ASRM 2016
Scientific Abstracts to be presented at the 72nd Scientific Congress of the American Society for Reproductive Medicine, October 17-19, 2016, Salt Lake City, Utah.

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October 17-19, 2016
Salt Lake City, Utah

These abstracts of research studies, printed as submitted by the authors, are presented in the ASRM 2016 congress sessions and are published in the order of their presentation. Abstracts of plenary lectures, symposia and interactive sessions are not included.
The first six papers are candidates for the ASRM Scientific Congress Prize Paper Awards. Six additional candidates will be presented during the Prize Paper Candidates’ session on Tuesday.

SCIENTIFIC CONGRESS PRIZE PAPER SESSION 1

O-1 Monday, October 17, 2016 11:15 AM

MATERNAL AND PATERNAL PRECONCEPTION PHTHALATE EXPOSURE AND BIRTHWEIGHT OF IVF SINGLETONS. C. Messerlian,a J. M. Braun,b L. Mingo-Muñoz-alarcon,c P. Williams,c J. B. Ford,c A. Calafat,c R. Hauser,a *Environmental Health, Harvard T. H. Chan School of Public Health, Boston, MA; bEpidemiology, Brown University School of Public Health, Providence, RI; bBiostatistics and Epidemiology, Harvard T. H. Chan School of Public Health, Boston, MA; cCDC, Atlanta, GA.

OBJECTIVE: Several phthalates are developmental and reproductive toxicants and reduce fetal weight in experimental animal studies. We examined the association between maternal and paternal urinary phthalate metabolite concentrations and birthweight among singleton infants conceived by in-vitro fertilization (IVF).

RESULTS: Father’s preconception urinary concentrations of mono-n-butyl phthalate (MBP) and the molar sum of 4 DEHP metabolites (Σ4DEHP) were associated with a significant decrease in birthweight. Each log,-unit increase in paternal preconception MBP and Σ4DEHP concentrations was associated with a 127 (95% CI: -231, -24) and 128 (95% CI: -228, -28) gram decrease in birthweight, respectively. Additional adjustment for respective maternal prenatal phthalate metabolite concentrations strengthened associations for DEHP metabolites and moderately attenuated the association for MBP. Although some maternal prenatal phthalate metabolite concentrations were also associated with birthweight, after adjustment for prenatal preconception concentrations these associations were no longer present. None of the 11 maternal preconception phthalate metabolites and a summary measure of di-(2-ethylhexyl) phthalate (DEHP) metabolites with birthweight using linear regression, and adjusted for a priori covariates, including maternal and paternal age, BMI and smoking status, maternal education, and infertility diagnosis.

CONCLUSIONS: Paternal preconception urinary concentrations of MBP and Σ4DEHP were associated with a significant decrease in birthweight among IVF conceived singletons.

Supported by: NIH grants R01 ES090718 and R01 ES024381 from the NIEHS. CM was supported by a fellowship from the Canadian Institutes of Health Research.

O-2 Monday, October 17, 2016 11:30 AM

EARLY LIFE DEVELOPMENTAL EXPOSURE TO ENDOCRINE DISRUPTING CHEMICALS INCREASES THE RISK OF ADULT ONSET OF UTERINE FIBROIDS BY PERMANENTLY REPROGRAMING THE EPIGENOME OF MYOMETRICAL STEM CELLS TOWARDS A PRO-FIBROID LANDSCAPE. Q. Yang,a L. Trevino,b A. Mas,c A. Laknaru,d M. P. Diamond,e C. L. Walker,f A. H-Hendy,f Og/BGN, Augusta University, Augusta, GA; fTexas AdM Health Science Center, Houston, TX.

OBJECTIVE: Increasing evidence supports the hypothesis that uterine fibroids (UFs) are monoclonal tumors arising from aberrant stem cells in the myometrium. We have identified Stro-1+/CD44+ myometrial stem cells (MSCs) capable of self-renewal and regeneration of myometrium tissues that give rise to fibroids upon xenotransplantation. We have also shown that early life exposures to endocrine disrupting chemicals (EDCs) increase UF penetrance and growth by inducing reprogramming of the epigenome. However, little is known if alteration of MSCs epigenome is the conduit by which early life EDCs environmental exposures lead to increased adult occurrence of UFs.

DESIGN: Laboratory research studies using Eker rat fibroid model: myometrium tissues as well as rat MSCs.

MATERIALS AND METHODS: Female newborn rats were treated S.C. with vehicle (VEH) or 1 μg/kg of diethylstilbestrol (DES, a tool compound of endocrine disrupting EDCs) on postnatal days 10-12, a key period of uterine development. MSCs were isolated from adult endometrium-free myometrium tissue (N=5 for each group) using Stro-1 and CD44 surface markers. To identify targets of epigenomic reprogramming in MSCs, whole genome RNA-sequencing and ChIP-sequencing (with an anti-H3K4me3 antibody) was performed in DES- and VEH-MSCs. In addition, Fisher’s exact test was used to examine the correlation between RNA expression and H3K4me3 enrichment of reprogrammed genes (estrogen responsive genes; ERGs). Finally, epigallocatechin gallate (EGCG, green tea extract) was used to determine whether the observed disease-causing reprogramming of ERGs can be reversed.

RESULTS: By RNA-sequencing, we identified 68 ERGs that were dysregulated in DES-MSCs compared to VEH-MSCs. Among them, 49 ERGs were markedly upregulated in DES-MSCs compared to VEH controls. We performed gene set enrichment analysis on the ChIP-sequencing data and identified enrichment of H3K4me3 (an active mark for gene transcription) at the promoters of 82 ERGs in DES-MSCs as compared to VEH-MSCs. Furthermore, the increased expression of ERGs was positively correlated with the elevated H3K4me3 mark (p<0.05). Using ChIP-qPCR and q-PCR, we validated the developmental reprogramming of key ERGs known to play a role in UFs tumor development, including ESR1, PGR, CD9, and CCL2 etc., in DES-MSCs. Importantly, EGCG treatment was capable of reversing the reprogramming of these key ERGs induced by early life exposure to DES in MSCs in a dose dependent manner.

CONCLUSIONS: These data suggest a new paradigm whereby early life developmental EDC exposure increases the risk of adult onset of UFs by permanently reprogramming the epigenome of MSCs towards a pro-fibroid epigenomic landscape.

References:

Supported by: This work was supported in part by an Augusta University Startup package, the Augusta University Intramural Grants Program (QY), and the National Institutes of Health grant HD04622811 (to AA).

O-3 Monday, October 17, 2016 11:45 AM

MTOR INHIBITORS PRESERVE FERTILITY IN A MURINE MODEL: A NOVEL PHARMACOLOGIC APPROACH TO FERTILITY PRESERVATION DURING GONADO TOXIC CHEMOTHERAPY. K. N. Goldman,a D. Chenette,a D. L. Keefe,a J. Grifo,a R. J. Schneider. aNew York University, New York, NY; bCancer Institute, NYU School of Medicine, New York, NY.

OBJECTIVE: Women with cancer have limited pharmacologic options for fertility preservation. We previously demonstrated that mTOR inhibitors administered alongside gonadotoxic chemotherapy (cyclophosphamide, CY) down-regulate the p70S6K/akt/mTOR pathway and prevent primitordial follicle activation in mice, thus preserving ovarian reserve. The objective of this study was to determine if mTOR inhibitors also preserve fertility in mice receiving chemotherapy.

DESIGN: Fertility was measured in vivo through breeding of a murine model.

MATERIALS AND METHODS: Female mice (C57BL/6, 8 weeks) were assigned to one of six treatment groups: Vehicle (PVP, “control”), 75 mg/kg CY intraperitoneal (IP) weekly for 4 weeks, RAD001 (mTORC1 inhibitor,
"RAD") or INK128 (mTORC1/2 inhibitor, "INK") by daily oral gavage (LG) for 4 weeks with or without 75mg/kg CY IP weekly. 8 weeks following the final treatment, mice were harem-bred with proven male breeders. Mice were given up to 8 weeks to breed and give birth. Infertility was defined as failure to conceive or pregnancy by 8 weeks in a harem-breeding cage with a fertile male partner. The following data were recorded: number of pups, percent of living pups, weight, and days from male interaction to birth. Data analysis was performed using student’s t-test (n=5 mice/group, mean ± SEM, Prism 6.0f). A power calculation determined that four female mice per treatment group would provide 80% power to detect a 50% difference in litter size with an alpha of 0.05.

RESULTS: 40% of CY-treated mice were infertile, and CY-treated mice had significantly fewer pups per litter compared to control (3.4 ± 1.7 [n=17 pups] vs. 8.8 ± 0.5 [n=44 pups] respectively, P<0.005). Mice treated with RAD+CY and INK+CY had litter sizes nearly 120% greater than CY alone. The mean litter size in the RAD+CY group was 7.4 ± 1.2 (n=37 pups) and in the INK+CY group 7.4 ± 0.9 (n=37 pups), both significantly greater than CY alone (3.4 ± 1.7, p<0.05). There were no differences in litter size between RAD-alone (7.8 ± 1.1, n=39 pups), INK-alone (8.6 ± 0.7, n=43 pups), RAD+CY, INK+CY, and control (p>0.05). The time from male interaction to birth was longer in mTOR inhibitor-treated groups compared to control. There were no differences in pup weight (mean 1.3 ± 0.03, percent of litter live-born (mean 85% ± 5.8) or pup anomalies between groups. mTOR inhibitors prevented CY-induced infertility and increased litter sizes by greater than two-fold.

CONCLUSIONS: mTOR inhibitors prevent CY-induced infertility in a murine model of DNA alkylating chemotherapy-induced gonadotoxicity. The mTOR inhibitor RAD001 (Everolimus) is clinically approved to treat multiple benign and malignant conditions, including endocrine resistant ER+ breast cancers. These data represent a potential fertility-sparing pharmacologic therapy to be administered alongside gonadotoxic chemotherapy. Future studies are needed to assess possible synergistic anti-cancer properties.

O-5 Monday, October 17, 2016 12:15 PM

CO-TRANSPLANTATION OF HUMAN OVARIAN TISSUE WITH AMH-PRODUCING ENDOTHelial CELLS INHIBITS RECRuMENT OF PRIMORDIAL FOLLICLES.


OBJECTIVE: The increasing frequency of cryopreservation of ovarian tissue for fertility preservation, poverts a surge in future demand for auto-transplantation. To meet this demand, quality and quantity of recoverable oocytes, must be improved. To this end, it is crucial to minimize ischemic injury to the transplant by reducing the latency period before neovascularization. Another determinant of follicular reserve is activation of signaling pathways within the graft. Anti-Mullerian Hormone (AMH), a member of the transforming growth factor beta superfamily, is a key player that inhibits the recruitment of primordial follicles into the pool of growing follicles. Using endothelial cells (EC) that were engineered to ectopically express AMH, we aimed to reduce premature follicular mobilization in tissue grafts co-transplanted with ECs.

MATERIALS AND METHODS: We generated lentiviral vectors that link a fluorescent reporter gene (mCherry) with expression of cDNA that encodes for AMH. Human umbilical vein ECs were transduced with these lentiviral particles. Human ovarian tissue was co-transplanted with AMH-ECs into the gluteus maximus of NSG oopherectomized mice aged 10-14 weeks (n=4); as controls we co-transplanted patient matched ovarian tissue with non AMH producing ECs (n=4). Engrafted tissue was harvested 2 weeks after transplantation. The ratio of primordial follicles in each treatment was assessed in histologic sections using light and confocal microscopy.

RESULTS: Our data demonstrates the efficient transduction of cultured ECs, with robust enrichment of AMH evident in cell supernatants, (more than 20 fold increase relative to control). Upon co-transplantation with human ovarian tissue, AMH-ECs produced AMH protein from ECs in proximity to the graft. At 2 weeks, tissue co-transplanted with AMH-ECs exhibited a two-fold increase in the percentage of primordial follicles relative to non-AMH producing ECs (57.34% vs 27.96%, P<0.05, n=4).

CONCLUSIONS: Co-transplantation of human ovarian tissue with AMH-ECs increases the volume of the primordial follicle pool after short-term xenotransplantation into NSG mice. Engineered ECs that express secreted factors are a powerful tool that can be used to interrogate molecular modulators of human ovarian physiology.

References:
4. C. Yding Andersen, M. Rosendahl, A.G. Byskov. Concentration of anti-Mullerian hormone and inhibin-B in relation to steroids and age

O-4 Monday, October 17, 2016 12:00 PM

VERIFICATION OF ACCURACY & SAFETY FOR OVARIAN RESERVE ASSESSMENT WITH OPTICAL COHERENCE TOMOGRAphY USING MOUSE OVARY.

S. Takae, K. Tsukada, N. Okamoto, Y. Sato, T. Kawahara, N. Suzuki. Obstetrics and Gynecology, St. Marianna University School of Medicine, Kawasaki City, Japan; aDepartment of Applied Physics and Physico-Informatics, Faculty of Science, Keio University, Yokohama City, Japan.

OBJECTIVE: Except for histological study, in clinical and basic research, so far there are no applicable techniques to detect and identify primordial follicles in the ovary for primary ovarian insufficiency (POI) patients who have undetectable AMH levels. The ability to locate and quantify follicles on ovarian cortex strips without fixation is valuable for patients who will receive ovarian tissue transplantation. Although optical coherence tomography (OCT) is a well-established high resolution imaging technique without fixation which has been widely applied in biomedicine, few reports are available on ovarian tissue imaging. Using the latest OCT equipment, our study aims to establish the standard images of follicles on each developmental stage, assess the accuracy of OCT to estimate ovarian reserve on par with histological imaging, and investigate the safety of OCT for optimal gamete viability.

DESIGN: This research is observational and experimental study which accordance with guideline of animal experimentation of our institution.

MATERIALS AND METHODS: The ovaries were obtained from day 3 (primordial follicle rich stage) and day 10 (primary follicle rich stage) and day 21 (secondary follicle rich stage), and 50 weeks old (menopausal stage or to resemble the POI model) female ICR mice (n=4 each). These ovaries were examined with OCT, then fixed by Bouin’s solution for making hematoxylin-and-eosin stained slides to compare between OCT images and histological images. Paired ovaries (day 3 and 50 weeks old) were inserted under each kidney capsule of the same 6 weeks old host mice that were ovariecto-

ized to increase endogenous gonadotropin levels. Two weeks after ovarian transplantation, they received 5 IU PMSG injection and 5IU hCG injection for 24 hours to encourage the retrieval of oocytes from day 3 ovaries. Then, retrieved oocytes were inseminated and cultured to the blastocyst phase for implantation into 10 weeks old ICR mice. After embryo transfer, newborn mice were delivered by Cesarean section. And the newborn mice were bred to screen for resulting anomalies from OCT.

RESULTS: The standard OCT images of follicles on each developmental stage were established. And OCT images were matched with histological images. Post ovulation induction, we obtained 10.2 ± 2.3 oocytes from transplanted day 3 ovaries, and no oocyte from transplanted 50 weeks old ovaries, and there were no abnormal newborns from day 3 ovaries that received OCT examination, and they have normal ability of reproduction.

CONCLUSIONS: In conclusion, the present study has demonstrated that OCT is a reliable and safe technique to detect primordial follicles, and to locate and quantify follicles on ovarian tissue. Further large scale studies are needed for clinical application.

Supported by: Entirely internal (CRM) funding.

O-6 Monday, October 17, 2016 12:30 PM

RANDOMIZED CONTROLLED TRIAL OF LOW (5%) VS. ULTRA-LOW (2%) OXYGEN TENSION FOR IN VITRO DEVELOPMENT OF HUMAN EMBRYOS, D. J. Kaser, a B. Bogale, a V. Sarda, b L. V. Farland, a c Racowsky, a b c Dept of Obstetrics & Gynecology, Brigham & Women’s Hospital, Harvard Medical School, Boston, MA; b Boston Children’s Hospital, Boston, MA; c Dept of Epidemiology, Harvard Chan School, Boston, MA.

OBJECTIVE: As the human embryo traverses the utero-tubal junction late on day 3, it is exposed to a step-down in O2 tension from 5-7% in the Fallopian tube to 2% in the uterus. The question therefore arises whether the IVF culture system should mimic this progressively hypoxic environment. The present study tested the hypothesis that sequential exposure first to 5% O2 from days 1 to 3, and then to 2% O2 from days 3 to 5, improves blastocyst yield and quality compared to continuous exposure to 5% O2.

DESIGN: Randomized controlled trial of sibling embryos.

MATERIALS AND METHODS: Donated sibling embryos (n=203), blocked on pronuclei (PN) status (2PN vs. 3PN), were randomized to either 5% O2 from days 1 to 5 (5-5% Group; n=102) or 5% O2 from days 1 to 3 and then 2% O2 to day 5 (5-2% Group; n=101). Stage and grade were assessed on day 5 by embryologists blinded to Group; usable blastocysts were those meeting freezing criteria. Cell counts of embryos from 3PNs were obtained by nuclear staining; 2PNs were used for ongoing gene expression studies. Odds ratios (OR) with 95% CI were calculated using generalized estimating equations to account for correlations among embryos from the same woman, adjusted a priori for oocyte age and source (autologous vs. donor), IVF vs. ICSI, PN number, fresh vs. thawed embryo and % good-quality embryo (GQE) on day 3. Differences in mean cell number and proportions of developmental stages were analyzed by independent t-tests and chi-square, respectively. Based on data comparing atmospheric (20%) vs. 5% O2, this study was powered to detect a 16.5% difference in day 5 GQE (α=0.05, β=0.80).

RESULTS: The percentage of day 3 GQEs did not differ between groups (5-5% O2 vs. 5-2% O2: 28.4% vs. 30.7%; OR=1.14 [CI=0.94-1.39]; P=0.31). Embryos in the 5-2% Group were less likely to arrest at cleavage and more likely to blastulate in vivo (Table). Notably, in the 5-2% Group, there was a two-fold increase in the odds of conversion to a usable blastocyst (OR 2.30 [CI=1.16-4.56]; P=0.02), yet blastocysts had fewer cells (Table).

CONCLUSIONS: These findings support our hypothesis that blastocyst yield and quality may be superior when O2 tension is reduced from 5% to 2% in the uterus. Further studies are warranted to confirm whether these preliminary findings translate into a paradigm shift for extended culture in clinical IVF, and to investigate the significance of lower cell counts in blastocysts cultured in 2% O2, particularly as related to the ‘quiet hypothesis’ for embryo metabolism.

References:

Table. Stage and cell count of embryos cultured from days 3 to 5 in low (5%) vs. ultralow (2%) O2.

<table>
<thead>
<tr>
<th>Stage per cleaved embryo n (%)</th>
<th>5-5% O2 Group</th>
<th>5-2% O2 Group</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cleavage arrest</td>
<td>52/89 (58.4)</td>
<td>34/87 (39.1)</td>
<td>0.38 (0.18, 0.80)</td>
</tr>
<tr>
<td>Morula</td>
<td>17/89 (19.1)</td>
<td>18/87 (20.7)</td>
<td>1.09 (0.47, 2.53)</td>
</tr>
<tr>
<td>Early blastocyst</td>
<td>11/89 (12.4)</td>
<td>23/87 (26.4)</td>
<td>2.59 (1.06, 6.32)</td>
</tr>
<tr>
<td>Full, expanded</td>
<td>9/89 (10.1)</td>
<td>12/87 (13.8)</td>
<td>1.43 (0.56, 3.64)</td>
</tr>
<tr>
<td>or hatching blastocyst</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any blastocyst</td>
<td>20/89 (22.5)</td>
<td>35/87 (40.2)</td>
<td>2.55 (1.27, 5.12)</td>
</tr>
<tr>
<td>Usable blastocyst</td>
<td>19/89 (21.3)</td>
<td>32/87 (38.6)</td>
<td>2.30 (1.76, 4.56)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Mean cell count ± SD</th>
<th>5-5% O2 Group</th>
<th>5-2% O2 Group</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early blastocyst</td>
<td>44.4 ± 2.1</td>
<td>35.5 ± 10.9</td>
<td>0.01</td>
</tr>
<tr>
<td>Full, expanded or</td>
<td>83.4 ± 15.9</td>
<td>62.0 ± 14.5</td>
<td>0.04</td>
</tr>
<tr>
<td>hatching blastocyst</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any blastocyst</td>
<td>60.7 ± 22.3</td>
<td>43.8 ± 17.3</td>
<td>0.01</td>
</tr>
</tbody>
</table>


Supported by: The Foundation for Embryonic Competence.

O-7 Monday, October 17, 2016 11:15 AM

EMPLOYER ENGAGEMENT AND EDUCATION INCREASES ACCESS TO CARE AND ESET UTILIZATION, G. Harton, a M. Larman, b K. Ajmani, c J. R. Tomassino, d G. Bartasi. e Progyny, New York, NY; e Pregnyn, San Francisco, CA; e Progyny, Inc., New York, NY; e Progyny; e Inc., 47th Floor, NY.

OBJECTIVE: Demonstrate that educating employers on ART practices, clinical outcomes and technology advances can increase access to care and utilization of ART by employees. Furthermore, will adoption of coverage by informed employers increase the use of elective single embryo transfer (eSET) and significantly reduce multiple gestations as a result of IVF treatment.

DESIGN: A retrospective analysis with historical company and national data.

MATERIALS AND METHODS: The funded ART benefit offered by a number of large, self insured employers was examined and analyzed to assess the associated expense to the employer for employees utilizing ART. The employers were informed and educated on innovations within the ART field. Beginning in January 2016 employees in two companies began utilizing a new fully funded ART benefit that included embryo selection and eSET. Historical company data on the cost of high order multiples from ART treatment in 2014 was compared to expected data based on eSET in the fully funded program. Additionally, the percentage of employees utilizing the benefit was compared to national averages in multiple states in the U.S.

RESULTS: In Q1 2016, 299 ART treatments were initiated (248 IVF and 51 IUI) for a predicted annual utilization rate of approximately 1%. When compared to utilization rates nationally and in the home state of the employers using 2013 SART data (0.25 %), the utilization thus far is four times higher. Nationally, in 2013, eSET was performed in 23.6 % of patients of all ages. Thus far in Q1 2016, with increasing employee awareness, the monthly percentage of eSET cycles reached 80% with an overall pregnancy rate of 56.9% (FHB+). With continued education on the advantages of eSET we expect the percentage of cycles with transfer of one embryo to continue to increase. At the end of Q1 there were no multiple gestations reported in this data.

CONCLUSIONS: The utilization rate for the two companies is 4 times higher than the national average and double the utilization rates seen in states with an ART mandate (0.48%). This data clearly shows that an employer offering a fertility benefit will increase utilization of IVF in the U.S. In SART 2013 data the average number of embryos transferred was 1.8 in women <35. Given that the medical costs associated with multiple gestations are at least 5-20 times higher than singletons, the use of eSET to increase the percentage of singleton births will result in a predicted savings of approximately $4 Million/employer based on our analysis of claims data and the Truven Health Analytics database. By engaging and educating employers with regards to the need for ART coverage and the medical and financial burdens associated with multiple gestations, it is anticipated that more than the current 25% of employers, which provide an ART benefit, will fund comprehensive coverage for IVF treatments in the coming years.

O-8 Monday, October 17, 2016 11:30 AM

INCREASED ACCESS TO CARE THROUGH CREATION OF PRIVATE FOUNDATIONS: THE CHICAGO EXPERIENCE, E. C. Feinberg, a A. Borowiecki, b R. Morris, c L. Rinehart, d N. Desai, e J. Eirishfeld-Cytron, f Fertility Centers of Illinois, Highland Park, IL; bKevin J. Lederer Life Foundation, Highland Park, IL; cIVF1, Naperville, IL; dLegal Care Consulting, Inc., Burr Ridge, IL; eBallard, Desai, & Miller, Chicago, IL; fFertility Centers of Illinois, Chicago, IL.

OBJECTIVE: Access to infertility care is a worldwide concern. Only 24% of infertile couples in the United States are able to access the medical care
needed to achieve pregnancy. ASRM held a summit meeting in Washington, D.C. in September 2015 to address this unmet need. The summit resulted in several strategies to broaden access to care and a task force was created to carry out actionable strategies. One such actionable strategy was the development of private foundations to which practitioners, industry or grateful patients could donate resources and/or money.

**DESIGN:** Observational study.

**MATERIALS AND METHODS:** The Kevin J. Lederer Life Foundation was created to promote health and alleviate the mental and physical distress of those diagnosed with infertility through education and financial assistance. The Life Foundation is a collaborative effort among Chicagoland REI practices to broaden access to fertility care in Illinois.

**RESULTS:** There are 19 clinics that provide ART services in Illinois. Nine of 19 (47%) participated in the Life Foundation, either by donation of medical service or volunteer service on the Foundation Board. The Foundation partnered with fertility clinics for provision of unreimbursed care and 11 IVF cycles were donated by 7 clinics. Community partners such as reproductive attorneys and third party agencies were solicited for service donations while industry partners and grateful patients were solicited for financial support. 2015 was the first fully operational year of the Life Foundation. A 5K race and a bowling fund-raiser was held to raise money to cover foundation operating costs and for financial grants. All Foundation members volunteer time, there is currently no paid support staff. A medical advisory board comprised of 4 board-certified REIIs selected grant recipients based on financial need and medical diagnosis. Eighty-five patients applied for grants and thirteen grants (15.3%) were awarded. Grants were a combination of donated IVF cycles and financial grants to defray the costs of associated with egg donation, gestational carrier use and adoption. 3 live births and 2 pregnancies have subsequently ensued. The Foundation also held educational events covering topics such as oocyte vitrification, adoption, male factor infertility and the psychological impact of fertility care. The Foundation newsletter has 1500 subscribers.

**CONCLUSIONS:** There remains a large unmet need within the United States for fertility care. Creation of private foundations is one mechanism to immediately increase access to care. Success of these foundations is dependent on widespread community engagement. Collaboration with organizations such as ASRM would be beneficial to streamline processes. Greater financial support is needed to help sustain growth and viability.

**O-9 Monday, October 17, 2016 11:45 AM**

**INFERTILITY & FAMILY-BUILDING PRIORITYs.** A. Duthie, A. Cooper, J. B. Davis, J. Sandlow, K. D. Schoyer, E. Y. Straw, K. E. Flynn. a Medical College of Wisconsin, Milwaukee, WI; b Duke University, Durham, NC; c Michigan State University, Grand Rapids, MI.

**OBJECTIVE:** To describe the family-building priorities most important to patients and partners seeking care from a reproductive endocrinologist and infertility specialist (REI) over time.

**DESIGN:** Longitudinal prospective cohort study of 85 infertility patients (pregnancy candidates, PCs) and 62 supporting partners (SPs) ≤1 week before a first consultation with a REI and ~12 months later.

**MATERIALS AND METHODS:** At both time points, respondents separately completed a novel Family-Building Priorities Ranking Tool which tasked them with prioritizing a list of 10 factors associated with different family-building paths (wording in Table). We describe the percentage of participants who ranked each factor among their highest (top three) priorities pre-consult and at 12 months and the agreement between partners within couples. We examined differences in priorities by role using chi-squared tests and changes in top priorities from pre-consult to 12 months using McNemar’s test (both α = 0.05).

**RESULTS:** We found significant differences between the top three priorities of PCs and SPs at both time points (Table). Other factors found general consensus: a majority of respondents in both roles highly prioritized maintaining their relationship with their partner, and ≤5% of respondents prioritized the ability to maintain privacy about their family-building methods. For PCs, more than half of those who prioritized being pregnant and giving birth pre-consult no longer included this factor among their highest priorities by 12 months post-consult (p = 0.04). There were no significant changes over time in highest priority rankings among SPs. At both time points, in >70% of couples, both members had in common 1 or 2 of their highest priorities; very few shared all 3 highest priorities (7% pre-consult; 4% at 12 months).

**CONCLUSIONS:** While there was general agreement among PCs and SPs about the importance of maintaining their relationships with their partners throughout their family-building process, consensus was lacking when it comes to the relative importance of other family-building priorities. REIs who provide support to patients and their partners in assessing the pros and cons of available family-building paths should be aware that becoming a parent may not be the highest priority for many of their patients. Family building is frequently a partnered activity, and the clinical discussions and treatment decisions that shape it should involve both prospective parents and incorporate awareness of the potential for discreet priorities.

*Supported by: Funding for this study came from R21HD071332 from the National Institute of Child Health and Human Development. Dr. Duthie received additional support from a National Research Service Award T32 HP10030. REDCap was supported by the National Center for Advancing Translational Sciences, National Institutes of Health, through UL1TR000055.

**O-10 Monday, October 17, 2016 12:00 PM**

**LETROZOLE + GONADOTROPIN PROTOCOL FOR SUPEROVULATION INDUCTION/INSEMINATION CYCLES: A NOVEL APPROACH TO INCREASE ACCESS OF CARE AND VALIDATED BY SUPPLY & DEMAND CURVE ANALYSIS.** M. X. Ransom. OB/GYN, Quillen College of Medicine, Johnson City, TN.

**OBJECTIVE:** To identify the benefits of offering a letrozole/FSH (follicle-stimulating hormone) hybrid protocol to clomiphene citrate-alone and letrozole-alone failures for superovulation induction insemination + intrauterine (SO/IUI) cycles prior to considering an FSH-alone protocol, and thereby increase access to care among an infertility population.

**DESIGN:** Patients attending a university infertility practice in Eastern Appalachia were recognized who had failed to conceive by clomiphene citrate and letrozole-alone cycles and were unable to financially consider either a gonadotropin-only/IUI or IVF (in vitro fertilization) cycle. Those patients were offered a letrozole/FSH combined cycle as an affordable alternative to abandonment of treatment.

### Table

<table>
<thead>
<tr>
<th>Percent of respondents ranking each factor among top 3 priorities</th>
<th>Pre-Consult</th>
<th>12 Months*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnancy Candidates (n = 82)</td>
<td>Supporting Partners (n = 61)</td>
<td>Pregnancy Candidates (n = 39)</td>
</tr>
<tr>
<td>That I become a parent one way or another</td>
<td>52% 38%</td>
<td>59% 33%</td>
</tr>
<tr>
<td>That my partner get(s) to be the person who is pregnant with and gives birth to my child</td>
<td>42% 36% 23% 38%</td>
<td>42% 36% 23% 38%</td>
</tr>
<tr>
<td>That my child has [pregnancy candidate’s] genes</td>
<td>22% 30% 31% 33%</td>
<td>22% 30% 31% 33%</td>
</tr>
<tr>
<td>That my child has [supporting partner’s] genes</td>
<td>20% 39% 26% 50%</td>
<td>20% 39% 26% 50%</td>
</tr>
<tr>
<td>That I have a child in the next year or two</td>
<td>55% 23% 39% 25%</td>
<td>55% 23% 39% 25%</td>
</tr>
<tr>
<td>Cost</td>
<td>24% 16% 13% 21%</td>
<td>24% 16% 13% 21%</td>
</tr>
<tr>
<td>That I can build my family in a way that doesn’t make it obvious to others that we had trouble</td>
<td>1% 0% 5% 0%</td>
<td>1% 0% 5% 0%</td>
</tr>
<tr>
<td>That I get to parent my child from birth</td>
<td>20% 16% 13% 21%</td>
<td>20% 16% 13% 21%</td>
</tr>
<tr>
<td>That I maintain a close and satisfying relationship with my partner</td>
<td>62% 79% 74% 58%</td>
<td>62% 79% 74% 58%</td>
</tr>
<tr>
<td>That I avoid side effects from medical treatments</td>
<td>2% 20% 10% 13%</td>
<td>2% 20% 10% 13%</td>
</tr>
</tbody>
</table>

Bold: significant difference by role; *Includes only respondents who are not pregnant/parenting
O-11 Monday, October 17, 2016 12:15 PM


OBJECTIVE: To analyze cumulative live birth/ongoing pregnancy rates and potential cost savings associated with MS-IVF and single embryo transfer (SET) in good prognosis patients.

DESIGN: A retrospective analysis comparing outcomes and costs of MS-IVF and traditional IVF in good prognosis patients.

MATERIALS AND METHODS: 137 good prognosis patients (defined as age <35, AMH >2.4, AFC >15, BMI <35, with diagnoses of PCOS, stage I-II endometriosis, thin ovarian tissue, or as a poor or moderate responder) underwent MS-IVF or traditional IVF based on the patient’s preferences. FSH was limited to 150 IU and gonadotropins were utilized. MS-IVF included 5 days of clomiphene citrate 100mg daily prior to administration of FSH. Traditional IVF cycles had a mean starting FSH of 244 IU. Monitoring by E2 was performed on alternate days throughout the cycle, hCG was administered when appropriate follicular maturation was attained. Both groups received a single IUI within 36 hours of hCG administration. Calculations were based upon patient responses who were unable to undergo FSH-alone protocols due to the economic principles of second degree price discrimination. Because this population has an inelastic demand for fertility treatment, a standard Supply and Demand curve was constructed and prices were modeled. Costs were calculated based on the above.

RESULTS: The cost of a cycle of IUI by Group 1 was significantly less than the cost for Group 2 cycles ($2377.64 versus $1154.17; p < 0.05). An estimated 48 more patients were able to undergo SOI/IUI by offering the Group 1 protocol compared to only 24 who were able to undergo Group 2 treatment. The calculated TR for Group 2 was $57.063.66 while for Group 1 cycles was $27,700.08 (p < 0.01). In addition, the hybrid cycle required fewer office visits for monitoring (2 versus 4, p < 0.05), lower average cost of medication ($493.92 versus $1233.39, p < 0.05) and less cost for monitoring ($484.03 versus $968.00, p < 0.01).

CONCLUSIONS: Among patients who have been ovulatory but unsuccessful in conceiving by both clomiphene citrate and letrozole-alone IUI cycles, a combined SOI/IUI induction cycle by letrozole and FSH is a reasonable and affordable alternative to patients who are otherwise unable to consider FSH-alone/IUI or IVF due to financial or travel concerns. In addition, applying supply and demand curve analysis, an economic advantage to offering a hybrid cycle is definable by utilizing center resources yet still generating revenue.

O-12 Monday, October 17, 2016 12:30 PM


OBJECTIVE: The incorporation of genetic testing into clinical practice has increased at a remarkable rate. Complete patient care involves discussion of testing and the impact of results with a genetic counselor. With one genetic counselor for every 80,000 people in the United States, genetic counselors struggle to be involved in the provision of every test. To address this gap, we developed a protocol for telecounseling and demonstrated its utility in increasing access to comprehensive genetic counseling (GC).

DESIGN: Prospective.

MATERIALS AND METHODS: We developed a scalable protocol for the provision of GC via telephone with a board-certified genetic counselor. Once carrier screening or non-invasive prenatal screening results are available, patients are counseled to schedule a consultation. Consults are performed in the context of genetic counselors. Informed consent was obtained.

RESULTS: Between May 2015 and March 2016, 697 responses were received. A total of 37 responses were excluded due to error in the GC donation portion of the protocol. To assess the uptake of this service, all patients were sent an online survey three weeks after receipt of results, querying whether they received genetic counseling. Informed consent was obtained.

RESULTS: Between May 2015 and March 2016, 697 responses were analyzed. 640 patients (92%) received GC. When analyzed in the context of carrier status, 96% of patients identified as carriers received GC; 94% of non-carriers received GC. 8 patients who received genetic counseling did not identify their carrier status. When asked to indicate their level of satisfaction with their counselor, 77% and 16% answered 5 or 4, respectively.

CONCLUSIONS: Telecounseling broadens access to GC services, and enables the personal interactions and comprehensive discussion of results and patient history to occur. This type of interaction allows for deeper engagement and further clarification than other methods of communication, such as pre-recorded videos. While telecounseling may not solve the current genetic counselor deficit, it can expand the reach of current genetic counselors to populations that may otherwise have testing without counseling. A significant uptake of our available counseling services by the patients polled shows that this offering is not only appreciated, but also sought after.

CONTRACEPTION AND FAMILY PLANNING

O-13 Monday, October 17, 2016 11:15 AM

A PROGRESSIVE ELIMINATION STRATEGY FOR SCREENING MEIOTIC INHIBITORS AS NOVEL CONTRACEPTIVES. C. Hanna,a S. Yao,a F. Xu,b R. Cuellar,b J. Jensen. aDivision of Reproductive and Developmental Science, Oregon National Primate Research Center, Beaverton, OR; bDepartment of Medical Chemistry, University of Minnesota, Minneapolis, MN. OBJECTIVE: Drugs targeting oocyte meiotic pathways are being evaluated as a new class of novel nonhormonal contraceptives. Screening for effects on both meiosis and mitosis is important to identify candidates before evaluation in nonhuman primates and clinical trials. Here we describe key steps in screening inhibitors for WEE2, an oocyte specific kinase, and potential contraceptive target.

DESIGN: Multiple independent analyses of compounds evaluating inhibitory activity of WEE2 kinase in a 4-step progressive elimination screening process.

MATERIALS AND METHODS: Step 1-In silico computational modeling of compound libraries was performed by high-throughput virtual screening followed by standard precision and extra precision docking into WEE2 model homology. Pharmacokinetic filters were applied and remaining hits were comparatively docked to WEE1 (the somatic cell homolog) for further restrictive selection. Step 2-From these libraries, potential WEE2 kinase inhibitors were identified and subjected to enzyme linked immunosorbent assay (ELISA) to measure inhibitory activity against WEE2 and WEE1. Step 3-Compounds in which inhibitory activity against WEE2 was only greater than against WEE1 were included in bovine cumulus oocyte complex cultures at multiple concentrations during in vitro maturation (IVM) and in vitro fertilization (IVF). Cell cycle progression was determined using flow cytometry and measurement of a fluorescent cell trace marker that becomes diluted with each round of mitosis. Mitotic activity was measured by enzyme linked immunosorbent assay (ELISA) to measure inhibitory activity against WEE2 and WEE1.

CONCLUSIONS: These results indicate that OVGP1 is expressed in the primate cervix as well as the primate oviduct, and strongly upregulated by estrogen in the proliferative phase and down-regulated by P during the secretory phase. The cervical epithelium would be easily accessible by biopsy or cervical brush, and OVGP1 could be assayed either by ELISA or by real-time PCR to provide a rapid and very sensitive method for identifying the effect of progestogen-based contraceptives on the cervix in clinical trials.

References:

Supported by: NICHD U54 HD055744(ODS); OD011092

O-15 Monday, October 17, 2016 11:45 AM

EFFICACY AND SAFETY OF A LOW-DOSE LNG-LEVONORGESTREL INTRUTERINE SYSTEM (LNG-IUS12) ACCORDING TO AGE, PARITY, AND BODY MASS INDEX OVER 5 YEARS OF USE. T. A. Faustmann,a K. Gemzell-Danielsson,b D. Apter,b C. A. Rosen,a T. Schmetter,c M. Merz,a A. Nelson.c Bayer Pharma AG, Berlin, Germany; Karolinska Institutet and Karolinska University Hospital, Stockholm, Sweden; VL-Medi Clinical Research Center, Helsinki, Finland; Bayer Healthcare, Whippany, NJ; Los Angeles Biomedical Research Institute, Torrance, CA.

OBJECTIVE: To assess the 5-year efficacy and safety of LNG-IUS12 according to age, parity, and body mass index (BMI).

DESIGN: In this randomized, open-label Phase III study, women used a levonorgestrel intrauterine contraceptive system (LNG-IUS12) for up to 5 years.

MATERIALS AND METHODS: Women aged 18-35 years and with regular menstrual cycles (21-35 days) requesting contraception were recruited.

RESULTS: The full analysis set included 1452 women who had ≥1 LNG-IUS12 placement attempt (mean age 27.1 years; 39.5% nulliparous; mean BMI 25.3 kg/m2). The 5-year Pearl Index (PI) was 0.29. Unadjusted 5-year PIs (95% confidence interval [CI]) were 0.18 (0.04-0.54) vs 0.36 (0.17-0.66) for women aged 18-25 vs 26-35 years; 0.24 (0.07-0.63) vs 0.32 (0.15-0.61) for nulliparous vs parous women, and 0.24 (0.11-0.64) vs 0.56 (0.3-1.42) for women with BMI <30 vs ≥30 kg/m2. The 5-year Kaplan-Meier cumulative failure rate was 1.4%. This rate was 1.2% vs 1.6% in nulliparous vs parous women, 0.9% vs 1.8% in women aged 18-25 vs 26-35 years, and 1.3% vs 2.2% in women with a BMI <30 vs ≥30 kg/m2. Only 250 women had a BMI ≥30 kg/m2; therefore, conclusions on contraceptive efficacy according to BMI cannot be drawn. Risk of partial/complete expulsion was low regardless of age, parity, or BMI. Cumulative 5-year

HORMONAL REGULATION OF OVIDUCTAL GLYCOPROTEIN 1 (OVGP1; MUC9) IN THE MACAQUE CERVIX: A NOVEL INDICATOR OF PROGESTGEN ACTION. Q. D. Slayden,a F. K. Friason,a R. A. Callhoun,a K. R. Bond, Reproductive & Developmental Sciences, Oregon National Primate Research Center, Oregon Health & Science University, Beaverton, OR.

OBJECTIVE: Progestogen-only contraception is reported to act by suppressing ovulation and/or altering cervical mucus secretion. Unfortunately, the effect of contraceptives on mucus quality is difficult to assess accurately by traditional Insler score or post-coital tests, and the lack of a molecular test for mucus quality has created a roadblock to the development of new contraceptives that target the cervix. Oviductal glycoprotein 1 (OVGP1; MUC9) is a hormonally regulated, carbohydrate-rich glycoprotein secreted by oviductal epithelial cells. In addition to the oviduct, the OVGP1 expression has been reported for the cervix of rabbits, mice and women, but hormonal regulation of OVGP1 in the cervix is poorly understood. The objective of this study was to characterize hormonal regulation and localization of OVGP1 in the macaque cervix as a novel marker of progesterogen action.

DESIGN: Real-time PCR and immunohistochemical analysis of the macaque cervix.

MATERIALS AND METHODS: Adult ovariectomized rhesus macaques (Macaca mulatta) were treated sequentially with estradiol (E2) and then E2 plus progesterone (P) to create artificial menstrual cycles. Reproductive tracts were collected in the artificial proliferative phase (E2 alone; n=13) and in the artificial secretory phase after 1, 3, 7, and 14 days of P (n=4, 5, 5, and 10, respectively). Total RNA was isolated from cervical samples and analyzed for expression of OVGP1 by TaqMan® real-time PCR and presented relative to expression of ribosomal (S10) RNA. Representative samples were analyzed by immunohistochemistry on cryosections with polyclonal antibodies specific to OVGP1. Representative sections were also stained for estradiol 1 (ESR1) and progesterone receptor (PGR) as independent assays for E2 and P action.

RESULTS: OVGP1 transcript was upregulated in the proliferative phase, maximal in the late proliferative phase, and maintained through day 1 of the secretory phase. There was a significant decrease (P<0.01) in OVGP1 expression between secretory phase day 1 and day 3 and a further significant decrease (P<0.05) by secretory phase day 7 and 14. IHC revealed specific OVGP1 staining in columnar cells of the mid cervix. Staining was strongest in the apical portion of the epithelial cells consistent with secretion into the cervix mucus. As expected, ESR1 and PGR was present in the cervix throughout the cycle. ESR1 and PGR staining was strongest in the cervix epithelium during the proliferative phase of the cycle.

CONCLUSIONS: These results indicate that OVGP1 is expressed in the primate cervix as well as the primate oviduct, and strongly upregulated by estrogen in the proliferative phase and down-regulated by P during the secretory phase. The cervical epithelium would be easily accessible by biopsy or cervical brush, and OVGP1 could be assayed either by ELISA or by real-time PCR to provide a rapid and very sensitive method for identifying the effect of progestogen-based contraceptives on the cervix in clinical trials.

Supported by: NICHD U54 HD055744(ODS); OD011092

FERTILITY & STERILITY®
expulsion rates were 3.7% for both age groups, 1.8% vs 5.0% for nulliparous vs parous women, and 3.1% vs 6.9% in women with BMIs <30 vs ≥30 kg/m². The cumulative 5-year ectopic pregnancy rate was 0.18 per 100 woman-years (range: 0.14-0.28 across all subgroups). Over 5 years, 328 (22.6%) women discontinued due to any adverse event (AE). This rate was 24.2% vs 21.5% in nulliparous vs parous women. Overall, the most frequent AEs that led to discontinuation were vaginal hemorrhage (3.5%), IUS expulsion (3.0%), and pelvic pain (3.0%).

CONCLUSIONS: LNG-IUS12 was highly effective over 5 years, regardless of age or parity. LNG-IUS12 was associated with low rates of expulsion and ectopic pregnancy. Overlapping 95% CIs for all groups suggest that no major differences exist between them. LNG-IUS12 offers women a lower-dose 5-year contraceptive option.

Supported by: Study and abstract funded by Bayer HealthCare

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FERTILITY CONCERNS ARE ASSOCIATED WITH LOWER CONTRACEPTION RATES IN BREAST CANCER SURVIVORS.
T. Toloubeydokhti, S. Lederhandler, T. Su. Reproductive Medicine, University of California, San Diego, La Jolla, CA.

OBJECTIVE: Contraception rates are lower in reproductive-aged female cancer survivors than in the general population. Longitudinal contraception patterns and factors related to contraceptive use are not known. This study evaluated changes in and factors related to contraceptive use in breast cancer survivors.

DESIGN: Prospective cohort

MATERIALS AND METHODS: 114 newly diagnosed, premenopausal breast cancer patients, mean age 39.5(SD 4.8), were enrolled at diagnosis and followed for up to 24 months. Contraception use, concern about future fertility, sexual activity were self-reported at enrollment and follow up visits via standardized questionnaires. Participants at risk of unintended pregnancy were categorized as 1) using contraception and 2) using WHO Tiers I/II contraception at enrollment and the first follow up occurring 12-24 months later. Paired data on contraception and use of Tiers I/II methods were compared using McNemar’s test. Participants characteristics and future fertility concern were compared by contraception status via Fisher’s Exact or Student’s t-test.

RESULTS: 85 participants were at risk of unintended pregnancy, excluding women who were pregnant, underwent hysterecyotomy or bilateral salpingoophorectomy, or were not sexually active. The majority was Caucasian (60%), 74% underwent chemotherapy, 20% were nulligravid, and 31% reported future fertility concerns. At diagnosis, 35% were not using contraception. A minority of contracting participants (41%) used Tier I/II methods. Compared to enrollment, follow up data showed 32% of participants were not using contraception (p=0.05); use of Tiers I/II methods was reported by 45% of those contracting (p=0.41). At follow up, contraception use and use of Tiers I/II methods were not associated with age, race, education, income, cancer characteristics or prior fertility preservation. Nulligravid women had a lower rate of contraception than those with prior pregnancy (RR 0.55, 95%CI 0.31-0.99, p=0.009). Participants with fertility concerns also had a lower rate of contraception (RR 0.67, 95% CI 0.42-1.08, p=0.05).

CONCLUSIONS: In the first two years after cancer diagnosis, no significant changes in contraception were seen in reproductive-aged breast cancer survivors. Many reported fertility concerns and were not contracting effectively, suggesting a need to improve family planning practices in this population.

Supported by: NIH HD058799-05, 5R01HD080952-03, HD MRSG-08-110-01-CCCE

O-17 Monday, October 17, 2016 12:15 PM


OBJECTIVE: To compare utilization of the etonogestrel contraceptive implant before and after a Medicaid payment policy change that allows device, facility and professional reimbursement while the patient is an inpatient postpartum, in addition to a bundled payment for obstetric delivery.

DESIGN: Retrospective cohort study

MATERIALS AND METHODS: Deliveries between January and April 2013, prior to inpatient availability of contraceptive implants, and January to April 2014, after inpatient insertion became available, were compared. Demographic characteristics, prenatal contraception plan, postpartum visit attendance, and utilization of long acting reversible contraception were obtained. Differences were compared using two-tailed independent sample t-tests for continuous variables and Chi-square or Fisher’s exact test for categorical variables.

RESULTS: 816 women were in the 2013 outpatient cohort and 847 women were in the 2014 inpatient cohort. Implant utilization increased from 4% to 21% (p<0.001) and was independent of parity or mode of delivery. Receipt of long acting reversible contraception increased from 12% to 26% of patients (p<0.001). Postpartum visit attendance was higher in women who received an inpatient implant (60% vs. 50%, p=0.024).

CONCLUSIONS: Improving access to contraceptive implants immediately postpartum via payment reform significantly increased uptake.

O-18 Monday, October 17, 2016 12:30 PM

ETHNIC AND RACIAL DIFFERENCES IN THE PREVALENCE OF INFERTILITY: NATIONAL SURVEY OF FAMILY GROWTH (NSFG). J. D. Peck, A. Janitz, L. B. Craig. “Dept of Biostatistics and Epidemiology, OU Health Sciences Center, Oklahoma City, OK; ”Dept of Biostatistics and Epidemiology, OU Health Science Center, Oklahoma City, OK; ”Section of REI, Dept of Ob/Gyn, OU Health Science Center, Oklahoma City, OK.

OBJECTIVE: Clinical and population-based comparisons of the racial/ethnic burden of infertility have identified disparities in infertility prevalence. The objective of our study was to estimate the prevalence of infertility in the U.S. population by race/ethnicity in a nationally representative sample of men and women aged 15-44 years.

DESIGN: Secondary analysis of existing cross-sectional data from the NSFG, a US population-based survey collecting data on infertility and receipt of infertility services.

MATERIALS AND METHODS: We analyzed female respondent data from the pooled NSFG cycles 2002, 2006-2010 and 2011-2013. Racial/ethnic groups were categorized as 1) Non-Hispanic (NH) white, 2) NH black, 3) NH other, or 4) Hispanic. Infertility was defined as >12 months of intercourse without pregnancy among married or cohabiting respondents in a continuous relationship for ≥12 months with no use of contraception. Impaired fecundity included women in 3 subgroups of nonsurgically sterile, subfertile, and long (3+ yr) interval without conception. Prevalence proportions and multivariable logistic regression analyses accounted for survey weighting. Prevalence odds ratios (POR) and 95% confidence intervals (CI) were adjusted for age, relationship status, education, poverty level, parity, body mass index, smoking, pelvic inflammatory disease treatment and gynecologic disorders. Power calculations indicated the planned study had 80% power to detect minimum PORs of 1.7 and 1.4 for infertility and impaired fecundity among other race/ethnicity compared to NH whites.

RESULTS: In the pooled data (n=25,523), the prevalence of infertility was 6.4% (95% CI: 5.7%, 7.0%) and the prevalence of impaired fecundity was 34.1% (95% CI: 33.0%, 35.1%). Compared to NH whites, NH blacks had a 43% higher adjusted odds of infertility (95% CI: 1.00, 2.03). Hispanics also had a higher adjusted odds of infertility compared to NH whites (POR: 1.28, 95% CI: 0.95, 1.74), whereas there was little difference for NH other (POR: 0.95, 95% CI: 0.60, 1.49). A significantly lower odds of impaired fecundity was observed among Hispanic (POR: 0.75, 95% CI: 0.65, 0.87) and NH other (POR: 0.74, 95% CI: 0.60, 0.92), with no difference for NH blacks (POR: 1.01, 95% CI: 0.87, 1.17), compared to NH whites.

CONCLUSIONS: Prevention of reproductive health disparities requires monitoring race-specific infertility prevalence and related risk factors to guide and monitor effective public health action strategies to safeguard reproductive health.

Supported by: This project is supported by the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services (HHS) under 1 R40MC29449-01-00. Support is also provided by Oklahoma Shared Clinical and Translational Research Institute NIGMS U54 GM104938. The information, content and/or conclusions are those of the authors and should not be construed as the official position or policy of, nor should any endorsements be inferred by HRSA, HHS or the U.S.
MALE REPRODUCTION AND UROLOGY: TRAVELING SCHOLARS

O-19 Monday, October 17, 2016 11:15 AM

MORE THAN A FLAGELLAR PROTEIN: IFT140 IS A MALE INFERTILITY CANDIDATE GENE THAT MAY MODULATE CELL SIGNALING. A. S. Herati,1 P. R. Butler,2 C. Cengiz,3 D. J. Lamb4 1Urology, Baylor College of Medicine, Houston, TX; 2Urology/Center for Reproductive Medicine/MCB, Baylor College of Medicine, Houston, TX.

OBJECTIVE: The intraflagellar transport 140 (IFT140) protein is involved in retrograde transport along the microtubules of the sperm axoneme and maintains flagellar structure and function. We previously identified a homo-zygous six nucleotide deletion in exon 22 of the IFT140 gene in a consan-guineous family of non-obstructive azoospermic (NOA) brothers using whole-exome sequencing. Recently published Drosophila and mouse data implicated IFT family proteins in extra-axonal functions, such as cell signaling, which may be essential for spermatogenesis. The objective of this study is to determine the effect of silencing the IFT140 gene dysregulates cell signaling pathways using a murine spermatogonial cell line.

MATERIALS AND METHODS: Ift140 function was silenced in GC-1 (ATCC CRL-2053), a type B spermatogonial murine cell line. Ift140 mRNA levels were evaluated using quantitative real-time PCR (qPCR). Transient knockdown studies were performed in triplicate on an oligonucleotide array of 84 cell signaling genes of various known signaling pathways using Ift140 siRNA and a scrambled control. Genes were considered dysregulated if their expression was more than 1.5x different between the experimental and control groups. Statistical significance in mRNA expression levels was assessed using a Student’s t-test with post-hoc Bonferroni correction for multiple, paired comparisons.

RESULTS: Ift140 knockdown efficiency was 96% at 72 hours after treatment with Ift140 siRNA. Overall 49 genes possessed greater than 1 fold up-regulation and 35 were down-regulated by less than 1-fold. Six of the 49 up-regulated genes (Bcl2a1, Wnt5a, Fabp1, Mmp7, Ifng, Tnfsf10) and 10 were more than 1.5x different between the two groups. In contrast, only 2 (Ccl5, Ldha) of the 35 down-regulated genes were greater than 1.5x different compared to scramble. We observed significant changes in the expression of key genes in the Wnt, NFkB, TGFβ, PPAR, and oxidative stress signaling pathways.

CONCLUSIONS: A complex network of extra-axonemal pathways are modulated by the silencing of Ift140. Functional studies are required to validate the findings of this study and determine the role of these genes in spermatogenesis.

Supported by: A.H. is a National Institutes of Health (NIH) K12 Scholar supported by a Male Reproductive Health Research Career (MRHRH) Development Physician-Scientist Award (HD073917-01) from the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) Program (to Dolores J. Lamb).

O-20 Monday, October 17, 2016 11:30 AM

IMPACT OF CLOMIPHENE CITRATE ON PROSTATE SPECIFIC ANTIGEN VALUES FOR MEN BEING TREATED FOR INFERTILITY. L. DiGiorgio, a D. Shin, b R. P. Bonitiz a Rutgers University, Newark, NJ; aUrology, Hackensack University Medical Center, Hackensack, NJ.

OBJECTIVE: Clomiphene Citrate (CC), a selective estrogen receptor modulator, is used in the empiric treatment of subfertile males to increase testosterone levels and improve spermatogenesis. Controversy exists in regard to the impact of rising serum testosterone on prostate specific antigen (PSA) levels. Because the effects of clomiphene citrate on the prostate and PSA levels are unknown, we assessed the impact of clomiphene citrate on hormonal and PSA values in subfertile men.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Chart review of 73 subfertile males who were treated with clomiphene citrate was performed. Serum follicle-stimulating hormone (FSH), luteinizing hormone (LH), total testosterone (TT), bioavailable testosterone (BT), estradiol (E), hemoglobin (Hgb), hematocrit (Hct) and PSA levels were measured at baseline and at 5 months during clomiphene citrate therapy. Paired t-test was used to compare pre- and post-treatment biochemical parameters.

RESULTS: The study included 73 men, mean age 36.1 ± 0.7 years (SEM). Mean baseline testosterone was 303.6 ± 13.4 ng/dl and mean baseline PSA level was 0.75 ± 0.06 ng/mL. Significant increases in FSH, TT, BT and E levels (p<0.05) were observed in response to clomiphene citrate treatment after 5 months of therapy. Slight but insignificant increase in PSA values was observed at 5 months of clomiphene citrate treatment (0.80 ± 0.06, p=0.51). No patient had a significant increase in PSA velocity or change in digital rectal exam requiring prostate biopsy.

CONCLUSIONS: Clomiphene citrate significantly increases total and bioavailable testosterone levels when used as empiric medical therapy for the treatment of subfertile males. However, the increase in testosterone levels seen with the use of clomiphene citrate does not result in significant increases in PSA levels at 5 months of therapy. Although there does not appear to be any short term adverse effects, further study of the long-term effects of clomiphene citrate on serum PSA is warranted.

Baseline vs. 5 months Post-CC Therapy

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<th>P-value</th>
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<td>FSH (mIU/mL)</td>
<td>5.3 ± 0.5</td>
<td>7.4 ± 0.8</td>
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<td>LH (mIU/mL)</td>
<td>6.5 ± 2.6</td>
<td>6.4 ± 1.0</td>
<td>NS</td>
</tr>
<tr>
<td>TT (ng/dL)</td>
<td>303.6 ± 13.4</td>
<td>509.5 ± 19.5</td>
<td>&lt;0.01</td>
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<td>BT (ng/dL)</td>
<td>165.7 ± 7.3</td>
<td>261.4 ± 14.0</td>
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<td>E (pg/mL)</td>
<td>22.3 ± 1.1</td>
<td>33.9 ± 1.8</td>
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<td>PSA (ng/mL)</td>
<td>0.75 ± 0.06</td>
<td>0.80 ± 0.06</td>
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<td>Hgb (g/dL)</td>
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<td>15.2 ± 0.1</td>
<td>NS</td>
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<td>Hct (%)</td>
<td>44.2 ± 0.4</td>
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PERIPUBERTAL BLOOD LEAD LEVELS AND SEMEN QUALITY IN A PROSPECTIVE COHORT STUDY OF RUSSIAN MEN. L. Miguez-Alarcon, a O. Sergeyev, b J. S. Burns, c P. Williams, d M. M. Lee, e K. S. Kerrick, e L. Smigulina, g B. A. Revich, b H. Hauser, i 1Department of Medicine, Brigham and Women’s Hospital, Harvard Medical School, Boston, MA; 2Department of Biostatistics and Epidemiology, Boston University School of Public Health, Boston, MA; 3Department of Genomics and Human Genetics, Vavilov Institute of General Genetics, Moscow, Russian Federation; 4Environmental Health, Harvard T.H.Chan School of Public Health, Boston, MA; 5Biostatistics and Epidemiology, Harvard T. H. Chan School of Public Health, Boston, MA; 6Department of Medicine, Brigham and Women’s Hospital, Harvard Medical Scho, Boston, MA; 7Chapaevsk Medical Association, Chapaevsk, Russian Federation; 8Environmental Health, Public Health, Moscow, Russian Federation; 9Harvard Chan School of Public Health, Boston, MA.

OBJECTIVE: To assess associations between peripubertal blood lead levels and semen parameters.

DESIGN: A prospective cohort study conducted in Chapaevsk, Russia. MATERIALS AND METHODS: From 2003 to 2005, 499 boys were enrolled at age 8-9 years and their growth and development were assessed annually for ten years. Blood lead levels (BLLs) were measured at enrollment using atomic absorption spectrometry. At ages 18-19 years, 137 young men provided up to two semen samples collected one week apart (264 samples) which were analyzed for volume, sperm concentration and motility according to NAFA and ESHRE-SIGA methods. Total sperm count and total motile sperm count were calculated. Linear mixed models were used to examine the relation between BLLs (<5 mcg/dL, CDC reference for childhood lead exposure) and semen parameters, with random intercepts to account for multiple semen samples per participant.

RESULTS: Men had a median total sperm count, total motile sperm count and motility of 126 million, 80 million and 64%, respectively. Higher peripubertal BLLs were associated with lower total sperm count and total motile sperm count. Men who had peripubertal BLLs ≥ 5 mcg/dL had 30% lower total sperm count (p-value=0.09) and 31% lower total motile sperm count (p-value=0.01) compared with men who had BLLs < 5 mcg/dL. BLLs were not associated with motility.

CONCLUSIONS: This is the first study to examine the association between peripubertal BLLs and semen quality in young adulthood. We observed suggestive evidence that peripubertal BLLs above the CDC reference level could be associated with poorer semen quality, indicating that the peripubertal period may be a sensitive window of exposure. Lead
exposure continues to be a major public health problem in the United States and Russia, thus these results add to our understanding of reproductive health risks from childhood lead exposure.

Supported by: NIH grants R01ES0014370, P30ES000002, EPA grant R82943701 and Russian Science Foundation grant 14-45-00065 (for OS and RH).

O-22 Monday, October 17, 2016 12:00 PM

ALLEVIATING EFFECTS OF VARIOUS CONCENTRATIONS OF ETHANOLIC EXTRACT OF Lycopodium Clavatum ON AGING INDUCED TESTICULAR PATHOLOGY IN WISTAR ALBINO RATS, G. Lakshmanan, P. Seppan. 1Department of Anatomy, Research Scholar, Chennai, India; 2Department of Anatomy, Associate Professor, Chennai, India.

OBJECTIVE: Delayed paternity in the modern society and decreased sexual activity provides reason to research on the effects of aging on male reproductive system and their possible treatment modalities. The crude ethanolic extract of Lycopodium clavatum commonly known as “club moss” has been reported to have good antioxidant properties. Traditionally lycopodium is used to treat sexual complaints of old aged men and is known to increase their ‘potency’ and considered as the ‘balm of old man’. However there is no scientific validation to confirm this effect.

DESIGN: To analyze the efficacy of ethanolic extract of Lycopodium clavatum on aging induced alteration in testicular function and to find its effective therapeutic concentration.

MATERIALS AND METHODS: Aged male wistar albino rats (24 months) were randomly divided into four groups (n=12), first group received distilled water, and the other three groups received ethanolic extract of Lycopodium clavatum at dosage of 250, 500, 1000 mg / kg b.w daily for 60 days by gavage. At the end of experimental period, serum testosterone was estimated. Sperm parameters including count, viability, motility, membrane permeability and nuclear condensation were done. Biochemical analyses of testicular antioxidant were done. Testicular mRNA expression of antioxidant and apoptotic genes were estimated by qPCR. The results were statistically analysed.

RESULTS: Aging induced pathological changes were noted in the aged untreated animals. Beneficial effects were significant in Lycopodium clavatum treated groups when compared to untreated aged rats. Depressed testosterone level in untreated aged rat was improved in all the treated rats however, significant improvement was seen with 500mg dosage. Sperm parameters were significantly improved in aged rats with 500 mg dosage when compared to the other two treated aged groups i.e. 250 & 1000mg. The gene expression studies emphasized the maximum beneficial effects under 500mg dosage.

CONCLUSIONS: This observation confirms that Lycopodium clavatum has therapeutic effect under aging induced reproductive disorder and the effect seem to be dosage dependent. Thus results signify that finding effective dose for given animal is a key factor for maximum therapeutic outcome.

O-23 Monday, October 17, 2016 12:15 PM

MAPPING GENETIC HETEROGENEITY OF VIABLE AND NON-VIABLE SPERM, L. Nagirnaja, M. J. Noordam, D. Conrad. 1Genetics, Washington University School of Medicine, St. Louis, MO; 2Clinical Genetics, Maastricht University, Maastricht, Netherlands.

OBJECTIVE: This study aimed to describe the genetic heterogeneity of viable and non-viable sperm selected from the total ejaculate of a healthy man.

DESIGN: Whole-exome sequencing was performed for bulk DNA of live and dead sperm in comparison to blood. Additionally, three DNA pools of live and dead sperm (42 vs 38 respectively). Due to the increased resolution in detecting rare mutations, sequencing of small pools of sperm revealed higher rates of de novo mutations with almost double counts in dead sperm (313 vs 172) and yielding in germline mutation rates of 4.6x10^-7 per bp of exome (0.29x spermin) in liquid cultures (4x0.51x spermin) in dead cells. 5x spermin were amplified to an average of 11% sperm cells (mean variant allele fraction, VAF=0.11) in bulk and 17% (VAF=0.17) in small sperm pools. Functional characterization of the identified de novo mutations with integrated CADD annotation predicted an increased deleterious impact of the rare variants identified in small pools of sperm compared to bulk (P=1.5x10^-7) and a similar increase in the ratio of non-synonymous to synonymous amino acid changes (Ka/Ks 3.4 vs 1.9, P<0.05). In small pools of dead sperm, the upper 5th percentile of mutations with the largest CADD score (n = 15) included variants in four genes highly relevant for sperm function (ADCY10, TSGA10, SPEF1 and BBS1). CONCLUSIONS: Characterizing the genetic differences between viable and non-viable sperm is an important step towards developing robust assays for mutation detection from bulk ejaculate. The results highlight the contribution of de novo mutations at the level of the biopsy in defining post syngamal characteristics of sperm. Furthermore, the increased rate of de novo mutations in dead sperm has relevant implications when selecting sperm in vitro for assisted reproduction procedures Supported by: This was supported by U.S. National Institutes of Health (grants R01HD078641 and R01MH101810 to D.F.C.).

O-24 Monday, October 17, 2016 12:30 PM

MOLECULAR MECHANISMS BEHIND GHRELIN-MEDIATED PREVENTION OF POST-SURGICAL ADHESIONS, E. Bianchi, K. Boekelheide, M. Sigman, S. J. Hall, H. Wong. 1Division of Urology, Brown University, Providence, RI; 2Brown University, Providence, RI; 3Surger (Urology), Brown University and Lifespan, Providence, RI; 4Pathology, Saucerstown, RI.

OBJECTIVE: Postoperative adhesions are a leading cause of infertility, chronic pelvic pain, and intestinal obstruction. A new reproducible mouse model of induction of adhesion has been developed to demonstrate the capability of ghrelin to reduce post-surgical adhesions in a growth hormone secretagogue receptor (GHSR-1a)-dependent manner. The present study was designed to assess the molecular mechanisms and the GHSR-1a signaling pathway has been optimized, characterized by lipopolysaccharide (LPS)-stimulated RAW264.7 murine macrophages in the presence or absence of ghrelin. Mice were divided into 6 groups and then gavaged to an average of 11% sperm cells (mean variant allele fraction, VAF=0.11) in bulk and 17% (VAF=0.17) in small sperm pools. Functional characterization of the identified de novo mutations with integrated CADD annotation predicted an increased deleterious impact of the rare variants identified in small pools of sperm compared to bulk (P=1.5x10^-7) and a similar increase in the ratio of non-synonymous to synonymous amino acid changes (Ka/Ks 3.4 vs 1.9, P<0.05). In small pools of dead sperm, the upper 5th percentile of mutations with the largest CADD score (n = 15) included variants in four genes highly relevant for sperm function (ADCY10, TSGA10, SPEF1 and BBS1). CONCLUSIONS: Characterizing the genetic differences between viable and non-viable sperm is an important step towards developing robust assays for mutation detection from bulk ejaculate. The results highlight the contribution of de novo mutations at the level of the biopsy in defining post syngamal characteristics of sperm. Furthermore, the increased rate of de novo mutations in dead sperm has relevant implications when selecting sperm in vitro for assisted reproduction procedures Supported by: This was supported by U.S. National Institutes of Health (grants R01HD078641 and R01MH101810 to D.F.C.).

DESIGN: In Vivo and In Vitro experiments were performed. Post-surgical adhesions were created in C57BL/6 wild type mice. Ghrelin or saline intraperitoneal injections were given from two days before surgery to 1, 4 and 20 days after surgery. An In Vivo model to test the ghrelin-activated GHSR-1a signaling pathway has been optimized, characterized by lipopolysaccharide (LPS)-stimulated RAW264.7 murine macrophages in the presence or absence of ghrelin. Mice were divided into 6 groups and then gavaged 15 included variants in four genes highly relevant for sperm function (ADCY10, TSGA10, SPEF1 and BBS1). CONCLUSIONS: Characterizing the genetic differences between viable and non-viable sperm is an important step towards developing robust assays for mutation detection from bulk ejaculate. The results highlight the contribution of de novo mutations at the level of the biopsy in defining post syngamal characteristics of sperm. Furthermore, the increased rate of de novo mutations in dead sperm has relevant implications when selecting sperm in vitro for assisted reproduction procedures Supported by: This was supported by U.S. National Institutes of Health (grants R01HD078641 and R01MH101810 to D.F.C.).

RESULTS: Aging induced pathological changes were noted in the aged untreated rats. Depressed testosterone level in untreated aged rat was improved in all the treated rats however, significant improvement was seen with 500mg dosage. Sperm parameters were significantly improved in aged rats with 500 mg dosage when compared to the other two treated aged groups i.e. 250 & 1000mg. The gene expression studies emphasized the maximum beneficial effects under 500mg dosage.

CONCLUSIONS: This observation confirms that Lycopodium clavatum has therapeutic effect under aging induced reproductive disorder and the effect seem to be dosage dependent. Thus results signify that finding effective dose for given animal is a key factor for maximum therapeutic outcome.

O-24 Monday, October 17, 2016 12:30 PM

MOLECULAR MECHANISMS BEHIND GHRELIN-MEDIATED PREVENTION OF POST-SURGICAL ADHESIONS, E. Bianchi, K. Boekelheide, M. Sigman, S. J. Hall, H. Wong. 1Division of Urology, Brown University, Providence, RI; 2Brown University, Providence, RI; 3Surge (Urology), Brown University and Lifespan, Providence, RI; 4Pathology, Saucerstown, RI.

OBJECTIVE: Postoperative adhesions are a leading cause of infertility, chronic pelvic pain, and intestinal obstruction. A new reproducible mouse model of induction of adhesion has been developed to demonstrate the capability of ghrelin to reduce post-surgical adhesions in a growth hormone secretagogue receptor (GHSR-1a)-dependent manner. The present study was designed to assess the molecular mechanisms and the GHSR-1a signaling pathway has been optimized, characterized by lipopolysaccharide (LPS)-stimulated RAW264.7 murine macrophages in the presence or absence of ghrelin. Mice were divided into 6 groups and then gavaged 15 included variants in four genes highly relevant for sperm function (ADCY10, TSGA10, SPEF1 and BBS1). CONCLUSIONS: Characterizing the genetic differences between viable and non-viable sperm is an important step towards developing robust assays for mutation detection from bulk ejaculate. The results highlight the contribution of de novo mutations at the level of the biopsy in defining post syngamal characteristics of sperm. Furthermore, the increased rate of de novo mutations in dead sperm has relevant implications when selecting sperm in vitro for assisted reproduction procedures Supported by: This was supported by U.S. National Institutes of Health (grants R01HD078641 and R01MH101810 to D.F.C.).

RESULTS: Aging induced pathological changes were noted in the aged untreated rats. Depressed testosterone level in untreated aged rat was improved in all the treated rats however, significant improvement was seen with 500mg dosage. Sperm parameters were significantly improved in aged rats with 500 mg dosage when compared to the other two treated aged groups i.e. 250 & 1000mg. The gene expression studies emphasized the maximum beneficial effects under 500mg dosage.

CONCLUSIONS: This observation confirms that Lycopodium clavatum has therapeutic effect under aging induced reproductive disorder and the effect seem to be dosage dependent. Thus results signify that finding effective dose for given animal is a key factor for maximum therapeutic outcome.

OBJECTIVE: The CSF family of ligands and their receptors are increasingly recognized to play important roles in embryo implantation and have recently been used as therapeutic targets for recurrent implantation failure and recurrent pregnancy loss. We, and others, have demonstrated cyclic regulation of the ligands, but cell-type specificity of ligand and receptor expression and function remains largely undefined. The aims of this study were to determine the expression and localization of the CSF ligand (1, 2, and 3) and receptor, CSF2A and CSF2B, mRNA in human whole and separated endometrium throughout the menstrual cycle and in stromal cells after in vitro decidualization.

DESIGN: Laboratory based analysis.

MATERIALS AND METHODS: Human endometrial biopsies from normal cycling volunteers throughout the menstrual cycle (n=24) were obtained timed by cycle day and urinary LH testing. Samples were divided into aliquots for whole tissue analysis and cell separation using enzymatic digestion. RNA was isolated from whole endometrium and separated epithelial and stromal cells. Primary stromal cell cultures (n=3) underwent decidualization in vitro by treatment with medroxyprogesterone, estradiol, and cAMP. Relative expression of CSF family ligands and receptors was determined by real-time RT-PCR. Differences were assessed using student’s t-test and ANOVA.

RESULTS: As in whole endometrium, CSF1 is cycle regulated in the stroma, with a fold increased expression in late secretory versus proliferative phase (p=0.008). While epithelial CSF1 expression is noted, no significant cyclic variation is observed (p=0.21). CSF2 is cycle regulated in whole endometrium, but not in separated epithelium or stroma. CSF3 is cycle regulated (p=0.04) with a 32-fold decrease from proliferative to mid-secretory phase in whole endometrium with similar relative changes in both separated stroma (p=0.03) and epithelium (p=0.008). In vitro, stromal CSF1 expression does not differ, while CSF2 and its receptors (CSF2RA and CSF2RB) all trend toward decreased with decidualization (p=0.73, 0.22, 0.34, 0.08 respectively). CSF3 is not expressed by stromal cells cultured on plastic, but is easily detected by those cultured on matrigel.

CONCLUSIONS: Whole endometrial expression of CSF1, CSF2 is cycle regulated, but regulation is not apparent in separated stromal or epithelial cells, suggesting that cyclic changes are likely due to resident immune and/or endothelial cells. Cyclic expression of CSF3 appears to be due to changes in both stromal and epithelial cells. CSF2, CSF2RA, and CSF2RB expression is likely reduced with decidualization, but an increased sample number will be needed to confirm the preliminary findings. Complimentary studies of CSF1 and CSF3 receptors are ongoing. These studies will allow a better understanding of ongoing and proposed trials of CSF ligand therapeutics in assisted reproduction.

REFERENCES:

Supported by: NIH/NICHD R01 HD067721.

LONGITUDINAL FOLLOW-UP IN FEMALE CHILDHOOD CANCER SURVIVORS: NO SIGNS OF ACCELERATED OVARIAN FUNCTION LOSS. A. L. van der Kooi, M. M. van den Heuvel-Eibrink, S. M. Pluijnm, J. S. Neergers, E. van Dulmen-den Broeder, W. van Dorp, J. S. Laven. Div. Reproductive Medicine, Erasmus Medical Center Rotterdam, Rotterdam, Netherlands; Pediatric Oncology, Princess Maxima Center, Utrecht, Netherlands; Pediatric Oncology/Hematology, Erasmus MC- Sophia Children’s Hospital, Rotterdam, Netherlands; Pediatric Oncology, Princess Maxima Center, Rotterdam, Netherlands; Pediatric Oncology/Hematology, Erasmus Medical Center Rotterdam, Rotterdam, Netherlands.

OBJECTIVE: Female Childhood Cancer Survivors (CCS) have an increased risk of gonadal impairment. It is conceivable that, in addition to this gonadal impairment, AMH shows a more rapid decline in female CCS than in healthy females. We assessed if the long-term decline of ovarian function, reflected by serum anti-Müllerian hormone (AMH) concentrations, is accelerated over time in female CCS.

DESIGN: A retrospective single-center cohort study was performed in Rotterdam, The Netherlands, between 2001-2014.

MATERIALS AND METHODS: Paired serum AMH levels of 192 adult female CCS were assessed, at least five years after cessation of treatment and at a second visit at least 2 years after the first measurement. The course of AMH levels was compared to the age-based median (p50) of AMH using the Mann-Whitney U test. The independent contribution of various treatment modalities on the course of AMH levels between the two visits was further evaluated using the Wilcoxon signed rank test.

RESULTS: At both the first visit and at the second visit, after a median of 3.2 years later (range 2.1-6.0 years), median AMH levels were below the age-based p50 of AMH (-0.59 μg/L; range: -4.07 - 17.05 versus -0.22 μg/L, range: -3.75 - 20.50, respectively). In women with a sustained ovarian function (AMH > 1.0 μg/L), analysis showed that the decline in AMH in CCS was not different from the decline seen in the normal population (difference in decline per year: -0.07 μg/L (range: -2.86 - 4.92), p=0.08). None of the treatment modalities of childhood cancer was associated with a significant acceleration of decline of AMH per year.

CONCLUSIONS: Our study shows that after initial impairment due to childhood cancer treatment, the further decline in ovarian function, as measured in AMH, is not accelerated in CCS. This finding may help physicians to counsel female CCS about the expected course of their ovarian function.

Supported by: FF7- PanCare LIFE.


OBJECTIVE: It can be a challenge for fertility specialists when good prognosis patients fail treatment for unexplained reasons. Conversely, poor prognosis patients often beat the odds and achieve live birth (LB). The aim of our study was to uncover subclinical, genetic factors that may help better stratify patients ahead of treatment decisions.

DESIGN: Retrospective cohort of 227 women undergoing IVF treatment at four fertility clinics in the US between 2012 and 2015.

MATERIALS AND METHODS: The likelihood of LB was calculated with a Cox proportional hazards model using retrospective data from >80,000 IVF treatment cycles across 12 clinics in the US. This model was used to stratify patients into 4 groups based on prognosis and outcome: (1) good prognosis (GP, upper quartile) and shorter time to LB (GP-SO), (2) GP and longer time to LB (>1 cycles to or no LB) (GP-LO), (3) poor prognosis (lower quartile) and SO (≤2 cycles to LB) (PP-SO) and (4) PP-LO (>2 cycles to or no LB). Whole genome sequencing was performed using the Illumina HiSeq platform with 30X min coverage on DNA extracted from whole blood. Genetic variants predicted to disrupt gene function were identified using a custom bioinformatics pipeline and annotated with pathway association using a fertility-centric, genomic knowledgebase. Paired-Wilcoxon test and median-polish method were applied to identify enriched pathways.

RESULTS: Analysis of the two groups revealed significant differences in mean age between GP and PP (29.7 vs. 35.8; p<0.001, respectively). The majority of the PP cohort were diagnosed with DOR (~57%) while the majority of GP patients were idiopathic (~49%). There
were no statistically significant differences in age or BMI between the GP-SO and GP-LO groups or between PP-SO and PP-LO. Of over 25 different biological pathways relating to reproductive function studied, oogenesis was the only pathway whose disruption was significantly associated with longer time to or lack of LB in both GP and PP patients.

CONCLUSIONS: This study suggests that subclinical, genetic markers of oocyte quality may hold diagnostic value independent of phenotypic biomarkers of fertility potential such as age and hormone levels. This information could bring much needed clarity to currently unexplained cases of infertility and help bring greater efficiency to infertility care.

Supported by: Celmatrix Inc.

O-28 Monday, October 17, 2016 12:00 PM

ISOLATION AND IDENTIFICATION OF EXTRACELLULAR VESICLES IN THE HUMAN ENDOMETRIAL FLUID. D. Bolumar,a I. Moreno,nett, S. Cabanillas, C. Simon, F. Vilella. *Research, Fundacion IVI, Paterna (Valencia), Spain; Fundacion IVI, Paterna (Valencia), Spain; Gynecologist, Valencia, Spain; Fundacion Instituto Valenciano de Infertilidad, Paterna, Spain; Fundacion IVI / Incliva, Paterna, Spain.

OBJECTIVE: To isolate and characterize the different types of extracellular vesicles (EVs) secreted by the human endometrium into the endometrial fluid (EF).

DESIGN: EF samples were obtained from healthy subjects throughout their natural cycles and processed for isolation of EVs, which were classified by morphology and size, and further characterized by their content.

MATERIALS AND METHODS: EVs were isolated by a modified ultracentrifugation protocol to obtain the different EV populations from the human EF. Morphology and size of the different EVs subpopulations were assessed by transmission electron microscopy (TEM). Size distribution was further investigated through Nanoparticle Tracking Analysis (NTA). The content of EVs was analysed by Western blot targeting against vesicle population-specific markers such as CD63, CD9, CD81, ARF6, annexin V and calnexin. Finally, DNA into the different EVs was analysed using LDS 751 that binds dsDNA.

RESULTS: EF contains EVs that can be classified into three categories. Apoptotic bodies, from 1.5 to 5 μm, are characterized by electron-dense grooves in the periphery of the vesicles. Micovesicles and exosomes are smaller in size (approx. 350 nm and 100 nm in average, respectively). Particle size distribution from NTA confirms the existence of the indicated populations, having the apoptotic bodies a size centre of 3.6 μm, 330 nm for micovesicles and 100 nm for exosomes. The different vesicle subpopulation can be phenotyped by a combination of the following markers: CD63, CD9, CD81, ARF6, annexin V and calnexin. LDS 751 fluorescence analysis shows that all the EVs populations contain DNA. In general, exosomes fraction were harvested. D5 and D7 implantation sites (IS) and D14 IS, placenta and fetus were harvested and weighed. Western blot analysis, H&E staining and immunohistochemistry were performed on tissue. F1 mice were weaned, bred, sacrificed and IS harvested and analyzed in similar fashion. Statistical analysis was performed using student t-test with significance at p<0.05.

RESULTS: Similarly F1 D5 IS showed no significant difference, however, a significant decrease in weight is noted in 1mgkg and 10mgkg BPA groups vs. control in D7 IS [0.0253g vs. 0.0181 (p<0.05) and 0.0197 (p<0.001)], as well as D14 IS [0.477 vs. 0.345 (p<0.05) and 0.390 (p<0.05)]. H&E staining confirmed D7 IS size difference between 10mgkg and control. (H2Ak119ub1, DNMT1) IS epigenetic regulators decreased in 10mgkg vs. control (p<0.05).

CONCLUSIONS: BPA exposure prior to implantation causes detrimental effect on pup weight at higher doses. BPA exposure disrupts decidualization causing poor embryonic growth through epigenetic changes in IS methylome, witnessed in subsequent generations without direct exposure. Further IS analysis needed to identify specific genes affected in order to delineate the perturbation mechanism.

Supported by: Support: NIEH Grant; Vivere Research Grant.

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*p<0.05

O-29 Monday, October 17, 2016 12:15 PM

BISPHENOL-A (BPA) EXPOSURE ON THE DAY OF IMPLANTATION ALTERS UTERINE EPIGENOME DISRUPTING FETAL GROWTH: A MOUSE MODEL. I. Robertshaw, J. M. Stoga, M. A. Thomas. Obstetrics and Gynecology, University of Cincinnati, West Chester, OH.

OBJECTIVE: To determine the effects of maternal BPA exposure prior to implantation on epigenetic regulation of decidualization and pregnancy progression.

DESIGN: Basic research IACUC approved animal study.

MATERIALS AND METHODS: Phase I: Female CD-1 mice were mated. Pregnant mice (F0) were exposed to subcutaneous injections of sesame oil, control, or BPA on day 4 (D4) of gestation. BPA group sub-divided into 10mg/kg/d, 1mg/kg/d, 0.1mg/kg/d, 0.01 mg/kg/d groups. A series of four 0.1mL injections administered at 2.5 hour intervals. Offspring (F1) litter size and weights were documented. Phase II: Mice mated and exposed to BPA as described above. On gestational D5, after implantation; D7, after decidualization, or D14, after embryo maturation and occurred, the mice were sacrificed. F0 uterus and ovaries were harvested. D5 and D7 implantation sites (IS) and D14 IS, placenta and fetus were harvested and weighed. Western blot analysis, H&E staining and immunohistochemistry were performed on tissue. F1 mice were weaned, bred, sacrificed and IS harvested and analyzed in similar fashion. Statistical analysis was performed using student t-test with significance at p<0.05.

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CONCLUSIONS: BPA exposure prior to implantation causes detrimental effect on pup weight at higher doses. BPA exposure disrupts decidualization causing poor embryonic growth through epigenetic changes in IS methylome, witnessed in subsequent generations without direct exposure. Further IS analysis needed to identify specific genes affected in order to delineate the perturbation mechanism.

References:

Supported by: Support: NIEH Grant; Vivere Research Grant.
GPER MEDIATED ACTION OF ESTROGEN IN EDOMETRIAL RECEPTIVITY OF WOMEN WITH HIGH SERUM ESTRADIOL LEVEL ON HCG DAY. Y. Shi, C. Fang, R. Huang, X. Liang. The Sixth Affiliated Hospital of Sun Yat-Sen University, Guangzhou, China.

OBJECTIVE: To investigate the influence of supra-normal serum estradiol level in the endometrial receptivity of infertile women. To reveal the mechanism of estrogen action mediated through its novel membrane receptor Gper.

DESIGN: Single-centre, prospective cohorts study. Two cohorts of endometrial samples of 40 infertile women were used: 30 women underwent controlled ovarian hyperstimulation with GnRH-agonist long protocols, the other 10 women underwent nature cycle.

MATERIALS AND METHODS: Forty infertile women with regular BMI aged <40 years were recruited for endometrial biopsies at day 5 after oocyte retrieval, respectively. Women who were undergoing their first IVF/ICSI cycle were infertile mainly due to tubal or pelvic disease, ovulatory dysfunction, or male infertility. Endometriosis, polycystic ovary syndrome, endometrial polyps, abnormal uterine development and hydrosalpinx etc. were excluded. Women with nature cycle were defined as group A, and serum estradiol concentrations on the day of human chorionic gonadotrophin (hCG) administration of the 30 women were categorized into two groups: group B <3000 pg/ml, group C <3000 pg/ml. The serum progesterone concentration on the hCG day of all the subjects was less than 1.5 ng/ml. Various genes expression were analyzed, including the novel estrogen membrane receptor: G protein-coupled estrogen receptor (Gper), and several endometrial receptive markers. In addition to the real-time PCR examination, the endometrial samples were also checked by histological results (histopathology and immunocytochemistry/immunohistochemistry) and TUNEL assay. Statistical tests were carried out using one-way analysis of variance (ANOVA).

RESULTS: Real-time PCR analysis of relative Gper expression revealed increased expression in the group C, which was significantly higher compared to group B (P < 0.05), with no difference between group A and B. Among the several receptive markers, mRNA of ITGβ3 and ITGβ53 expression in group C were significantly decreased than in group B (P < 0.05). There were no significant changes of other markers. However, the immunoreactive protein abundance of Gper did not parallel mRNA abundance. Its protein expression was significantly decreased in group C (P < 0.05). All protein expression of ITGβ5, LIF (P < 0.01) and ITGβ3, EGFR (P < 0.05) were decreased in group C than that of group B. The result of TUNEL showed significantly increased apoptosis signals in group C than in group B, with no difference between group A and B.

CONCLUSIONS: High serum estradiol concentrations on hCG day down regulated the protein expression of Gper. The increased apoptosis of endometrial cells was probably due to the impairment of estrogen response through Gper resulting from high serum estradiol concentrations, which may adversely affect the receptivity of endometrium. The present data suggests a potential role for Gper in the hormonal regulation of endometrial receptivity, which should be taken into consideration for future hormonal treatment strategies.

Supported by: This project was supported by the Natural Science Fund of Guangdong Province (2014A030310149).

REPRODUCTIVE SURGERY 1

O-30 Monday, October 17, 2016 12:30 PM

HUMAN ADHESION FIBROBLASTS ARE CHARACTERIZED BY A REDUCTION IN THE LEVEL OF PLURIPOTENCY MARKERS AS COMPARED TO NORMAL PERITONEAL FIBROBLASTS. N. M. Fletcher, A. Juhani, M. S. Abusamaan, M. P. Diamond, G. M. Saed. Obstetrics and Gynecology, Wayne State University School of Medicine, Detroit, MI; Wayne State University, Detroit, MI. August University, Augusta, GA.

OBJECTIVE: Pluripotency is promoted and stabilized by pluripotent-cell specific genes including the transcription factors octamer-binding transcription factor-4 (Oct4), MIX (sex determining region Y)-box 2 (Sox2) and homeobox protein NANOG. The objective of this study was to determine the level of key pluripotency markers in fibroblasts isolated from normal peritoneum and adhesion tissues collected from the same patient. Additionally, determine whether hypoxia contributes to less pluripotency in normal peritoneal fibroblasts.

DESIGN: Experimental study.

MATERIALS AND METHODS: Fibroblasts established from normal peritoneum and adhesion tissues from the same patients (n=2) were exposed to normal (20% O2) or hypoxic (2% O2) conditions for 24 hours. Total RNA was extracted; cDNA was synthesized and subjected to real-time RT-PCR to measure mRNA levels of NANOG, Oct4b, and Sox2.

RESULTS: Baseline levels of NANOG, Oct4b and Sox2 are significantly lower in adhesion fibroblasts compared to normal peritoneal fibroblasts. There is no significant difference in expression of Oct4b between the 2 cell lines. Treatment of normal peritoneal fibroblasts with hypoxia resulted in a significant decrease in levels of NANOG (from 5.8 ± 0.1 to 4.3 ± 0.07 fg/μg RNA) and Sox2 (from 34.0 ± 0.3 to 15.7 ± 1.2 fg/μg RNA) while increasing Oct4b (from 224.2 ± 13.6 to 388.5 ± 15.9 fg/μg RNA) (p<0.05). Treatment of adhesion fibroblasts with hypoxia also resulted in a significant increase in Oct4b (from 170.0 ± 26.4 to 283.5 ± 16.6 fg/μg RNA, p<0.05) and Sox2 (from 8.2 ± 1.8 to 14.3 ± 0.9 fg/μg RNA, p<0.05) while also increasing NANOG, but not quite significantly.

CONCLUSIONS: The results indicate significant changes in expression of pluripotency markers in adhesion fibroblasts as compared to normal fibroblasts, which suggest the involvement of peritoneal stem cells in the development of peritoneal adhesions. Furthermore, treatment of normal peritoneal fibroblasts with hypoxia results in a more differentiated phenotype, similar to baseline adhesion fibroblasts.

O-32 Monday, October 17, 2016 11:30 AM

DEMOGRAPHIC CHARACTERISTICS OF WOMEN WITH UTERINE FACTOR INFERTILITY SEEKING INFORMATION ON UTERINE TRANSPLANTATION. S. Arian, R. Flyckt, A. G. Tzakis, T. Falcone. Obstetrics, Gynecology, and Women’s Health Institute, Cleveland Clinic, Cleveland, OH; Transplant Surgery, Cleveland Clinic Florida, Weston, FL.

OBJECTIVE: The objective of this study is to describe characteristics of women with uterine factor infertility (UFI) who were screened as candidates for a uterine transplantation clinical trial at our institution.

DESIGN: This is a descriptive study.

MATERIALS AND METHODS: Reproductive-aged women with UFI contacted our institution between 4/2015 to the present regarding our uterine transplantation clinical trial. Descriptive and demographic characteristics of screened patients are reported below.

RESULTS: 239 women with UFI were screened for our uterine transplantation protocol. The mean age was 31 years (range 18-52). 32% (n=78) had UFI secondary to prior hysterectomy. One patient had an introspection diagnosis. There were 5 male to female trans-gender applicants (2%) and one case of androgen insensitivity syndrome. The mean age in the MRKH group was 28 versus 33 in the acquired UFI group. 15% of patients with MRKH had a single kidney. The most common cause for seeking uterine transplantation was prior hysterectomy, with indications for surgery including 50% benign conditions (fibroids, endometriosis), 25% obstetric complications (post-partum hemorrhage, placenta abnormalities) and 25% gynecological malignancies (Table 1). 67% of candidates were Caucasian. 94% of women lived in the United States and 6% were international. 64% of screened women were legally married, 29% in a stable relationship and 7% were single. 17% of the screened candidates had at least one child.

CONCLUSIONS: Uterine transplantation is a novel treatment for UFI, a condition that affects approximately 1.5 million women worldwide. Given recent reported live births, uterine transplant has now reached its clinical experimental stages at several institutions. Candidates are actively seeking uterus transplantation programs internationally and in the U.S. These women have wide-ranging ages, social and religious situations, and medical histories. The greater number of patients with acquired versus congenital UFI had at least one child.

Table 1

<table>
<thead>
<tr>
<th>Condition</th>
<th>Total</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acquired UFI</td>
<td>154</td>
<td>64%</td>
</tr>
<tr>
<td>Hysterectomy for benign conditions</td>
<td>77</td>
<td>50%</td>
</tr>
<tr>
<td>Hysterectomy for malignancy</td>
<td>39</td>
<td>25.3%</td>
</tr>
<tr>
<td>Hysterectomy for OB complications</td>
<td>38</td>
<td>24.7%</td>
</tr>
</tbody>
</table>
References:

O-33 Monday, October 17, 2016 11:45 AM
UTERINE AND OVARIAN VIABILITY IN THE BABOON WITH BILATERAL UTERO-OVARian MICROVASCULAR ANASTOMOSES ALONE. B. D. Beran, a K. S. Arnold, a M. E. Shockley, a K. Rivas, b M. L. Sprague, c M. Medina III, d P. Escobar, e A. G. Tzakis, f T. Falcone, f S. Zimberg. f Division of Minimally Invasive Gynecology, Cleveland Clinic Florida, Weston, FL; bMannheimer Foundation, Home-stead, FL; cPlastic Surgery, Cleveland Clinic Florida, Weston, FL; dGynecologic Oncology and Reproductive Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX; eTransplant Surgery, Cleveland Clinic Florida, Weston, FL; fObstetrics & Gynecology, Cleveland Clinic, Cleveland, OH.

OBJECTIVE: To determine uterine and ovarian viability with microsurgical anastomoses of utero-ovarian vessels alone in a baboon model for translation to future human uterine transplantation efforts.

DESIGN: Prospective observational study of uterine and ovarian viability in Papio hamadryas baboons with surgically-altered uterine perfusion.

MATERIALS AND METHODS: Three baboons underwent laparotomy to alter uterine perfusion. Bilateral uterine arteries and veins were surgically ligated. A circumferential colpotomy was made and repaired. One utero-ovarian artery and vein were identified on each side, divided, and re-anastomosed end-to-end using a microsurgical technique. Intra-operative perfusion of the uterus was documented with near-infrared perfusion angiography. Resumption of menstrual blood flow with appearance of uterus on transabdominal ultrasound and cervical biopsies confirmed presence of uterus in all animals 6-10 weeks after surgery, while cyclical changes of the sex skin demonstrated continued ovarian function.

RESULTS: All surgeries occurred without incident, and near-infrared perfusion angiography confirmed intra-operative uterine perfusion after completion of microsurgical anastomoses. One baboon acquired cellulitis of the skin incision which resolved with antibiotics. Trans-abdominal ultrasound confirmed presence of uterus in all animals 6-10 weeks after surgery, and simultaneous cervical biopsies verified normal cervical tissue. Within the first 60 days post-laparotomy, all animals demonstrated at least one menstrual bleed, and cyclical pattern of sex-skin changes in accordance with normal baboon physiology.

CONCLUSIONS: The baboon uterus can be adequately perfused by bilateral microsurgical anastomosis of the utero-ovarian vessels in the absence of the uterine artery and veins, and cervico-vaginal vessel branches. This technique did not disrupt ovarian function and shows promise for future human transplantation trials to occur without meticulous uterine artery and vein dissection, and instead to rely solely on utero-ovarian vasculature.

O-34 Monday, October 17, 2016 12:00 PM
UNILATERAL SALPINGECTOMY AND METHOTREXATE ARE ASSOCIATED WITH SIMILAR RECURRENCE RATE OF ECTOPIC PREGNANCY IN PATIENTS UNDERGOING IVF. M. Irani, a A. Robles, b V. Gunnnala, c Z. Rosenwaks,d S. D. Spandorfer.e 1. Reproductive Endocrinology and Infertility, Weill Cornell Medicine, New York, NY; 2. Resident Physician at NYP Weill Cornell, New York, NY; 3. OB/GYN, REI Fellow, New York, NY; 4. Weill Cornell Medicine - Center for Reproductive Medicine, 1305 York Avenue, New York, NY; 5. Cornell University Medical Center, New York City, NY.

OBJECTIVE: Treatment of ectopic pregnancy (EP) with Methotrexate (MTX) or unilateral salpingectomy is associated with comparable risk of recurrence of EP in patients who conceive naturally. It is not clear whether such treatment modalities are associated with comparable risk of recurrence of EP following IVF. In the present study, we aim to determine whether different treatment approaches of EP affect its recurrence risk in IVF.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Patients with history of previous ectopic pregnancy who achieved pregnancy following IVF cycles between January 2004 and May 2013 were included. Recurrence risk of EP was compared between patients who underwent different treatment approaches for previous EP, χ² test and Fisher's exact test were used for categorical variables. Odds ratio (OR) with 95% confidence intervals (CI) were calculated and adjusted for potential confounders.

RESULTS: A total of 486 patients were included; 14 of them (2.8%) had recurrence of EP following IVF. Patients who underwent unilateral salpingectomy (n=191) to treat ectopic pregnancy had comparable risk of recurrent ectopic pregnancy following IVF with those who received MTX (n=233) (3.6 % vs 3.0 %; p=0.7; OR=1.2; 95% CI=0.4-3.5). This odds ratio remained unchanged after adjusting for patient’s age, number of previous ectopic pregnancies, number of transferred embryos, and peak estradiol level during stimulation (aOR=1.0; 95% CI=0.3-3.2). None of the patients who underwent bilateral salpingectomy (n=41) had recurrence of EP following IVF.

CONCLUSIONS: Treatment of EP with MTX has comparable risk of recurrence of EP following IVF with unilateral salpingectomy. In patients who are not candidate for MTX and who consider IVF as their sole method to achieve pregnancy, bilateral salpingectomy should be considered to treat EP because it is associated with a significantly lower recurrence rate than unilateral salpingectomy.

O-35 Monday, October 17, 2016 12:15 PM
ASSESSING IMPORTANCE OF REPRODUCTIVE SURGERY TRAINING IN GRADUATING REPRODUCTIVE ENDOCRINOLOGY AND INFERTILITY FELLOWS. L. R. Goodman, a Z. Khan, b J. M. Goldberg. c 1. Women’s Health Institute, Cleveland Clinic, Cleveland, OH; 2. Reproductive Endocrinology & Infertility, Mayo Clinic, Rochester, MN.

OBJECTIVE: Across the United States, physicians graduating from reproductive endocrinology and infertility (REI) fellowship programs are expected to have an adequate exposure to reproductive endocrinology, infertility and reproductive surgery during the 36-months of subspecialty training. Management of infertility, though a small part of the learning objectives for fellowship in REI, has become a prime focus of most training programs nationwide. With a change in clinical practice and more fellowship

<table>
<thead>
<tr>
<th>Objective</th>
<th>Strongly Agree</th>
<th>Agree</th>
<th>Neutral</th>
<th>Disagree</th>
<th>Strongly Disagree</th>
</tr>
</thead>
<tbody>
<tr>
<td>There is a role for surgery in patients with infertility</td>
<td>18 (52.9%)</td>
<td>12 (35.3%)</td>
<td>4 (11.8%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>I feel prepared to perform reproductive surgery</td>
<td>11 (33.3%)</td>
<td>11 (33.3%)</td>
<td>9 (27.3%)</td>
<td>2 (6.1%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>The ability to perform reproductive surgery will enable me to provide better patient care</td>
<td>17 (50%)</td>
<td>13 (38.2%)</td>
<td>4 (11.8%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>The ability to perform reproductive surgery will make me a competitive job applicant</td>
<td>14 (41.2%)</td>
<td>12 (35.3%)</td>
<td>5 (14.7%)</td>
<td>3 (8.8%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>I would be interested in a 1-year reproductive surgery fellowship</td>
<td>4 (11.8%)</td>
<td>3 (8.8%)</td>
<td>11 (32.3%)</td>
<td>9 (26.5%)</td>
<td>7 (20.6%)</td>
</tr>
</tbody>
</table>
trained minimally invasive gynecologic surgeons, REI practices and trainees have had further reduction in exposure to reproductive surgery. In this study we assess the exposure to reproductive surgery in graduating REI fellows and determine if there would be interest in further training in reproductive surgery.

DESIGN: Cross-Sectional study using survey design.

MATERIALS AND METHODS: We sent a survey to all REI fellows enrolled in fellowships across the United States graduating in June 2016. We used survey monkey to create and distribute our survey and calculate results.

RESULTS: All 44 graduating fellows across 39 programs nationwide were sent the survey with a response rate of 77% (34/44). The majority (30/34; 88.2%) attested to the importance of reproductive surgery and most (22/33; 66.6%) felt well prepared to perform reproductive surgery. A significant proportion (7/34; 20.6%) would consider enrolling in an additional 1-year reproductive surgery fellowship.

CONCLUSIONS: It appears that most graduating REI fellows feel comfortable with performing reproductive surgery, however, 1 in 5 graduating fellows would be interested in additional surgical training. Information regarding the amount of surgical exposure and level of surgical expertise will be helpful in understanding our results better and to determine if additional surgical training should be incorporated into the existing REI fellowships. Future directions include polling the same fellows following graduation to determine practice patterns and comfort level with reproductive surgery.

O-36 Monday, October 17, 2016 12:30 PM

THE INCIDENCE OF RENAL ANOMALIES IN PATIENTS WITH SEPTATE UTERI. D. E. Broughton, K. Anderson, E. Jungeheim, C. Siegel. Obstetrics and Gynecology, Washington University, St. Louis, MO; Radiology, Washington University, St. Louis, MO.

OBJECTIVE: To determine the prevalence of renal anomalies in patients with uterine septums.

DESIGN: Retrospective chart review.

MATERIALS AND METHODS: This was a retrospective chart review performed in an academic tertiary care center. The electronic medical record was queried for all radiologic studies containing the terms “uterine septum” or “septate uterus” from 2005 to present. A genitourinary radiologist reviewed the images to determine if a uterine septum was present. Patients were included if a uterine septum was noted and renal imaging was available. A uterine septum was defined as separation of the uterine horns >1 cm in length when measured from a transverse line connecting the cornu. Designation as a septate uterus required less than 1 cm of fundal indentation, with >1 cm indicating bicorannate morphology. Other data obtained from the pelvic imaging included the presence or absence of a cervical and/or vaginal septum. If a septate uterus was identified, the kidneys were examined for the presence or absence of renal anomalies. Dec 66 patients met the inclusion criteria. Of those, 98 (77%) had an MRI available for review, but CT scans, hysterosalpingograms and ultrasounds were also reviewed. In this cohort of patients with a uterine septum, 35 (28%) had a duplicated cervix and 21 (17%) had a vaginal septum. All patients with a vaginal septum also had cervical duplication. Renal anomalies were identified in 11 patients (8.7%), and these included: renal agenesis (N=6), horseshoe kidney (N=2), pelvic kidney (N=1), a duplicated collecting system (N=1) and unilateral kidney malrotation (N=1). Of patients with renal anomalies, 4 (36.3%) had a duplicated cervix and vaginal septum.

CONCLUSIONS: Historically, renal anomalies have been associated with defects in fusion of the Mullerian ducts, leading to anomalies such as unicorannate uterus or uterine didelphys. Fusion of the ducts is thought to occur prior to midline resorption in the caudal-cranial direction. However, many mixed anomalies are identified in the clinical context. For example, a septate uterus is considered a resorption defect, but may be seen with a defect in fusion such as a double cervix. This prompted us to investigate the relationship between renal anomalies and uterine septums, previously considered to be rarely associated. Our study found a substantial prevalence of renal anomalies in patients with a uterine septum. We also found a high percentage of duplicated cervices and vaginal septums in our cohort, indicating that resorption may occur bidirectionally. These findings challenge the traditional step-wise theory of Mullerian embryologic development and highlight the clinical significance of mixed anomalies.

The diagnosis of a uterine septum should warrant a consideration of renal imaging.

O-37 Monday, October 17, 2016 11:15 AM

EXPERIENCE IN TRANSABDOMINAL OOCYTE RETRIEVALS: A CASE SERIES. C. C. Shenoy, C. Coddington, Z. Khan, T. L. Jones, J. Jensen. Reproductive Endocrinology & Infertility, Mayo Clinic, Rochester, MN.

OBJECTIVE: While the transvaginal route is currently the standard approach to oocyte retrieval during in vitro fertilization (IVF) procedures, the transabdominal approach may be an alternative for situations with difficult ovarian access. Case reports and one case control study showed that transabdominal oocyte retrieval can be safe and efficacious (1-5). However, among the reports that specified technique, the majority utilized a transabdominal ultrasound probe during the oocyte retrieval. We report six cases of successful transabdominal oocyte retrieval using the transvaginal ultrasound probe.

DESIGN: This study reports six IVF cases with difficult ovarian access that required transabdominal retrieval and discusses optimal retrieval technique.

MATERIALS AND METHODS: We identified all cases of abdominal oocyte retrieval at Mayo Clinic from 2012-2015. Operative reports were reviewed. Indications, outcomes and complications were recorded. All patients underwent standard ovarian stimulation protocols with individualized gonadotropin dosing based on ovarian reserve parameters and were triggered when 2 or more follicles reached 18mm or greater. Serial monitoring by abdominal and vaginal ultrasonography was performed to confirm follicle development and ovarian location prior to retrieval. Two patients had retrieval under monitored anesthesia care. The other four underwent general anesthesia. Chlorhexidine was utilized for abdominal prep. A sterile saline wash was subsequently applied. For all procedures a standard transabdominal ultrasound probe (3.5MHz curvilinear probe) was used initially to visualize the ovaries and a transvaginal ultrasound probe (3-10MHz ultrasound wand) with needle guide was placed on the abdominal wall to perform the retrieval. For the aspiration, a 16-gauge 35cm single lumen aspiration needle (Ova-Stiff™ EchoTip®; Cook Medical) and a suction pressure of 130mmHg were utilized.

RESULTS: Indications for abdominal retrieval included: oophoropexy, positive vaginal margins for cervical carcinoma, müllerian agenesis, and central obesity. The most common indication for abdominal retrieval was oophoropexy (66%). An average 11.5 oocytes were retrieved and 6.8 embryos created. One patient had a complication of ovarian hyperstimulation syndrome which required hospitalization and paracentesis. Three patients have kept their embryos in cryopreservation to date. One patient underwent her first transfer utilizing a gestational carrier which resulted in a live birth; a subsequent transfer was unsuccessful. Her third transfer resulted in another live birth. One patient had an autologous transfer which resulted in a live birth. The patient had a transfer to a gestational carrier which resulted in an ongoing pregnancy.

CONCLUSIONS: Transabdominal oocyte retrieval utilizing a transvaginal ultrasound probe is an alternative for patients with difficult ovarian access.

References:
HOME-BASED ULTRASOUND MONITORING FOR IN VITRO FERTILIZATION IS A FEASIBLE METHOD OF IN CYCLE MONITORING. N. Resetkova, D. Sakkas, S. Bayer, A. Penzias, M. M. Alper, Obstetrics and Gynecology, Beth Israel Deaconess Medical Center, Boston, MA; Boston IVF / Harvard Medical School, Waltham, MA; Boston IVF, Waltham, MA.

OBJECTIVE: This study evaluates the feasibility of home-based Self Operated Endovaginal Telemonitoring (SOET) of women undergoing controlled ovarian stimulation with gonadotropins for In Vitro Fertilization by comparing it to facility-based testing.

DESIGN: Prospective feasibility study.

MATERIALS AND METHODS: Study subjects (n=6) performed home-based SOET in parallel with standard of care clinic based ultrasound monitoring of follicle maturation. Subjects underwent a one hour instructional session involving use and functionality of the home ultrasound monitoring kit and image acquisition. All subjects demonstrated competence on use of the system prior to departing the clinic with the kit. Subjects performed home based ultrasounds daily from stimulation day 4 through to the day prior to oocyte retrieval. Home acquired images were securely transmitted electronically to study personnel. Comparative analysis was made at the conclusion of cycle monitoring. Subjects evaluated their experience after cycle completion using a survey instrument.

RESULTS: Subject and cycle characteristics are outlined in Table 1. Follicle size comparison was made between home and clinic monitoring for each day the subject underwent clinic based monitoring. The correlation coefficient between the 68 direct pair follicle size comparisons was 0.92. The average number of patient communications with the study personnel was 8 emails during the course of the cycle. Using two or more 18 mm lead follicles as the minimum trigger criterion, the decision to trigger would have occurred on the same cycle day in all subjects, with home based monitoring leading to a preferred day of trigger in one subject. If home based monitoring were used exclusively, the estimated time saved per subject would have been 5.5 hours, inclusive of about 60-70 minutes of total driving time.

CONCLUSIONS: This study shows that images acquired by home-based SOET correlate well with clinic based monitoring. The critical decision to administer a trigger injection compared favorably to clinic based ultrasound. Objective and subjective measures suggest a high degree of user satisfaction. The second phase of this study involves substituting routine clinic based monitoring with SOET imaging throughout a cycle in order to help minimize the time burden and inconvenience of conventional in cycle monitoring.

**TABLE 1. Subject and Cycle Characteristics**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Average Value</th>
<th>S.D.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>34</td>
<td>3.5</td>
</tr>
<tr>
<td>BMI</td>
<td>24.8</td>
<td>4.1</td>
</tr>
<tr>
<td>Infertility Duration (months)</td>
<td>22.5</td>
<td>12.4</td>
</tr>
<tr>
<td>IVF Cycle Number</td>
<td>1.7</td>
<td>0.8</td>
</tr>
<tr>
<td>Parity</td>
<td>0.2</td>
<td>0.4</td>
</tr>
<tr>
<td>AMH</td>
<td>2.4</td>
<td>1.5</td>
</tr>
<tr>
<td>Days of Stimulation</td>
<td>8.7</td>
<td>1.2</td>
</tr>
<tr>
<td>SOET Ultrasounds per cycle</td>
<td>6.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Facility Based Ultrasounds per cycle</td>
<td>3.0</td>
<td>1.0</td>
</tr>
</tbody>
</table>

Supported by: Three SonAur SOET kits were lent to our institution for the purpose of monitoring patients through this study.

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DESIGN: Pilot study in 44 healthy female volunteers around basal, periovulatory and midluteal menstrual cycle phases. Transvaginal scans were performed in 2D, 3D and power-Doppler, with and without intravenous ultrasound contrast (Sonovue®).

MATERIALS AND METHODS: 41 healthy 18-30 years old nulliparous volunteers were finally recruited, after comprehensive inclusion criteria were applied. On 4th day of cycle (E1), periovulatory (E2: periovulatory follicle and proliferative endometrium) and midluteal phase (E3: luteal follicle and secretory follicle), the following ultrasound tests were performed. Voluson®E80 Expert (GE Healthcare®) was used: -2D/3D/PowDoppler-2D-CE-US. 2.4 mL intravenous bolus of Sonovue® was inoculated according to data sheet. Two independent explorers delineated clips, defining endometrium and whole uterus; one of the delineators was asked to include the cervix, the other was not. Delineated clips were analyzed by Ymaging (Barcelona, Spain), calculating: a) Perfusion Index [Plarbrituris.(AU)]; b) FMBV (%), considering cardiae-cycle (systole and diastole), Time-Intensity Curves (TIC) and color-graphs were developed. Statistically processed using SPSS® v.20.0.

RESULTS: Basal characteristic were homogeneous. 95 CE-US clips were analyzed (34 in E1, 28 in E2 and 33 in E3): - CE-US Pglobal: E1 vs E2 [CI: (-1.91)—(-0.66); p<0.05]; E2 vs E3 [CI:0.28—1.62; p>0.05]. - CE-US Pendometrium: E1 vs E2 [CI: (-2.75)—(-4.45); p=0.004] and E2 vs E3 [CI: (0.06—1.91); p=0.034]. - CE-US Pmyometrium: E1 vs E2 [CI: (-2.82)—(-5.36); p=0.007]. Delineating correlation index was higher in globular analysis than in endometrium (k = 0.817, k = 0.640). 92 FMBV clips were suitable to be analyzed (32 in E1, 30 in E2 and 30 in E3): - FMBVglobal: E1 vs E2 [CI: 1.75—12.62; p<0.05] and E1 vs E3 [CI: 2.21—12.64; p<0.05]; E2 vs E3, pNS; - FMBVmyometrium: E1 vs E2 [CI: 1.37—7.33; p=0.02] and E1 vs E3 [CI: 1.89—7.86; p=0.01] and E2 vs E3 [pNS].

Similar data obtained when global cardiac cycle was evaluated. Interobserver correlation for FMBV was 0.171.

CONCLUSIONS: CE-US is a new, valid and good inter-observer correlation technique to evaluate uterus perfusion depending on anatomic area and menstrual cycle phases. Periovulatory PI is higher than in menstrual and luteal phases. Endometrium PI is higher than myometrium PI along the menstrual cycle. CE-US is more powerful than FMBV.

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OBJECTIVE: To define a new contrast-enhanced ultrasound method (CE-US) to describe uterine and endometrial functionality and to compare it with Fractional Movement Blood Volume technique (FMVB).

DESIGN: IRB approved retrospective study at an academic fertility center.

MATERIALS AND METHODS: Medical records of 194 women undergoing SIS in preparation for ET on two or more occasions from 2008-2013 were reviewed. During that time, according to the policy at our center, SIS was performed within 6 months before every embryo transfer, even if a prior SIS was normal. The incidence of an abnormal SIS during the first study was the primary outcome studied. Secondary outcomes included the incidence of an abnormal SIS in a subsequent study if initial SIS is normal, and incidence of an abnormal SIS in a subsequent study if the initial SIS is abnormal. Descriptive statistics were used to evaluate the data.

RESULTS: The initial SIS was abnormal in 35 of 194 women (18%), and 33/35 underwent a corrective hysteroscopy. Endometrial polyps were the most common uterine abnormality, and polyps were confirmed by pathology in 60.6% of all hysteroscopies. A second SIS was performed in 82 women. Of 64 with a normal initial SIS, 57 (89%) remained normal and 7 (11%) became abnormal. Of 18 who had an abnormal initial SIS, 15 (83%) were normal and 3 (17%) were again abnormal during the second SIS. Approximately 20% of women were abnormal at both 6 and 12 months. As expected, women with an abnormal SIS result had significantly more days of menstrual bleeding than those with a normal SIS (mean 5.2 vs. 4.7, p=0.02). Peak endometrial thickness was significantly greater in women with an abnormal SIS than in those with a normal SIS (p=0.02). The live birth rate were significantly higher in...
patients with a normal SIS compared to those with an abnormal SIS, even af-
ter correction (p=0.04). None of the other variables examined were signifi-
cantly different between the two groups.

CONCLUSIONS: The optimal time to repeat endometrial assessment in wom-
ens preparing for assisted reproduction procedures has not been estab-
lished, and there is very little evidence in the literature to provide guid-
ance. The incidence of uterine abnormalities is high in infertile women un-
dergoing assisted reproduction procedures. Endometrial polyps may re-
duce endometrial receptivity (1), and hysteroscopic removal is recom-

References:
1. Rackow BW, Jorgensen E, Taylor HS. Endometrial polyps affect uter-
2. Kodaman PH. Hysteroscopic polypectomy for women undergoing IVF treat-

Supported by: Carolinas HealthCare System Cannon Summer Scholars Program.

O-41 Monday, October 17, 2016 12:15 PM

OPTIMAL FOLLICULAR SIZE FOR OVULATORY TRIGGER IN NATURAL AND CLOMIPHENE CITRATE INTRAUTERINE INSEMINATION CYCLES. K. Hancock, N. Pereira, J. P. Lekovich, P. H. Chung, Z. Rosenwaks. The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: Intrauterine insemination (IUI) during a natural cycle (NC) or following ovulation induction with clomiphene citrate (CC) forms the mainstay of fertility treatment in many young patients. IUIs in such patients are frequently performed after administration of a human chorionic gonadotropin (hCG) ovulatory trigger. The primary objective of this study is to iden-
tify the optimal lead follicular size for an ovulatory trigger in either NC or CC
IUI cycles.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Patients <40 years of age, with patent fallopian tubes, a normal uterine cavity, and a male partner with >15 million sperm/mL undergoing an IUI in either a NC or CC ovulation in-
duction cycle between 2004 and 2013 were analyzed for inclusion. All pa-
tients with a spontaneous LH surge or undergoing successive IUIs in the same treatment cycle were excluded. The hCG ovulatory trigger was adminis-
tered either subcutaneously or intramuscularly, after visualization of a >17 mm follicle in the NC group or >19 mm follicle in the CC group, and an endometrial thickness of >7 mm in both groups. IUIs were performed 24-30 hours following the ovulatory trigger. Clinical pregnancy rates were plotted for the NC and CC groups against lead follicular size, in increments of 1 mm beginning at 17 mm. Odds ratios (OR) for clinical pregnancy at different lead follicular sizes were calcu-
lated by using 17 mm and 19 mm as reference values for the NC and CC
groups, respectively.

RESULTS: 3272 IUI cycles met inclusion criteria: 1201 NC and 2071 CC. The median age in the NC and CC groups was 35.4 (31.4-41.4) years and
34.3 (29.8-38.8) years, respectively. In the NC group, the clinical pregnancy rate (14%) was highest when the ovulatory trigger was adminis-
tered at a lead follicular size of 19 mm compared to the reference group of 17 mm (8%). However, these odds were not statistically significant (OR 1.80, 95% CI 0.73-4.41). The aforementioned odds remained unchanged even after adjusting for age. In contrast, the clinical pregnancy rate in the CC group was highest when the lead follicular size was 22 mm at the time of the ovulatory trigger (16%). Compared to the reference group of 19 mm, the odds for clinical pregnancy with a lead follicle of 22 mm was 2.14 times higher (OR 2.14, 95% CI 1.20-3.83; P=0.01). The higher odds for clinical pregnancy persisted even after stratifying for age: 25-35 years (OR 2.55, 95% CI 1.25-5.20) and 35-40 years (OR 1.90, 95% CI 1.01-3.58).

CONCLUSIONS: Our results suggest that administration of a hCG ovulatory trigger at a lead follicular size of 22 mm is associated with higher odds of clinical pregnancy in patients undergoing IUI following ovulation induction with CC. Although triggering at a lead follicular size of 19 mm in the NC group is also associated with an increased odds of clinical preg-
nancy, these odds remain non-significant when compared to the reference group of 17 mm.

PREIMPLANTATION GENETIC TESTING 1

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THE DIFFERENCE IN SIZE BETWEEN SINGLE PRONUCLEI AF-

OBJECTIVE: Some embryos derived from 1PN zygotes after conven-
tional IVF procedures (cIVF-1PN) have been known to be diplod and have the potential to develop into healthy babies. In contrast, most embryos derived from 1PN zygotes after ICSI procedures (ICSI-1PN) have been re-
ported to contain abnormal chromosome configurations. In this study, we
analyze the clinical outcomes of cIVF-1PN and ICSI-1PN and investigate
why ICSI-1PN zygotes failed to produce pregnancy.

DESIGN: A retrospective study involving 7497 frozen-thawed single blas-
tocyst transfers. All patients received HRT and the study spanned from
January 2011 to December 2014. Time-lapse observations were made on
79 1PN zygotes from January 2013 to February 2015.

MATERIALS AND METHODS: Clinical pregnancy rates, miscarriage rates, live birth rates and malformation rates resulting from blastocysts
derived from cIVF-1PN and ICSI-1PN were compared with blastocysts
derived from cIVF-2PN and ICSI-2PN. Blastocysts derived from ICSI-1PN
zygotes were transferred when there were no embryos derived from 2PN
zygotes. Among 79 1PN zygotes, which were observed by a time-lapse
system, the size of the single pronucleus from 40 ICSI-1PN zygotes were
compared with those from 39 cIVF-1PN zygotes immediately before the
breakdown of their pronuclear membranes.

RESULTS: A total of 7497 frozen-thawed single blastocyst transfers re-
sulted in 3088 (40.8%) clinical pregnancies. Clinical pregnancy rates in
cIVF-1PN, cIVF-2PN, ICSI-1PN, ICSI-2PN were 36.1% (26/72), 42.1% (2244/5352), 0% (0/20), 37.6% (814/2165) respectively. Among the 26 preg-
nancies derived from cIVF-1PN, 21 babies were born, 4 women miscarried
and 1 case lost contact. A minor malformation (pneumothorax) was reported
in 1 baby among the 21 postpartum babies. Among the 2244 pregnancies
derived from cIVF-2PN, 1681 babies were born, 528 women miscarried
and 35 cases lost contact. Malformations were reported in 30 babies among
the 1681 postpartum babies. There were no statistical differences in clinical pregnancy rates, miscarriage rates, live birth rates and malformation rates be-
 tween cIVF-1PN and cIVF-2PN. In contrast, the pregnancy rate from ICSI-
1PN zygotes was zero, which was significantly lower than that in ICSI-2PN.
The average size of cIVF-1PN was 66.4μm² (±105.2) and was significantly
less than that of cIVF-1PN 72.8μm² (±114.4) (p=0.028). Student’s t-test or
the chi-square test was used for statistical analyses where appropriate.

CONCLUSIONS: Zygotes derived from ICSI-1PN produced blastocysts
but no pregnancies, while healthy babies were born from cIVF-1PN zygotes.
There was no statistical difference in pregnancy rates between blastocysts
derived from cIVF-1PN and cIVF-2PN. In contrast, the pregnancy rate from ICSI-
1PN zygotes was zero, which was significantly lower than that in ICSI-2PN.

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the embryo was based solely upon the TE result. Results from the EC were retrospectively compared to TE from the corresponding blastocysts. The incidence of cell exclusion and the correlation in ploidy between EC and corresponding TE cells were evaluated retrospectively. Chi square analysis was used for statistical analysis.

RESULTS: A total of 103 embryos from 18 patients were analyzed by aCGH or NGS for aneuploidy screening and 24 blastocysts contained EC. Overall, 52% (54/103) of blastocysts were euploid. The euploidy rate in blastocysts with no EC as compared to those with EC was similar (51% (41/80) vs 54% (13/24)); p = 0.8. Chromosome analysis revealed that all EC contained DNA, however 33% (8/24) exhibited chaotic profiles. Full results were obtained for 67% (18/24). All EC were aneuploid. Results of EC relative to corresponding blastocysts revealed two patterns: euploid TE and aneuploid/chaotic EC or aneuploid TE cells and aneuploid/chaotic EC. The frequency of the two patterns was 54% (13/24) vs 46% (11/24) respectively. Aneuploid TE results were not associated with euploid excluded cells and euploid TE results were not associated with euploid EC.

CONCLUSIONS: Although preliminary, the incidence of euploidy appears similar between blastocysts that do not contain excluded cells and those that do. Therefore, cell exclusion is likely not indicative of aneuploidy in the blastocyst. In this series, excluded cells were always aneuploid and were not representative of the embryo. We believe that abnormal cells excluded during blastulation may reflect a mechanism of self-correction in low-mosaic embryos.

O-44 Monday, October 17, 2016 11:30 AM

DOES EUPLOID EMBRYO RANKING BY TROPHECTODERM CELL MITOCHONDRIAL DNA CONTENT CORRESPOND WITH RANKING BY BLASTOCYST MORPHOLOGY WITHIN AN INDIVIDUAL PATIENT’S COHORT OF BLASTOCYSTS? J. Kort, R. Lathi, B. Behr. Stanford Fertility and Reproductive Medicine Center, Palo Alto, CA.

OBJECTIVE: This study aimed to determine whether ranking of euploid embryos by trophectoderm mitochondrial DNA content is consistent with or discordant to ranking by traditional morphology within an individual patient’s embryo cohort.

MATERIALS AND METHODS: This was a retrospective chart review of all pre-implantation genetic screening cases utilizing next generation sequencing with the availability of normalized mitochondrial DNA counts at a single academic infertility clinic between November 2015 and April 2016. The PGS and mitochondrial DNA quantification was obtained from a single reference lab, using the ReproSeq low pass whole-genome sequencing with the availability of normalized mitochondrial DNA counts. The highest ranked embryo available for transfer although five of these cases were due to the two best embryos by morphology having the same Gardner blastocyst grading system. Each patient’s cohort rank order of euploid embryos by morphology was determined by the laboratory who performed the preimplantation genetic screening. The highest ranked embryo available for transfer was selected. All transferred embryos were transferred in a subsequent frozen embryo transfer (FET) cycle, as part of a hormone replacement, or supplemented natural FET cycle.

RESULTS: The study population included 50 IVF-PGS cycles from 46 patients. Twenty-one (42%) patients (median age 38.5) only had one euploid embryo, and embryo ranking was not possible. Of the 29/50 (58%) patients who had two or more euploid embryos, the highest ranked embryo from, 9/29 (31%) patients had embryo hierarchies entirely concordant between morphology and mtDNA ranking, while 20/29 (69%) had discrepant rankings between a morphology based hierarchy and a mtDNA content based ranking. In 18/29 (62%) cycles, there were discrepancies involving the highest ranked embryo available for transfer although five of these cases were due to the two best embryos by morphology having the same Gardner grade. Ignoring the day of blastocyst expansion and biopsy with regards to the morphology ranking, 14/29 (48.3%) cases had discrepancies regarding the best euploid blastocyst available. There have been thirteen frozen embryo transfers from blastocyst cohorts with >1 euploid embryo of which eleven have resulted in early ongoing pregnancies. The blastocysts resulting in ongoing pregnancies are heterogeneous regarding their mtDNA content and morphology rankings, and include those with the best and worst cohort rankings by mtDNA content and morphology. Somatic and mosaic embryos resulted in ongoing pregnancies.

CONCLUSIONS: In over half the IVF-PGS cycles with >1 euploid blastocyst available for transfer, there are discrepancies in choosing the best euploid embryo to transfer when comparing ranking by morphology with ranking by trophectoderm mitochondrial content. Given the high discordance in embryo ranking methods, additional studies are needed to identify the best method to select the euploid embryo most likely to lead to a successful pregnancy.

O-45 Monday, October 17, 2016 11:45 AM

PREVALENCE AND CLINICAL SIGNIFICANCE OF SEGMENTAL ANEUPLOIDY IN HUMAN OOCYTES AND PREIMPLANTATION EMBRYOS. D. Babarinya, a E. Fragouli, a S. Alfarawati, b K. Spath, a A. Raberi, a S. Taylor, a N. Kubikova, a D. Wells, b "Nutfield Department of Obstetrics and Gynaecology, University of Oxford and Reprogenetics UK, Oxford, United Kingdom; b Reprogenetics UK, Oxford, United Kingdom.

OBJECTIVE: To investigate the incidence, origin and clinical significance of segmental aneuploidy in human oocytes and preimplantation embryos.

MATERIALS AND METHODS: 452 human oocytes, 1,762 cleavage stage and 1,890 blastocyst stage embryos were investigated. Comprehensive cytogenetic analysis, involving microarray comparative genomic hybridisation (aCGH) or next generation sequencing (NGS), was applied to polar bodies or cells biopsied from embryos.

RESULTS: The incidence of segmental aneuploidy differed according to the stage at which the analysis was performed, affecting 10.39% (47/452) of embryos vs 46% (11/24) of embryos vs 46% (11/24) vs 46% (207/1327) of blastocysts. Hence, the frequency increased significantly after fertilisation (p<0.0001) but declined between the cleavage and blastocyst stages (p<0.0001). This suggests that most segmental aneuploidies spontaneously arise during the first few mitotic divisions. Patient age had no correlation with segmental aneuploidy. Analysis of the sites of chromosome breakage revealed hotspots occurring in specific regions, some corresponding to known fragile sites. The use of NGS for the analysis of 563 trophectoderm biopsies provided an insight into mosaicism. Mosaic segmental abnormality was detected in 122/563 biopsy specimens, higher than the incidence of such abnormalities affecting all of the biopsied cells (43/563) (p<0.0001). Transfer of embryos with mosaic segmental aneuploidy (8/13) was associated with a greater chance of ongoing pregnancy compared with embryos mosaic for whole chromosomal aneuploidy (4/31) (p=0.002).

CONCLUSIONS: Segmental aneuploidies are common in human embryos, yet the understanding of their genesis and clinical relevance is poor and appropriate clinical management is unclear. Should embryos with segmental aneuploidy be discarded or transferred? Our results show that the site of chromosomal breakage is predictive of the stage at which the abnormality arose and that this in tum influences the likelihood that the abnormality is mosaic. Importantly, this is of relevance to embryo viability and the potential to produce a healthy child.

O-46 Monday, October 17, 2016 12:00 PM

PGS ANALYSIS OF OVER 33,000 BLASTOCYSTS USING HIGH RESOLUTION NEXT GENERATION SEQUENCING (HRNGS) OF OVER 33,000 BLASTOCYSTS USING HIGH RESOLUTION NEXT GENERATION SEQUENCING (HRNGS). S. Munne, a L. Babarinya, b L. Ribustello, a J. Blazek, c F. Gouw, a J. Grifo, a G. Haddad, a W. Chang, a G. M. Grunert, a A. Huang, b F. Yelian, j M. Hughes, k aReprogenetics, Living- ston, NJ; aGenetics, Houston, TX; aResearch and Development, Genesis Genetics, Houston, TX; bReprogenetics, Los Angeles, CA; cNYU Langone Medical Center, New York, NY; dHouston Fertility Institute, Tomball, TX; eART Reproductive Center, Southern California Reproductive Center, Beverly Hills, CA; fHouston Fertility Specialists, Houston, TX; gReproductive Partners Medical Group, Redondo Beach, CA; hReproduction Endocrinology, Life IVF Center, Irvine, CA; iMolecular Genetics, Genesis Genetics, Plymouth, MI.

OBJECTIVE: hr-NGS detects mosaicism in trophectoderm (TE) biopsies when 10%-90% of cells are abnormal. Mosaic TE biopsies may come from embryos that result from euploid, aneuploid or mosaic pregnancies. Mosaic biopsies have higher risk of miscarrying, lower implantation potential but some may go to term. Mosaic embryos should be classified in between euploid and euploid in their priority for transfer. This study aims to
determine the rate of euploidy, mosaicism and other abnormalities according to maternal age in a large cohort of embryos for purpose of patient counseling.

DESIGN: Analysis of PGS procedures involving TE biopsy and hr-NGS performed by two large genetic reference laboratories serving over 250 fertility clinics.

MATERIALS AND METHODS: Two laboratories analyzed 4277 and 2303 PGS procedures using TE biopsy by whole genome amplification method (SurePlex), assay for hr-NGS (VeriSeq PGS assay, Illumina), sequencer (MiSeq, Illumina) and software (BlueFuse Multi analysis, Illumina). EMRs (dIVF, practiceHwy and lab’s own) used to query the data. Embryos with 1 or 2 aneuploid chromosomes or 1 aneuploid chromosome and 1 mosaic chromosome were called aneuploid. Embryos with 3 aneuploid chromosomes or two aneuploid and 1 or more mosaic chromosomes were complex abnormal. Embryos with a mixture of normal cells and abnormal were called mosaic.

RESULTS: Rate of euploidy, mosaicism and complete abnormalities (aneuploidy, complex or polyploidy) was 41% and 47%, 20% and 14%, and 39% and 39%, respectively. The combined results for both datasets shown (Table1).

CONCLUSIONS: Being a postmeiotic abnormality, mosaicism does not increase with advancing maternal age (the apparent decrease in the table is due to some mosaics that are also aneuploid being classified as aneuploid). Differences between the two labs were attributed to difference in scoring criteria where the threshold to call an embryo normal or euploid was set due to some mosaics that are also aneuploid being classified as aneuploid). Regardless, the amount of mosaic embryos, which have lower potential than euploid embryos, is considerable, 11-23% depending on maternal age.

O-47 Monday, October 17, 2016 12:15 PM

SINGLE EMBRYO TRANSFER (SET) FOLLOWING COMPREHENSIVE CHROMOSOME SCREENING (CCS) IS MORE COST EFFECTIVE THAN UNSCREENED SEQUENTIAL SET. S. Neal, J. S. Morin,*, J. M. Franasiak,*, C. R. Juneau,*, Y. Zhan,*, R. T. Scott,*, RMANJ, Basking Ridge, NJ; *EFC, NJ, NJ.

OBJECTIVE: Detectors of CCS have argued that it serves only to increase the cost of care given that the cumulative live birth rate per stimulation cycle is equivalent in CCS cycles and sequential unscreened SET cycles until either pregnancy is achieved or their embryo cohort is exhausted. This study models the overall costs of IVF/CCS and euploid SET versus SET of unscreened embryos when considering an embryo cohort obtained from a single oocyte retrieval.

DESIGN: Retrospective cost effectiveness analysis.

MATERIALS AND METHODS: Using the sustained implantation rate of 60% for euploid embryos consistently demonstrated in prior CCS studies, a mathematical model was created to determine the average number of unscreened SET cycles required to produce either of 2 endpoints: live birth or frozen embryo transfer (FET) cycles (§3,812). A baseline fresh embryo transfer rate was set at 30% for unscreened SETs based on actual outcome data. This was assumed that all CCS transfers occurred in a subsequent FET cycle.

RESULTS: A total of 11,848 CCS cases were used to compare both models. No euploid embryos were produced in 2,098 cycles (17.7%). An estimated total of 25,179 embryo transfers were required to achieve either endpoint in the unscreened group (3554 fresh; 21,625 FETs) versus 9750 in the CCS group. The average cost to achieve a delivery of at least one live born out of all available blastocysts was higher in the unscreened sequential SET group than the CCS group ($7972.80 vs. $7137.99, p<0.001).

CONCLUSIONS: When considering only cycle related costs, aneuploidy screening is a more cost effective strategy for achieving live birth than planned sequential unscreened SET. Additionally, these findings represent the bare minimum in cost savings provided by CCS. They do not take into account hidden additional costs of unscreened SETs. These include 1) increased need for surgical procedures and time out of work associated with increased miscarriage risk, 2) increased time out of treatment following futile transfers and associated difficulties in subsequent cycles, and 3) costs associated with a viable aneuploid pregnancy.

O-48 Monday, October 17, 2016 12:30 PM

UNRAVELING THE COMPLEXITIES OF MOSAICISM IN HUMAN BLASTOCYSTS. S. McReynolds, M. Schweitz, S. McCormick, J. C. Parks, W. B. Schoolcraft, M. Katz-Jaffe. Colorado Center for Reproductive Medicine, Lone Tree, CO.

OBJECTIVE: With the implementation of high resolution Next Generation Sequencing (HR-NGS) for comprehensive chromosome screening, the presence of chromosome mosaicism is more frequently identified in trophoderm (TE) biopsies. The aim of this study was to evaluate the clinical significance of mosaicism in human blastocysts using HR-NGS.

DESIGN: Prospective blinded study.

MATERIALS AND METHODS: Forty human blastocysts identified as chromosomally mosaic embryos, mosaic monosomies (n=26) and mosaic trisomies, (n=14), were donated with patient consent (mean maternal age = 36.3 years). Initial diagnosis of chromosome mosaicism was performed using HR-NGS (VeriSeq; Illumina). Mosaic blastocysts were rebiopsied into three separate segments, individually subjected to whole genome amplification, and blindly re-analyzed using the same HR-NGS platform (n=120 samples). After un-blinding chromosome results, all four biopsies were compiled together for a complete picture of each individual blastocyst.

RESULTS: The overall incidence of chromosome mosaicism following biopsy of 3,677 human blastocysts was observed at only 3.8%. Multiple segmental re-analysis of 40 mosaic blastocysts confirmed the original mosaicism diagnosis in 50% of these blastocysts (n=20; ≥1 of the re-analyzed segments). Of these, 7 blastocysts were the result of mitotic cell division errors identified by the reverse aneuploidy in the re-biopsy segments. In the remaining 20 mosaic blastocysts, 6 displayed a different mosaic chromosome in the re-biopsied segments, and 14 showed only the mosaic chromosome in the original biopsy (n=7 monosomies; n=7 trisomies). The chromosomes involved in these 14 mosaic blastocysts are typically not compatible with a viable outcome. Closer examination of the percentage of mosaicism within the original biopsy diagnosis revealed estimates of 30-60% in blastocysts that the original mosaicism diagnosis was confirmed in the re-biopsied segments, and lower percentages of <30% were noted when the mosaic chromosome was only observed in the original biopsy.

CONCLUSIONS: This novel study exposes the complexity surrounding chromosomal mosaicism in human blastocysts and reveals that the origin of mosaicism is not a single mechanism. The question regarding the future developmental competence of each type of mosaicism remains unpredictable. Certainly it would be presumed that the mosaic blastocysts generated from a mitotic cell division error that contain three cell lines: monosomy, trisomy and disomy, should have compromised implantation potential. However, the clinical fate of mosaic blastocysts with smaller proportions of either trisomy or monosomy cells remain to be determined.
ART: CLINICAL 1

O-49 Monday, October 17, 2016 11:15 AM


OBJECTIVE: First-trimester noninvasive prenatal screening (NIPS) for aneuploidy using cell-free DNA (cfDNA) in maternal blood, a relatively new screening approach, has improved validity over conventional methods. While general OB-GYNs have been slow to adopt cfDNA, fertility practices may easily incorporate this screening. We describe the first report of acceptability and outcomes of cfDNA NIPS among patients in a single fertility practice.

DESIGN: Retrospective chart review.

MATERIALS AND METHODS: Beginning 1 June 2014, all non-oocyte-recipient women presenting with first-trimester singleton pregnancies in our practice were offered NIPS using cfDNA. Charts were extracted for demographics, genetic and pregnancy histories, diagnosis, treatment, and index pregnancy details. Descriptive and comparative statistics were used to analyze NIPS acceptance and outcomes.

RESULTS: NIPS using cfDNA was offered to 233 women of whom 81.5% presented for infertility and 18.5% for recurrent spontaneous abortion (RSA). cfDNA screening was accepted by 188 (80.7%). Demographic, historical, and diagnostic parameters were not associated with acceptance; 79% with infertility and 86.0% with RSA accepted cfDNA NIPS. NIPS was done at a mean 74.4±6.4 (SD) days' gestational age (GA); median 73, IQR 70-76, range 64-111), and showed low probability of aneuploidy (LO) in 91.4%, high probability in 1.6% [trisomy 21 (2); trisomy 18 (1)], and no result (NR) in 7.0%. NR trended toward a negative association with GA (OR 0.94/day, 95% CI 0.879-1.008, p=0.058). Six of the 10 women with NR advised to repeat testing did so; 4 were again NR and 2 LO, giving a definitive result in 174/185 (94.1%) overall. cfDNA fetal fraction (FF) was >4%, as needed for validity, in 91.3%, and was negatively correlated with maternal weight (r=-0.53, p<0.0001). A NIPS result was not returned in 2.6% of 152 women weighing <200 lb, but in 27.3% of 33 women >200 lb (p<0.0001). At first, all tests were sent to a single lab (Lab1), which used single nucleotide polymorphism (SNP)-based sequencing. For the heavier women, we switched to a second lab using massively parallel sequencing; it returned a result in 10/10, while Lab1 did so in only 13/22 (p=0.03). Fetal sex information was requested by 94.1% of couples; 47.2% were reported as female, 46.6% as male, and 6.2% gave no result. Of the 188 screened women, all 99 livebirths to date have confirmed the screen findings, including one trisomy.

CONCLUSIONS: First-trimester noninvasive prenatal screening (NIPS) for aneuploidy using cell-free DNA (cfDNA) in maternal blood, a relatively new screening approach, has improved validity over conventional methods. While general OB-GYNs have been slow to adopt cfDNA, fertility practices may easily incorporate this screening. We describe the first report of acceptability and outcomes of cfDNA NIPS among patients in a single fertility practice.

O-50 Monday, October 17, 2016 11:30 AM


OBJECTIVE: It is commonly recognized that the gender ratio at birth is biased towards male infants conceived by in vitro fertilization (IVF). Additionally, blastocyst stage embryo transfer has been associated with a higher proportion of male embryos. This study explored the live born gender ratio following blastocyst biopsy, comprehensive chromosome screening (CCS) and frozen single euploid blastocyst transfer without patient requested sex selection.

DESIGN: Retrospective analysis of a large consecutive cohort of live births (n=535).

MATERIALS AND METHODS: Infertility patients (mean maternal age = 37.1 years) underwent IVF with intracytoplasmic sperm injection using autologous oocytes and ejaculated sperm with no severe male factor infertility. Blastocyst culture, trophoderm biopsy for CCS (day 5 or 6), were followed by embryo vitrification. Only euploid blastocysts were selected for single embryo transfer with morphology as the secondary selection index. There was no patient requested sex selection. Statistical analysis was performed using Student t-test and Chi square test with Yates correction where appropriate, significance at p<0.05.

RESULTS: At the blastocyst stage, the gender ratio of biopsied blastocysts was equivalent (female = 49.8% vs. male = 50.2%) with similar embryo grading. Conversely, live births following a frozen single euploid blastocyst transfer were significantly associated with a gender bias towards male infants (n=239 females, 44.7% vs. n=296 males, 55.3%; p<0.05). Further analysis of these live births relative to the day of blastocyst biopsy showed the same gender bias on both days of biopsy independently. Specifically, there were 188 day 5 biopsied male infants (55.8%) and 149 day 5 biopsied female infants (44.2%), which was comparable to the 108 day 6 biopsied male infants (54.5%) and the 90 day 6 biopsied female infants (45.5%).

CONCLUSIONS: A significant deviation in the live birth gender ratio was observed following a frozen single euploid blastocyst transfer even though a comparable embryo gender ratio was observed at the blastocyst stage following biopsy. Imprinted X chromosome inactivation (iXCI) is one of the major epigenetic barriers for the developmental competence of female embryos. Precocious or impaired iXCI in female blastocysts may account for preferential female mortality at early post-implantation stages and thereby variations in gender ratios at birth. Ongoing research into the causes of live birth IVF gender bias is crucial.

REFERENCES:


O-51 Monday, October 17, 2016 11:45 AM


OBJECTIVE: Infertility patients often expect that young oocyte donors will provide them the most successful outcome. This study sought to compare the two extremes in oocyte donor ages to determine if there are better cycle outcomes for recipients with younger oocyte donors (age 21-23) versus “older” oocyte donors (age 28-31).

DESIGN: Retrospective Cohort Study.

MATERIALS AND METHODS: Analysis was performed on 485 patients’ electronic medical records from January 8, 2011 to February 18, 2016. Only the initial oocyte donor cycle was included in the analysis. Data was divided into two groups: Group A, age 21-23; Group B age 28-31. Subjects with an AMH level < 1.2 ng/ml and an antral follicle counts < 12 were automatically excluded per our program’s protocol. Oocyte donors underwent standard ovarian stimulation using antagonist or lupon down regulation protocol and transvaginal ultrasound guided aspiration. ICSI was performed on M2 oocytes and embryos cultured to the blastocyst stage. Outcome parameters analyzed included total number of oocytes retrieved, total number of blastocysts, aneuploidy rate and recipient ongoing pregnancy rates. Statistical analysis was performed using student’s t-test or

<table>
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<th>Variable</th>
<th>Young Donors (N=261)</th>
<th>Old Donors (N=224)</th>
<th>P Value</th>
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<tbody>
<tr>
<td>Basal Antral Follicle Count</td>
<td>17.1 ± 9.1</td>
<td>16.7 ± 9.0</td>
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<td>AMH Level (ng/ml)</td>
<td>5.0 ± 3.04</td>
<td>4.7 ± 3.67</td>
<td>0.6</td>
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<tr>
<td>Total Number Oocytes Retrieved</td>
<td>21.54 ± 9.85</td>
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<tr>
<td>Total Number of Blastocysts</td>
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</tr>
<tr>
<td>Use of Comprehensive Chromosomal Screening</td>
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<td>16.5%</td>
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<tr>
<td>Aneuploidy Rate</td>
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<td>0.7</td>
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<td>Ongoing Pregnancy</td>
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<td>69.1%</td>
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</tr>
</tbody>
</table>
chi square where applicable. Multivariable logistic regression was performed to account for possible confounding.

RESULTS: There was no significant difference in baseline AMH or antral follicle counts among groups (Table 1). Number of oocytes retrieved and blastocyst development rate were similar between all four groups. There was no significant difference in ongoing pregnancy rates. (72.6% and 69.1%).

CONCLUSIONS: Extremes of oocyte donor age does not predict cycle outcomes. Donors age 21-23 at the time of oocyte donation produced comparable number of oocytes and blastocysts when compared with donors age 28-31. More importantly, the two groups had comparable clinical pregnancy rates and aneuploidy rates. Given the frequent request from donor oocyte recipients to use younger donors, the findings of this study are of practical clinical importance for patient counseling.

**O-52** Monday, October 17, 2016 12:00 PM

**ASSISTED REPRODUCTIVE TECHNOLOGY CYCLE AND OBSTETRIC OUTCOMES AMONG UNDERWEIGHT AND OVERWEIGHT WOMEN.** J. F. Kawass,

1 A. Kulkarni,

2 H. Hipp,

3 S. Crawford,

4 D. M. Kinsin,

5 D. J. Jamieson. 1Reproductive Endocrinology and Infertility, Emory University Reproductive Center (& CDC). Atlanta, GA; 2Division of Reproductive Health, Centers for Disease Control and Prevention, Atlanta, GA; 3Gynecology and Obstetrics, Emory University School of Medicine, Atlanta, GA; 4CDC, Atlanta, GA.

OBJECTIVE: To investigate the association between body mass index (BMI) and in vitro fertilization (IVF) and pregnancy outcomes among women using Assisted Reproductive Technology (ART).

DESIGN: Retrospective cohort study using the National ART Surveillance System (NASS).

MATERIALS AND METHODS: We assessed BMI trends among women undergoing fresh autologous IVF in the US from 2008-2013 (n=494,077 cycles) using the NASS. We calculated pregnancy outcomes (intratruine pregnancy, live birth rates) among non-canceled transfers (n=402,742) in underweight (BMI <18.5 kg/m2), normal weight (BMI 18.5-24.9 kg/m2), and obese women (BMI >30kg/m2). Among cycles resulting in pregnancy (n=180,855), we calculated miscarriage rate. We calculated low birth weight (<2500g) and preterm (<37 weeks) delivery rates among singleton and twin pregnancies separately. We used log-binomial regression to investigate the relationship between BMI and pregnancy outcomes.

RESULTS: Among women undergoing IVF, pre-pregnancy BMI affects pregnancy outcomes. Although underweight status may have limited impact on pregnancy and live birth rates, it is associated with increased preterm and low birth weight delivery risk. Obesity negatively affects all pregnancy outcomes investigated.


OBJECTIVE: Recent studies have suggested a detrimental effect of the hyperestrogenic milieu during ovarian stimulation on perinatal outcomes. To this effect, we investigate the existence of a supraphysiological estradiol (E2) threshold for the pathogenesis of adverse perinatal outcomes.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: All patients <40 years undergoing fresh IVF and embryo transfer (ET) at our center between 2004 and 2013 resulting in live singleton births were included. Patients with vanishing twins or multiple gestations were excluded. Demographics and ovarian stimulation parameters of the study cohort were recorded. Perinatal outcomes analyzed included LBW (<2500 grams), very LBW (<1500 grams), early PTB (<34 weeks), and late PTB (≥34 to <37 weeks). LBW was further classified as term LBW or term very LBW. Rates of the aforementioned perinatal outcomes were plotted against peak E2 levels, in increments of 500 pg/mL (<500 to ≥4000 pg/mL). Odds ratios (OR) for perinatal outcomes at various peak E2 levels were calculated by using the median E2 level of study cohort as the referent group. A receiving-operator-characteristic (ROC) curve was constructed to identify a E2 threshold, with a corresponding area-under-the-curve (AUC) calculation.

RESULTS: A total of 4071 patients with live singleton births were included. The median age, peak E2 level and birth weight for the study cohort...
was 36 (33-39) years, 1554 (1112.7-2179) pg/mL, and 3289 (2920-3628) grams, respectively. The overall rate of LBW was 209/4071 (5.14%) and PTB was 378/4071 (9.29%). Although there was no difference in the odds of PTB across all E2 quartiles, the odds of LBW were higher in the top E2 quartile compared to the median E2, suggesting an E2-dependent effect. Upon analyzing the LBW group as term LBW or term very LBW, the odds of term LBW with E2 levels >2500 pg/mL were 6.11-7.89 times higher compared to the median E2. In contrast, the odds of term very LBW remained unchanged across all E2 quartiles. The ROC curve indicated an E2 level of 2900 pg/mL as the threshold beyond which statistically significant odds of term LBW was observed (AUC=0.83).

CONCLUSIONS: Using term LBW as a surrogate, our results suggest that an E2 level >2900 pg/mL may serve as a supraphysiologic threshold for adverse perinatal outcomes in fresh IVF-ET cycles. These results emphasize the importance of utilizing conservative step-down stimulation protocols and careful monitoring of serum E2 to minimize the supraphysiologic elevations of E2 levels in fresh IVF-ET cycles, and thereby circumvent adverse perinatal outcomes.

EMBRYO BIOLOGY 1

O-55 Monday, October 17, 2016 11:15 AM

COMPREHENSIVE CHROMOSOME SCREENING AND GENE EXPRESSION ANALYSIS FROM THE SAME TROPHETODERM BIOPSY. N. R. Treff,† Y. Wang,† X. Tao,† R. T. Scott.† †RMANJ, Rutgers-RWJ, Basking Ridge, NJ; ‡The Foundation for Embryonic Competence, Basking Ridge, NJ.

OBJECTIVE: While comprehensive chromosome screening (CCS) has demonstrated improvement in outcomes in 3 published randomized trials, many euploid embryos fail to implant and progress to delivery illustrating the need for additional biomarkers of reproductive potential. The transcriptome represents a provocative target for investigation. However, methods which allow simultaneous assessment have not been established. This study aims to develop and validate a new methodology in which both RNA and DNA can be evaluated from the same trophoderm biopsy.

MATERIALS AND METHODS: Phase 1 - Validation of the Methodology: Optimization of cell lysis methodology was performed using 6-cell samples from 2 cell lines, one euploid and one with trisomy 16 and 21. Gene expression quantitation by qRT-PCR was compared for consistency between a portion of the 6-cell lysate and a large quantity from the same cell cultures. In parallel, qPCR based CCS was performed from the remaining portion of the 6-cell lysate and evaluated against the expected karyotypes. Phase 2: Evaluation of Human Embryos: 18 previously diagnosed aneuploid embryos were rebiopsied and evaluated using the validated method. Expression levels of 48 genes related to stem cell pluripotency were assessed in parallel with CCS from the same biopsy. CCS results were compared to the original diagnosis and expression profiles were evaluated for correlation within the same embryo and among unrelated embryos. Trisomy 21 embryos (known to possess implantation potential) were compared to monosomy 21 embryos (known not to possess reproductive potential) to evaluate whether any significant differences could be identified in association with putative reproductive competence.

RESULTS: In phase 1, cells-to-CT lysis buffer with RNase inhibitor provided the ability to obtain 100% CCS diagnostic consistency and gene expression profiles consistent with large quantities of cells when splitting the lysate among CCS and qRT-PCR. When applied to human embryos the correlation of expression profiles with each embryo (r=0.96) was significantly higher than when unrelated embryos were evaluated (r=0.93) (p=6.3e-10). In addition, monosomy embryos expressed significantly less LAMC1 (p=0.003), a marker of differentiation, and more GABRB3 (p=0.016) and GDF3 (p=0.015), both markers of pluripotency. In addition, 96% (64/67) of the CCS results were consistent with the original diagnosis.

O-56 Monday, October 17, 2016 11:30 AM

MITOCHONDRIAL DNA CONTENT IS INCREASED IN THE ANEUPLOID MOUSE BLASTOCYST. X. Tao,† J. N. Landis,‖ R. T. Scott,‖ II. N. Treff,† A. Lontzek.‖ †Foundation for Embryonic Competence, Basking Ridge, NJ; ‡RMANJ, Rutgers-RWJ, Basking Ridge, NJ.

OBJECTIVE: The age-related increase in aneuploidy has been observed in both humans and mice. Therefore, mice have the potential to be a useful model system to study the origins, etiology, and mechanisms of human aneu- ploidy. Previous research has provided a basis for new therapeutic strategies. To further establish relevance to this model system, this study aims to validate a method capable of mitochondrial (mt)DNA quantitation in the mouse blastocyst and evaluate putative association with aneuploidy.

DESIGN: Prospective, blinded, and observational.

MATERIALS AND METHODS: A tumor-derived mouse cell line (Cor- telli Cell Repository ID GM05384) was treated with ethidium bromide in order to create samples expected to possess less mitochondria. Single cell samples were collected to mimic a polar body or oocyte, and 100-cell samples were collected to represent a blastocyst. Samples were subject to whole genome amplification (GenomePlex WGA4, Sigma) and next generation sequencing (NGS) using an Ion Proton. The number of reads which aligned to the mitochondrial genome was normalized by dividing it by the total sum of reads aligning to the autosomes from the same sample. The results were compared to data obtained from large quantities of cells from the same cell culture without WGA. 40 pairs of matched first polar bodies and oocytes were analyzed for mtDNA content. The percent of mtDNA in the polar body relative to the matched oocyte samples was evaluated. Blastocysts produced from young and reproductively aged female mice were obtained and the chromosomal copy number was assayed based on a previously validated method for mouse NGS based CCS. Mitochondrial content was calculated and compared between euploid and aneuploid blastocysts.

RESULTS: Single and 100-cell samples provided results equivalent to large quantities of cells. The first polar body contained between 0.1- 8.8% of the total mtDNA content of the oocyte from which it was removed. Aneu- plloid blastocysts (n=19) possessed a significantly higher (1.8-fold) quantity of mtDNA compared to euploid blastocyst (n=90) (P<0.001).

CONCLUSIONS: This study has established validity of a new method for simultaneous CCS and RNA analysis, providing a foundation for the development of transcriptional biomarkers of reproductive potential.

O-57 Monday, October 17, 2016 11:45 AM

USE OF SINGLE NUCLEOTIDE POLYMORPHISM (SNP) ARRAYS AND NEXT GENERATION SEQUENCING (NGS) TO STUDY THE INCIDENCE, TYPE AND ORIGIN OF ANEUPLOIDY IN THE HUMAN PREIMPLANTATION EMBRYO. M. Konstantinidis,† K. Milligan,‡ A. S. Berkley,† J. Kennedy,‡ W. Maxson,‡ C. Racowsky,‡ D. Wells,† S. Munne,§ Reprogenetics, Livingston, NJ; ‡NYU Fertility Center, NYU School of Medicine, New York, NY; §Seattle Reproductive Medicine, Seattle, WA; ¶IVF Florida Reproductive Associates, Margate, FL; ¶Brigham and Women’s Hospital ART Center, Boston, MA; †Reprogenetics, Oxford, United Kingdom.

OBJECTIVE: To perform a thorough investigation using a combination of the most advanced technologies available in an effort to decipher the aneu- plody ‘code’ in the human preimplantation embryo.

DESIGN: Quantitative assessment and genotyping were undertaken concurrently for human blastocysts using SNP arrays and NGS.

MATERIALS AND METHODS: Single trophoderm biopsies were ob- tained from blastocysts of couples undergoing in vitro fertilization (IVF) with preimplantation genetic diagnosis (PGD) for single gene disorders (SGD) and aneuploidy screening. Karyomapping SNP array (Illumina, USA) was used for PGD of SGD while, NGS via the VeriSeq PGS assay (Illumina) was utilized for comprehensive chromosome screening. Fisher’s exact test (GraphPad Software, USA) was used for statistical analysis.
RESULTS: In total, over 19,000 chromosomes were screened in 417 embryos from 75 couples [maternal age: 34.1±0.5 years (mean ± SE)]. At least one chromosomal abnormality was detected in 49.2% (205/417) of the embryos assessed, with 48.3% of the embryos exhibiting only abnormalities of meiotic origin. 40% of abnormal embryos and the remainder of the embryos presenting both types of abnormalities. Notably, maternal meiosis was associated with an equal number of events leading to gain vs. loss of chromosomal material (74 gains vs. 75 losses) and prevailed over paternal meiosis which consisted of events mainly involving loss of chromosomal material (27 losses vs. 1 gain) with almost half of the losses (40.7%) being partial. Of the overall number of aneuploidies detected, 15.7% were determined to be partial with the size of segments gained or lost ranging from 7.8 to 145.6 megabases. Incidences of maternally-derived meiotic errors and overall mitotic errors detected are presented in the table below in relation to maternal age:

<table>
<thead>
<tr>
<th>Maternal Age Group</th>
<th>Maternal Meiotic Errors</th>
<th>Overall Mitotic Errors</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 34</td>
<td>45/257 (17.5%)&lt;sup&gt;a,b&lt;/sup&gt;</td>
<td>63/257 (24.5%)</td>
</tr>
<tr>
<td>35-39</td>
<td>56/131 (42.7%)&lt;sup&gt;a,c&lt;/sup&gt;</td>
<td>34/131 (26.0%)</td>
</tr>
<tr>
<td>&gt; 40</td>
<td>22/29 (75.9%)&lt;sup&gt;a,b&lt;/sup&gt;</td>
<td>9/29 (31.0%)</td>
</tr>
</tbody>
</table>

Meiotic errors: <sup>a</sup> difference statistically significant at P<0.0001; <sup>b</sup> difference statistically significant at P<0.001; <sup>c</sup> difference statistically significant at P<0.01.

Conclusions: The incidence of maternal meiotic abnormalities was associated with increasing age, consistent with the higher rates of implantation failure and miscarriage experienced by older women. Mitotic errors, potentially producing mosaicism, were also common. Interestingly, aneuploidy of male meiotic origin was characterized by a predominance of monosomies compared with that of female origin, suggesting a sex-specific difference in the mechanism underlying segregation errors. 

Conclusions: This novel study revealed compromised transcriptional states for aneuploid blastocysts and a potential mechanism for differential implantation potential among aneuploid blastocysts.

O-58 Monday, October 17, 2016 12:00 PM
TRANSFER OF BLASTOCYSTS WITH LOWER MITOCHONDRIAL DNA (mtDNA) QUANTITIES IMPROVES IVF OUTCOMES. K. Ravichandran, C. McCaffrey, J. Grifo, M. Perlo, A. M. Rosen, T. Singer, S. Moore, D. Wells, E. Fragouli, Reprogenetics, Livingston, NJ; OB/Gyn, NYU Fertility Center, New York, NY; NYU Langone Medical Center, New York, NY; Georgia Reproductive Specialists, Atlanta, GA; Mercy Hospital and Medical Center, Chicago IL, Manhattan Beach, CA; OB/Gyn, Lenox Hill Hospital, Roslyn, NY; Reprogenetics, Oxford, United Kingdom.

Objective: To evaluate embryo selection based upon mtDNA quantification in a clinical setting and to determine its impact on IVF outcomes.

Design: Retrospective study.

Materials and Methods: A total of 1505 euploid blastocysts were generated from 490 couples (average maternal age 34.7±0.14 years) undergoing preimplantation genetic diagnosis for aneuploidy. Embryo biopsy specimens were subjected to whole genome amplification (WGA) followed by comprehensive chromosome screening using next generation sequencing. At a later date the same WGA products were examined using quantitative PCR to determine relative mtDNA quantities. Results were considered with respect to pregnancy outcomes, where available. Samples were derived from 12 different clinics.

Results: Elevated mtDNA was detected in 9.2% (139/1505) of the euploid blastocysts. To date, 238 have been replaced in single embryo transfer cycles, with a pregnancy rate of 65.4% (185/283). 249 of these contained normal/low levels of mtDNA, including all of the embryos that implanted. Moreover, none of the 33 embryos determined to contain elevated mtDNA implanted, giving a 100% negative predictive value for mtDNA selection. If these embryos had been excluded from transfer, the pregnancy rate would have been significantly higher (~74%) (185/238) (P<0.001).

Conclusions: This study demonstrates the clinical applicability and validity of mtDNA assessment as an independent biomarker for predicting the implantation potential of euploid blastocysts. A clear difference in the frequency of implantation between mtDNA-elevated and mtDNA-normal embryos was observed (P<0.001). Although the study was retrospective, the large data set strongly suggests that mtDNA measurement could lead to significant improvements in embryo selection and hence pregnancy rate per transfer (provided embryos with lower mtDNA quantities are available).

O-59 Monday, October 17, 2016 12:15 PM
RNA SEQUENCING OF ANEUPLOID BLASTOCYSTS REVEALS ENRICHED PATHWAYS ASSOCIATED WITH COMPROMISED IMPLANTATION POTENTIAL. B. R. McCallie, J. C. Parks, M. Demomme Tignanelli, W. B. Schoolcraft, M. Katz-Jaffe.

Objective: The implantation potential of aneuploid blastocysts differs greatly across chromosomes. With the exception of Turner syndrome, implantation of autosomal monosomies is extremely low compared to corresponding trisomies, which can initially develop in utero but contribute to pregnancy loss. The aim of this study was to investigate the mechanistic pathways underlying differential implantation potential among aneuploid blastocysts.

Design: Research study.

Materials and Methods: Surplus cryopreserved human blastocysts were donated with patient consent: monosomy 11 (n=5), monosomy 15 (n=5), trisomy 11 (n=5), trisomy 15 (n=4), and euploid donor oocyte blastocysts (n=5). Individual samples underwent RNA isolation ( Molecular Devices), RNA amplification (ClonTech) and small cell number RNA-seq (Illumina) to determine the global transcriptome. Reads generated were mapped to the human genome (hg19) by gSNAP, expression derived by Cufflinks, and statistical analysis with ANOVA in R. Pathway analysis was completed using Ingenuity Pathway Analysis (Qiagen). Transcription validation (n=20) was performed using qPCR with REST® statistical software. A p-value of <0.05 was considered significant.

Results: RNA sequencing generated between 33-54 million reads per blastocyst sample (mean = 44 million). A total of 775 genes were observed to be differentially expressed between monosomy 11 blastocysts, and 280 genes in monosomy 15 blastocysts compared to euploid controls (p<0.05). For their trisomy counterparts there was a total of 361 differentially altered genes in trisomy 11 blastocysts and 278 genes in trisomy 15 blastocysts (p<0.05). Chromosomal location of these differentially expressed genes did not reveal exclusivity to the chromosome involved in the error. Pathway analysis identified significant enrichment for necrosis, cell death, apoptosis, and decreased cell proliferation in both groups of monosomy blastocysts compared to controls (p<0.0001). A higher association to cell death was observed for monosomy 11 compared to monosomy 15 blastocysts. Conversely, both groups of trisomy blastocysts were primarily enriched for negative regulators of transcription, predicting a decrease in RNA expression and promoter activation (P<0.0001). Indicators of cell death were also significantly increased in trisomy blastocysts but to a lesser degree than in monosomy blastocysts (P<0.0001). qPCR validation confirmed an increase of BAX, a pro-apoptotic gene, and a decrease of BCL2L1, an anti-apoptotic gene, in aneuploid blastocysts compared to euploid controls (p<0.05).

Conclusions: This study demonstrated compromised transcriptional states for aneuploid blastocysts and a potential mechanism for differential implantation potential among autosomal monosomies and trisomies. Specifically, the enrichment of apoptotic genes observed for autosomal monosomies suggests that the absence of an autosomal chromosome is detrimental to cell survival and development.

O-60 Monday, October 17, 2016 12:30 PM

Objective: Male offspring may often weigh more than females as a result of endogenous androgen-driven in utero development. Whether embryonic sex influences on growth in the peri-implantation period or is confined to late pregnancy is not known. While HCG is not a direct measurement of embryonic growth, it represents the trophoblastic cell mass and signifies pregnancy progression. Female fetuses may produce higher HCG
ET of male vs. female embryos: patient demographics, cycle characteristics and outcome

<table>
<thead>
<tr>
<th></th>
<th>Female blastocysts</th>
<th>Male blastocysts</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient age</td>
<td>36.9 ± 4.2</td>
<td>36.6 ± 4.3</td>
<td>NS</td>
</tr>
<tr>
<td>Oocyte age</td>
<td>36.0 ± 4.1</td>
<td>35.6 ± 4.3</td>
<td>NS</td>
</tr>
<tr>
<td>BMI</td>
<td>23.2 ± 4.0</td>
<td>23.3 ± 4.2</td>
<td>NS</td>
</tr>
<tr>
<td>Peak Estradiol</td>
<td>544.1 ± 463.4</td>
<td>517.6 ± 446.8</td>
<td>NS</td>
</tr>
<tr>
<td>Day 3 FSH</td>
<td>6.1 ± 3.4</td>
<td>6.3 ± 3.2</td>
<td>NS</td>
</tr>
<tr>
<td>Endometrial thickness</td>
<td>9.0 ± 2.0</td>
<td>9.2 ± 2.1</td>
<td>NS</td>
</tr>
<tr>
<td>at transfer (mm)</td>
<td>0.0 ± 0.0</td>
<td>0.0 ± 0.0</td>
<td>NS</td>
</tr>
<tr>
<td>Implantation rate</td>
<td>58.6% (329/561)</td>
<td>60.9% (333/547)</td>
<td>NS</td>
</tr>
<tr>
<td>Clinical pregnancy rate</td>
<td>53.7% (301/561)</td>
<td>56.5% (309/547)</td>
<td>NS</td>
</tr>
<tr>
<td>Early pregnancy loss</td>
<td>5.0% (28/561)</td>
<td>4.4% (24/547)</td>
<td>NS</td>
</tr>
<tr>
<td>rate post ET</td>
<td>96.9 ± 100.1</td>
<td>108.9 ± 108.5</td>
<td>NS</td>
</tr>
<tr>
<td>Serum HCG 9 days from</td>
<td>163.0 ± 0.6%</td>
<td>152.0 ± 4.7%</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>day 9 to 11 post ET</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

levels, with reports of this phenomenon confined to the late first, second and third trimester of pregnancy. This study sought to determine if there are embryonic sex-related differences in early pregnancy.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Patients underwent single, euploid, frozen blastocyst transfers (FET) from 2011-2016. Blastocysts, from autologous and donor oocytes, underwent day 6 biopsy and comprehensive chromosome screening (CCS). FETs of male and female embryos were compared (Table). Maternal serum HCG measured 9 and 11 days post-FET were analyzed to determine sex-related differences in embryonic implantation and early dynamics of trophoblast progression. Student’s T test, chi square and binary logistic regression were used.

RESULTS: Of 1108 FET cycles, 561 female and 547 male embryos were transferred. Patient demographics and cycle characteristics were similar in patients who had female vs. male embryos transferred (Table). Embryonic sex did not significantly influence odds of implantation (OR 0.9 [95% CI 0.7-1.2], p=0.45), clinical pregnancy (OR 0.9 [95% CI 0.7-1.1], p=0.34) or pregnancy loss (OR 1.2 [95% CI 1.0-7.2-1], p=0.53). Implanted female embryos had increased rise in HCG from day 9 to 11 post-FET (OR 1.5 [95% CI 1.04-2.0], p=0.02).

CONCLUSIONS: IVF with CCS enables accurate evaluation of sex-related differences in embryonic competence and early development. Controlling for pregnancy status, embryos transferred, and the endometrial environment, male and female blastocysts implant and progress at similar rates. Female fetuses demonstrated a significantly increased rise in serum HCG in the early implantation period, prior to the establishment of the fetal hypothalamic-pituitary-gonadal axis. Therefore, the differential HCG production is more likely mediated by sex chromosomes of the trophoblast, whereby genes on the X chromosome that escape inactivation may be overexpressed by the placenta in the presence of a female fetus. Validation of this theory could be provided by an analysis of gene expression within female and male placentas.

EMBRYO TRANSFER

O-61 Monday, October 17, 2016 11:15 AM

EMBRYO SPECIFIC GRAVITY CAN DETECT CRYODAMAGE, GENETIC INFORMATION AND ESTABLISH PREGNANCY. C. E. Wessels, L. Penrose, S. Prien. Animal Science, Texas Tech University, Lubbock, TX; Department of Obstetrics and Gynecology, Texas Tech University Health Sciences Center, Lubbock, TX; Obstetrics, Texas Tech University Health Sciences Center, Lubbock, TX.

OBJECTIVE: Studies have suggested single embryo transfer (SET) could prevent risks from multiple gestations. However, embryos are currently selected by morphological appearance and developmental rate, which have been shown inadequate to ensure success after SET. Because multiple embryos are created during IVF, SET often leads to cryopreservation of super numerical embryos for later transfer attempts. However, cryopreservation has its own inherent risks to embryo viability. The objective of this study was to identify if embryo density can be used to detect cryodamage.

DESIGN: Culture based study.

MATERIALS AND METHODS: Previous research from this lab suggested embryo weight could detect cryodamage in sheep. To further examine this observation, mice embryos were cultured to blastocysts. Fresh blastocysts were analyzed using a modified specific gravity technique (MSGT). Blastocysts were then frozen using global® Blastocyst Fast Freeze® Kit. Embryos were stored in cryotanks for a minimum of two weeks. Embryos were thawed with global® Blastocyst Fast Freeze® Thawing Kit. Thawed blastocysts were then re-evaluated using the MSGT. Blastocysts were cultured for 48 hours. Survival was determined by blastocysts hatching out of zona pellucida.

RESULTS: Data from an earlier sheep study suggest a difference in the density of embryos in sheep that conceived versus those who did not (P < 0.046). Embryos with average to slow descent times (low density) blastocysts established more pregnancies that survived to term than faster descending blastocysts, which often did not establish pregnancy at all. Post-thaw mice embryo data supported sheep study with embryos with average to slow descent times hatching at a higher rate than embryos that descended rapidly thru the MSGT (P<0.029). Mice embryos that showed fewer differences, which had similar weights pre-freeze and post-thaw survived at a greater rate than embryos with large differences in weight (P<0.016).

CONCLUSIONS: Embryo density could suggest biochemical information that cannot be determined from morphological assessment. Cryodamage can be detected by variability of embryo density, possibly because damaged embryos have lost the ability to osmoregulate themselves due to membrane disruption, making them denser. Current studies are examining if MSGT can be used to weight differences in X and Y chromosomes. This data continues to support the use of MSGT as a noninvasive means of assessing embryo quality.

Supported by: Laura W. Bush Institute for Women’s Health South Plains Foundation.

O-62 Monday, October 17, 2016 11:30 AM

RECURRENT RISK OF ECTOPIC PREGNANCY IS NOT INCREASED FOR PATIENTS WITH PREVIOUS ECTOPIC PREGNANCY COMPARED WITH THOSE WITHOUT PREVIOUS ECTOPIC PREGNANCY IN FROZEN BLASTOCYST TRANSFER CYCLES: A STUDY BASED ON MORE THAN 30,000 CYCLES. T. Du, Y. Fan, Q. Chen, Q. Lyu, Y. Kuang. Department of Assisted Reproduction, Shanghai Ninth People’s Hospital, Shanghai, China.

OBJECTIVE: To evaluate the effect of frozen-thawed blastocyst transfer on recurrence rate of ectopic pregnancy (EP) in patients with previous EP.

DESIGN: Strictly controlled retrospective cohort study.

MATERIALS AND METHODS: Women undergoing 31,871 frozen-thawed embryo transfer (FET) cycles of in vitro fertilization (IVF)/intracytoplasmic sperm injection (ICSI) in the period between March 2003 and May 2015 were enrolled, and those with uterine abnormalities, uterine disorders or disorder history, uterine or uterine cavity surgery and other conditions that were incompatible for management were excluded. Additionally, history and those without EP history (control group) were strictly matched by age, number of cycles, number of prior full-term births, type of infertility, presence of Fallopian tubal diseases, previous Fallopian tubal surgery, polycystic ovary syndrome, endometriosis and male factor infertility, type of endometrial preparation, number of embryos transferred, stage of embryos transferred and endometrial thickness on embryo transfer (ET) day, and then divided into four groups by according to the status of embryos transferred: cleaved embryo transfer group (n=1,938 FETs), blastocyst transfer group (n=251 FETs), and their respective control groups. Statistical analyses were carried out by SPSS version 19.0. The normality of quantitative data was tested both by Kolmogorov-Smirnova test and Shapiro-Wilk test, and the Mann-Whitney U test, Chi-square test or Fisher’s exact test were applied to obtain group comparisons as appropriate. P<0.05 was considered statistically significant.
RESULTS: Main baseline characteristics including age, body mass index, number of cycles, number of prior full-term births, profiles of type of infertility, indications for IVF/ICSIs and pre-existing conditions including previous Fallopian tube surgery and FET characteristics including profile of type of endometrial preparation, number of embryos transferred, number of good-quality embryos transferred, estradiol and progesterone levels and endometrial thickness on ET day had no statistically significant differences between experimental groups and their respective control groups. As for pregnancy outcome, cleaved embryo transfer group had a statistically significant higher EP rate than its control group (6.3% vs. 3.8%, P = 0.017, relative risk increase: 65.8%, 95% confidence interval: 11.9%-119.7%). However, the EP rates of blastocyst transfer group and its control group had no statistically significant difference (2.8% vs. 0%, P = 0.123).

CONCLUSIONS: In frozen-thawed blastocyst transfer cycles of IVF/ICSIs, recurrence risk of EP is not increased for patients with previous EP.

Supported by: National Natural Science Foundation of China.
**O-66 Monday, October 17, 2016 12:30 PM**

**COMPARISON OF ANEUPLOID RATES AMONG DAY 5, 6, AND 7 BIOPSIED BLASTOCYSTS.** J. Shah, A. C. Vanijgul, S. Chauhan, R. D. Dunn, W. A. Wu, UT-Houston/Memorial Hermann Hospital, Houston, TX; Houston Fertility Specialists, Houston, TX; Houston Fertility Specialist, Sugarland, TX; Houston Fertility Specialists, Houston, TX; IVF lab, SART, Houston, TX.

**OBJECTIVE:** To transfer euploid embryos is a continuing actively pursuing goal in the IVF field. Currently, the embryo morphology and developmental speed are the parameters to select. The correlation of developmental speed with euploid rate is unclear. Capalbo et al (2014) reported no significant correlation while Taylor et al (2014) reported a significant higher euploid rate for a fast growing blastocyst. This study intends to utilize big data to examine any significant correlation of embryo growing speed with the euploid rate.

**DESIGN:** All trophectoderm biopsy cases with comprehensive chromosome screening (CCS) during January 2014 - February 2016 were included. In total, there are 863 cases with 2781 biopsied blastocysts. There were 287 blastocysts with no results or without complete information. 2494 blastocysts with clear information were included in the analysis.

**MATERIALS AND METHODS:** The trophectoderm biopsy is done when the blastocyst is at full expansion or a more advanced stage. The mean age is 35.3 with a range 25-45. Depending on the blastocyst stage, the biopsy is performed at day 5, day 6, or day 7. The CCS is done by the Genesis Genetics lab. Logistic analyses were used for statistical analysis. The significance level is defined at P < 0.05.

**RESULTS:**

<table>
<thead>
<tr>
<th>Day 5 vs Day 6</th>
<th>Day 5 vs Day 7</th>
<th>Day 6 vs Day 7</th>
</tr>
</thead>
<tbody>
<tr>
<td>P &lt; 0.0001</td>
<td>P &lt; 0.0001</td>
<td>P &lt; 0.05</td>
</tr>
<tr>
<td>P &gt; 0.05</td>
<td></td>
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</tr>
</tbody>
</table>

**Table 1:** Comparison of blastocyst euploidy rate in patients who had trophectoderm biopsies on day 5, 6 and 7

**RESULTS:**

**CONCLUSIONS:** The results agrees with the Taylor et al (2014) report that fast growing blastocysts (day 5) have significant better chance to be euploid than the slow growing blastocysts (day 6 or day 7). Selecting a quality embryo to transfer is especially important in elective single embryo transfer cases. The results support the use of embryo growing speed as a selection criterion for a quality embryo.

**References:**


FRUIT AND VEGETABLE INTAKE AND THEIR PESTICIDE RESIDUES IN RELATION TO OUTCOMES OF ASSISTED REPRODUCTIVE TECHNOLOGY. Y. Chiu, A. J. Gaskins, P. Williams, M. W. Gillman, L. Mingez-Arbron, T. L. Toth, R. Hauser. 1Department of Nutrition, Harvard T.H. Chan School of Public Health, Boston, MA; 2Bioestatistics and Epidemiology, Harvard T. H. Chan School of Public Health, Boston, MA; 3Obesity Prevention Program, Department of Population Medicine, Harvard Medical School and Harvard Pilgrim Health Care Institute, Boston, MA; 4Environmental Health, Harvard T.H. Chan School of Public Health, Boston, MA; 5OB/GYN, Massachusetts General Hospital, Boston, MA.

OBJECTIVE: Animal experiments have shown that very low dose ingestion of pesticide mixtures before implantation decreases the number of live-born pups. Whether the same is true in humans is unknown. We examined the association of intake of pesticides residues in fruits and vegetables (FV) with outcomes of infertility treatment using assisted reproductive technology (ART).

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: During 2007-2015, 300 women presenting to an academic fertility center completed a validated food frequency questionnaire and subsequently underwent 493 ART cycles. FVs were categorized as having high or low-to-moderate (L-M) pesticide residues using a validated method based on surveillance data from the US Department of Agriculture. Data on implantation, clinical pregnancy and live birth were abstracted from medical records. Pregnancy loss was defined as a loss after -hCG and 202 (41%) resulted in a live birth. Higher intake of high-pesticide residue FVs was associated with a lower probability of live birth. The adjusted probability (95%CI) of a positive ART was 1.0 (0.7,1.6) and 2.5 (1.7,3.4) servings/day, respectively. Of 493 initiated ART cycles, 2,823 of 56,607 genes analyzed were differentially expressed in exposed vs. non-exposed animals with gene expression changes ranging from -645 to +7742-fold difference. Examples of key differentially expressed genes included acyl-CoA synthetase, apolipoprotein, and ATPase.

CONCLUSIONS: In this study female mice were exposed to the EDC plasticizer, DEHP, at an environmentally relevant dose, comparable to human exposure. Exposure to DEHP resulted in significant changes in the expression of genes involved in energy production and apoptosis in adipose tissue and ovarian tissue. Our study may have important implications for ovarian function and fertility in humans.


Supported by: T32HD040135-14 (NMG).

O-69 Monday, October 17, 2016 11:45 AM

MULTI-CENTER STUDY: INNOVATIVE CONTROL OF AMBIENT AIR QUALITY IN MULTIPLE IVF LABORATORIES IS ASSOCIATED WITH STATISTICALLY SIGNIFICANT IMPROVEMENTS IN CLINICAL OUTCOMES - ANALYSIS OF 5319 CYCLES. S. Palter, K. DiPaola, A. E. Sparks, S. Degelos, G. T. Koulmianos, J. Young, C. Halicigil, T. Yalcinkaya, E. She, A. Bartolucci. 1Gold Coast IVF, Woodbury, NY; 2University of Cincinnati, West Chester, OH; 3University of Iowa, Iowa City, IA; 4The Center for Reproductive Medicine, Mobile, AL; 5The Fertility Center, Grand Rapids, MI; 6Carolina's Fertility Institute, Winston Salem, NC; 7NEFI, Stanford, CT; 8CARS, Farmington, CT.

OBJECTIVE: Successful preimplantation embryogenesis and the reproductive potential of the human embryo are critically dependent upon a number of variables including the changing organic chemistry of the ambient air (AA) within the IVF laboratory. AA contains dynamic levels of embroyotoxic volatile organic compounds (VOCs) and viable particulates (VPs), which play a critical role in preimplantation toxicology and in the influence of AA on epigenetic processes. This report represents the largest cohort study evaluating the impact of comprehensive remediation of airborne pathogens on measures of embryogenesis and patient outcomes in multiple IVF programs using a proprietary air purification system (APS). Using targeted engineered molecular media and genomically modeled biological inactivation, the APS was designed to comprehensively remediate airborne embryotoxic pathogens.

DESIGN: Retrospective analysis with historical controls.

MATERIALS AND METHODS: Clinical outcome data from all non-donor IVF patients (n = 5319) cycling through 9 independent IVF programs was evaluated over a 24-48 month period. Data was collected for 2761 patients cycling in an environment protected by pre-existing mechanisms of air filtration and 2558 patients after the installation of the APS. Blastocyst conversion rate (BCR) was defined by zygotes.
reaching the blastocyst stage by Day 5, implantation rate (IR) by positive fetal cardiac activity (FCA) per transferred embryo, ongoing pregnancy (OP) by positive FCA and loss rate (LOR) as an intrauterine gestational sac without subsequent FCA. Multivariable analyses (MVA) evaluated differences in patient demographics, sperm and post-APS pediatric, and pre- and post-installation variables. Statistical analyses included odds ratios calculated with 95% confidence intervals and \( \alpha = 0.05 \) using MedCalc Software 13.1.2, Ostend, Belgium.

RESULTS: Embryos cultured after installation of the APS demonstrated a significant increase in BCR (33.7% vs. 54.4% [p<0.0001]), IR (29.7% vs. 41.4% [p<0.0001]) and OP (42.7% vs. 57.6% [p<0.0001]) from all matched pairs, respectively. Those embryos cultured in the APS-controlled environment demonstrated a significant decrease in LOR (27.7% vs. 20.3% [p=0.0001]). No other variables were significant by MVA.

CONCLUSIONS: Embryotoxic VOCs and VPs play a critical role in preimplantation toxicology and in the influence of AA on epigenetic processes. Concomitant with comprehensive removal and control of airborne pathogens within the in vitro culture environment was a statistically significant increase in BCR, IR, OP and a decrease in LOR. Comprehensive control of the AA is critical to successful preimplantation embryogenesis.

O-70 Monday, October 17, 2016 12:00 PM

EXPOSURE TO PHTHALENAL, AN ENDOCRINE DISRUPTING CHEMICAL, ALTERS FIRST TRIMESTER PLACENTAL GENETIC EXPRESSION IN WOMEN. N. M. Grindler, I. Yang, K. Rajendiran, K. Kannan, M. A. Schwartz, A. J. Polotsky, T. L. Powell, T. Jansson. OBGYN, Division of REI, University of Colorado, Aurora, CO; Department of Medicine and Integrated Center for Genes, Health, and Environment, University of Colorado, Aurora, CO; New York State Dept of Health, Albany, NY; OBGYN, Division of Family Planning, University of Colorado, Aurora, CO; Pediatrics, University of Colorado, Aurora, CO; OBGYN, Division of Reproductive Sciences, University of Colorado, Aurora, CO.

OBJECTIVE: Altered placental function can result in abnormal fetal development and pregnancy complications and may affect health in later stages of life. Exposure to endocrine disrupting chemicals (EDCs), like di(2-ethylhexyl) phthalate (DEHP), a common plasticizer, has been shown to alter the placental transcriptome in animal models. We tested the hypothesis that exposure to phthalates alters first trimester placental gene expression in women.

DESIGN: Cross-sectional cohort study.

MATERIALS AND METHODS: Placental tissue and paired maternal urine were collected from anonymous elective first trimester terminations of pregnancy (n = 52) and frozen. The concentrations of 22 phthalate metabolites were analyzed in urine using high performance liquid chromatography-tandem mass spectrometry (HPLC-MS/MS) and GC-MS. DEHP refers to molar sum of each of the individual DEHP metabolites and we compared high and low \( \Sigma \)DEHP levels based on quartile distributions. Spearman correlation was used to assess the dependence of \( \Sigma \)DEHP on maternal age, body mass index (BMI) and gestational age (GA). Placental tissue RNA was isolated using the Qiagen method. Placental gene expression was analyzed using Agilent’s Sureprint G3 8x60K array. Differential gene expression was determined using t-test and a cut-off of \( p < 0.005 \) between high and low \( \Sigma \)DEHP groups.

RESULTS: The mean maternal age was 27.2 years, BMI was 22.8, and GA was 7.7 weeks. The distribution of each of the 22 phthalates and \( \Sigma \)DEHP (mean 47.9 nmol/L) was determined for all subjects. There was no correlation between any of the phthalate metabolites and GA, maternal age, or BMI. We found 45 of 58,202 genes analyzed were differentially expressed, in high vs. low \( \Sigma \)DEHP groups including genes involved in transcriptional activation, energy production, mitochondrial function, and genes required for early embryonic stem cell development. Gene expression changes ranged from -6 to +12-fold differences in placental tissue obtained from high compared to low \( \Sigma \)DEHP levels.

CONCLUSIONS: Exposure to DEHP is associated with altered expression of critical genes in the first trimester human placenta, which may impact fetal development. Future studies are needed to determine the underlying mechanisms and the functional consequences of these changes in gene expression.

spermatozoa (p=0.030 for soy milk) and decreased progressive spermatozoa (p=0.045 for soy milk). Higher daidzein levels in seminal plasma were associated to a significant increase in total diploidy (p=0.008). Increased autosomal disomies were found with higher daidzein levels in urine (p=0.031) and seminal plasma (p=0.004). Increased levels of genistein in seminal plasma were significantly correlated to increased sex chromosomes disomies (p=0.027) and ejaculate volume (p=0.025). We also found a correlation between m-paraben in seminal plasma and the percentage of non-progressive spermatozoa (p=0.003); and between increased urine p-paraben and increased sex chromosomes disomies (p=0.008). Finally, MEHP urine levels were correlated with sperm concentration (p=0.035).

CONCLUSIONS: We are highly exposed to several EDCs found in our daily routine, environment and food that could be found in the urine and seminal plasma, altering sperm quality and aneuploidy rates. More attention to lifestyle and EDCs exposure (especially soy-derived phytoestrogens and parabens) should be paid.

Supported by: Supported by Illumina.

FERTILITY PRESERVATION

O-73 Monday, October 17, 2016 11:15 AM

PREDICTING THE LIKELIHOOD OF LIVE BIRTH FOR ELECTIVE OOCYTE CRYOPRESERVATION: A COUNSELING TOOL FOR PHYSICIANS AND PATIENTS. R. H. Goldman, a C. Racowsky, c L. V. Farland, a S. Munne, c L. Ribustello, b J. H. Fox, d Dept of Obstetrics and Gynecology, Brigham and Women’s Hospital and Harvard Medical School, Boston, MA; Reprogenetics, Livingston, NJ.

OBJECTIVE: As more women consider elective oocyte cryopreservation as a means to preserve fertility and defer childbearing, a counseling tool is needed to predict the likelihood of live birth as a function of age and number of mature eggs frozen. The purpose of this study was to develop such a counseling tool using outcomes from a population of presumably fertile women undergoing ART.

DESIGN: Data from 423 first fresh IVF/ICSI cycles for which male-factor infertility was the sole diagnosis were collected from a single university-based clinic between January 2011 and March 2015. In conjunction with aggregate Reprogenetics data on euploidy rates, a model was designed to predict the likelihood of having at least one live birth based on age and the number of mature oocytes retrieved.

MATERIALS AND METHODS: Poisson regression was used to develop an equation that calculates the proportion of mature oocytes that fertilize and develop into blastocysts as a function of age (years, y) at retrieval, using our exclusive male-factor population. The age-specific probabilities of euploidy for a single blastocyst were then estimated from Reprogenetics data of 18,000 preimplantation genetic screening (PGS) results using array comparative genomic hybridization. Finally, the probability of having at least one live birth was calculated using the projected proportion of euploid blastocysts based on patient age and number of mature oocytes. Our model assumed 95% survival of thawed oocytes and that 60% of transferred euploid blastocysts result in live birth on average, based on published data.

RESULTS: Based on our dataset, the probability that each mature oocyte (n=5,311) will fertilize and develop into a blastocyst can be described by the equation: exp(2.5571-0.1044x age). For example, women age 34y, 37y, or 42y, each with 8 mature oocytes, would be expected to have 3, 2, or 1 blastocyst(s), respectively. Incorporation of age-specific PGS data for prediction of the euploid blastocyst formation rate enabled development of the prediction tool. The table shows the likelihood (%) of a patient having at least one live birth for selected ages and number of mature oocytes cryopreserved.

<table>
<thead>
<tr>
<th>No. Mature Oocytes Frozen</th>
<th>Age (y)</th>
<th>Likelihood (%) of at least one live birth</th>
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<tbody>
<tr>
<td></td>
<td>&lt;35</td>
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<tr>
<td>1</td>
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<td>50</td>
<td>97</td>
<td>97</td>
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</table>

CONCLUSIONS: Our model will help women desiring fertility preservation decide how many cycles to undergo and when additional cycles would bring diminishing returns for future family building. This tool will be a valuable counseling resource for physicians as more women elect to cryopreserve their oocytes. A prospective study is encouraged to validate our model.

O-74 Monday, October 17, 2016 11:30 AM

SECOND CHILDREN BORN AFTER AUTOTRANSPLANTATION OF CRYOPRESERVED OVARIAN TISSUE IN A YOUNG PATIENT PREVIOUSLY TREATED WITH CHEMOTHERAPY FOR ASKIN’S DISEASETHE SUCCESSFUL FERTILITY PRESERVATION PROGRAM. F. Lorenzo, a M. Villamayor, c J. Viola, b M. Tiveron, b E. Young, d Reproductive Medicine, IFER, Buenos Aires, Argentina; Fertility, IFER, Ciudad Autonoma de Buenos Aires, Argentina.

OBJECTIVE: Oncological treatment was associated with a reduced ovarian reserve, the chance of a successful pregnancy is currently around 1/3 for those with ovarian-tissue autotransplantation. Ovarian tissue cryopreservation is an effective option, gaining ground as a valid method for fertility preservation especially for pre-pubertal patients and patients who have a short time between diagnosis of a disease and gonadotoxic treatment. More than 62 children worldwide have now been born following this procedure.

DESIGN: Case report and a retrospectively analyze, of patients whose underwent ovarian tissue cryopreservation at IFER, Argentina between 1999-2015. One of these women, had orthotopic transplantation, after chemotheraphy premature ovarian failure (POF) has now conceived again following natural conception. She gave birth to a healthy girl on 7/2015 and is therefore the second woman in the world to have had two children, from separate pregnancies, born as a result of transplanting frozen/thawed ovarian-tissue.

MATERIALS AND METHODS: 68 patients referred from private oncological units underwent cryopreservation of ovarian tissue before gonadotoxic therapy for malignant disease. 7 patients (10,3%) died during follow-up due to recurrence of disease. 24 post-pubertal patients without the need for grafts of cryopreserved tissue. 4 patients had undergone ovarian tissue transplantation in order to restore their fertility after remission of the disease and one of these women became pregnant twice and gave birth to two healthy babies.

RESULTS: In 2005 a 28 year old patient was referred for fertility preservation before undergoing aggressive chemotherapy for Askin tumor. Several strips of ovarian cortical tissue were obtained by laparoscopy and cryopreserved . The patient underwent surgical treatment, and chemotherapy (CVEA), ovarian failure was established. In 2009 orthotopic transplantation of frozen-thawed ovarian tissue was carried out by laparoscopy in the right ovary. Three months after transplantations she resumed regular menses. Four IVF cycles were performed with no pregnancy. 9/2012 POF was established. In 2/2013 another laparoscopy was performed with replacement of ovarian tissue this time in the left ovary. In 5/2013 spontaneous menses began. An Intrauterine Insemination resulted in pregnancy. In 2/2014, and after an uneventful pregnancy, a healthy baby boy was born.

The patient was breastfeeding her first baby and returned to our fertility clinic in 9/2014 a pregnancy test revealed a high pregnancy already confirmed, after an uneventful pregnancy a normal healthy girl was born in 7/2015.

CONCLUSIONS: The present result supports cryopreservation of ovarian tissue as a valid method of fertility preservation to be used in women facing gonadotoxic treatment. However alternative procedures such as oocyte or embryo cryopreservation should be considered as first options especially for older patients.

REFERENCES:

O-75 Monday, October 17, 2016 11:45 AM

RANDOM START STIMULATION ALLOWS FOR MINIMAL TREATMENT DELAYS WITH NEOADJUVANT BREAST CANCER TREATMENT. J. Letourneau,a K. A. Wald,a N. Sinha,a E. Harris,a E. Mok-Lin,a M. Rosen.b Obstetrics, Gynecology and Reproductive Sciences, University of California, San Francisco, San Francisco, CA; OB/GYN, University of Washington, Seattle, WA.
OBJECTIVE: Time delay to cancer treatment places increased anxiety upon the patient and oncology team. These potential delays have prevented women from undergoing fertility preservation treatment. Most recently, the movement toward neoadjuvant therapy for breast cancer has increased the potential for delay. Alternative ovarian stimulation strategies have been implemented to minimize delays to cancer treatment. In the study, we sought to determine whether random start stimulation allows for minimal delays to neoadjuvant chemotherapy start in breast cancer patients.

DESIGN: Case-control study.

MATERIALS AND METHODS: 42 women were diagnosed with breast cancer at UCSF with a treatment plan for neoadjuvant chemotherapy and were seen for fertility preservation consultation. Referrals for fertility preservation evaluation came from breast cancer diagnostic centers, often prior to medical oncology consultation. Women in the control group did not undergo ovarian stimulation for fertility preservation (No FP), and women in the case group did undergo ovarian stimulation for fertility preservation (FP). The time from diagnosis to FP, the time from diagnosis to chemotherapy treatment, and the time from FP consult to chemotherapy treatment were calculated. T-tests were utilized to determine if there were differences in time from diagnosis to chemotherapy based on whether patients underwent FP or not.

RESULTS: Average age of women in our study was 34 +/- 5 years old. After consultation with a reproductive endocrinologist, 24 women underwent ovarian stimulation for fertility preservation and 18 did not. The time from cancer diagnosis to neoadjuvant chemotherapy start was not significantly different between the FP and No FP groups (Table 1).

CONCLUSIONS: These findings suggest a random start ovarian stimulation allows for minimal delays, even in a neoadjuvant setting. However, an early referral is paramount to avoid delays. Patients undergoing neoadjuvant chemotherapy should be enabled to undergo FP treatment and be informed of these findings to avoid unnecessary anxiety due to delays.

O-76 Monday, October 17, 2016 12:00 PM

IN VITRO MATURATION OOCYTE COLLECTION AT DIFFERENT PHASES OF THE MENSTRUAL CYCLE AMONG WOMEN REQUIRING URGENT CHEMOTHERAPY. H. Creux, a P. Monnier, 1,b W. Son, c T. Tulandi, d W. Buckett, e Obstetrics and Gynecology, MUHC Reproductive Center, Montreal, QC, Canada; c MUHC Research institute, Montreal, QC, Canada; d Obstetrics and Gynecology, McGill University, Montreal, QC, Canada; e McGill University, Montreal, QC, Canada.

OBJECTIVE: To evaluate the feasibility and the efficacy of in vitro maturation (IVM) collection performed in early follicular, late follicular and luteal phases among women requiring urgent chemotherapy.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Patients: The study group consisted of 156 patients with cancer who underwent IVM treatment for fertility preservation in the period of January 2003 to January 2016, with a total of 176 cycles. All cancer types were taken into account. The patients were grouped into three categories: the early follicular phase, the late follicular phase (defined by day 7 of the menstrual cycle combined with endometrium > or = 6 mm and one follicle > or = 10 mm), and the luteal phase (defined by the presence of a corpus luteum and date of the cycle). Fertilization and embryo freezing were performed in 57 cycles.

Outcome measures: Number of oocytes collected, maturation rates after 48h of culture, total number of oocytes cryopreserved. Fertilization rates and number of embryos cryopreserved were also evaluated when appropriate.

STATISTICAL ANALYSIS: Quantitative data were expressed as mean +/- standard deviation. Non-parametric Kruskal-Wallis rank-sum tests with multiple comparison Z test were performed to compare variables among the different phases of the menstrual cycle. Results were considered significant at a p-value of less than 0.05.

RESULTS: Number of oocytes collected, maturation rates after 48h of culture, total number of oocytes cryopreserved were similar in all groups. Where applicable, fertilization rate and number of embryos cryopreserved were similar in all groups (Table). Conclusions: Our study confirms the feasibility of IVM collection at anytime during the menstrual cycle. IVM treatment appears an attractive alternative when chemotherapy cannot be delayed or if ovarian stimulation is contraindicated. At present, long-term outcome data are lacking.

O-77 Monday, October 17, 2016 12:15 PM

COST EFFECTIVENESS OF EGG BANKING FOR CANCER PATIENTS. B. M. Lyttle, a N. S. Grover, b T. B. Mesen, c A. Z. Steiner, d J. E. Mersereau. a Obstetrics and Gynecology, Division of Reproductive Endocrinology, University of North Carolina, Chapel Hill, NC; b Hematology, University of North Carolina, Chapel Hill, NC; c Obstetrics and Gynecology, Division of Reproductive Endocrinology, University North Carolina Chapel Hill, Chapel Hill, NC; d University of North Carolina, Chapel Hill, NC; e REI, UNC, Chapel Hill, NC.

OBJECTIVE: Determine the cost-effectiveness of fertility preservation (FP) in cancer patients undergoing treatment with high risk (HRT) and low risk (LRT) gonadotoxic therapy.

DESIGN: Decision-tree analysis.

MATERIALS AND METHODS: Decision tree models were constructed to determine the cost-effectiveness of FP versus no FP prior to chemotherapy for patients ages 25-40 years. A 5 year horizon from diagnosis to attempt at pregnancy was assumed. The decision tree included the following probabilities: amenorrhea after LRT or HRT (ASCO), natural conception (Time to Conceive, a prospective time-to-pregnancy study), miscarriage, and live birth for both cryopreserved oocytes and fresh autologous oocytes from IVF (In-tegraMed and CDC database). If no live birth with cryopreserved or fresh oocytes, donor egg was added as final strategy. Costs were averaged from actual charges estimated from 7 diverse US fertility centers. Overall probability and cost of live birth at each age of diagnosis were calculated for LRT and HRT. Incremental Cost Effectiveness Ratio (ICER) was determined for each strategy.
Probability of LB when undergoing HRT and LRT

<table>
<thead>
<tr>
<th>Age at Diagnosis (YRS)</th>
<th>HRT</th>
<th>LRT</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>FP</td>
<td>FP</td>
</tr>
<tr>
<td>25</td>
<td>0.18</td>
<td>0.66</td>
</tr>
<tr>
<td>30</td>
<td>0.17</td>
<td>0.63</td>
</tr>
<tr>
<td>35</td>
<td>0.12</td>
<td>0.51</td>
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<tr>
<td>40</td>
<td>0.05</td>
<td>0.26</td>
</tr>
</tbody>
</table>

RESULTS: For patients who receive HRT, FP (compared to no FP) increases the probability of live birth most when banking is done at a younger age. In contrast, patients who receive LRT have the greatest increase when banking occurs at an older age (Table1). For those who did not conceive with their own eggs (FP or IVF), donor egg IVF increased chance of LB for women in HRT and LRT groups on average by 48% and 25%. ICER suggests egg banking is more cost-effective in HRT groups at 25 versus 40 years of age (ICER $333,911 and $74,170). Egg banking is most cost-effective in LRT groups at 40 versus 25 years of age (ICER $50,511 and $78,105).

CONCLUSIONS: FP at any age for both LRT and HRT is more effective and costly than no FP. Women less than 35 years of age undergoing HRT are the most likely group to benefit from FP.

References:

O-79 Monday, October 17, 2016 11:15 AM

HYPERANDROGENISM IS ASSOCIATED WITH PREFERENTIAL FAT DEPOSITION OF VISCERAL VERSUS SUBCUTANEOUS (SC) ABDOMINAL FAT IN LEAN POLYCYSTIC OVARY SYNDROME (PCOS) WOMEN. A. L. Akopians, a V. Madrigal, a E. Ramirez, b D. Margolis, c M. K. Sarma, c M. A. Thomas, c D. Trogan, d H. Abbott, e R. Haykal, e G. D. Chazenbalk, d A. D. Dumesic. e OB/GYN, UCLA, Los Angeles, CA; bMedicine, UCLA, Los Angeles, CA; cRadiological Science, UCLA, Los Angeles, CA; dMedicine Statistics Core, UCLA, Los Angeles, CA; eOB/GYN, Wisconsin National Primate Research Center, Madison, WI.

OBJECTIVE: Accumulation of small SC abdominal adipocites in humans as a sign of impaired adipogenesis underlying insulin resistance (IR) (1) also has been reported in prenatally testosterone (T)-treated monkeys and sheep (2,3). This study examines whether a similar accumulation of SC abdominal adipocites accompanies an increase in abdominal fat mass in lean PCOS women compared to normoandrogenic ovulatory (NL) women.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: Six lean non-Hispanic, Caucasian PCOS women (by 1990 National Institutes of Health criteria) ages 18-35 years and 14 NL women, age- and body mass index (BMI, 18.5-25 kg/m²)-matched, underwent examination; serum hormone/metabolic measures; frequently sampled intravenous glucose tolerance testing; total body dual-energy x-ray absorptiometry; abdominal magnetic resonance imaging; and SC abdominal fat biopsy. Student’s test and regression analyses were performed and adjusted for BMI. Variables were log transformed as appropriate.

RESULTS: PCOS women had elevated serum luteinizing hormone (P<0.01), total T (P<0.005), free (f) T (P<0.0001), and androstenedione (A4) (P<0.03) levels, along with increased fasting serum insulin levels (P<0.01) with euglycemia, and acute insulin responses to glucose infusion (P<0.05). PCOS women also had increased total abdominal fat mass due in part to more visceral fat mass than NL women (P<0.05, both fat deposits). Total fat mass and % body fat were comparable between female types (P=NS). Similar to prenatally T-treated monkeys and sheep (2,3), PCOS women had a greater proportion of small SC abdominal adipocites than NL women (P<0.05). In all women combined, total abdominal fat mass positively correlated with visceral (r=0.73, P<0.001) and SC abdominal fat (r=0.87, P<0.001) masses, which in turn were predicted by waist size (r=0.61, P<0.01) and BMI (r=0.73, P<0.001), respectively. Adjusting for BMI, visceral fat mass positively correlated with serum total T (r=0.51, P<0.05), FT (r=0.52, P<0.05), A4 (r=0.57, P<0.025), fasting insulin (r=0.56, P<0.025), non-HDL cholesterol (r=0.59, P<0.01) and triglyceride (r=0.54, P<0.025) levels. In contrast, SC abdominal fat mass positively correlated with total body fat (r=0.85, P<0.001). However, the proportion of small SC abdominal adipocites in all women combined was positively linked with serum T (r=0.71, P<0.005) and A4 (r=0.65, P<0.005) levels.

CONCLUSIONS: Hyperandrogenism in lean PCOS women favors preferential fat deposition of visceral versus SC abdominal fat as a sign of impaired adipogenesis and may have its developmental origin during fetal life.
SATURATED FAT INGESTION STIMULATES SUPPRESSOR OF CYTOKINE SIGNALING-3 (SOCS-3) AND TOLL-LIKE RECEPTOR-4 (TLR-4) GENE EXPRESSION IN POLYCYSTIC OVARY SYNDROME (PCOS). O. A. Abdelhadi,1 R. V. Considine,1 A. J. Acton,1 F. Gonzalez,a Obstetrics and Gynecology, Indiana University School of Medicine, Indianapolis, IN;1 Medicine, Indiana University School of Medicine, Indianapolis, IN.

OBJECTIVE: SOCS-3 is a proinflammatory inhibitor of insulin signaling. Lipopolysaccharide (LPS) from gut-related bacteria enters the circulation with saturated fat ingestion and binds the TLR-4 receptor to stimulate inflammation. We previously reported increases in plasma LPS and the mononuclear cell (MNC) mRNA content of SOCS-3 and TLR-4 in women with PCOS compared with ovulatory controls; and its relation to insulin sensitivity and the ovarian androgen response to HCG administration.

MATERIALS AND METHODS: We studied 16 women with PCOS (8 lean, 8 obese) between ages 18-40, diagnosed on the basis of oligomenorrhea and hyperandrogenemia, and 16 ovulatory controls (8 lean, 8 obese) of similar age. Subjects ingested 100 ml of dairy cream and received a single 5000 IU IM injection of HCG within 5-8 days of menses. Plasma LPS was measured by fluorescence and SOCS-3 and TLR-4 mRNA content was determined by real-time quantitative PCR in isolated MNC from blood samples drawn while fasting and 2 hours after cream ingestion. Androgens were measured from blood samples drawn at 0, 24, 48 and 96 hours after HCG administration. Insulin sensitivity was derived by ISOGTT.

RESULTS: The change from baseline (Δ%) in SOCS-3 was greater (p<0.03) in lean and obese women with PCOS (30.6±16.9, 47.7±13.1) and PCOS-like monkeys (31.9±10.9) compared with lean controls (-1.9±11.5). Compared with weight-matched controls, women with PCOS exhibited greater area under the curve (AUC) following HCG administration for testosterone (T) (lean: 6932±791 vs. 3154±447, p<0.002; obese: 7078±1236 vs. 3754±226, p<0.005), and androstenedione (A) (lean: 517±15 vs. 286±24, p<0.0001; obese: 511±15 vs. 333±41, p<0.0004). The Δ% SOCS-3 was negatively correlated with ISOGTT (r=-0.64, p<0.0001), and positively correlated with AUC for T (r=0.46; p<0.008) and A (r=0.41; p<0.03). The Δ% LPS was greater (p<0.02) in obese women with PCOS (98.4±15.1) compared with obese controls (42.1±18.8); and was greater (p<0.0001) in obese controls compared with either lean group (PCOS: -2.8±15.2; controls: -8.2±13.3). The Δ% TLR-4 was higher (p<0.03) in the obese groups (PCOS: 53.3±24.1; controls: 42.7±26.7) compared with the lean groups (PCOS: -22.5±9.3; controls: -21.9±14.2); and was positively correlated with the Δ% LPS (r=0.46; p<0.009).

CONCLUSIONS: In PCOS, saturated fat ingestion increases SOCS-3 independently of obesity. However, lipid-stimulated increases in LPS and TLR-4 are obesity-related phenomena made worse by PCOS. Lipid-stimulated upregulation of proinflammatory gene expression may promote insulin resistance and excess ovarian androgen production in PCOS.

References:

Supported by: NIH grant R01 DK107605 to F.G.

ANTI-INFLAMMATORY THERAPY SUPPRESSES PROINFLAMMATORY CYTOKINE SECRETION FROM MONONUCLEAR CELLS AND REDUCES HYPERANDROGENISM IN LEAN WOMEN WITH POLYCYSTIC OVARY SYNDROME (PCOS). F. González,1 R. V. Considine,1 O. A. Abdelhadi,1 A. J. Acton.1 Obstetrics and Gynecology, Indiana University School of Medicine, Indianapolis, IN;1 Medicine, Indiana University School of Medicine, Indianapolis, IN.

OBJECTIVE: We have shown that in PCOS, saturated fat ingestion increases proinflammatory cytokine secretion from mononuclear cells (MNC) even in the absence of obesity, and that suppression of NFκB activation with saltsalate treatment improves ovarian dysfunction.1,2 We now examine the effect of saltsalate treatment on lipid-stimulated proinflammatory cytokine secretion from MNC and the concurrent effects on the ovarian androgen response to HCG administration in lean insulin-sensitive women with PCOS.

DESIGN: Longitudinal Pilot Study.

MATERIALS AND METHODS: Seven lean women with PCOS diagnosed on the basis of secondary amenorrhea and hyperandrogenemia were selected for study. They had a normal BMI (23.1±0.5 kg/m²), normal insulin sensitivity (glucose disposal rate >4.45 mg/kg/min during a glucose clamp) and normal abdominal adiposity (% ratio of truncal fat to total body fat <42% measured by DEXA). Measurements were performed at baseline and following treatment with saltsalate 3 gm daily for 12 weeks. Subjects ingested 100 ml of dairy cream and received a single 5000 IU IM injection of HCG within 5-8 days of menses. MNC were cultured following isolation from blood samples drawn while fasting and 2, 3, and 5 hours after cream ingestion. TNFα and IL-6 secretion was measured by ELISA in response to LPS, TNFα and IL-6-stimulated increases in LPS were greater (p<0.009). The absolute change in lipid-stimulated cytokine secretion (pg/ml) from the fasting baseline declined at 2 hours (TNFα: 19.7±13.5 vs. 0.6±6.7, p<0.05; IL-6: 17.4±7.3 vs. 0.1±3.0, p<0.02) and 3 hours (TNFα: 19.8±11.8 vs. 0.1±6.5, p<0.03; IL-6: 12.9±4.8 vs. 0.1±5.6, p<0.007) and was similar to baseline at 5 hours (TNFα: 1.6±0.5 vs. 1.3±1.2, p=0.80; IL-6: 0.3±1.2 vs. 0.6±0.5, p=0.70). Saltsalate treatment also reduced basal T levels (67.6±34.6 ng/dl, p<0.003) and the HCG-stimulated androgen response to HCG administration in lean insulin-sensitive women with polycystic ovary syndrome. Fertil Steril 2015; 104 (2 Suppl):21.

Supported by: NIH grant R01 DK107605 to F.G.

CHANGES IN OVARIAN MORPHOLOGY ASSOCIATED WITH BARIATRIC SURGERY AMONG WOMEN WITH POLYCYSTIC OVARY SYNDROME (PCOS). J. Christ T. Falcone. Cleveland Clinic, Cleveland, OH.

OBJECTIVE: To assess the impact of bariatric surgery on ovarian morphology among women with PCOS.

DESIGN: A retrospective chart review was completed.

MATERIALS AND METHODS: Records of all women who had presented to the Cleveland Clinic Foundation for bariatric surgery from...
2009 to 2015 were reviewed and those patients with a diagnosis of PCOS were identified. Medical records were reviewed for pre- and postoperative total testosterone, free testosterone, dehydroepiandrostro- stenedione (A) (lean: 507 ± 343 ng/dL), area under the curve (AUC) for testosterone (T) (lean: 6324 ± 2971 pg/mL), hemoglobin A1C, fasting glucose, weight, body mass index (BMI), and ovarian volume. Ovarian morphology was assessed using ovarian cross-sectional measurements reported in patients’ medical records. Ovarian volume was calculated using the formula (π/6) X(transverse diameter)X(anteposterior diameter)X(longitudinal diameter) and averaged between the right and left ovary for each patient. Pre- and postoperative values were compared using Wilcoxon rank sum test.

RESULTS: A total of 930 women underwent bariatric surgery from 2009 to 2015, of which 33 had a diagnosis of PCOS. Postoperative weight (kg) and BMI (kg/m²) were significantly reduced compared to preoperative values (95.7 ± 23.2 vs. 126.3 ± 37.6, 37.4 ± 10.3 vs. 47.5 ± 13.9, respectively p<0.0001). Postoperative ovarian volume (mL) was significantly less than preoperative values (7.7 ± 4.8 vs. 14.0 ± 9.8, p=0.036). Total testosterone (ng/dL), free testosterone (pg/mL), and DHEAS (ug/dL) trended towards a postoperative decrease compared to preoperative values, but did not reach statistical significance (38.4 ± 24.1 vs. 56.1 ± 25.6, 4.5 ± 4.4 vs. 10.3 ± 5.8, 132.9 ± 79.4 vs. 196.3 ± 114.3, respectively).

CONCLUSIONS: Bariatric surgery is an effective method of weight loss among women with PCOS. Postoperatively, women with PCOS have decreased ovarian volume and have a trend towards a decline in markers of androgen excess. These results suggest that weight loss associated with bariatric surgery may result in resolution of the key characteristics associated with PCOS including androgen excess and ovarian enlargement.

O-83 Monday, October 17, 2016 12:15 PM
INCREASED LIPID-STIMULATED INTERLEUKIN-6 (IL-6) RELEASE FROM MONONUCLEAR CELLS (MNC) IS LINKED TO EXCESS OVARIAN ANDROGEN SECRETION IN POLYCYSTIC OVARY SYNDROME (PCOS). O. A. Abdelhadi,* R. V. Considine,* A. J. Acton,* F. Gonzalez,* X(transverse diameter)X(anteposterior diameter)X(longitudinal diameter) and averaged between the right and left ovary for each patient. Pre- and postoperative values were compared using Wilcoxon rank sum test.

RESULTS: A total of 930 women underwent bariatric surgery from 2009 to 2015, of which 33 had a diagnosis of PCOS. Postoperative weight (kg) and BMI (kg/m²) were significantly reduced compared to preoperative values (95.7 ± 23.2 vs. 126.3 ± 37.6, 37.4 ± 10.3 vs. 47.5 ± 13.9, respectively p<0.0001). Postoperative ovarian volume (mL) was significantly less than preoperative values (7.7 ± 4.8 vs. 14.0 ± 9.8, p=0.036). Total testosterone (ng/dL), free testosterone (pg/mL), and DHEAS (ug/dL) trended towards a postoperative decrease compared to preoperative values, but did not reach statistical significance (38.4 ± 24.1 vs. 56.1 ± 25.6, 4.5 ± 4.4 vs. 10.3 ± 5.8, 132.9 ± 79.4 vs. 196.3 ± 114.3, respectively).

CONCLUSIONS: Bariatric surgery is an effective method of weight loss among women with PCOS. Postoperatively, women with PCOS have decreased ovarian volume and have a trend towards a decline in markers of androgen excess. These results suggest that weight loss associated with bariatric surgery may result in resolution of the key characteristics associated with PCOS including androgen excess and ovarian enlargement.

O-84 Monday, October 17, 2016 12:30 PM
THE MORPHOKINETIC CHARACTERISTICS OF EMBRYOS DERIVED FROM PCOS PATIENTS. N. Aono,* R. Obata,* S. Maekawa,* N. Oka,* T. Takeuchi,* H. Igarashi,* K. Kyono,* Kyono ART Clinic Takenak, Minatoku, Tokyo, Japan; *Kyono ART Clinic, Sendai, Miyagi, Japan.

OBJECTIVE: Polycystic ovary syndrome (PCOS) patients are extremely sensitive to stimulation with exogenous gonadotropins and are at an increased risk of developing ovarian hyperstimulation syndrome (OHSS) during ART treatment. Such patients are therefore likely to greatly benefit from using the in vitro maturation (IVM) technique. However, IVM oocytes have been found to exhibit lower viability and developmental potential than in vitro matured oocytes. The objective of this study was to compare morphokinetics of early stage embryos from IVM oocytes to that of mature oocytes obtained after controlled ovarian stimulation (COS) in PCOS patients, while mature oocytes from stimulated non-PCOS ovaries served as a control.

DESIGN: Retrospective study.

MATERIALS AND METHODS: From Jan. 2014 to Dec. 2015, zygotes were divided into three groups according to oocyte maturity and patient characteristics. A total of 66 zygotes derived from 15 IVM cycles in PCOS patients (Group A), 33 zygotes from 8 COS cycles in PCOS (Group B), and 43 zygotes from 10 COS cycles in non-PCOS patients (Group C) were involved. Following ICSI insemination, morphokinetic parameters of each zygote were recorded and evaluated by a time-lapse monitoring system (EmbryoScope™).

RESULTS: In Group B, embryos developing to the 3-cell and 4-cell stage were significantly slower than those in Group C (39.2 ± 6.6 hours vs. 35.1 ± 67.2 hours, 43.2 ± 7.5 hours vs. 39.5 ± 6.7 hours) (P<0.05). The time for the initiation of the compaction and the time to the morula stage were remarkably shorter in Group A (92.8 ± 7.4 hours, 104.3 ± 9.5 hours) than in Group C (102.6 ± 5.7 hours, 114.4 ± 7.0 hours) (P<0.05). CONCLUSIONS: Embryos derived from PCOS patients, regardless of the maturity at oocyte retrieval, showed faster development from the initiation of compaction onwards in comparison to non-PCOS patients. These results suggest that the state of PCOS may cause changes in morphokinetic behavior of early embryos.

OUTCOME PREDICTORS: ART I

O-85 Monday, October 17, 2016 11:15 AM
SERUM ANTI-MULLERIAN HORMONE (AMH) LEVELS INDEPENDENTLY PREDICT MISCARRIAGE RATES FOLLOWING IN VITRO FERTILIZATION-EMBRYO TRANSFER. B. Tarasconi,* T. Tadores,* E. Adda-Hertzog,* S. Belfoc,* J. Ayoubi,* R. Fanchin,* Reproductive Medicine, Hospital Antoine Beclere-University of Paris Sud, Chatillon, France; *Eylau-Unilabs Laboratory, Paris, France; *Ob-Gyn, Hospital Foch-University of Paris Ouest, Suresnes, France.

OBJECTIVE: AMH is a confirmed quantitative marker of ovarian follicles. Yet, doubts persist on its possible relationship with oocyte competence. Whereas, for some authors, serum AMH levels are an age-independent marker of pregnancy and live birth rates after IVF-ET, for others they are not. These conflicting views may result from the confounding role of the intensity of the ovarian response to COH, which is stronger in patients with increased AMH levels. In addition, scarce data is available on the possible link between AMH and miscarriage rates in IVF-ET, an indirect marker of
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MATERNL AND NEONATAL OUTCOMES IN WOMEN OF ADVANCED MATERNAL AGE (AMA) UNDERGOING TWO IN VITRO FERTILIZATION (IVF) SINGLETON PREGNANCIES, AS COMPARED TO ONE IVF TWIN PREGNANCY. S. Amran,a P. Ghosh,a D. E. Reichman,b Z. Rosenwaks,c S. E. Gelber,b Obstetrics and Gynecology, New York Presbyterian-Weill Cornell Medicine, New York, NY; cCenter for Reproductive Medicine and Infertility, Weill Cornell Medical College, New York, NY.

OBJECTIVE: This study seeks to compare maternal and neonatal outcomes for women of AMA undergoing two IVF pregnancies resulting in singleton gestations versus women with one IVF pregnancy resulting in a twin gestation.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Patients 37 years old and greater at the time of oocyte retrieval, who had either two consecutive singleton gestations from IVF (n = 45) or one twin gestation from IVF (n = 175), were included. Both IVF and delivery at our center were required. Maternal and neonatal outcomes were obtained by chart review. Primary maternal outcomes included antepartum admission, length of hospital stay, preeclampsia, PPROM, and cesarean section. Primary neonatal outcomes included low birth weight (LBW), very low birth weight (VLBW), intrauterine growth restriction (IUGR), neonatal intensive care unit (NICU) admission, length of NICU hospital stay, and severe neonatal morbidity including retinopathy of prematurity (ROP), intraventricular hemorrhage (IVH), sepsis, and bronchopulmonary dysplasia (BPD). For singleton pregnancies, outcomes were counted as having occurred if present in one or both pregnancies. Continuous outcomes were log-transformed. Bivariate tests were performed using t-tests for continuous variables, and chi-square type or Fisher’s exact test for categorical variables. Outcomes with p-values <0.10 were tested in regression frameworks to obtain odds ratios.

RESULTS: There were significantly increased rates of antepartum admission (OR 5.22, 95% CI 1.54-17.66), PPROM (OR 8.92, 95% CI 1.18-67.39), cesarean section (OR 10.08, 95% CI 4.58-22.47), LBW (OR 24.52, 95% CI 8.35-72.02), and NICU admission (OR 5.12, 95% CI 2.17-12.10) in the twin group as compared to the singleton group. Length of neonatal hospital stay and length of NICU stay were also longer in the twin group (OR 1.14, 95% CI 1.04-1.24) and OR 1.28, 95% CI 1.09-1.49) in the twin group as compared to the singleton group. Length of neonatal hospital stay and length of NICU stay were also longer in the twin group (OR 1.14, 95% CI 1.04-1.24) and OR 1.28, 95% CI 1.09-1.49) in the twin group as compared to the singleton group. Length of neonatal hospital stay and length of NICU stay were also longer in the twin group (OR 1.14, 95% CI 1.04-1.24) and OR 1.28, 95% CI 1.09-1.49) in the twin group as compared to the singleton group. Length of neonatal hospital stay and length of NICU stay were also longer in the twin group (OR 1.14, 95% CI 1.04-1.24) and OR 1.28, 95% CI 1.09-1.49) in the twin group as compared to the singleton group.

CONCLUSIONS: In women of AMA, undergoing two subsequent IVF singleton pregnancies is associated with more severe neonatal morbidity including severe morbidity and neonatal mortality were relatively rare in the twin group. Patients with the goal of having two children should be counseled about the neonatal and maternal risks associated with twin pregnancies as compared to two consecutive singleton pregnancies, prior to making decisions about how many embryos to transfer.

O-88 Monday, October 17, 2016 12:00 PM

RETRIEVAL OF LARGER OOCYTE COHORTS MAXIMIZES IN VITRO FERTILIZATION (IVF) BIRTH RATES PER CYCLE. M. T. Connell,a K. S. Richter,a M. J. Tucker,a J. Graham,a A. DeCherny,a M. J. Hill,a M. Levy,a NH, Bethesda, MD; aShady Grove Fertility Reproductive Science Center, Rockville, MD.

OBJECTIVE: To determine if retrieval of larger cohorts of oocytes adversely affects IVF treatment outcomes.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: A retrospective cohort study of all autologous IVF cycles among patients under 35 years from 2009-2014 was performed. Excluded from the analysis were patients with a diagnosis of diminished ovarian reserve, uterine factor, chromosomal abnormalities, or cancer, patients being treated for fertility preservation, use of preimplantation genetic screening, oocyte or embryo cryopreservation prior to the blastocyst stage, or incomplete insemination of the retrieved cohort. All embryo...
cryopreservation was performed using vitrification protocols at the expanded blastocyst stage (minimum ICM and trophoderm grades of BB) on day 5 or 6 after oocyte retrieval. Potential births from the transfer of all vitrified blastocyst were estimated based on our observed birth rate (35%) per vitrified/warmed blastocyst among autologous patients in this age range.

RESULTS: At total of 8,573 cycles were evaluated. Cycles with retrieval of 1-4 oocytes or 5-9 oocytes were much less likely to have viable embryos available for transfer or cryopreservation, had much lower live birth rates per fresh embryo transfer cycle, and had many fewer children per freshly transferred embryo compared to larger retrieved oocyte cohorts. The numbers of surplus blastocysts that were cryopreserved per fresh embryo transfer cycle, and the estimated total number of live born children resulting from the transfer of all fresh and cryopreserved embryos per oocyte retrieval cycle, both increased substantially with each incremental increase in the size of the retrieved oocyte cohort.

CONCLUSIONS: Previous data has suggested there may be lower mean # of embryos harvested (7.2 ± 4.8) or number of embryo transferred (3.4 ± 1.9). The overall pregnancy rate per transfer was 17.2% (117/680), of which 82.1% (96/117) ended in a pregnancy loss. Although there was no difference in IVF outcomes between age groups, an overall clinical pregnancy rate of 8.8% (60/680) and delivery rate of 3.1% (21/680) were found. 20/21 live births were in the 45 year old group and one live birth was found in women age 46. There was no live births in any patient with ≤ 4 oocytes retrieved.

CONCLUSIONS: IVF may be a reasonable option for women age 45 with an acceptable ovarian reserve, however with very low prognosis. Patients with ≤ 4 follicles should be counseled appropriately that based on these results positive pregnancy seems highly unlikely.

OBJECTIVE: To determine IVF outcomes in women 45 years and older using autologous oocytes.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: 1,077 fresh IVF cycles in women 45 years and older were reviewed from 1/1995-6/2015. PGD/S, natural IVF, and donor egg cycles were excluded. Patient demographics, IVF cycle characteristics, total pregnancy loss, clinical pregnancy and live birth rates were analyzed for the different age groups (age 45 n = 773, age 46 n = 221, age 47 n=57, age 48 n=22, age 49 n=5). Fisher exact t test, Kruskal-Walis, and Chi-square were used to evaluate the data and p < 0.05 was considered significant.

RESULTS: Mean age of patients in the study cohort was 45.4 ± 0.72. 11.7% of patients did not start due to an elevated FSH or cyst and 28.5% of patients were canceled prior to oocyte retrieval. There was no difference in demographic characteristics between age groups as well as no difference in mean # of oocytes harvested (7.2 ± 4.8) or number of embryo transferred (3.4 ± 1.9). The overall pregnancy rate per transfer was 17.2% (117/680), of which 82.1% (96/117) ended in a pregnancy loss. Although there was no difference in IVF outcomes between age groups, an overall clinical pregnancy rate of 8.8% (60/680) and delivery rate of 3.1% (21/680) were found. 20/21 live births were in the 45 year old group and one live birth was found in women age 46. There was no live births in any patient with ≤ 4 oocytes retrieved.

CONCLUSIONS: IVF may be a reasonable option for women age 45 with an acceptable ovarian reserve, however with very low prognosis. Patients with ≤ 4 follicles should be counseled appropriately that based on these results positive pregnancy seems highly unlikely.

O-90 Monday, October 17, 2016 12:30 PM

DOES A WORSENING IN ENDOMETRIAL STRIPE PATTERN CORRELATE WITH INCREASING PROGESTERONE LEVELS IN IVF CYCLES? M. W. Healy, H. Wolfe, B. Yauger, R. Chason, N. Banks, C. M. Owen, A. DeCherney, J. Cookmy, M. J. Hill. National Institutes of Health- NICHD, Bethesda, MD; Department of OB/GYN, Walter Reed National Military Medical Center, Bethesda, MD.
OBJECTIVE: To longitudinally assess the relationship of serum progesterone (P) and endometrial stripe (EMS) pattern during IVF stimulation and to determine if EMS pattern could predict elevated P.

RESULTS: The rate of appearance of each traced AA was calculated as an EMS pattern that worsened in the last 2 days of stimulation, but there was no association with a rise in P (<0.14) or a high absolute P value (P=0.33). There was no association with final EMS pattern and serum P values on the last day of stimulation (A pattern 1.03 ng/ml, B pattern 1.06, and C pattern 1.12, P=0.64). EMS pattern and thickness were both associated with pregnancy. Rates for EMS thickness were 25%, 65%, 51%, and 41% (P=0.03). Pregnancy rates for EMS thickness were 65%, 10mm. There was no association between EMS pattern and thickness of the endometrium and the measurement of serum P to assess for endometrial advancement.

These papers are candidates for the ASRM Scientific Congress Prize Paper Awards. Six additional candidates will be presented during the Prize Paper Candidates session on Monday.

SCIENTIFIC CONGRESS PRIZE PAPER SESSION 2

O-91 Tuesday, October 18, 2016 11:15 AM


OBJECTIVE: To investigate the effects of isocaloric PPR with and without folate supplementation on AA kinetics, glutathione (GSH) production, and mitochondrial ultrastructure (MU) and function in the rat cumulus oocyte complex (COC).

RESULTS: Wistar rats (n=24) were assigned to 3 isocaloric dietary groups (n=8 each) for 40 days; control (C, 20% protein), LP (6% protein) and LPF (6% protein + 5mg/kg folate). 15U of pregnant mare serum gonadotropin was administered on day 34. The LPF group was paralleled by a decline of fasting insulin (by 31.8%, P<0.007) and increase of the Insulin Sensitivity Index (by 66.3%, P<0.04). In a similar fashion, DHEAS significantly declined in the Resveratrol group (by 23.1%, P<0.002). Improvement of hyperandrogenemia in the Resveratrol group was paralleled by a decline of fasting insulin (by 31.8%, P<0.007) and increase of the Insulin Sensitivity Index (by 66.3%, P<0.04). However, resveratrol had no significant effect on BMI, ovarian theca-interstitial cells, testosterone, estradiol, insulin, androstenedione, androstenedione, lipid profile, or markers of inflammation and endothelial function.

CONCLUSIONS: This study, to our knowledge, is the first clinical trial evaluating the effects of resveratrol on PCOS. It is apparent that resveratrol significantly reduces serum levels of testosterone and DHEAS, suggesting an
effect on ovarian as well as adrenal androgen production. These effects may be, at least in part, related to an improvement of insulin sensitivity and a decline of insulin level.

Supported by: Intramural Funding.

O-93 Tuesday, October 18, 2016 11:45 AM

GENOME-WIDE DNA METHYLATION CHANGES IN MOUSE ZYGOTES ASSOCIATED WITH SUPEROVULATION. B. Yu,1,2  
1OBGYN, University of Washington, Seattle, WA; 2Albert Einstein College of Medicine, Bronx, NY.

OBJECTIVE: Several animal and human studies have shown Assisted Reproductive Technologies (ART) procedures can result in abnormal methylation of some imprinted genes in early embryos. However, it is not known what genome-wide effect these ART procedures may have, and which ART manipulations cause these changes. The objective of this study is to identify DNA methylation changes in pre-implantation mouse embryos after ovarian hyperstimulation.

DESIGN: Basic research using animal model.

MATERIALS AND METHODS: Using Whole Genome Bisulfite Sequencing (WGBS) method, we compared DNA methylomes in mouse pre-implantation embryos from superovulated and negative control mice (n=3 in each group). Superovulated mice were injected with 10IU of PMSG to stimulate multiple oocyte growth, followed by 10IU of hCG 48 hours later to induce ovulation. The negative control (or natural ovarian hyperstimulation) study group. Both groups were mated with fertile male mice overnight, and zygotes were harvested the next morning. All zygotes were pooled from each female mouse. WGBS was performed according to our established protocol and libraries were sequenced on HiSeq-2500 with 150-bp single-end reads.

RESULTS: Significant differences in CpG methylation levels were observed in zygotes from superovulation group compared to natural mating group, with 31223 differentially methylated regions (600bp in size) (p<10^-6) that distributed throughout the genome. Promoters and/or gene bodies of 2262 genes were located in these DMRs. Among the differentially methylated genes, some examples such as Igf2r, Cagf2, Dmnt3a may be of interests for further research, as they indicate possible mechanistic links between ART and potential DNA methylome establishment errors.

CONCLUSIONS: Our results demonstrated superovulation, which is an essential part of Assisted Reproductive Technologies, may result in significant genome-wide DNA methylation changes in mouse pre-implantation embryos. These preliminary findings will need to be confirmed in future studies.

References:

_SUPPORTED by: American Society for Reproductive Medicine (ASRM) research grant; Reproductive Scientist Development Program; Howard and Georgeanna Jones Foundation for Reproductive Medicine; American College of Obstetrics and Gynecology.

O-94 Tuesday, October 18, 2016 12:00 PM

CAN WE EXPECT TO IMPROVE AGE AT MENOPAUSE PREDICTIONS WITH REPEATED AMH MEASUREMENTS? A. C. de Kat,1 Y. T. van der Schouw,1 R. Eijkemans,2 M. Verschuren,3 F. J. Broekmans,1 "Reproductive Medicine and Gynecology, University Medical Center Utrecht, Utrecht, Netherlands; 2Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, Netherlands; 3National Institute for Public Health and the Environment, Bilthoven, Netherlands.

OBJECTIVE: Anti-Müllerian hormone (AMH) levels are considered to be an indicator of ovarian aging and thus time to menopause, but to date this is mostly based on cross-sectional research in selected and small populations. We previously unraveled longitudinal decline trajectories of AMH with age. Here, we aimed to relate longitudinal anti-Müllerian hormone (AMH) levels to time to menopause in the general population, in order to lay the groundwork for dynamic age at menopause prediction with multiple AMH measurements.

DESIGN: This study included 1,857 women enrolled in the prospective, population-based Doetinchem Cohort Study, with a known age at natural menopause (ANM). All women completed at least 1 of 5 consecutive visits with 5-year intervals between 1987 and 2010, resulting in a maximum follow-up time of 20 years. At each visit, data collection included a questionnaire, anthropometric measurements and blood withdrawal.

MATERIALS AND METHODS: AMH was measured with the picoAMH assay (AnshLabs) in a total of 7,666 plasma samples. Time to menopause was modeled with the use of mixed model analyses, taking non-linear changes of AMH with age into account for each individual, and correcting for confounders. The association of age at menopause with AMH levels at baseline (t0), and the rate of AMH decline between t0 and t1 were furthermore compared.

RESULTS: The mean age at baseline was 44.5 (range 20-60) years and on average, women had an ANM of 50.3 (range 17-65) years. At any given age, a 19% lower AMH level was associated with being 1 year closer to menopause on average (proportional difference 0.81, 95% CI 0.79-0.83). AMH levels at t0 and t1, combined with the rate of decline between t0-t1, were simultaneously associated with age at menopause in women who became postmenopausal between 45-55 years (p<0.001 for all three predictors).

CONCLUSIONS: This longitudinal study confirms the overall association of AMH levels with time to menopause, while taking into account individual AMH changes with time. These results furthermore suggest that repeated AMH measurements might improve the prediction of age at menopause for a selected group of women.

O-95 Tuesday, October 18, 2016 12:15 PM

OOCYTES WITH IMPAIRED MEIOTIC MATURATION CONTAIN AN INCREASED LOAD OF MUTATED MITOCHONDRIAL DNA. J. Kolins,1 M. Seth-Smith,1 D. H. McCulloh,1 Y. G. Kramer,1 J. Grifo,2 D. L. Keefe,3 "Division of Reproductive Endocrine/Infertility, NYU, New York, NY; 2NYU, New York, NY; 3Obstetrics and Gynecology, New York University Fertility Center, New York, NY; 4NYU Fertility Center, New York, NY; 5NYU Langone Medical Center, NY, NY; 6ObGyn, New York University Langone Medical Center, New York, NY.

OBJECTIVE: Meiotic competence is a major goal of controlled ovarian stimulation. But do factors intrinsic to the oocyte also contribute to oocyte maturation? Deletions in mitochondrial dna (mtDNA) accumulate in long lived, post mitotic tissues, and are found in human oocytes, so we sought to determine whether mtDNA deletion load, measured by a novel PCR assay- deletion ratio- affects meiotic maturation of human oocytes.

DESIGN: Translational science research.

MATERIALS AND METHODS: IRB approval was obtained for use of human discard material for the purpose of genetic analysis. A total of 146 oocytes (66 patient cycles) were obtained from egg freeze and in vitro fertilization patients during 2015 at our center. Discarded GV oocytes were obtained for our research protocol. Oocytes were obtained 2 hours post retrieval and cultured in a time lapse incubator for 48 hours. Oocytes remained in G2 wash culture media. Images were captured every 5 minutes and timing of germinal vesicle break down and polar body extrusion ascertained. After 48 hours of culture oocytes were frozen and stored for future analysis. A real time PCR assay was developed to measure both mitochondrial copy number and proportion of mtDNA harboring the 4977 base pair common deletion. The mtDNA deletion ratio was then calculated. ANOVA was used to compare the absolute copy number and deletion ratio of oocytes arrested at GV or M1 to those that progressed to M2 in culture. Logistic regression of 14
clinical parameters as well as the deletion ratio were used to confirm the findings.

RESULTS: 68.8% of oocytes matured to M1 and 51% reached M2. Mean deletion ratios in GV, M1, and M2 oocytes were 28%, 31.5% and 19.8% respectively. Oocytes arrested at M1 had higher deletion ratios than those which progressed to M2 (31.5% M1 v 19.8% M2; p-value < 0.0003). Logistic regression models incorporated the following parameters- day 2/3 fsb, day2/3 E2, total gonadotropins, number of oocytes retrieved, %GV, %M1, %M2, % atretic, total copy number, total ND4, and deletion ratio. Number of oocytes retrieved was negatively correlated with maturation in vitro as was the deletion ratio. These factors had a synergistic effect in the model. MDNA copy number did not differ significantly different among GV, M1 and M2 stage oocytes.

CONCLUSIONS: The mtDNA deletion ratio has been described in other long lived, post mitotic tissues, e.g. cardiac, as a marker for aging. This is the first report of an association between the mitochondrial deletion ratio and maturation in vitro of human oocytes. Oocytes with impaired meiotic maturation contain an increased load of mutated mtDNA. Future studies should establish whether mitochondrial deletion ratio, like mtDNA copy number, may predict competence at other stages of development.

O-96 Tuesday, October 18, 2016 12:30 PM
LOW LEVEL MOSAICISM: INCIDENCE AND IMPLICATIONS ON CLINICAL PREGNANCIES. D. A. Kelk,a J. Lo,a J. Martin,b M. Hughes. aYale Fertility Center, Yale University, Ob/Gyn, New Haven, CT, bOb/GYN Dept, Yale University, REI Section, Yale REI, New Haven, CT.

OBJECTIVE: Preimplantation genetic screening (PGS) has been shown to decrease miscarriage rates and improve live birth outcomes particularly for older women where rates of aneuploidy are highest (1). As methods for PGS testing have evolved, so has awareness of embryonic mosaicism, the presence of two or more chromosomally distinct cell lines. The clinical significance of mosaicism is not well understood but mosaic embryos have resulted in healthy live births (2). However some mosaic embryos may be diagnosed as aneuploid and potentially be discarded despite an unclear potential viability. Mosaicism is detected on the single cell level. The main concern with mosaic embryos is that these may be cultured to blastocyst, transferred and result in a live birth with a condition or abnormality associated with mosaic cell line.

METHODS: We evaluated routine PGS of blastocysts from January 2013 to January 2016 at Yale University Fertility Center. Business as usual methodology was used. For each patient, blastocysts were cultured in utero for 5 days and biopsied for PGS. Mosaicism was detected by single cell next generation sequencing (NGS) on each cell. Mosaicism was defined as a genetic variant in >1% of the cells.

RESULTS: Of the freeze embryo cycles, 35% had blastocysts biopsied. Of these, 26% were diagnosed as mosaic. The detection rate was higher in blastocysts derived from patients over the age of 35 and in cases that were failed IVF attempts. Of the mosaic embryos transferred, 36% exhibited levels of mosaicism ranging from 15-45%. Due to a double embryo transfer of 1 mosaic and 1 non-mosaic embryo, implantation rates could be confirmed for 34 of the embryos transferred. Mosaic embryos had a 50% implantation rate compared to 64% for those with no mosaicism observed. This difference was not statistically significant.

CONCLUSIONS: Embryos with low level mosaicism exhibited respectable implantation (50%) and clinical pregnancy (54%) rates. Although these implantation and pregnancy rates are lower than those for embryos with no mosaicism (64% and 65% respectively), the difference was not statistically significant. Dividing the euploid embryos into two groups (with and without mosaicism observed) could potentially allow for enhanced selection of embryos with the greatest reproductive potential. Further studies in this area will certainly elucidate better understanding of the clinical significance of embryo mosaicism.


ACCESS TO CARE 2
OBJECTIVE: To understand disparities in In-Vitro Fertilization (IVF) patient-reported outcomes according to a patient’s household income (HHI), occupation at the time of treatment, and level of educational attainment.

DESIGN: A retrospective analysis of 1,123 survey responses collected from IVF patients reported on FertilityIQ.com between July, 2015 and November, 2015. Each patient attested to the accuracy and truthfulness of their information. The majority of patients were able to provide a document to investigators demonstrating they had been treated in the United States within the previous 10 years.

MATERIALS AND METHODS: All data was aggregated at FertilityIQ.com, stored in Qualtics survey software and analyzed using R statistical software (3.2.2). The chi-squared test was used for multi-variate regression at a 95% Confidence Interval (CI). All observations controlled for variables in income, age, level of educational attainment, race and geographical distribution.

RESULTS: Patients who reported earning $99,000 or more in annual household income (HHI) recorded an 80% higher likelihood of success than patients who reported earning less than $99,000 HHI (CI 95%, P = .03). Patients earning $99,000 or greater of HHI recorded undergoing 21% more treatment cycles.

Patients who reported their occupation as “teacher” during the time of treatment recorded a six-fold higher likelihood of success, after controlling for variables like age, income, race and geographical location (CI 95%, P < .01). Patients who reported working in fields categorized as “Sales, Marketing and Public Relations” recorded a two-fold higher rate of success (CI 95% P < .04). Meantime patients working in “ traditionally-male” dominated fields like investment banking or engineering recorded a 60% lower likelihood of success, but results did not meet statistical significance (CI 95%, P = .15) likely due to insufficient study power.

Patients attaining increasingly higher levels of education recorded higher rates of treatment success, with a cessation in outcome disparity at, or beyond, the bachelor’s degree level.

CONCLUSIONS: Patients undergoing IVF treatment in the United States may experience differing levels of success correlated to their income or ability to afford additional courses of treatments. Similarly, disparities in outcomes may also correlate to a patient’s occupation, after controlling for variables like income, age, race, and geography. Patients working in the fields of education, sales, marketing and public relations may benefit in ways patients employed in other categories do not. A patient’s level of education may well correlate with an increased likelihood of treatment success, yet such a correlation ceases to exist at or beyond the attainment of a bachelor’s degree.

O-99 Tuesday, October 18, 2016 11:45 AM
THE IMPORTANCE OF PRAYER AND RELIGIOUS LEADERS TO US. WOMEN FACING INFERTILITY. S. Kim, E. Chan, S. C. Collins. Department of Obstetrics, Gynecology, and Reproductive Sciences, Yale University School of Medicine, New Haven, CT; Sociology, Yale University, New Haven, CT.

OBJECTIVE: Religion, spirituality, and prayer are influential to many American women, providing coping mechanisms for stressful life events and guidance on complex topics. Our objective was to determine how important prayer and the counsel of religious leaders are to US women facing infertility and to identify demographic predictors of choosing these support mechanisms.

DESIGN: Cross-sectional study.

O-100 Tuesday, October 18, 2016 12:00 PM
ART OF INFERTILITY: CURATING PATIENT-CENTERED PERSPECTIVES VIA AN ARTIFACT ORAL HISTORY METHODOLOGY. E. Walker, M. Novotny. The ART of Infertility, Jackson, MI.

OBJECTIVE: The objective of this presentation is to respond to the question posed by Atkinson et al’s (2014): Is there a radical potential for the medical humanities? The authors in this article cited potential in the areas of art activism as a heuristic to disrupt and shift current limitations in medical definitions and practices. The authors of this presentation agree with Atkinson et al’s view that art has potential for the medical humanities. Specifically, we expand this within the context of infertility - providing an overview of how we, as the ART of Infertility, utilize arts-based workshops and artifact-based interview methodologies to construct an infertility oral history project.

DESIGN: The ART of Infertility travels the U.S. hosting arts-based workshops. Infertile men and women are invited to attend these workshops where they bring in objects related to their infertility. These objects include: syringes for ART treatment, pill bottles, medical statements pertaining to their infertility, and failed pregnancy tests. Participants then co-opt these objects to make new pieces of art that incorporate the infertility artifact. We then conduct interviews using artifact-based inquiry practices. This methodology asks individuals to narrate an experience they had pertaining to their infertility through their artifact.

To date, we have an n= 100.

MATERIALS AND METHODS: We use oral history methods to collect life stories pertaining to infertility. This project is IRB protected.

RESULTS: We at the ART of Infertility seek to collect a variety of perspectives and narratives pertaining to infertility. As such, we have collected stories from trans-youth making the decision to preserve their eggs for fertility treatment in the future, LGBTQ individuals who have had to use gestational surrogates, male factor perspectives of infertility, individuals who have
sought out medical tourism in the Czech Republic, as well as the perspectives of single parents by choice.

This presentation will highlight the diversity of these stories and share clips of participants detailing how their artifacts speak to their experiences.

CONCLUSIONS: The intention of sharing this with the ASRM community is to facilitate more cross-talk amongst patients and physicians. Our hope is that the use of artifact-based methods may be useful to facilitate and cultivate relationships with patients to improve health-care decision making in reproductive medicine, particularly related to fertility treatment. As such, we as the speakers will articulate the need for more arts-based medical approaches to reproductive medicine. We believe this to be essential to improving access to care, as well as increasing the health literacy around the topic of fertility.

References:

O-101 Tuesday, October 18, 2016 12:15 PM

LIMITATIONS ON THE COMPENSATION OF GAMETE DONORS: A SURVEY OF PUBLIC SUPPORT AND OPINION. M. S. Lee, L. V. Farland, S. A. Misserm, E. S. Ginsburg. Dept of Obstetrics & Gynecology, Brigham & Women’s Hospital and Harvard Medical School, Boston, MA; Dept of Epidemiology, Harvard Chan School, Boston, MA, Boston, MA.

OBJECTIVE: ASRM recommendations regarding limitations on gamete donor compensation have been controversial. Our aim was to determine public opinion regarding gamete donor compensation, and if support varies by demographic factors.

DESIGN: Cross-sectional web-based survey.

MATERIALS AND METHODS: A nationally representative sample of adult U.S. residents completed an online questionnaire in February 2016. Responders who support limitations on gamete donor compensation were compared with those who were neutral or in opposition using log binomial regression, adjusted a priori for age and gender, to calculate relative risk ratios (RR) and 95% confidence intervals (CI).

RESULTS: Of the 1,574 respondents, 1,427 completed the survey. 51(4%) disagreed with use of IVF for any indication. 232(16%) felt egg and/or sperm donation are unacceptable practices. Of the remaining 1,185 respondents, 953(80%) were in support of and 41(4%) were against paying sperm donors; 1,063(90%) were in support of and 24(2%) were against paying egg donors; the remainder were neutral.

559(47%) supported placing a limit on sperm donor and 544(46%) on egg donor compensation. Individuals who self-identified as Republicans compared to Democrats, or had a personal knowledge of someone who had used ART, were more likely to support a limitation on both egg and sperm donation (Table). Divorced compared to married respondents were less likely to support a limit on both egg and sperm donor compensation. Men were less likely than women to support a limit on sperm donor compensation only. Participants with a yearly income of >$60,000, those with a college degree, those with a personal knowledge of someone with infertility, and Catholics compared to Protestants were more likely to support limits on egg donor compensation only. Participants without biological children and those who identified as sexual minorities were less likely to support limitations on egg donor compensation only. Age and race were not associated with support.

CONCLUSIONS: The vast majority of respondents in a nationally representative sample support compensation for sperm and egg donors. Less than half of the respondents support limitations on gamete donor compensation. Supported by: Funded by a Dept of ObGyn Expanding the Boundaries Grant.

O-102 Tuesday, October 18, 2016 12:30 PM

COMPASSIONATE CORPS: CREATING ACCESS TO IVF MEDICATIONS FOR INJURED VETERANS. J. A. Drum. EMD Serono, Morrisville, NC.

OBJECTIVE: Implement program to assist wounded Veterans with IVF medications for family building where no coverage or assistance existed.

DESIGN: More than 2,000 people who have served in the military have been diagnosed with infertility after suffering from major injuries. However, when active members of the U.S. military and U.S. veterans injured during service are faced with infertility, they become an underserved population. According to law, the Department of Veterans Affairs
is prohibited from covering in vitro fertilization treatments for injured veterans, therefore creating a gap in coverage for their fertility benefits and significant cost barriers. In July of 2014 Compassionate Corps launched to raise awareness of fertility coverage gaps and to help alleviate these cost barriers by developing a program tailored for injured U.S. veterans.

MATERIALS AND METHODS: Compassionate Corps provides IVF stimulation medications at no charge for up to 2 cycles for qualifying applicants. Compassionate Corps is the first patient assistance program to completely eliminate the cost [AD1] of [AD2] fertility medications (Gonal-F, Cetrodix, & Ovidrel) for eligible U.S. Veterans who are infertile due to a service-related injury. • Patient Attested • Patient confirms that he/she/spouse is a medically retired member of the military • Physician confirms that the patient has no insurance coverage for the infertility treatments or related medications needed • Physician Attested • Physician confirms that the patient has service-related injuries that have caused infertility • Physician confirms that IUl/OIl would be suboptimal or impossible • Physician submits a valid prescription for an eligible drug • Medications Provided • Program is valid for a maximum of 2 cycles per calendar year • Medications are shipped to IVF clinic.

RESULTS: To date, more than 80 U.S. veterans have attained access to medications for in vitro fertilization and advanced reproductive technology through the Compassionate Corps program.

CONCLUSIONS: The Compassionate Corps program was designed and implemented to create access for injured U.S. Veterans who required IVF due to injuries sustained while actively serving in the military. The coverage gap that currently exists creates tremendous financial burdens and barriers to treatment for this very deserving population. The 80 approved applicants were given a chance to build a family because of Compassionate Corps when no other program existed and no legislation had been mandated to protect our heroes who bravely served their country.

REPRODUCTIVE SURGERY 2

O-103 Tuesday, October 18, 2016 11:15 AM

IMPORTANCE OF MALE INFERTILITY MICRO SURGERY TRAINING. F. Neto, B. Stone, P. V. Bach, B. B. Najari, M. Feliciano, P. S. Li, P. N. Schlegel, M. Goldstein. Urology, Weill Cornell Medical College, New York, NY; ²Weill Cornell Medical College, New York, NY; ³Weill Cornell Medical College, New York, NY; ⁴Male Reproductive Medicine, and Urology, Weill Cornell Medical College, New York Presbiterian, New York, NY.

OBJECTIVE: Male infertility microsurgery (MIM) is technically and mentally challenging, and outcomes are heavily dependent on surgeon’s skills[1]. Training programs in MIM are important for acquisition and improvement of surgeon’s microsurgical skills and outcomes. In this report, we describe our MIM training program, the trainees’ profile and outcomes.

<table>
<thead>
<tr>
<th>Trainees’ characteristics</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean years (±SD)</td>
<td>37.5 (±6.9)</td>
</tr>
<tr>
<td>No previous experience</td>
<td>7 (43%)</td>
</tr>
<tr>
<td>Self-taught</td>
<td>6 (37%)</td>
</tr>
<tr>
<td>Basic training</td>
<td>3 (20%)</td>
</tr>
<tr>
<td>Fellowship</td>
<td>0</td>
</tr>
<tr>
<td>Full practice</td>
<td>0</td>
</tr>
<tr>
<td>Years performing microsurgery: 0-5 years</td>
<td>10 (62%)</td>
</tr>
<tr>
<td>Years performing microsurgery: &gt; 5</td>
<td>6 (38%)</td>
</tr>
<tr>
<td>Number of MIM cases/week: 0-2 cases</td>
<td>11 (68%)</td>
</tr>
<tr>
<td>Number of MIM cases/week: &gt; 2 cases</td>
<td>5 (32%)</td>
</tr>
<tr>
<td>Academic practice</td>
<td>13 (81%)</td>
</tr>
<tr>
<td>Non-academic practice setting</td>
<td>3 (19%)</td>
</tr>
</tbody>
</table>

DESIGN: Retrospective review of trainees’ demographic data and training evaluation forms.

MATERIALS AND METHODS: All urologists who attended our MIM training course from May 2015 to April 2016 were included. Briefly, the MIM training program at our institution is a two-week training course offered to urologists interested in male infertility and held in a dedicated MIM training lab. During the first week, the trainees are taught how to manipulate basic microsurgical equipment. They practice under operating microscopes, using a latex practice card, microsurgical instruments and sutures (10-0 and 9-0). During the second week, and depending on their skill levels, the trainees perform MIM procedures, such as vasovasostomy (VV) and vasopelidiodyotomy (VE) in rats. Our training protocol is approved by the Institutional Review Board, and instructors provide close supervision and continuous evaluation during all phases of the training. Trainees also observe microsurgical cases performed at our institution. Evaluations of microsurgical skills are performed using a structured score form composed of 18 items, in which the lowest score is 18 points and the highest is 90 points. VV and VE patency rates are also reported.

RESULTS: We identified 16 urologists that completed our MIM training program and had evaluation data available. Demographic data is shown on table 1. The average time spend in the microsurgical training lab was 72.1 (±28.8) hours, and the average number of rat procedures performed per trainee was 8.9 (±3.6). The patency rates for VV and VE were 96% and 73% respectively. The average final evaluation score was 14 (±7.1) points, and the average improvement from baseline was 21.2 (±3.5) points. No baseline characteristics were predictive of the outcomes.

CONCLUSIONS: A MIM training program is an effective tool for teaching MIM skills. A well-equipped training lab provides the ideal environment for acquisition of microsurgical skills, even for experienced surgeons.

References:

Supported by: The project was supported by The Frederick J. and Theresa Dow Wallace Fund of the New York Community Trust.

O-104 Tuesday, October 18, 2016 11:30 AM

UTERINE VIABILITY FOLLOWING INTERRUPTION OF THE UTERINE VEIN: A PILOT STUDY TO ASSESS ALTERNATIVE VENOUS RETURN FOR UTERINE TRANSPLANT. K. Arnold, B. Beran, M. Shockley, K. Rivas, M. L. Sprague, T. Azakie, T. Falcone, S. Zimberg. Gynecology, Cleveland Clinic Florida, Weston, FL; ²Manheimer Foundation, Homestead, FL; ³Transplant, Cleveland Clinic Florida, Weston, FL; ⁴OB GYN, Cleveland Clinic, Cleveland, OH.

OBJECTIVE: To assess uterine viability after disruption of the uterine vein (UV) for the purpose of uterine transplant.

DESIGN: Prospective observational study of three female Papio hamadryas baboons undergoing interruption of the UV, cervical detachment and repair.

MATERIALS AND METHODS: Three baboons underwent laparotomy during which the uterine arteries and veins were isolated and the UV was ligated and transected bilaterally. Colpotomy was performed and the cervix was reanastomosed to the vaginal cuff. Following this, Isocyanine green (ICG) was administered and the SPY Elite imaging system (Novadaq Tech Inc.) documented vascular perfusion of the uterus and the cervicovaginal (CV) junction in real time. 6 weeks postoperatively, the subjects underwent transabdominal sonography, vaginoscopy and endocervical biopsy. The baboons were released into the primate colony and observed.

RESULTS: Three baboons underwent uncomplicated suture ligation and transection of the left and right uterine vein followed by colpotomy with cervicovaginal anastomosis. Near-infrared perfusion confirmed blood flow throughout the uterus and CV anastomosis in all cases. The operative time was 115 ± 20 min. On transabdominal ultrasound 6 weeks postoperatively, a normal appearing uterus was visualized in all subjects and vascular color flow was confirmed at both ovarian and uterine vascular insertions. Vaginoscopy showed a well-healed CV anastomosis and all endocervical biopsies showed non necrotic tissue. Postoperatively, cyclical sex skin turgescence and menstruation was observed in all subjects.
animals between 7 and 13 days and they continued normal menstrual cycles since.

CONCLUSIONS: In published series of uterine transplantation, the UV was dissected from the internal iliac vein to the uterus. This was considered in part for the length of intervention in the donor. In this alternative approach, where the UV was ligated, the uterus remains viable through the uterine artery and uteroovarian vessels with venous drainage only through the uteroovarian vein. All baboons developed sex skin turgescence, deturgescence and menstruation in the average time expected for a baboon menstrual cycle [1]. This suggests that disruption of UV and reanastomosis of the cervix did not hinder the baboon’s ability to continue normal menstruation. Intraoperative uterine perfusion was confirmed by near-infrared perfusion. A limitation of the study is that the syngeneic experimental condition with no immunosuppression did not test a true uterine transplant surgery, though this has been successfully performed in the human [2]. If the donor procedure for uterine transplant could be simplified by avoiding dissection of the UV and instead, using the uteroovarian vein for venous outflow, this could facilitate the technique and shorten surgical time for live donors.

References:

O-105 Tuesday, October 18, 2016 11:45 AM

UNEXPLAINED INFERTILITY: LAPAROSCOPY FIRST OR ART DIRECTLY. A. Algergawy, 1 A. Alhalwagy, 1 A. Shehata, 1 H. Salem, 1 A. Abd Alnaby, 1 Obstetrics and Gynecology Department, Faculty of Medicine, Tanta University, Tanta, Egypt; 2 Obstetrics and Gynecology Department, Clinical Pharmacist, Tanta, Egypt.

OBJECTIVE: To evaluate the outcome of two approaches for treatment of unexplained infertility; laparoscopic surgery (diagnostic and therapeutic) or ART directly.

DESIGN: Randomized prospective clinical trial.

MATERIALS AND METHODS: 423 patients diagnosed as having unexplained infertility based on normal semen parameters, normal HSG findings, regular ovulation as detected by ovulation testing and normal hormonal profile, were randomized according to their will into two groups: group I: patients treated with diagnostic and therapeutic laparoscopy and IUI up to 3 trials, if failed ICSI was performed. Group II included 218 patients managed with laparoscopy with aim of diagnosis and treatment. Cumulative pregnancy outcome were calculated for each group after one year.

RESULTS: in group I, 86 cases (41.95%) got pregnant, 26 cases (12.6%) by IUI, and 60 cases (29.26%) by ICSI. In group II, laparoscopy revealed the followings minimal to mild endometriosis in 68 cases (31.1%) moderate to severe endometriosis in 36cases (16.5%) managed by adhesiolysis and ablation - excision of endometriotic implants the pregnancy rate after one year was 55.88% (38cases), 38.9% (14 cases) in both respectively, significant peridural and pelvic adhesions was found in 33 cases (15.1 %) managed by adhesiolysis with pregnancy occurred in 18 cases (54.5%), while laparoscopy revealed hypo plastic tubes in 27 cases (12.3%), and 54 cases (24.7%) remained unexplained. expectant management result in pregnancy rate as 22.6% (6 cases), and 14.8% (8 cases) respectively. The over all pregnancy rate in group II is 84 cases (38.53%). OHSS occurred in 3 cases, multiple pregnancy in 13 cases, abortion and miscarriage 6 cases in group I, while 2 cases of ectopic pregnancy in group II, and no significant operative complications in both groups.

CONCLUSIONS: the performance of laparoscopy in unexplained infertility provided diagnostic findings which are helpful in global management of the cases, enables a significant number of patients to have spontaneous pregnancy comparable to pregnancy rate with ART while avoiding psychological, physical, and economic burdens associated with ART: Complications like OHSS, multiple pregnancy and abortion are higher in cases treated with ART while ectopic pregnancy rate was higher in cases treated with laparoscopic surgery. If ART is needed in the cases formerly treated with laparoscopic surgery, the chances of success are not affected but even facilitated.

O-106 Tuesday, October 18, 2016 12:00 PM

UTERINE VIABILITY IN THE BABOON FOLLOWING INTERRUPTION OF THE UTERINE ARTERIES AND VEINS BILATERALLY. M. E. Shockley, 1 K. S. Arnold, 1 B. D. Beran, 1 K. Rivas, 1 M. L. Sprague, 1 A. G. Tzakis, 1 P. Escobar, 1 T. Falcone, 1 Z. S. Zimberg. 1 Minimally Invasive Gynecolgy, Cleveland Clinic Florida, Weston, FL; 2 Mannheimer Foundation, Homestead, FL; 3 Transplant Surgery, Cleveland Clinic Florida, Weston, FL; 4 Gynecologic Oncology, University of Texas, MD Anderson Cancer Center, Houston, TX; 5 Obstetrics & Gynecolgy, Cleveland Clinic, Cleveland, OH.

OBJECTIVE: To contribute to a novel surgical approach for uterine transplantation by assessing uterine viability after interruption of the bilateral uterine arteries and veins in a baboon model.

DESIGN: Prospective observational study of uterine viability in Papio hamadryas baboons undergoing surgical interruption of the bilateral uterine arteries and veins.

MATERIALS AND METHODS: Three baboons underwent laparotomy during which uterine arteries and veins were isolated, ligated, and transsected bilaterally. A circumferential colpotomy was made and the cervix was reattached to the vagina. Intraoperative perfusion of the uterus and the cervico-vaginal junction was documented with near-infrared perfusion angiography following intravenous administration of indocyanine green dye. Postoperatively the animals were monitored for resumption of menses and changes in sex skin turgescence. All baboons underwent transabdominal ultrasonography, vaginoscopy, and cervical biopsy 7 weeks post-laparotomy.

RESULTS: Surgeries were performed without complication and intraoperative near-infrared angiography in all cases confirmed prompt blood flow throughout the entire uterus and along the cervico-vaginal anastomosis. Recovery of all animals was also uncomplicated. A normal appearing uterus with a thin and homogenous endometrial stripe was visualized on ultrasound performed 7 weeks after surgery in all subjects. Post-operative vaginoscopy permitted visualization of well approximated cervico-vaginal anastomoses and cervical biopsies revealed normal cervical tissue without evidence of necrosis. For each of the baboons, the first post-operative menstrual bleed occurred within 30 days of surgery and lasted for 2-3 days, consistent with normal baboon menses. Sex skin turgescence occurred in predictable cyclic patterns postoperatively, in accordance with each baboon’s respective menstrual cycle. Histopathological results, ultrasound imaging, and resumption of menstrual cycles demonstrated postoperative uterine viability in all 3 baboons, establishing that bilateral uterine artery and vein ligation does not affect uterine function.

CONCLUSIONS: The surgical technique of interrupting uterine vasculature, combined with disconnection and reanastomosis of the cervix and vagina, is designed to simulate implantation of a donor uterus that is connected to the recipient exclusively by utero-ovarian vessels. Eliminating dissection of the uterine artery and vein from donor hysterectomy shows great potential for future human uterine transplant trials, as it offers a more efficient, less risky, and less technically challenging technique to live donor uterus procurement.

O-107 Tuesday, October 18, 2016 12:15 PM

REPRODUCTIVE SURGERY MALPRACTICE PATTERNS. L. R. Matthews, 1 F. A. Alvi, 1 M. P. Milad. 1 OB/GYN, Northwestern Feinberg School of Medicine, Chicago, IL; 2 Department of Obstetrics and Gynecology, Northwestern University Feinberg School of Medicine, Chicago, IL; 3 Northwestern University, Chicago, IL.

OBJECTIVE: 74% of physicians practicing obstetrics and gynecology are projected to face a malpractice claim by the age of 45. "Major patient injury” is the most frequent primary allegation of all gynecologic claims. The
OBJECTIVE: Evaluate whether the order of performance of Office hysteroscopy (OH) and endometrial biopsy (EMBx) during the same office encounter for evaluation of abnormal uterine bleeding (AUB) affects patient’s pain perception, adequacy of the endometrial sample, duration of the procedure and optimal visualization of the uterine cavity.

DESIGN: Prospective Randomized Single Blinded study.

MATERIALS AND METHODS: Patients presenting to UF Fibroid and Endometriosis center for evaluation of AUB with concurrent OH and EMBx between 10/2015 and 4/2016 were randomized to have either OH followed by EMBx (Group 1) or EMBx followed by OH (Group 2). Procedures were performed using standard Gynecologic techniques. Patients were blinded to the order of performance of the procedures. Patients were asked to describe their pain perception based on Visual analogue scale (VAS) from 0-10 at the end of the procedures. The adequacy of the endometrial sample was determined from the pathology report. The duration of the entire procedure as well as the quality of image of the endometrial cavity were recorded as fair, good and excellent. (Fair = No tubal ostia visualized, the anterior and posterior wall of the uterus not clearly visible; Good = Both tubal ostia identified but only anterior or posterior wall of the uterus was clearly visible; Excellent = Bilateral tubal ostia as well as posterior and anterior uterine wall clearly visible). These variables were analyzed based on the order of performance of OH or EMBx.

RESULTS: A total of 30 patients were enrolled and randomized to group 1 (n=15) and group 2 (n=15). Data are portrayed in table 1. There were no significant differences in age or indications for the procedure between the two groups. Visualization of the endometrial cavity was significantly better when OH was performed as the first procedure, although patients who had OH first required more passes with the Pipelle. There were no differences in global pain perception, duration of the procedure and adequacy of samples obtained between the two groups.

CONCLUSIONS: In patients having concurrent OH and EMBx for evaluation of AUB, performance of OH first was associated with optimal visualization of the uterine cavity but more passes of the Pipelle was required in order to obtain sufficient samples for histologic diagnosis. The duration of the procedures and reported pain score were independent of the order of performance of the OH or EMBx.

Table 1: Summarized result of demographic, primary and secondary outcomes variables.

<table>
<thead>
<tr>
<th></th>
<th>OH First</th>
<th>EMBx First</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient Age</td>
<td>44.1±6.5</td>
<td>39.4±7.2</td>
<td>0.07</td>
</tr>
<tr>
<td>Indications for procedure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fibroids</td>
<td>8 (53.3%)</td>
<td>10 (66.7%)</td>
<td>0.39</td>
</tr>
<tr>
<td>Adenomyosis</td>
<td>2 (13.3%)</td>
<td>3 (20%)</td>
<td></td>
</tr>
<tr>
<td>Polyps</td>
<td>0</td>
<td>1 (6.7%)</td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>5 (33.3%)</td>
<td>1 (6.7%)</td>
<td></td>
</tr>
<tr>
<td>Reported global pain score</td>
<td>7 (2-10)</td>
<td>7 (0-10)</td>
<td>0.67</td>
</tr>
<tr>
<td>Duration of procedure (min)</td>
<td>3 (1-6)</td>
<td>4 (2-10)</td>
<td>0.126</td>
</tr>
<tr>
<td>Number of passes with Pipelle during endometrial biopsy</td>
<td>2 (1-3)</td>
<td>1 (1-2)</td>
<td>0.001</td>
</tr>
<tr>
<td>Visualization of endometrial cavity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Excellent</td>
<td>8 (53.3%)</td>
<td>0 (0%)</td>
<td>0.007</td>
</tr>
<tr>
<td>Good</td>
<td>3 (20%)</td>
<td>5 (33.3%)</td>
<td></td>
</tr>
<tr>
<td>Fair</td>
<td>3 (20%)</td>
<td>8 (53.3%)</td>
<td></td>
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</tbody>
</table>
MALE REPRODUCTION AND UROLOGY: CLINICAL 1

O-109 Tuesday, October 18, 2016 11:15 AM

POLICY ON POSTHUMOUS SPERM RETRIEVAL: SURVEY OF 50 MAJOR ACADEMIC MEDICAL CENTERS, N. Waler, R. Ramasamy. "UMM School of Medicine, Miami, FL; University of Miami, Miami, FL.

OBJECTIVE: Very few studies have addressed attitudes on posthumous sperm retrieval due to the ethical and legal ramifications of the use of gametes after death. We evaluated the presence and content of a policy on posthumous sperm retrieval at the 50 major academic medical centers.

DESIGN: Questionnaire based telephone study / web survey.

MATERIALS AND METHODS: We surveyed the 50 major academic medical centers as ranked for research in 2016 by U.S. News & World Report. We gathered data on presence and content of posthumous sperm retrieval policies. If not published, we contacted the legal counsel for the medical center, the ethics and compliance offices, as well as the Urology Department for each center.

RESULTS: Out of the 50 major academic medical centers, we gathered data on posthumous sperm retrieval from 14 (28%). Of the 14 institutions, five (35.7%) had policies regarding posthumous sperm retrieval and the remaining nine (64.3%) did not have a policy. Four of the nine medical centers without policies have discussed development of a policy but did not formalize it due to lack of legal guidance as a barrier to policy adoption.

CONCLUSIONS: Very few, less than 1/3, of the surveyed academic medical centers can adopt individualized policies based on guidelines published by the American Society for Reproductive Medicine.

Table: Medical Center Posthumous Sperm Retrieval Policies

<table>
<thead>
<tr>
<th>University</th>
<th>Policy</th>
<th>Consent</th>
<th>Bereavement</th>
<th>Published</th>
</tr>
</thead>
<tbody>
<tr>
<td>Columbia University/ Cornell University (Weill)</td>
<td>Yes</td>
<td>Written, surviving wife</td>
<td>1 year</td>
<td>Yes</td>
</tr>
<tr>
<td>Mayo Medical School</td>
<td>No</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ohio State University</td>
<td>No</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tufts University</td>
<td>Yes</td>
<td>Written with specified recipient, medical record with specified recipient, surviving partner with judicial authorization</td>
<td></td>
<td>Yes</td>
</tr>
<tr>
<td>University of Iowa (Carver)</td>
<td>Yes</td>
<td>Written with specified recipient</td>
<td></td>
<td></td>
</tr>
<tr>
<td>University of Miami (Miller)</td>
<td>No</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>University of Texas Southwestern Medical Center</td>
<td>No</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>University of Virginia</td>
<td>Yes</td>
<td>Written with specified recipient, medical record with specified recipient, surviving partner with judicial authorization</td>
<td>1 year</td>
<td>Yes</td>
</tr>
<tr>
<td>USC (Keck)/UC Davis/UC Irvine</td>
<td>No</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vanderbilt University</td>
<td>No</td>
<td></td>
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</table>

O-110 Tuesday, October 18, 2016 11:30 AM


OBJECTIVE: We aim to assess changes in the practice pattern of U.S. urologists performing male infertility procedures (vasal reconstruction, sperm retrieval, varicocelectomy) from 2004 to 2015.

DESIGN: Retrospective review of American Board of Urology (ABU) case logs.

MATERIALS AND METHODS: We examined self-reported procedural volume from urologists undergoing certification and re-certification, focusing on vasal reconstruction, sperm retrieval, and varicocectomy. The study period was stratified into early (2004-2007) and recent (2012-2015) time periods and assessed for temporal variation in practice patterns and by urology sub-specialty.

RESULTS: A total of 9,389 urologists submitted case logs, with 2,642 vs. 3,316 urologists submitting case logs during the early vs. recent time periods. During 2004-07, 1,069 urologists (40%) performed at least one infertility procedure compared to 1,097 urologists (33%) during 2012-15 (p=0.001).

CONCLUSIONS: Our data demonstrates a significant decline over time in the proportion of urologists who perform male infertility cases. While the majority of male infertility procedures are performed by general urologists, there is a growing proportion of procedures being performed by andrologists. As fellowship training becomes more commonplace in urology and more urologists start identifying with subspecialties, we would expect male infertility procedures to continue shifting to andrologists over time.

Supported by: The project was supported by The Frederick J. and Theresa Dow Wallace Fund of the New York Community Trust. The project was also supported by grant number T32HS00066 from the Agency for Healthcare Research and Quality. The content is solely the responsibility of the authors and does not necessarily represent the official views of the Agency for Healthcare Research and Quality.

Table: Number and proportion of male infertility procedures performed by andrologists

<table>
<thead>
<tr>
<th>Procedure</th>
<th>early cohort (p%)</th>
<th>recent cohort (p%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All male infertility</td>
<td>807 (22.9%)</td>
<td>1068 (25.9%)</td>
<td>p=0.002</td>
</tr>
<tr>
<td>procedures</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Varicocelectomy</td>
<td>409 (19.2%)</td>
<td>594 (25.2%)</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Sperm retrieval</td>
<td>205 (33.6%)</td>
<td>234 (35.7%)</td>
<td>p=0.476</td>
</tr>
<tr>
<td>Vasal reconstruction</td>
<td>193 (24.7%)</td>
<td>240 (21.8%)</td>
<td>p=0.160</td>
</tr>
</tbody>
</table>
RELATIONSHIP BETWEEN MALE AGE AND SUCCESS OF VASECTOMY REVERSAL. J. M. Rehmer, L. H. Sayles, A. Perkins, S. L. Gustin, S. H. Marks, C. M. Deibert. Department of Obstetrics and Gynecology, University of Nebraska Medical Center, Omaha, NE; Department of Biostatistics, University of Nebraska Medical Center, Omaha, NE; International Center for Vasectomy Reversal, Tucson, AZ; Division of Urologic Surgery, University of Nebraska Medical Center, Omaha, NE.

OBJECTIVE: To assess if male age at the time of vasectomy reversal plays a role in patency irrespective of obstructive interval.

DESIGN: Retrospective analysis of vasectomy reversal patient and partner data collected from a single institution from December 1989 through December 2015.

MATERIALS AND METHODS: The original dataset contained 4,259 observations. Reasons for vasectomy reversal included infertility (n = 3,789), pain (n = 126), pain/fertility (n = 3), pain/personal (n = 1), personal (n = 6), religious (n = 6), or unspecified (n = 327). The following analyses are limited to the 3,789 observations who reported fertility as the lone reason for reversal. Of these individuals 87 patients had a missing date of surgery reported. There are 9 patients who do not have an age at surgery. The remainder range from 21 to 81, however only 0.4% are 25 or younger and only 1.0% are older than 62, with 10.2% being over 50. There are 54 patients who are missing a value for time since original vasectomy. Removing these patients from the analysis left 3,696 patients for inclusion. Of these patient we analyzed the age of individual and association with patency post-reversal and the obstructive interval and association with patency post-reversal.

RESULTS: Patency data was plotted in relationship to both the patient age at surgery and years of obstructive interval individually. Using a Lowess smoothed estimate of the mean regression model, there is a trended increase in patency early on as age and years since vasectomy increase followed by a long steady decline. In a logistic regression model predicting patency with male age at reversal and years since vasectomy as independent variables, only the vasal obstructive interval is predictive (OR 0.977, p = 0.002). Male age does not predict patency (OR 0.988, p = 0.124).

CONCLUSIONS: After controlling for years since vasectomy, there is not a significant association between age at reversal and likelihood of patency (p = 0.124). Understanding this may be helpful in counseling older men seeking vasectomy reversal.

O-111 Tuesday, October 18, 2016 11:45 AM

RNA-SEQUENCING TO ASSESS EMBRYONIC DEVELOPMENTAL COMPETENCE OF THE MALE GAMETE. T. Cozzubbo, N. Pereira, S. Cheung, Z. Rosenwaks, G. D. Palermo. Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: Evaluation of the reproductive quality of the male gamete by standard semen analysis and chromatin integrity (CI) test is often inadequate, particularly with ART. Therefore, we explored the expression levels of genes devoted to DNA repair and apoptosis regulation in relation to the sperm’s ability to generate offspring.

MATERIALS AND METHODS: The nucleic acid quality and spermatozoal RNA concentration was measured. The RNA samples were then made into paired-end libraries. Pilot paired-end 76bp RNA-Seq using an Illumina platform (NextSeq 500) was carried out and expanded to 60M reads. Expression values were calculated in fragments per kilobase of transcript per million mapped reads (FPKM).

RESULTS: Of the 25 consenting men, 5 had a mean age of 37.6 ± 3.6 an average sperm concentration of 27.3 ± 27.5 million/ml, motility of 46.6 ± 24.8, 5.0 ± 2% normal morphology, TUNEL assessment yielded 15.6 ± 7% chromatin fragmentation rate, and RNA concentration of 14.3 ± 6 ng/µL (9.1 - 21.3). These men underwent ICSI with their female partner with a mean age of 34.8 ± 3 years and achieved a fertilization rate of 71.4% (30/42), however, failed to obtain a pregnancy. The control couples (n = 3) with a female age of 38.3 ± 5 and male age of 33.6 ± 7 years had normal semen parameters with a 8.7 ± 1% chromatin fragmentation and delivered 3 healthy offspring by natural conception. A total of 86 genes were differentially expressed (P < 0.0005) between the study and control cohort. Of them, 24 genes were overexpressed and 62 underexpressed when compared to the control. Specifically, DNA repair genes (APLF, CYB5R4, ERCC4 and TGFβ2) and apoptotic modulating genes (MORC1, PIWIL1 and ZFAND6) were remarkably underexpressed (P < 0.0003).

CONCLUSIONS: Transcriptome profiling utilizing RNA-Seq in human spermatozoa reveals that genes related to DNA repair and apoptosis may be predictive of ICSI reproductive outcome. The borderline positive of the sperm chromatin fragmentation did not predict clinical outcome and this was confirmed by the weak correlation with gene expression. Sperm RNA-Seq is a reliable and reproducible technique that may aid in providing information on embryo developmental competence of the male gamete where semen parameters and chromatin fragmentation seem inadequate.

O-113 Tuesday, October 18, 2016 12:15 PM

POSTVASECTOMY REVERSAL SEMEN ANALYSIS: A PREDICTOR OF PREGNANCY. A. Majzoub, A. S. Polackwich, R. Sharma, A. Agarwal, E. S. Sahaneh. Urology, Glickman Urological and Kidney Institute, Cleveland Clinic Foundation, Cleveland, OH; Urology, Columbus University Medical Center, Miami Beach, FL; Urology, American Center for Reproductive Medicine, Cleveland, OH; Urology, Cleveland Clinic, Cleveland, OH.

OBJECTIVE: Vasectomy reversal (VR) is commonly performed on men who wish to regain fertility after elective sterilization. Despite a thorough understanding of predictors of vasal patency after surgery, little is known about the predictors of pregnancy post vasectomy reversal. The aim of this study is to investigate the postoperative pregnancy rate and explore semen analysis reference values associated with it.

DESIGN: A retrospective study.

MATERIALS AND METHODS: The records of 171 patients who underwent VR at the Glickman Urological and Kidney Institute from 2011-2014 were reviewed. Data regarding patient/spouse age, obstructive interval, intraoperative findings, procedure performed, postoperative semen results and spontaneous pregnancy outcome was collected. Pearson’s test was used to analyze categorical data, while appropriate T-tests were used to examine numerical data. A p-value of <0.05 was considered significant. Analysis was performed using the SPSS software, version 21.

RESULTS: The mean obstructive interval was 9.5 ± 1.2 years. Spontaneous pregnancy was achieved by 49.6% (30/61) of patients and was directly related to better intraoperative sperm quality and postoperative sperm concentration, total motility and normal morphology (p < 0.001). The reference ranges of postoperative semen parameters of patients with spontaneous pregnancy were presented in table 1. Spontaneous pregnancy was reported by 15% of patients with a sperm concentration <5 million/ml; 21.3% patients with total sperm motility <10% and 14.8% of patients with normal morphology <1% (p < 0.001).

CONCLUSIONS: Semen parameters associated with pregnancy after vasectomy reversal are significantly lower than reference ranges reported in the WHO 2010 normal ranges. Consideration of these ranges allows better post reversal counseling of patients.

Reference values of semen parameters from patients with documented pregnancy post VR

<table>
<thead>
<tr>
<th>Centiles</th>
<th>5th</th>
<th>95th</th>
<th>CI 10th</th>
<th>25th</th>
<th>50th</th>
<th>75th</th>
<th>95th</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume</td>
<td>0.74</td>
<td>0.4-1.4</td>
<td>1.28</td>
<td>1.62</td>
<td>2.5</td>
<td>3.4</td>
<td>5.9</td>
</tr>
<tr>
<td>Sperm concentration</td>
<td>3.56</td>
<td>0.1-5.89</td>
<td>5.17</td>
<td>13.1</td>
<td>23.7</td>
<td>45.5</td>
<td>119.6</td>
</tr>
<tr>
<td>Total Motility</td>
<td>4.45</td>
<td>3.7-7.3</td>
<td>5.9</td>
<td>13</td>
<td>25.5</td>
<td>37.7</td>
<td>63.2</td>
</tr>
<tr>
<td>TMC</td>
<td>0.58</td>
<td>0.1-1.6</td>
<td>0.82</td>
<td>4.7</td>
<td>14.7</td>
<td>42.7</td>
<td>152.2</td>
</tr>
<tr>
<td>Normal Forms</td>
<td>0</td>
<td>0-1</td>
<td>1</td>
<td>3</td>
<td>5.75</td>
<td>14.1</td>
<td></td>
</tr>
</tbody>
</table>

OBJECTIVE: The male factor in worldwide infertility incidence is 20-30%. Sperm has high energy requirement for maturation, capacitation and motility. Many factors affecting sperm quality act through decreasing energy and increasing reactive oxygen species (ROS) by causing mitochondrial dysfunction. Sperm is vulnerable to ROS causing sperm immobilization, impairment of acrosomal reaction, abnormal morphology, DNA fragmentation and cell death.

DESIGN: To determine the effect of antioxidant supplementation containing L-carnitine, acetyl-L-carnitine, fructose, citric acid, selenium, coenzyme Q10, vitamin C, vitamin B12 and zinc on sperm quality in subjects with oligo- or astheno-teratozoospermia, with and without varicocele and history of difficulty conceiving.

MATERIALS AND METHODS: This was a monocentric, randomized, DBPC with a total of 104 patients, 52 in the supplementation and 52 in the placebo arm, that were recruited in 6 months. The enrollment was divided in 52 patients with varicocele grade I-III and 52 patients without varicocele. The study evaluated the efficacy of 6 months of supplementation (2 sachet daily) versus placebo (2 sachet daily). Spermogram evaluation, according to the WHO guidelines, was done at the beginning of treatment (V1) and at the end of the 6 month treatment (V2).

RESULTS: Sperm count (number x 10⁶/mL) in patients with varicocele was 39.3 +/- SD 16.8 in placebo group and 49.4 +/- 18.9 in supplementation group (percentage change 25.7% vs. 0.05 Student test); in patients without varicocele 47.5 +/- 7.9 in placebo group and 52.3 +/- 9.1 in supplementation group (percentage change 9.9% vs. 0.05). Total sperm motility in patients with varicocele was 33.9% +/- 6.9 in placebo group and 43.8% +/- 8.0 in supplementation group (percentage change 18.6% vs. 0.05); in patients without varicocele was 35.0 +/- 7.5 in placebo group and 39.9 +/- 8.0 in supplementation group (percentage change 13.8% vs. 0.05). Progressive sperm motility in patients with varicocele was 23.1 +/- SD 6.7 in placebo group and 27.4 +/- 7.9 in supplementation group (percentage change 18.6% vs. 0.05); in patients without varicocele was 25.1 +/- 7.0 in placebo group and 29.7 +/- 9.1 in supplementation group (percentage change 18.6% vs. 0.05).

CONCLUSIONS: In our study, at the end of the treatment we observed a marked increase in quality parameters of sperm such as count and in total and progressive motility especially in varicocele patients. The supplementation was safe and no adverse events were observed. On this basis it can be established that the use of carnitines and other functional substances can form part of an efficacious strategy to handle male infertility.

Supported by: Sigma-tau HealthScience provided supplement product for the study.

REPRODUCTIVE ENDOCRINOLOGY: CLINICAL 1


OBJECTIVE: To investigate differences in implantation (IR), pregnancy (PR), ongoing pregnancy (OP) rates and delivery among women undergoing transfer at the blastocyst stage in their first IVF/ICSI cycle randomized to fresh cycles (ET), deferred embryo transfer (DET), or personalized embryo transfer (pET) after endometrial receptivity analysis (ERA).

DESIGN: Prospective multicenter, randomized, open label, controlled trial that started in October 2013, with preliminary outcome evaluated in April 2016. Patients were allocated through computer-generated randomization into ET, DET, or pET groups. Sample size calculated for the endpoint of delivery rate per embryo transfer was 182 patients per arm.

MATERIALS AND METHODS: We investigated the reproductive outcome of infertile women under 38 years in their first IVF/ICSI cycle with elective blastocyst transfer randomly allocated to be performed in a fresh cycle (ET), after freezing all embryos (DET) or after identification of the personalized window of implantation (WOI) with the ERA test (pET). Patients have BMI of 18.5-30 and AFC criteria were recurrent pregnancy loss and/or severe male factor. Statistical comparisons between groups were performed using Chi-square test (p<0.05).

RESULTS: Preliminary results have been analyzed after recruiting 356 patients of the 546 planned.

<table>
<thead>
<tr>
<th>Variable</th>
<th>GROUP A Fresh EmbryoTransfer ET</th>
<th>GROUP B Deferred EmbryoTransfer DET</th>
<th>GROUP C Personalized EmbryoTransfer pET</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recruited (n)</td>
<td>117</td>
<td>122</td>
<td>117</td>
</tr>
<tr>
<td>Embryo transfer (n)</td>
<td>60</td>
<td>74</td>
<td>49</td>
</tr>
<tr>
<td>Implantation rate (%)</td>
<td>36/102 (35.3)</td>
<td>53/128 (41.4)</td>
<td>43/90 (47.8)</td>
</tr>
<tr>
<td>Pregnancy rate/ET (%)</td>
<td>37/60 (61.7)*</td>
<td>45/74 (60.8)*</td>
<td>42/49 (85.7)*</td>
</tr>
<tr>
<td>Pregnancy loss (%)</td>
<td>11/37 (29.7)</td>
<td>12/45 (26.7)</td>
<td>15/42 (35.7)</td>
</tr>
<tr>
<td>Biochemical pregnancies (%)</td>
<td>8/37 (21.6)</td>
<td>3/45 (6.7)</td>
<td>5/42 (11.9)</td>
</tr>
<tr>
<td>Ectopic pregnancies (%)</td>
<td>1/37 (2.7)</td>
<td>0/45 (0.0)</td>
<td>1/42 (2.4)</td>
</tr>
<tr>
<td>Clinical miscarriages (%)</td>
<td>2/37 (5.4)</td>
<td>9/45 (20.0)</td>
<td>9/42 (21.4)</td>
</tr>
<tr>
<td>Ongoing pregnancy/ET (%)</td>
<td>26/60 (43.3)</td>
<td>33/74 (44.6)</td>
<td>27/49 (55.1)</td>
</tr>
<tr>
<td>Twins (%)</td>
<td>8/28 (28.6)</td>
<td>11/42 (26.2)</td>
<td>7/36 (19.4)</td>
</tr>
<tr>
<td>Singleton (%)</td>
<td>20/28 (71.4)</td>
<td>31/42 (73.8)</td>
<td>29/36 (80.6)</td>
</tr>
</tbody>
</table>

Supported by: Sigma-tau HealthScience provided supplement product for the study.
CONCLUSIONS: PET is associated with significant improvement in PR and trend towards increase IR and OP versus regular ET or DET. Personalization of the endometrial factor in the diagnostic work-up of the infertile couple must be considered.


O-116 Tuesday, October 18, 2016 11:30 AM
DIMINISHED BUT NOT DECLINING: LONGITUDINAL ANDROGEN PRODUCTION AND FOLLICULAR MEASURES OF OVARIAN RESERVE IN CANCER SURVIVORS COMPARED TO HEALTHY CONTROLS. K. Cameron,1 M. D. Sammel,2 M. M. Prewitt,3 M. E. Lynch,4 C. Gracia,5 University of Pennsylvania, Philadelphia, PA;6Biostatistics and Epidemiology, Univ. of Pennsylvania, Perelman School of Medicine, Philadelphia, PA;7Obstetrics and Gynecology, University of Pennsylvania School of Medicine, Philadelphia, PA;8University of Pennsylvania School of Medicine, Ardmore, PA.

OBJECTIVE: Recent studies have examined levels and the rates of change of follicular measures of ovarian reserve in cancer survivors over time. No data exist examining androgen production in this population, which is important for folliculogenesis and sexual health. This study sought to examine levels and rate of change in testosterone and dehydroepiandrosterone sulfate (DHEAS) for a cohort of cancer survivors compared to similar-aged healthy controls.

DESIGN: Prospective cohort.

MATERIALS AND METHODS: Participants were seen for annual visits that included early follicular phase hormone analyses and pelvic ultrasound. Changes in free testosterone, DHEAS, anti-mullerian hormone (AMH) and antral follicle count (AFC) were modeled over the study period using random effects linear regression. Exogenous hormone use was an exclusion criterion.

RESULTS: One hundred and nine cancer survivors (age range 18-39 years, mean 10 years after treatment) and 86 controls were followed on average for 15 months. The absolute levels of hormones differed between the groups. In adjusted models, geometric mean (GM) AMH levels in the cancer survivors at age 30 were 70% lower than in controls (0.63 ng/mL vs. 2.14 ng/mL, p<0.001), AFC was 52% lower (GM 23 vs. 11 follicles, p<0.001), testosterone was 25% lower (GM 0.45 nmol/L vs. 0.60 nmol/L, p<0.001) and DHEAS was 33% lower (GM 0.91 nmol/L vs. 1.36 nmol/L, p<0.001). The rate of change over time in AMH and AFC differed in the 2 groups: AMH declined at a rate of 0% per year in survivors, compared to 4% per year in controls (p=0.048). Decline in AFC was 0.1% per year for survivors, compared to 3% in controls (p=0.11). In both controls and survivors, the levels of testosterone and DHEAS remained stable, (p=0.73 and 0.66, respectively). Neither BMI nor race confounded associations.

CONCLUSIONS: This is the first longitudinal study to examine changes in androgens and follicular measures of ovarian reserve over time in young cancer survivors. The rate of change of measures of ovarian reserve is faster in controls than survivors, likely related to lowered baseline levels in survivors. However, despite different baseline androgen levels, neither group show appreciable decline over time. These measures may have implications for follicle quality, fertility, and long term sexual health; additional longitudinal data in this population is needed.

Supported by: IR01HD062797

O-118 Tuesday, October 18, 2016 12:00 PM
FSH PROMOTES PREMATUeRE PROGESTERONE OUTPUT IN HU-MAN GRANULOSA CELLS WITHOUT LUTEINIZATION BY UP-REGULATING THE EXPRESSION OF 3β-HSD AND INDUCING DISPROPORTIONAL INCREASES BETWEEN 17α-OH AND OTHER STEROIDENZEN ECIES. N. Akin,1 G. Bildik,1 A. Seyhan,2 B. Urman,3 O. Oktem,4 School of Medicine and the Graduate School of Health Sciences, Koc University, Istanbul, Turkey;2Women’s Health Center Assisted Reproduction Unit, American Hospital, Istanbul, Turkey;3Obstetrics and Gynecology, Koc University School of Medicine, Istanbul, Turkey.

OBJECTIVE: Serum progesterone (P) level may prematurely rise before ovulation trigger in stimulated IVF cycles. We aimed in this study to explore if gonadotropin stimulation up-regulates the expression of the enzyme 3β-HSD, which converts pregnenolone to P, and alters the expression of ovarian steroidogenic enzymes that facilitates premature P output without luteinization.

DESIGN: A translational research study.

MATERIALS AND METHODS: Human ovarian cortical samples (n=15) and non-luteinizing mitotic granulosa cells (GGrC1) were stimulated with FSH (n=30). The mRNA levels of 3β-HSD were determined using qRT-PCR of tissues from patients undergoing pure natural (n=20) and stimulated IVF cycles with GnRH agonist (n=30) and antagonist (n=30) protocols. Real-time quantitative qRT-PCR, immunoblotting and ELISA assays were used.

RESULTS: Intracellular cAMP level was significantly increased in a concentration manner in the mitotic granulosa cells with a baseline level of 2.2 nM to 4.9, 7.9 and 13 nM after stimulation with FSH at 12.5, 25 and 50 mM concentrations respectively. FSH at the same doses induced 1.52, 1.78 and 2.63 fold increases in the mRNA level of 3β-HSD at 24 hrs compared to baseline level (p<0.001). There was a dose-dependent increase in the protein levels of 3β-HSD and
P on quantitative immunoblotting confirming that FSH induced up-regulation in the transcription was accompanied by increased translation at protein level. Overall, when all time points and FSH doses were analyzed collectively, FSH significantly increased the expression of its own receptor (4.52 fold, p<0.001), sARK (2.92-fold, p<0.01), SCC (2.56-fold, p<0.01), aromatase (5.32-fold, p<0.001), 3β-HSD (2.48 fold, p<0.01) 17β-HSD (2.46 fold, p<0.01) but not 17α-OH (1.56 fold p>0.05). Similar results were obtained in the luteal granulosa cells of the IVF cycles. Compared to pure natural ones, stimulated IVF cycles with GnRH agonist and antagonist protocols were characterized by 2.8 and 2.6 fold increases respectively, in the expression of all steroidogenic enzymes with a notable exception of 17α-OH, of which the expression did not increase in proportion with the others (1.4 and 1.6 folds). Stimulation of the ovarian tissue samples with FSH for 48hrs significantly increased their in vitro E2 (776±147pg/mL, respectively; p<0.01) and P productions (1.3±0.4 vs. 0.2±0.1ng/mL, respectively; p<0.01) compared to those cultured without FSH.

CONCLUSIONS: Ovarian stimulation may promote progesterone output by up-regulating 3β-HSD expression and creating a relative shunting in the ovarian steroidogenesis at the 17 hydroxylation step that diverts high input precursor steroids generated during multifollicular development into progesterone pathway.

O-119 Tuesday, October 18, 2016 12:15 PM

ABSTRACT WITHDRAWN

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O-120 Tuesday, October 18, 2016 12:30 PM

REPEAT IN VITRO FERTILIZATION SUCCESS RATES ARE LOWER IN PATIENTS WHO DELIVER VIA CESAREAN SECTION WHEN USING EMBRYOS FROM THE SAME COHORT. M. K. Hayes,a,b P. A. Bergh,a C. M. Bergh,c T. A. Molinaro,d RMA, Basking Ridge, NJ; bDrexel University College of Medicine, Philadelphia, PA; cNursing, RMANJ, Basking Ridge, NJ; dReproductive Medicine Associates of New Jersey, Eatontown, NJ.

OBJECTIVE: Determine if previous mode of delivery affects outcome of subsequent in vitro fertilization attempt.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Patients who conceived at a single infertility care center, delivered, and returned to the center for a subsequent pregnancy attempt, transferring frozen embryos from the same cohort that resulted in the initial pregnancy, were evaluated. Cycles from Aug 2006 to Dec 2015 meeting this criteria were analyzed to determine if the initial pregnancy resulted in a Cesarean Section (C-Section) or vaginal delivery. Ongoing pregnancy and implantation rates were compared between patients who had delivered their initial pregnancy via C-Section versus those who had delivered vaginally.

Chi-square and t-tests were performed to compare demographics between groups. This study was powered to detect a 5% difference between groups.

RESULTS: A total of 975 patients met inclusion criteria; 521 (53.4 %) delivered via C-Section and 454 (46.6 %) vaginally. The mean oocyte age was higher in the C-Section group than in the vaginal group (33.3 vs. 32.1 years, p = 0.000). Patients who delivered via C-Section opted for pre-implantation genetic diagnosis (PGD) testing of their embryos more often those who delivered vaginally (42.5 % vs. 34.4 %, p = 0.010).

CONCLUSIONS: Outcomes appear to be adversely affected by a history of previous C-section. Further investigation is warranted before patients can be advised that mode of delivery adversely impacts future rates of sustained pregnancy.

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O-121 Tuesday, October 18, 2016 11:15 AM

ANDROGEN AND ESTROGEN PROMOTE MACAQUE PREANTRAL FOLLICLE SURVIVAL AND GROWTH IN THE ABSENCE OF FSH DURING 3-DIMENSIONAL CULTURE. T. Baba,a,b A. Y. Ting,a O. Tkachenko,a J. Xu,b R. L. Stouffer,a “Division of Reproductive & Developmental Sciences, Oregon National Primate Research Center, Oregon Health & Science University, Beaverton, OR; bDepartment of Obstetrics and Gynecology, Sapporo Medical University, Hokkaido, Japan.

OBJECTIVE: In vivo development of primate follicles is generally considered independent of follicle stimulating hormone (FSH) until the antral stage. However, previous data suggest that FSH promotes the survival of human and macaque preantral follicles in vitro. In this study, we investigated whether local factors, androgen and anti-Müllerian hormone (AMH), can replace FSH in supporting the development of macaque preantral follicle during 3-dimensional culture.

DESIGN: Nonhuman primate model; randomized, controlled study.

MATERIALS AND METHODS: Macaque secondary follicles (n=24/group x 3 animals) were encapsulated in 0.25% alginate and divided into 4 groups: 1) control (CTRL, 44 mL/uml FSH); 2) No FSH (-FSH); 3) -FSH plus 17α estradiol (E2, 100pg/ml) and dihydrotestosterone (DHT, 50ng/ml), E2/DHT; and 4) -FSH plus AMH (100ng/ml). Follicles were cultured at 37°C and 5% O2 for 5 wks [1]. Follicle survival and antrum formation rates as well as follicle diameters were determined. Surviving follicles were categorized based on their wk5 diameter: no-grow (<250 um), slow-grow (250-500 um) and fast-grow (>500 um). Peak levels of progesterone (P4, wk5), E2 (wk5) and AMH (wk3) in the media were measured. Statistical difference (p ≤ 0.05) was determined using SigmaPlot.
RESULTS: As expected, FSH deprivation decreased (p < 0.05) follicle survival rates in the FSH group (16 ± 5%), compared to CTRL (66 ± 9%). The addition of E2/DHT (49 ± 5%), but not AMH (27 ± 8%), restored follicle survival rate to the CTRL level. Similarly, antrum formation rates were higher (p < 0.05) in CTRL (56 ±6%) and E2/DHT groups (51 ±1%), compared to -FSH (0 ±0%) and AMH (11 ±11%) groups. However, follicle growth rate after antrum formation and follicle diameter at wk5 was reduced (p < 0.05) in the E2/DHT group (405 ± 25 μm), compared to CTRL (522 ± 29 μm). Indeed, the proportion of fast-grow follicles was higher in CTRL (29 ±5%), compared to E2/DHT (10 ±3%). No fast-grow follicles were observed in -FSH and AMH groups. AMH levels at wk3 remained similar in all groups. However, media concentrations of P4 and E2 at wk5 were lower (p < 0.05, undetectable) in -FSH, E2/DHT and AMH groups, compared to CTRL (P4 = 93 ±10 ng/mL; E2 = 4 ±1 ng/mL).

CONCLUSIONS: At the preantral stage, E2/DHT, but not AMH, can support FSH’s action to promote primordial follicle survival, growth and antrum formation. However, after antrum formation, E2/DHT cannot support further follicle growth or steroidogenesis in the absence of FSH. Thus, E2 and DHT may act as local survival and growth factors for pre-antral follicles independent of FSH. Studies are ongoing to examine whether E2 or DHT alone supports preantral follicle development in a FSH-deprived milieu.

References:

Supported by: NIH 5P50HD071836, 8P51OD011092

O-122 Tuesday, October 18, 2016 11:30 AM

OCYTE-SPECIFIC EMBRYONIC POLY (A)-BINDING PROTEIN (EPAB) IS REQUIRED FOR GRANULOSA CELL ERK SIGNALING IN RESPONSE TO FSH. C. Yang, K. Lowther, M. D. Lalioti, H. S. Taylor, E. Seli. Department of Obstetrics, Gynecology, and Reproductive Sciences, Yale School of Medicine, New Haven, CT.

OBJECTIVE: Embryonic poly (A)-binding protein (EPAB) is an oocyte-specific RNA-binding protein required for translational regulation of gene expression in oocytes and early embryos. Ebap−/− females are infertile due to impaired oocyte maturation, cumulus expansion, and ovulation. The aim of this study was to characterize the molecular mechanisms of follicular somatic cell dysfunction in Ebap−/− mice.

DESIGN: Experimental study.

MATERIALS AND METHODS: Granulosa cells (GCs) were obtained from ovaries of 12- to 13-week-old WT and Ebap−/− mice, cultured to preconfluence, serum starved 2-12 hours depending on the experiment, and treated with vehicle alone (negative control), FSH (100 mIU), or Forskolin (20 μM; positive control); activates adenylyl cyclase and increases intracellular levels of cAMP independent of FSH and its receptor). Estradiol production by GCs was measured by ELISA. Expression of aromatase and EGR-1 (Early Growth Response-1) mRNA and protein by was detected by quantitative reverse transcription-polymerase chain reaction (qRT-PCR) and Western Blot analysis, respectively. To determine whether the ERK signaling in response to FSH receptor activation is affected in GCs of Ebap−/− mice, down-stream mediators p-ERK1/2, p-MEK1/2 and p-90RSK was examined by Western blot analysis and normalized to house keeping gene GAPDH.

RESULTS: Estradiol production in response to FSH was significantly decreased in Ebap−/− GCs (p < 0.05). Similarly, FSH-induced expression of aromatase and Egr-1 were significantly decreased in the GCs of Ebap−/− mice (p < 0.05). FSH strongly activated ERK signaling in WT GCs, such that p-ERK1/2, p-MEK1/2 and p-90RSK significantly increased following 5 and 10 min of FSH treatment. However, FSH treatment of Ebap−/− GCs did not result in an increase in p-ERK1/2, p-MEK1/2 and p-90RSK.

CONCLUSIONS: In granulosa cells, EPAB-deficiency results in impaired ERK signaling in response to FSH, associated with decreased aromatase expression and estradiol production. Our findings demonstrate that oocyte-specific EPAB is important for regulating the function of GCs, and that the FSH signaling pathway is, at least in part, responsible for somatic cell dysfunction in Ebap−/− mice.

Supported by: R01HD095909 from the National Institute of Health (NIH), O-123 Tuesday, October 18, 2016 11:45 AM

UTILIZATION OF ADIPOSE DERIVED STEM CELLS FOR THE IN VITRO MATURATION OF PRIMARY AND EARLY SECONDARY OVARIAN FOLLICLES. L. J. Green, H. Zhou, A. Shikanov; OB-GYN, University of Michigan, Ann Arbor, MI; University of Michigan, Ann Arbor, MI.

OBJECTIVE: The mammalian ovary is comprised of a multitude of follicles within various stages of development. The more numerous, early stage follicles are gonadotropin independent and are regulated by paracrine and autocrine factors from the surrounding somatic cells. Mimicking this micro-environment in vitro has proved challenging in the past requiring co-culture with various “feeder” cells for follicular development. Adipose tissue is an easily accessible source to derive stem cells, which can be expanded in culture, and used to secrete various repair and growth factors that are useful for follicular development. To further mimic the native micro-environment of growing follicles, we utilized follicle encapsulation in alginate hydrogels, which is an established method of three-dimensional follicle cultures that maintains follicular morphology. Our objectives were to 1) determine if adipose derived stem cells (ADSCs) could improve survival of early stage follicles encapsulated in alginate hydrogels 2) to assess the meiotic competence of follicles co-encapsulated with ADSCs.

DESIGN: Prospective experimental study.

MATERIALS AND METHODS: Ovarian follicles ranging from 80-110 μm, from day 10-12 day old, B6CBAF1 mice were mechanically isolated and co-encapsulated with ADSC within 0.25% alginate hydrogel beads for 9-11 days. Folliucle media was changed every two days, follicle diameter and morphology were assessed using light microscopy. After 14 days of culture, the alginite beads were lysed and follicles matured in vitro.

RESULTS: In this follicle co-encapsulation system, we observed an increase in follicular survival, growth, and antrum formation of early stage follicles. Follicle survival was significantly higher (p < 0.05) in the co-encapsulation group (follicle with stem cells), with overall survival of 44.5% (n=110) compared to 9% (n=64) of controls (follicle only). Of surviving co-encapsulated follicles, 92.5% underwent germinal vesicle breakdown (GVBD), with 63.6% metaphase II (MII) oocytes.

CONCLUSIONS: To our knowledge this is the first report of an in vitro system utilizing stem cells to support follicular development. Our findings suggest that co-encapsulation of ADSCs with early stage follicles supports follicular development, through secretion of growth factors that promote follicular survival, antrum formation and meiotic competence within a hydrogel based in vitro culture system. This unique culture system has translational implications, as ADSCs could be used as an autologous source for in vitro maturation of early stage human follicles.

O-124 Tuesday, October 18, 2016 12:00 PM

A MOUSE 5-FLUOROURACIL-BASED SUBMYEOXABOLATION MODEL FOR THE STUDY OF BONE MARROW-DERIVED CELL TRAFFICKING IN REPRODUCTION. R. Tal, Y. Liu, N. Pluchino, S. Shaikh, R. Mamillapalli, H. S. Taylor. Yale School of Medicine, New Haven, CT.

OBJECTIVE: Bone marrow (BM)-derived cells (BMDCs) contribute to endometrial regeneration. Most animal models to date investigating BMDCs recruitment to the uterus utilized irradiation prior to BM transplant (BMT), which leads to ovarian failure. Therefore, such models cannot be used to study the role of BMDCs in various reproductive processes such as pregnancy. 5-fluorouracil (5-FU) is non-gonadotoxic but is associated with very low BM engraftment (<3%) when given as single dose. Our objective was to develop a non-gonadotoxic BMT model for the study of BMDCs trafficking in reproduction.

DESIGN: Animal study.

MATERIALS AND METHODS: 6wk-old female C57BL/6J mice (n=12/group) received i.p. either a single (150mg/Kg) 5-FU dose 24h before BMT (CT1), or paired-dose 5-FU with stem cell factor (SCF) 150μg/Kg on days -5 and -1 prior to BMT (CT2+SCF). Control mice received BMT or saline. For BM, 20×10⁶ BM cells obtained from green-fluorescent protein (GFP) mice were injected intravenously into recipients. For fertility experiment, mice were
O-125 Tuesday, October 18, 2016 12:15 PM

DETERMINATION OF TIMING AND MECHANISM OF DIPLOIDIZATION OF HAPLOID PARTHENOGENETIC AND ANDROGENETIC HUMAN EMBRYOS. L. C. Grossman, a,b G. Chia, a M. Zuccaro, a S. Sadovsky, a R. Prosser, a M. V. Sauer, a,b D. Egli, a,c Columbia University Medical Center, New York, NY; bCenter for Women’s Reproductive Care at Columbia University, New York, NY; cThe New York Stem Cell Foundation (NYSCF), New York, NY.

OBJECTIVE: Most stem cell lines derived from haploid human embryos are diploid.d This study aims to determine the timing and potential mechanism of diploidization.

DESIGN: Laboratory study using human gametes.

MATERIALS AND METHODS: Fresh oocytes were obtained from women ages 22-29 years who consented to undergo an oocyte donor cycle to donate oocytes to stem cell research under Institutional Review Board protocol from 8/2015 - 4/2016. Metaphase II (MII) oocytes were manipulated within 4 hours of donation, while immature oocytes were cultured in global total media for up to 48 hours and then used if they became a MII oocyte. MII oocytes were either activated by an electrical pulse and puromycin to create parthenogenetic (P) embryos, or enucleated and injected with sperm via intracytoplasmic sperm injection to create androgenetic (A) embryos. Embryos were incubated and the morphology was assessed daily. Embryos with poor morphology or delayed growth were fixed in 4% paraformaldehyde, stained for human centromere protein A and analyzed by confocal microscopy, including 36 P (8 2-4 cell, 11 cleavage stage, 6 multi-cell, 3 morula, 8 blastocyst TE biopsy) and 33 A (5 2-4 cell, 8 cleavage stage, 7 multi-cell, 5 morula, 8 blastocyst TE biopsy). One cell was found to be diploid in a morula in a P embryo, while all other diploid cells were found at the blastocyst stage (Table 1). Binucleated cells were noted at all stages of development, with highest percentage in TE cells. There was no significant difference in diploidization or binucleated cells in comparing P and A embryos at each developmental stage.

CONCLUSIONS: Diploidization of haploid cells begins as the embryo becomes a blastocyst. Binucleated cells, seen as early as the 4 cell stage, could explain how diploidization occurs. Understanding the mechanism and timing of diploidization is the key to improve the success of growing and maintaining haploid stem cell lines, which could be used in autosome recessive disease research, stem cell therapy, and potentially gamete production in the future.

References:

Supported by: NYSCF

O-126 Tuesday, October 18, 2016 12:30 PM

THE RHO GUANINE NUCLEOTIDE EXCHANGE FACTOR (RHO-GEF) DOMAIN OF AKINASE ANCHORING PROTEIN-13 (AKAP13) IS NECESSARY FOR OPTIMAL GONADOTROPIN SIGNALING IN GRANULOSA CELLS. K. C. Cayton, a C. M. Owen, a P. Driggers, a J. Segars, a ¢GYN/OB, Johns Hopkins School of Medicine, Baltimore, MD; ¢NIH/NICHD/PRAE, Bethesda, MD.

OBJECTIVE: AKAP13 plays an active role in gonadotropin-dependent gene transcription. We previously showed that AKAP13 augments cyclic AMP response element binding protein (CREB) activation in granulosa cells (GCs) and is required for optimal follicle stimulating hormone signaling. Since the exact mechanisms by which AKAP13 mediates gonadotropin signaling through CREB remains unclear, we sought to further explore regions of AKAP13 required for CREB activation.

DESIGN: Laboratory Research Study.

MATERIALS AND METHODS: COV434, a GC tumor line, or COS-7 cells were serum-starved overnight prior to transfection with a cyclic-AMP response element (CRE) luciferase reporter plasmid (CRE-Luc), AKAP13 expression vector, an AKAP13 expression vector encoding a tyrosine to phenylalanine mutation that eliminates RhoA (Ras homolog family member A) binding by the GEF domain (Y2153F; GEF-), or empty vector control. COS-7 cells were transfected with C3 (Clostridium Botulinum toxin 3, an inhibitor of RhoA) exoenzyme or luteinizing hormone receptor (LHR) expression vectors. Transfections were performed 24hrs prior to treatment with empty vehicle, protein kinase A activator forskolin (FSK), or human chorionic gonadotropin (hCG). Cells were harvested after 24hrs treatment and luciferase assays were performed.

RESULTS: Transfection of COV434 cells with AKAP13 expression vector resulted in an increase of CRE-Luc activity by ~7 fold in untreated cells compared to controls (P < 0.05). Addition of AKAP13 GEF mutant reduced CRE-Luc activity by 48% in untreated COV434 cells (P < 0.001). The reduction of CRE-Luc activity by AKAP13 GEF mutant was also observed in FSK treated COV434 cells. Transfection of COS-7 cells with AKAP13 GEF mutant resulted in a decrease of CRE-Luc activity compared to wild-type AKAP13. In addition,
O-127 Tuesday, October 18, 2016 11:15 AM

COMPROMISED DEVELOPMENTAL COMPETENCE OF DAY 7 HUMAN BLASTOCYSTS. S. McCormick, K. A. LaRocque, K. Hammes, J. M. Stevens, W. B. Schoolcraft, M. Katz-Jaffe. Colorado Center for Reproductive Medicine, Lone Tree, CO.

OBJECTIVE: To evaluate the chromosome constitution and developmental competence of day 7 human blastocysts.

DESIGN: Retrospective analysis with maternal age matched controls.

MATERIALS AND METHODS: A total of 938 day 7 blastocysts, created from 610 IVF cycles performed between 2011 and 2015, were biopsied for comprehensive chromosome screening prior to vitrification. Standard protocols for a hormone replacement frozen embryo transfer (FET) were employed and only euploid blastocysts were selected for transfer. Statistical analysis included Fisher’s exact and Chi-square test where appropriate.

RESULTS: Chromosome numeration of D7 blastocysts revealed a 37% euploidy rate with parental age being a significant factor contributing to aneuploidy (maternal 35.8% vs. 39.1 years; paternal 38.3% vs. 40.7 years, respectively; both p<0.0001). The majority of the aneuploid D7 blastocysts involved a single error (59%) with 25% containing 2 chromosome errors and only 16% three or more errors. There was a significant association between chromosome constitution and blastocyst grading with a higher proportion of euploid grade 5 and grade 6 blastocysts (P<0.0001). The gender proportion for D7 blastocysts was only slightly biased with 50.9% euploid males compared to 49.1% euploid females. Following transfer of only D7 euploid blastocysts (n=76 FETs; mean maternal age = 37.1±3.9 years), infertile women achieved poorer clinical outcomes compared to maternal age matched counterparts with D5 or D6 euploid blastocysts (n=1,314 SETs; mean maternal age = 37.1±3.6 years). Biochemical pregnancy (D7 = 47.8% vs. D5/D6 = 79.2%; P<0.0001), clinical pregnancy with fetal heart tone (D7 = 32.9% vs. D5/D6 = 65.8%; P<0.0001), miscarriage (D7 = 12.0% vs. D5/D6 = 4.2%; ns) and live birth rates (D7 = 29.0% vs. D5/D6 = 63.0%; P<0.0001) were all significantly impacted with D7 slower blastocyst development.

CONCLUSIONS: Significant compromised developmental competence was observed for D7 euploid blastocysts compared to maternal age matched counterparts with transferred D5/D6 euploid blastocysts. Biochemical, metabolic and epigenetic processes that can impact embryo viability, independent of chromosome numeration, are potential contributors to the observed halving of the live birth rate for D7 euploid blastocysts. Despite poorer outcomes, these data would suggest that trophoectoderm biopsy of D7 blastocysts is a clinical option for poor prognosis infertility patients since viable euploid blastocysts may result.

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CHANGE IN DAY OF EMBRYO TRANSFER (ET) BY AGE AND PRIMARY DIAGNOSIS IN A REAL-WORLD US DATABASE STUDY OF 66,051 TRANSFERS OVER 6.5 YEARS. K. S. Richter, a G. L. Motta, a B. Kaplan, a B. Hayward, a M. C. Mahony, a Research, Shady Grove Fertility Reproductive Science Center, Rockville, MD; bResearch, Shady Grove Fertility Reproductive Science Center, Annapolis, MD; cFertility Centers of Illinois, Chicago, IL; dEMD Serono, Inc., Rockland, MA.

OBJECTIVE: To evaluate the practice changes in day of ET in IVF cycles for women in the US by age and primary diagnosis from a large real-world database.

DESIGN: Non-randomized, observational, retrospective, large US real-world database analysis.

MATERIALS AND METHODS: Data from all autologous IVF cycles with fresh ET between July 2009 and Dec 2015 within a large US clinical database were analyzed by age (SART categories) and primary diagnoses (diminished ovarian reserve [DOR], ovulation disorders/PCOS, male infertility, unexplained infertility).

RESULTS: ETs occurred on Day 3 in 16,548 women (25,524 cycles) and on Day 5/6 in 28,474 women (38,008 cycles). Mean (SD) female age at the time of IVF was higher for Day 3 ETs compared with Day 5/6 ETs (36.4 [4.42] vs 33.7 [4.27] years, p<0.0001), and Day 1 antral follicle counts were lower (11.7 [7.36] vs 17.4 [9.53], p<0.0001), respectively. Number of embryos transferred per ET and pregnancy and live birth outcomes stratified by day of transfer for all patients and by primary diagnosis are shown (see table). Of note, over the 6.5 years of the study, the percentages of ETs shifted gradually and steadily away from Day 3 and towards Day 5/6 ETs (p<0.0001). Most cycles were DETs; but SET rates were significantly increased in all groups for Day 5/6 vs Day 3, except for DOR where >2 embryos were routinely transferred. Transfer of >2 embryos was greater with Day 3 vs Day 5/6 ETs across groups. CPR per ET was lower after Day 3 vs Day 5/6 ET. Across the groups, live births were predominantly singletons; all groups for both Day 3 and Day 5/6 ETs had comparable rates of singleton and twin births.

CONCLUSIONS: Diagnosis did not impact day of transfer treatment decisions except for DOR. SET rates were increased in Day 5/6 ETs as >2 ETs were routinely transferred.
decreased but DETs were predominant and similar whether ET was Day 3 or Day 5/6. Day 5/6 ETs resulted in significantly higher LBRs per ET than Day 3 ETs. Overall, the increased rate of SET in Day 5/6 ETs likely contributed to multiple birth rates lower than the national average (26.6%) while maintaining high LBRS.

References:

Supported by: Study supported by EMD Serono, Inc., Rockland, MA, USA (a business of Merck KGaA, Darmstadt, Germany).

O-129 Tuesday, October 18, 2016 11:45 AM

INTRAUTERINE HUMAN CHORIONIC GONADOTROPIN (HCG) INFUSION PRIOR TO EMBRYO TRANSFER (ET) MAY BE DETRIMENTAL TO PREGNANCY RATE. M. Volovsky, a M. Healey, b V. B. MacLachlan, b B. J. Vollenhoven. c aMonash University, Melbourne, Australia; bUniversity of Melbourne, Malvern East, Australia; cMonash IVF, Victoria, Australia; fObstetrics and Gynaecology, Monash University, Melbourne, Australia.

OBJECTIVE: The process of embryo implantation is influenced by both embryonic and endometrial factors. The receptivity of the endometrium is vital to the process and hence much attention has been given to enhancing the intrauterine environment. A hormone thought to have beneficial effects on the intrauterine environment is HCG. It has been postulated that an intrauterine HCG infusion prior to ET could potentially increase implantation rates. However, up to this point, evidence on the matter is conflicting. Therefore, our aim was to investigate whether intrauterine HCG at the time of ET improves pregnancy rate.

DESIGN: The study design was a matched case control study based on a standardised database from a multi-site private in vitro fertilisation clinic.

MATERIALS AND METHODS: Initial analysis involved all patients including those using multiple adjuvants (n=1153). A second analysis was performed in which no additional adjuvants other than intrauterine HCG infusions were used (n=667). In both analyses there were two groups: an intervention group of those given an intrauterine HCG infusion, and a control group of patients receiving no infusion. Cases were matched according to the following variables: maternal age, number of embryos transferred, embryo age, tubal factor infertility, progressive number of ETs since a live birth, IVF clinic site. In the initial analysis matching also included the use of melanotan, intralipid, growth hormone, testosterone, cefuroxime and flargristim. Matching was performed with the MatchIt module in R, using the "genetic" method with a case control ratio of 1:2. The outcomes were defined as: chemical pregnancy, clinical pregnancy, clinical pregnancy loss and a live birth.

RESULTS: The sample in which adjuvants were allowed demonstrated statistically significant reductions in chemical pregnancy (OR 0.78 CI 0.63-0.96), clinical pregnancy (OR 0.71 CI 0.57-0.88) and live birth rates (OR 0.67 CI 0.53-0.86) when intrauterine HCG infusions were used prior to ET. Analysis where no additional adjuvants were used similarly found that intrauterine HCG use produced declines in chemical pregnancy (OR 0.65 CI 0.48-0.87), clinical pregnancy (0.67 CI 0.49-0.90) and live birth rates (0.65 CI 0.46-0.93) when compared to a control group. Sub-analysis of frozen embryo transfers (FET) revealed a marked decrease in chemical pregnancy, clinical pregnancy and live birth rates in the setting of intrauterine HCG infusions in both the initial and second analyses.

CONCLUSIONS: Intrauterine HCG prior to ET was shown to not only have no benefit on pregnancy outcomes but a potentially negative effect, particularly when used before FET. Hence, there is an indication for prospective randomised studies in this area. Moreover, as there is now documented potential for harm, use of HCG infusions prior to ETs should be limited to within such trials. Less may be more for some patients.

References:

O-130 Tuesday, October 18, 2016 12:00 PM

AS GOOD AS IT GETS: DONOR EGGS AND A GESTATIONAL CARRIER. R. J. Chektowski, a A. C. Eisenberg. a Alta Bates IVF, Berkeley, CA; bAlta Bates IVF, Oakland, CA.

OBJECTIVE: To compare live birth (LB) and embryo implantation (IR) rates in donor egg cycles with and without a gestational carrier (GC). Since the former treatment optimizes both embryonic and recipient-related variables while the latter approach optimizes only embryonic components, this comparison provides an estimate of the relative magnitudes of these two major components of successful outcome.

DESIGN: A case control study using anonymous compensated egg donors 2:1 for their age and year of treatment.

MATERIALS AND METHODS: The study group (SG) includes 19 egg retrievals (ER) in egg donors followed by 23 embryo transfers (13 fresh and 10 frozen ETs) into screened GCs. The control group (CG) consists of 38 ERs in matched egg donors with 84 ETs (51 fresh and 33 frozen) into infertile recipients. The principal outcome measures are: 1. cumulative LB/ER; 2. IR calculated for both fresh and frozen ETs up to and including the first LB, but excluding any subsequent deliveries; 2. LB/ET; 3. IR defined as total # of infants/total # of embryos transferred. Additional outcome measures include: number of embryos/ET, multi-fetal pregnancies, recipients’ age, endometrial thickness, fibroids, abnormalities of uterine cavity, ease of transfer and BMI. Chi-square and t-tests are used with P<0.05 indicating significance.

RESULTS: All three primary outcome measures are more favorable in the SG than in the CG: cumulative LB/ER 94.7% vs 72.2% (P=0.041); LB/ET 78.3% vs 46.4% (P=0.007); IR 40.0% vs 21.4% (P=0.010). There are no significant differences between egg donors in the two groups. The number of embryos transferred (2.0 vs 2.2) and twin deliveries (27.8% vs 25.6%) are similar with no high order multiple births. GCs are younger (33.6 vs 44.0; P=0.001), have more children (2.5 vs 0.3; P=0.001) and a thicker lining (10.4 vs 9.5 mm; P=0.029) than the infertile recipients. Only infertile recipients have fibroids (0% vs 40.4%; P=0.002) and abnormal uterine cavity (0% vs. 44.2%; P=0.001). Difficult ETs (4.3% vs 7.2%) and BMI (26.2 vs 25.8) are comparable.

CONCLUSIONS: Donor eggs with a surrogate result in better outcomes than donor eggs alone as evidenced by all three measures of clinical success: cumulative LB/ER (“take-home baby rate”), LB/ET and IR. This pilot study suggests that the relative impact of the embryonic and recipient-related factors are 70-75% and 20-25%, respectively. Fibroids and abnormal uterine cavity are the most common recipient-related variables which are absent in screened GCs and which may thus account in part for the observed difference in treatment outcomes.

References:

O-131 Tuesday, October 18, 2016 12:15 PM

ARE WE TRANSFERRING TOO MANY EMBRYOS IN THE MOST FAVORABLE GROUP OF FRESH AUTOLOGOUS IVF CYCLES: A 2013 UPDATE. S. Keyhan, a K. S. Acharya, a C. R. Acharya, b S. J. LL, c S. J. Maunder, a Division of Reproductive Endocrinology and Infertility, Duke University Medical Center, Durham, NC; bDept. Of Biostatistics and Bioinformatics, Duke Computational Biology and Bioinformatics, Durham, NC.

OBJECTIVE: Our group has reported a high rate of non-compliance with the American Society for Reproductive Medicine/Society for Assisted Reproductive Technologies (ASRM/SART) embryo transfer (ET) guidelines in first fresh autologous cycles from 2011-2012, especially for blastocyst stage transfers. This led to an unacceptable multiple pregnancy rate (MPR) in patients <35 years. The objective of this study was to determine the noncompliance rate for first fresh IVF cycles.
with excess cryopreserved embryos, using the 2013 SART data and assess the impact of this on MPR in this most favorable group of patients.

**DESIGN:** Retrospective cohort study.

**MATERIALS AND METHODS:** 2,249 first fresh autologous IVF cycles in women under the age of 35 and with excess embryos for cryopreservation undergoing ET from the 2013 SART registry were stratified based on stage of embryo transfer. Cycles were classified as compliant (C) or noncompliant (NC) based on their adherence to published 2013 ASRM/SART guidelines for favorable prognosis patients. Main outcomes were the percentage of C and NC cycles in each ET group as well as the MPR (≥2 fetal heart beats on ultrasound) in each of these groups. P-values were obtained from t-tests and chi-square test and were appropriately adjusted for multiple comparisons using the Benjamini-Hochberg method.

**RESULTS:** Among cycles involving cleavage stage ET, 97.1% were compliant. There was no significant difference in clinical pregnancy rate (CPR), live birth rate (LBR), multiple LBR and MPR between C and NC compliant among cleavage stage ET cycles. On the other hand, the majority of cycles involving blastocyst stage ET were noncompliant. Although the NC group had a significantly higher CPR and LBR, the MPR and multiple LBR were also significantly higher compared to the C group. Results are shown in the table.

**CONCLUSIONS:** The vast majority of cycles involving cleavage stage ET were compliant but the MPR was still high (35%). Non-compliance in the blastocyst embryo transfer group remains high at 61% in patients <35 years. The transfer of ≥2 blastocyst embryos in this group of patients continues to lead to an exceptionally high MPR (50%) and multiple LBR (43%). Elective single embryo transfer, preferably at the blastocyst stage, needs to be encouraged in these young, favorable prognosis patients.

**O-132 Tuesday, October 18, 2016 12:30 PM**

**EVALUATING PREGNANCY AND LIVE BIRTH OUTCOMES IN A REAL-WORLD ANALYSIS OF A US DATABASE OF 66,051 TRANSFERS OVER 6.5 YEARS.**

K. S. Richter,a G. L. Mottla,b B. Kaplan,c B. Hayward,d M. C. Mahony.e Research, Shady Grove Fertility Reproductive Science Center, Rockville, MD; bResearch, Shady Grove Fertility Reproductive Science Center, Annapolis, MD; cFertility Centers of Illinois, Chicago, IL; dEMD Serono, Inc., Rockland, MA.

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<td>5503/11,722 (46.9)</td>
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<td>4501/11,817 (38.1)</td>
<td>3596/11,817 (30.4)</td>
<td>3596/4501 (79.9)</td>
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<td>10,147/17,316 (58.6)</td>
<td>8322/17,316 (48.1)</td>
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<td>6135/24,120 (25.4)</td>
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<td>14,683/31,921 (46.0)</td>
<td>14,683/18,087 (81.2)</td>
<td>11,215/14,683 (76.4)</td>
<td>3347/14,683 (22.8)</td>
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Higher-order multiples = ≥3 live births.

Data are limited to transfers occurring before January 1, 2015, to allow for follow-up of birth outcomes.

All between-group comparisons were significantly different (p<0.0001).
OBJECTIVE: To evaluate pregnancy and live birth outcomes with IVF with single embryo transfer (SET) and >1 embryo transfer (ET) over time in assisted reproductive technology cycles for women in the US from a large real-world database.

DESIGN: Non-randomized, observational, retrospective, large US real-world database analysis.

MATERIALS AND METHODS: Data from all autologous IVF cycles with fresh ET between Jul 2009 and Dec 2015 within a large US clinical dataset were analyzed.

RESULTS: Among a total of 66,051 transfers, over time, there was an overall increase in SETs, from 20.6% of transfers in Jul 2009 to 45.8% in Dec 2015, resulting from a decrease in double ETs (DETs), from 53.6% of transfers in Jul 2009 to 44.5% in Dec 2015, and a dramatic decrease in >2 ETs, from 25.8% of transfers in Jul 2009 to 9.7% in Dec 2015. Of the 66,051 transfers, 25,522 were on Day 3 and 38,003 were on Day 5/6. For Day 5/6 transfers, there was an increase in SETs and a decrease in DETs over time, with similar proportions of each (approximately 45% of total transfers) occurring by 2015. Pregnancy and live birth outcomes following SETs, DETs, and >2 ETs for Day 3 versus Day 5/6 transfers are shown (see Table). From Jul 2009 to Dec 2014, the proportion of Singleton/Birth increased (from 74.4% to 82.2%), while twins and higher-order multiples decreased (from 24.5% to 17.0% and 1.1% to 0.8%, respectively). Further outcomes analyses by primary diagnosis and Society for Assisted Reproductive Technology age groups will be presented.

CONCLUSIONS: From 2009 to 2015, the proportion of SETs increased and the proportion of DETs and >2 ETs decreased. With Day 5/6 transfer, clinical pregnancy rates (CPRs) were similar with SET and >1 ET, but the incidence of twin and multiple live births was greater with >1 ET. Thus, in appropriate patient populations, SET performed at Day 5/6 has the ability to optimize CPR/live birth rate and the proportion of singleton live births, thereby minimizing and equalizing the number of twin and higher-order multiple pregnancies, respectively.

Supported by: Study supported by EMD Serono, Inc., Rockland, MA, USA (a business of Merck KGaA, Darmstadt, Germany).

OOCYTE BIOLOGY

O-133 Tuesday, October 18, 2016 11:15 AM

MITOCHONDRIAL STRESS RESPONSE IS REQUIRED FOR FEMAAL FERTILITY. T. Wang, E. Babayev, K. Lowther, E. Seli. Department of Obstetrics, Gynecology, and Reproductive Sciences, Yale School of Medicine, New Haven, CT.

OBJECTIVE: Mitochondrial unfolded protein response (mt-UPR) is a highly conserved mechanism by which cells maintain homeostasis in the presence of cellular and metabolic stress. ClpP (caseinolytic peptidase P) plays a central role in this process by promoting degradation of unfolded mitochondrial proteins. We hypothesized that mt-UPR is essential for oocyte and early embryo development and investigated fertility parameters in mice lacking ClpP.

DESIGN: Experimental study.

MATERIALS AND METHODS: Mature (12-weeks-old) ClpP knockout (ClpP−/−) female mice were compared to wild type (WT). Follicle development was assessed in serial ovarian sections stained with hematoxylin and eosin. Ability to generate oocytes (germinal vesicle [GV] and metaphase II [MII]) 2-cell embryos and blastocystcs was assessed after injection with PMSG (5IU) or PMSG and hCG (5IU) and mating with WT males as indicated. Spindle morphology was determined in in vivo and in vitro matured oocytes by staining with tubulin and DAPI. Mitochondrial membrane potential was measured by JC-1, and mitochondrial ATP levels were measured by bioluminescent assay (Abcam). Reactive oxygen species (ROS) levels were measured by staining oocytes with 6-carboxy-2',7'-dichlorodihydrofluorescein diacetate (carboxy-H2DCFDA), followed by fluorescence detection using confocal microscopy. Mitochondrial DNA (mtDNA) copy number was measured in individual oocytes by cloning of mitochondria specific gene (Cox3) as a standard, followed quantitative real-time PCR (qPCR). ANOVA, student’s t-test, and Chi Square analysis were used for statistical analysis as appropriate.

RESULTS: Number of preantral and antral follicles was similar in ClpP−/− and WT mice ovaries, as was the number of GV oocytes obtained following PMSG stimulation. However, ClpP−/− mice generated a significantly lower number of MII oocytes (7.8 vs 25, p<0.05) and 2-cell embryos (3 vs 24, p<0.01), and no blastocysts (0 vs 12.75, p<0.05). In vitro maturation revealed that ClpP−/− oocytes had a significantly lower rate of GVBD after 9h (30.5 vs 86.5%, p<0.01) and 18h (37.9 vs 98.5%, p<0.05), and a significantly higher number of ClpP−/− oocytes had abnormal spindles at MI (76.3 vs 19.6%, p<0.01) and MII oocyte stage (74.4 vs 14.4%, p<0.01). Both mitochondrial membrane potential (0.97 vs 1.72, p<0.001) and ATP levels (13.5 vs 19.6, p<0.001) were significantly decreased in ClpP−/− oocytes, while ROS levels (74.6 vs 41.4 pixel intensity, p<0.001) and mtDNA copy number (384.105 vs 188.154, p<0.001) were increased.

CONCLUSIONS: Loss of mt-UPR by homozygous deletion of ClpP results in female infertility due to impaired oocyte and embryo development, associated with decreased energy production and accumulation of detrimental ROS. As mt-UPR pathway is implicated in longevity and mtDNA copy number is associated with embryo viability in IVF, further exploration of this pathway may have diagnostic and therapeutic implications for infertility.

Supported by: R01HD059909 from the National Institute of Health (NIH).

O-134 Tuesday, October 18, 2016 11:30 AM


OBJECTIVE: To determine whether immature oocytes can be efficiently recovered from ovarian tissue harvested for freezing and matured in vitro, to enable oocyte or embryo cryopreservation in tandem.

DESIGN: Prospective Study.

MATERIALS AND METHODS: 65 females (mean age 32.1±0.71; range of 24-38) underwent fertility preservation (FP) with ovarian tissue cryopreservation for cancer; 12 of which already initiated chemotherapy. At the time of the harvesting, small antral follicles were aspirated either laparoscopically, or by a fine gauge needle in the laboratory (n=52). Alternatively, small preantral follicles were excised (n=55) from the tissue before being punctured in a separate dish. GV oocytes were subjected to IVM and cryopreserved for single adults or pediatric patients, or were fertilized for embryo cryopreservation in adult women with partners.

RESULTS: Of the 65 women, at least one GV oocyte was recovered in 93.8% (61/65) with a mean of 9.93±0.86 (0-31) oocytes/patient. Oocyte recovery was less likely in chemo-exposed compared to non-exposed (9/12 vs. 52/53, p=0.02) with fewer oocytes recovered/patient (10.42±0.96 in chemo vs. 16.5±3.78 non-exposed; p=0.02). Of all GV oocytes, 3.9±4.53 matured into MII in vitro (range 1-18) and 12.9±3.66% of women cryopreserving at least one mature oocyte (range 1-18). Chemotherapy exposure significantly reduced the IVM rate; 41.56±3.45% in no exposure vs. 25.3±7.6% in chemo exposed (p=0.05). The method of oocyte recovery did not affect the IVM rates; 43.7±4.50% with aspiration vs. 38.1±3.90% after excision (p=0.34). An IVM media did not statistically significantly improve IVM rates compared to blastocyst culture media (43.7±4.75% vs. 32.4±6.21%, respectively; p=0.31). Of the oocytes of 22 adult females who requested embryo cryopreservation, 64.70±7.5% was fertilized, yielding a mean of 1.64±0.32 cryopreserved embryos (range 1-6) per patient. Overall, 76.92% (50/65) of the patients had at least one oocyte or embryo cryopreserved in addition to ovarian tissue.

CONCLUSIONS: This is the largest prospective study on the combined approach of GV oocyte recovery and in vitro maturation with ovarian tissue cryopreservation as a FP strategy. Our data indicates that this strategy is efficient, enabling the performance of additional established FP procedures. However, chemotherapy exposure immediately prior to ovarian tissue reduces oocyte yield and IVM rates. The GV oocyte recovery followed by IVM should be combined with all ovarian tissue cryopreservation cases.

O-135 Tuesday, October 18, 2016 11:45 AM

EFFECT OF GALACTOSE AND ITS METABOLITES ON DEVELOPMENT AND QUALITY OF MURINE EMBRYOS PRODUCED IN VITRO. M. Thakur, F. Sheib, H. Kohan-Ghadr, S. Khan, F. Qadir, G. Konik, H. Abu-Soud. Division of Reproductive
Endocrinology and Infertility, Department of Obstetrics and Gynecology, Wayne State University School of Medicine, Detroit, MI; ²CS Mott Center for Human Growth and Development, Department of Obstetrics and Gynecology, Wayne State University School of Medicine, Detroit, MI; ³Department of Obstetrics and Gynecology, Wayne State University School of Medicine, Detroit, MI.

OBJECTIVE: A majority of women with classic galactosemia suffer from premature ovarian insufficiency and infertility. Recently, we have shown that galactose and its metabolites, galactose 1-phosphate and galactitol deteriorate oocyte quality by a mechanism that involves the enhancement of reactive oxygen species. The objective of this study was to explore the role of these compounds on oocyte quality postovulation.

RESULTS: At 24 hours post insemination, majority of the oocytes exposed to galactose and its metabolites appeared granulared and failed to fertilize, however the cleavage rate 24 hours post-fertilization was not statistically significant in the different exposure groups. The rates of embryo development at 48 hours were significantly lower in oocytes exposed to galactitol (5%) and galactose 1-phosphate (5%) as compared to controls (45%). The arrested embryos were highly fragmented and at (2.5%), galactitol (0) and galactose 1-phosphate (2.5%) in comparison to controls (37.5%). A similar trend was also observed in oocytes exposed to D-Galactose (17.5%) but did not reach statistical significance. Most of the zygotes exhibited fragments and a large perivitelline space. After 96 hours post-insemination, the rates of expanded blastocysts were significantly lower in all three treatment groups; D-galactose (2.5%), galactitol (0) and galactose 1-phosphate (2.5%) in comparison to controls (45%). The arrested embryos were highly fragmented and atretic. In summary, galactose and its metabolite disturbed the spindle structure and chromosomal alignment due to oxidative stress, with significant decline in oocyte cleavage and blastocyst development after in-vitro fertilization.

CONCLUSIONS: Our results confirm that galactose and its metabolites adversely affect oocyte quality and this damage is mediated by oxidative stress. Strategies that lower plasma galactose metabolites and/or antioxidant supplements could improve oocyte quality in females with classic galactosemia, and extend their window of fertility.

References:

Supported by: Wayne State Research and Development Fund, SRERE Women’s Cure Fund.

O-135 Tuesday, October 18, 2016 12:00 PM

EPAB IS REQUIRED FOR THE DEVELOPMENT OF OOCYTE-SOMATIC CELL COMMUNICATION IN PREANTRAL FOLLICLES. K. Lowther, C. Yang, H. S. Taylor, E. Seli. Department of Obstetrics, Gynecology and Reproductive Sciences, Yale School of Medicine, New Haven, CT.

OBJECTIVE: EPAB (Embryonic-Poly(A) Binding Protein) is an oocyte-specific RNA binding protein required for translational activation of maternal mRNAs. EPAB knockout (Epab⁻/⁻) mice are infertile due to defects in oocyte maturation, cumulus expansion, and ovulation. To further understand the role of EPAB during folliculogenesis, we investigated whether oocyte-somatic communication is disrupted as a result of EPAB deficiency.

DESIGN: Experimental study.

MATERIALS AND METHODS: Gap junction (GJ) function was examined by injecting AlexaFluor488 into preantral follicle-enclosed oocytes (FEOs) and measuring the ratio of oocyte and granulosa cell fluorescence. Transzonal processes (TZPs) were examined by fixation and phallolidin staining of F-actin. Follicle growth was measured after 6 days of culture in the presence or absence of oocyte-secreted factors (OSFs) FGF9, BMP15, and FGFB. Gene expression was examined by qRT-PCR.

RESULTS: In Epab⁻/⁻ FEOs smaller than 125 um, the ratio of fluorescence was comparable to WT FEO’s (0.6 vs 0.7; ns) indicating that GJs were functional. However, in Epab⁻/⁻ FEO’s larger than 125 um, the dye was retained in the oocyte and the ratio of fluorescence was significantly lower (0.6 vs. 0.25; P<0.0001). Consistent with the timing of GJ dysfunction, F-actin staining of TZPs was similar in WT and Epab⁻/⁻ FEOs < 125 um, but was dramatically reduced in Epab⁻/⁻ FEO’s > 125 um. Since TZPs are important for secretion of OSFs that promote folliculogenesis, the in vitro growth of WT and Epab⁻/⁻ preantral FEOs was examined. After 6 days of culture, WT FEOs reached the early antral stage (272 um) whereas Epab⁻/⁻ FEOs did not grow beyond the preantral stage (182 um). Addition of OSFs to the culture restored the growth of Epab⁻/⁻ FEO’s (182 um vs. 258 um; P<0.0001) while WT FEO’s were unaffected (272 um vs. 250 um; n.s.). Furthermore, expression of glycolytic transcripts (LdhA, Pfkpa, Pkm2) that are regulated by OSFs was significantly lower in cumulus cells from Epab⁻/⁻ mice. Lastly, Epab expression during folliculogenesis was examined. The copy number of Epab transcripts in the oocyte increased significantly from the primary to preantral stage (98,053 vs. 247,084; P<0.05) and remained steady until the antral stage (279,382).

CONCLUSIONS: Our findings demonstrate a precise role for oocyte-specific EPAB at the preantral stage of folliculogenesis in promoting oocyte-somatic communication.

Supported by: R01HD059909 from the National Institute of Health (NIH).

O-137 Tuesday, October 18, 2016 12:15 PM

RELATIONSHIP BETWEEN PRE ICSI MEIOTIC SPINDLE ANGLE, OVARIAN RESERVE, GONADOTROPIN STIMULATION AND PREGNANCY OUTCOMES. A. Mahfoudh, J. Moon, S. Henderson, W. Son, Dahan. “MUHC Reproductive Center, Montreal, QC, Canada; ²Stanford Children Hospital Fertility and Reproductive Health, Sunnyvale, CA; ³McGill University, Montreal, QC, Canada.

OBJECTIVE: The goals of this study are: 1) to analyze the clinical pregnancy rate as a function of the pre-ICSI oocyte spindle angle, 2) to determine factors which can be associated with different spindle angles, if clinically relevant.

DESIGN: Retrospective study.

MATERIALS AND METHODS: 58 patients, who underwent their first ICSI cycle from January-December 2013, were included. Oocytes were collected after gonadotropin stimulated IVF cycles. Protocols used included long-agonist, antagonist and microdose-flare. Human chorionic gonadotropin (hCG) was injected 35 hours before oocyte retrieval. 830 oocytes were collected, 648 were metaphase-II (MII) on retrieval day. Oocytes were evaluated using the Polscope™ to visualize the meiotic spindle. Spindles were characterized in terms of visibility and their position in relation to the first polar body (PB). Among the 648 MII oocytes, 581 (89%) had visible spindles and were separated into 3 groups based on angle: (group 1; n=297) 0°-29°; (group 2; n=212) 30°-89°; (group 3; n=72) ≥90° and those with no visible spindle (group 4; n=67). All patients had single embryo transfer. ANOVA and posterior testing were used to compare baseline data. Chi-squared was used to compare pregnancy rates. P-value ≤0.05 was considered significant.

RESULTS: The rate of blastocyst development was associated with the spindle angle (p=0.002). The rate of good quality blastocysts were: group 1 (42%), group 2 (30%), group 3 (35%), group 4 (19%) (p=0.02). Pregnancy and live birth rates were also affected (p=0.007; p=0.046, respectively). Antral follicle count (AFC) (p=0.001), total FSH stimulating dose (p=0.001) and peak serum estradiol level (p=0.001) were associated with spindle angle grouping. Miscarriage rates trended different (p=0.07). On the other hand, female age (p=0.77), male age (p=0.91), day 3 follicle-stimulating hormone (FSH) levels (p=0.08) were not associated with spindle angle grouping. Plot analysis revealed that inclusion in group 4 was more common among lower AFC subjects than groups 1 to 3, as was use of higher FSH doses and higher peak stimulated estradiol.

CONCLUSIONS: Embryos resulting from oocytes with pre-ICSI spindle angles between 0°-29° were associated with better blastocyst, 55/FERTILITY & STERILITY®
CONCLUSIONS: Our results define a critical role for an mRNA decay factor in the downregulation of transcription activators leading to germline transcription elongation.

Supported by: H. Cook-Andersen was supported by the Women’s Reproductive Health Research grant K12 HD001259 and by a grant from the American Society for Reproductive Medicine, University of California, San Diego, La Jolla, CA; University of California, San Diego, La Jolla, CA.

OBJECTIVE: Global transcriptional silencing during the transition from the fully differentiated oocyte to the totipotent embryo is a highly conserved evolutionary event that is poorly understood despite its critical role in the earliest developmental stages of animals from worms to humans. Here, we report the unexpected finding that this germline-specific, genome-wide event depends on an mRNA decay activator.

MATERIALS AND METHODS: Oocyte-specific mouse knockout of Zfp36l2.

RESULTS: We find that oocyte-specific loss of ZFP36L2, an RNA-binding protein critical for decay of a subset of cellular mRNAs, prevents global transcriptional silencing in oocytes during folliculogenesis. Female Zfp36l2 conditional knockout mice are infertile, and oocytes deficient in ZFP36L2 are developmentally incompetent, with defects in oocyte survival and maturation, as well as a complete failure to undergo normal fertilization. Single-cell RNAseq analysis of peri-ovulatory oocytes revealed that ZFP36L2 regulates scores of genes that are candidates to mediate global transcriptional silencing, including factors with roles in histone modification, DNA methylation, transcription initiation, and transcription elongation.

OVARIAN STIMULATION

O-139 Tuesday, October 18, 2016 11:15 AM

THE CONCENTRATION OF COMMERCIAL HCG TRIGGER IS IMPRECISE AND INACCURATE. I. Woo,1 E. Davenport,1 S. A. Ingle,2 F. Z. Stancyk,2 K. Chung,3 K. Bendikson,4 R. Paulson.1 1University of Southern California, Los Angeles, CA; 2Preventive Medicine, University of Southern California, Los Angeles, CA; 3Obstetrics & Gynecology, Keck School of Medicine of USC, Los Angeles, CA.

OBJECTIVE: During controlled ovarian hyperstimulation for IVF, human chorionic gonadotropin (HCG) is administered to induce oocyte maturation approximately 34–35 hours before oocyte aspiration. Post-trigger serum HCG levels have been shown to correlate with incidence of OHSS. One strategy used to prevent this complication is to reduce the HCG dose. Due to the variability in serum HCG post-trigger, we hypothesized serum HCG concentration from the manufacturer may not be consistent. The primary objective of this study was to measure the concentration of HCG in commercially available preparation. Secondary objectives were to determine if other factors were associated with serum HCG including: BMI, oocyte maturity, and risk for OHSS.

MATERIALS AND METHODS: Each bottle of HCG trigger containing approximately 10,000 IU of HCG was mixed with 1mL of water and subsequently 0.1mL of each vial was analyzed for actual HCG concentration. Calculation was performed to determine the true dose patient received from the remaining 0.9mL. Patients returned the following day to measure serum HCG to ensure proper administration and absorption. All HCG concentration were measured with Immulite 2000. Descriptive statistics was performed along with a stepwise multiple regression analysis to predict whether dose, time from trigger injection, or BMI would influence serum HCG.

RESULTS: 108 patients were identified between Nov 2015–March 2016. Patient’s HCG trigger concentration ranged from 6,591–24,766 IU/mL with a mean 13,191±3,670 IU/mL. The dose patients actually received ranged from 7,361-22,289 IU/mL, instead of the expected 9,000IU. Serum HCG overall ranged from 76-637mIU/mL with mean 301±114mIU/mL. Patient’s weight was significantly correlated with serum HCG level (R² = 0.27, p < 0.01) after adjusting for dose and time from trigger. When stratifying BMI into normal, overweight, and obese categories, for each increasing BMI category, serum HCG levels were dropped by approximately 70mIU/mL (likelihood ratio test p = 0.0001). Serum HCG was not correlated with number of oocytes retrieved, percent mature oocytes, pregnancy, or OHSS. OHSS occurred in 3 patients, with serum HCG ranging from 312-544mIU/mL.

CONCLUSIONS: Variability in serum HCG post-trigger is due to inconsistent HCG concentrations in commercial formulations and due to patient weight. The large variability in HCG concentrations in the vials makes it difficult to choose an optimal dose. Decreasing the dose of HCG to prevent OHSS may not be effective unless the actual concentration of HCG is calculated.
Table: Outcomes in progesterone supported and control groups with Odds Ratio

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Control group N=147 (% ± standard deviation)</th>
<th>Progesterone group N= 151 (% ± standard deviation)</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical pregnancy</td>
<td>18.4 ± 3.8 (27/147)</td>
<td>13.2 ± 3.4 (20/151)</td>
<td>0.68 (0.36 - 1.26)</td>
</tr>
<tr>
<td>Ongoing pregnancy</td>
<td>14.7 ± 3.5 (22/147)</td>
<td>12.2 ± 3.3 (18/151)</td>
<td>0.77 (0.39 - 1.48)</td>
</tr>
<tr>
<td>Total pregnancy</td>
<td>24.0 ± 4.3 (36/147)</td>
<td>17.3 ± 3.7 (24/151)</td>
<td>0.58 (0.33 - 1.03)</td>
</tr>
<tr>
<td>Biochemical pregnancy</td>
<td>6.0 ± 2.8 (9/147)</td>
<td>2.7 ± 3.3 (4/151)</td>
<td>0.42 (0.13 - 1.31)</td>
</tr>
<tr>
<td>Spontaneous abortion</td>
<td>3.3 ± 4.1 (5/147)</td>
<td>1.4 ± 1.2 (2/151)</td>
<td>0.38 (0.0 - 1.74)</td>
</tr>
</tbody>
</table>

**O-142 Tuesday, October 18, 2016 12:00 PM**

**THE EFFECT OF LUTEAL PHASE SUPPORT ON PREGNANCY RATES IN INTRAUTERINE INSEMINATION CYCLES FOLLOWING OVARIAN STIMULATION WITH GONADOTROPINS- A RANDOMIZED CONTROLLED TRIAL.**  
J. Han, T. Motan, Obstetrics and Gynecology, University of Alberta, Edmonton, AB, Canada; University of Alberta, Edmonton, AB, Canada.

OBJECTIVE: To investigate if luteal phase support with vaginal progesterone in controlled ovarian hyperstimulation (COH) using gonadotropins and intrauterine insemination (IUI) improves conception rates in couples with infertility.

DESIGN: Single centre, open label randomized controlled trial.

PARTICIPANTS: Couples with infertility meeting inclusion criteria underwent 298 cycles of COH with gonadotropins and IUI.

MATERIALS AND METHODS: Couples meeting inclusion criteria had treatment at the Fertility and Women’s Endocrine Clinic at the Royal Alexandra Hospital using gonadotropin COH and IUI between December 2013 and December 2015. Inclusion criteria were: 1) More than 12 months of unprotected intercourse without conceiving, 2) Confirmed bilateral tubal patency, 3) More than 10 million motile sperm available for IUI. Randomization was done prior to the IUI with the study group receiving vaginal micronized progesterone (Endometrin 100 mg vaginally BID) from the day of IUI for at least 16 days until clinical pregnancy test. Control group patients received no luteal phase support. Clinic COH protocols were followed for all participants including baseline investigations and cycle monitoring. Ovulation was triggered with hCG when at least one follicle > 17 mm was seen, and IUI was performed approximately 36-hours later. Patient demographics, cycle characteristics and outcomes were analyzed. The primary outcome was clinical pregnancy rate (presence of a fetal heart beat after 6-weeks gestational age). Secondary outcomes were biochemical pregnancy rate, non-viable pregnancy rate and ongoing pregnancy rates (continuing past first trimester).

RESULTS: There were no statistically significant differences (Fisher’s Exact) between the treatment and control groups in primary and secondary outcomes (table). There were no clinically significant differences in demographic, baseline characteristics and stimulation cycles between groups.

CONCLUSIONS: This randomised control trial indicates that luteal phase support with vaginal progesterone does not affect the conception rate in intrauterine insemination cycles following ovarian stimulation with gonadotropins.

Supported by: Ferring Pharmaceuticals subsidised the Endometrin used.
PROSPECTIVE DOUBLE-BLIND RANDOMIZED PLACEBO CONTROLLED CLINICAL TRIAL COMPAREING PREGNANCY RATES AFTER CO-ADMINISTRATION OF LOW DOSE hCG AT THE TIME OF GnRH-AGONIST TRIGGER OR 35 HOURS LATER, FOR THE PREVENTION OF OHSS.

OBJECTIVE: To compare the effectiveness of adjuvant hCG administration at the time of GnRH-agonist (GnRH-a) trigger or 35 hours later.

Design: Prospective double-blind randomized clinical trial at large university based infertility center.

Materials and Methods: Subjects at high risk for OHSS (age <35, AMH 3.5 or diagnosis of PCOS, and >14 follicles) undergoing GnRH antagonist cycles were randomly assigned to receive one of two previously published adjuvant hCG protocols. Arm 1 received 1000 IU hCG+GnRH-a trigger and placebo 35 hours later (at retrieval). Arm 2 received placebo+GnRH-a trigger and 1500 IU hCG 35 hours later. The groups were blinded to both physicians and patients. Subjects with E2 levels ≥ 4,000pg/mL and with subjects with <14 mature follicles were excluded. All subjects had OHSS evaluation 9 days after trigger and were followed until negative pregnancy test or final pregnancy outcome. Sample size calculation yielded 40 subjects in each arm to detect a significant difference in mean luteal phase ovarian volume between the arms (p < 0.05). All subjects having blastocyst transfer were included for final analysis. 34 subjects were randomized to Arm 1 and 37 subjects were randomized to Arm 2. There was no difference in the number of subjects excluded after randomization between the two arms (p = 0.36). Of those included in the final analysis, 26/34 (76.5%) were randomized to Arm 1 and 31/37 (83.8%) were randomized to Arm 2. Demographic and cycle data for the two arms are presented in Table 1. There were 4 cases of OHSS (2 in Arm 1, 1 in Arm 2 and 1 in Arm 1, p = 0.39). All were categorized as mild or moderate and managed conservatively. There was no difference in mean luteal phase ovarian volume between the arms (p = 0.06). Clinical pregnancy, ongoing pregnancy, and live birth rates were 63.2%, 59%, and 50%, respectively. Clinical pregnancy rate was 65.4% in Arm 1 and 61.3% in Arm 2 (p = 0.75). Ongoing pregnancy rate was 53.8% in Arm 1 and 48.4% in Arm 2 (p = 0.68). There was no significant difference in loss rates (22.7% vs. 29.2%, p = 0.62) or live birth rate (53.8% vs. 48.4%, p = 0.68) between the two arms.

Conclusions: No significant difference was noted in outcomes between the two adjuvant low-dose hCG treatment groups. Both treatments afforded excellent ongoing pregnancy rates and should be considered in women at high risk for OHSS.

Supported by: Supported in part by an unrestricted educational grant from Merck Pharmaceuticals ( Rahway, NJ)
Values are median (25th - 75th percentile), *mean (standard deviation) or number (percentage).

Technologies®. A total of 179 participants were randomized. Eighty-eight women were allocated to the fresh transfer group and 91 to the frozen transfer group. 1-2 embryos were transferred according to embryo availability and patient preference.

RESULTS: Comparison of fresh and frozen transfers of euploid blastocysts that were expanded and biopsied on day 5 (excluding frozen transfers of day 6 embryos).

CONCLUSIONS: Our findings suggest similar implantation and ongoing clinical pregnancy rates of euploid expanded blastocysts in both treatment groups. Fresh transfers may be more affordable and slightly faster, but can be logistically challenging for patients and staff and may be associated with a higher incidence of low birth weight and preterm births compared to frozen cycles (1-3). Freezing all embryos may facilitate scheduling and allow for careful consideration of the CCS results of all embryos rather than just the day 5 cohort on the day of transfer. This RCT showed there is no difference in implantation and pregnancy rates between transfer protocols suggesting that the preferred strategy may be to vitrify all embryos and transfer in a subsequent cycle.

References:

Supported by: Institutional support.

O-146 Tuesday, October 18, 2016 11:30 AM
COMPREHENSIVE REVIEW OF CHROMOSOME REARRANGEMENT CASES ANALYZED BY PREIMPLANTATION GENETIC SCREENING, E. Cameron, J. Klavianin, T. T. Gordon, M. R. Hughes. Genesis Genetics, Plymouth, MI.

OBJECTIVE: Patients with structural chromosome rearrangements are at increased risk for adverse reproductive outcomes, including recurrent miscarriage, offspring with congenital anomalies, and reduced fertility. Many of these patients pursue in vitro fertilization with preimplantation genetic screening (PGS) to improve pregnancy outcome. Previous publications have routinely focused on blastomere biopsy samples from translocation carriers alone. The purpose of this study was to catalogue PGS data from couples with various types of chromosome rearrangements, including inversions, in order to provide more accurate risk estimates for physicians and patients.

DESIGN: Retrospective observational study. PGS results from couples with a known chromosome rearrangement who underwent testing between January 2014 and December 2015 were classified according to type of rearrangement (inversion, reciprocal translocation, or Robertsonian translocation) and data was analyzed for overall euploid/aneuploid rates. Complex rearrangements, sex chromosome rearrangements, and common inversion 9 cases were excluded.

MATERIALS AND METHODS: 1,763 biopsy samples (272 blastomere; 1,491 trophectoderm) were examined from 276 families. All embryo biopsy samples were subjected to whole genome amplification using SurePlex DNA amplification (Illumina) and Quantifluor dsDNA kits (Promega). Chromosome copy number was assessed by Illumina's 24-Sure+ Translocation microarrays (924 samples) or VeriSeq Next Generation Sequencing (839 samples); all data profiles were analyzed using the Illumina BlueFuse Multi software.

RESULTS: 1,660 of 1,763 embryos subjected to PGS were successfully analyzed, yielding a no result rate of 5.8% due to amplification failure or data below quality thresholds. Data is summarized in Table 1.

CONCLUSIONS: To our knowledge, this study demonstrates the largest data set of embryo biopsy samples from couples with different types of structural chromosome rearrangements. These data indicate that euploid rates differ according to the type of chromosome rearrangement present and allow for more targeted counseling of this patient population. Future analyses should further classify euploid/aneuploid rates of these various rearrangements according to maternal age and gender of transmitting parent.

O-147 Tuesday, October 18, 2016 11:45 AM
NO DIAGNOSIS AFTER DAY 3 BIOSPY: INDICATIVE OF EMBRYO PROGNOSIS OR BIOSPY ERROR. E. Yeboa, S. Munne, T. Escudero, N. Cekleniak, J. L. Frattarelli, D. Tortoriello, S. G. Prough, A. Coates, Reprogenetics, Livingston, NJ; IRMS Reproductive Medicine at Saint Barnabas, Livingston, NJ; Fertility Institute of Hawaii, Honolulu, HI; Sher Institute for Reproductive Medicine, New York, NY; Tulsa Fertility Center, Tulsa, OK; Oregon Reproductive Medicine, Portland, OR.

OBJECTIVE: Although more IVF centers are adopting trophectoderm biopsy for PGS instead of “cleavage stage” (D3), some clinics still offer these two options to their patients. One of the main challenges with D3 biopsy procedures is the limited amount of genetic material available to perform analysis. Limited genetic material may give a no result diagnosis or a chaotic profile, which are common in apoptotic cells and/or DNA damage during biopsy. These results lead to inconclusive diagnoses posing a burden on reproductive care providers on whether to biopsy these “no conclusive” embryos or to discard them. The aim of this study was to determine the likelihood that a D3 biopsy without a diagnosis, will have a genetically assigned diagnosis when allowed to grow to day 5/6, and to compare that diagnosis to a control group of blastocysts of similar maternal age, to determine if blastocysts resulting from day 3 “no result” embryos have a poorer prognosis than the control group.

DESIGN: Retrospective data analysis by Array Comparative Genomic Hybridization (aCGH).

MATERIALS AND METHODS: Data collected from 1,240 patients who underwent aCGH testing with a total of 8,000 embryos were analyzed. All embryos that had a diagnosis of “Degraded DNA” (N= 79) or a “No
Diagnosis (N=41) - also referred to as “no result” after the initial biopsy and were subsequently rebiopsied for repeat aCGH testing were included in this analysis (n=120). As a control group, 12,222 blastocyst were analyzed from patients (similar to the test group) who underwent aCGH testing between 2012 to February 2016.

RESULTS: The results attained from the analysis of all blastocyst with the same average age (35yrs) and time frame (control group) was concordant to the blastocysts rebiopsied from the “non conclusive” blastomeres.

CONCLUSIONS: This observed concordance between the control and the experimental group suggests that the plausible explanation for the “no result” diagnosis primarily originates from anuclear or apoptotic cells, damaged cells during biopsy, or faulty biopsy, but not an intrinsic problem of the embryo. The majority of blastomeres that were rebiopsied on day 5/6 received a diagnosis, and of those, they showed very similar rates of euploidy as the control group, indicating that these embryos are equally competent genetically, and should not be discarded but rebiopsied.

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OBJECTIVE: Chromosome abnormality is one of the major causes of infertility. In Japan, only PGD regarding patients with severe genetic disorders and balanced translocations experienced with recurrent abortion are permitted. The purpose of this study is to compare results of ART without PGD between reciprocal translocation and Robertsonian translocation.

DESIGN: This is a retrospective analysis of clinical outcome between January of 1999 and July of 2014.

MATERIALS AND METHODS: Thirty-nine reciprocal translocations (29 men and 10 women) and 24 Robertsonian translocations (21 men and 3 women) were enrolled in the study. Among 29 couples with men’s reciprocal translocation, 61 fresh embryo transfers and 33 frozen-thawed embryo transfers were performed. Among 10 couples with women’s reciprocal translocation, 14 fresh embryo transfers and 8 frozen-thawed embryo transfers were performed. On the other hand, among 21 couples with men’s Robertsonian translocation, 38 fresh embryo transfers and 29 frozen-thawed embryo transfers were performed. Among 10 couples with women’s Robertsonian translocation, 4 fresh embryo transfers and 1 frozen-thawed embryo transfer were performed.

RESULTS: The clinical pregnancy rate per embryo transfer among couples with men’s reciprocal translocation was comparable with that among couples with women’s reciprocal translocation (26.6% vs 27.3%). The delivery rate per embryo transfer among couples with men’s reciprocal translocation was as well comparable with that among couples with women’s reciprocal translocation (14.9% vs 13.6%). On the other hand, the clinical pregnancy rate per embryo transfer among couples with men’s Robertsonian translocation was comparable with that among couples with women’s Robertsonian translocation (40.3% vs 40.0%). The delivery rate per embryo transfer among couples with men’s Robertsonian translocation was also comparable with that among couples with women’s Robertsonian translocation (31.3% vs 40.0%). Next, the clinical pregnancy rate per embryo transfer among couples with reciprocal translocation was comparable with that among couples with Robertsonian translocation (26.7% vs 40.3%). The abortion rate per embryo transfer among couples with reciprocal translocation was also comparable with that among couples with Robertsonian translocation (21.4% vs 12.5%). However, the delivery rate per embryo transfer among couples with reciprocal translocation was significantly lower than that among couples with Robertsonian translocation (14.7% vs 31.9%; P<0.01).

CONCLUSIONS: In the case of performing ART without PGD, the delivery rate per embryo transfer among couples with reciprocal translocation was significantly lower than that among couples with Robertsonian translocation.

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IS PREIMPLANTATION GENETIC SCREENING WITH FROZEN SINGLE EMBRYO TRANSFER SUPERIOR TO FRESH IN-VITRO FERTILIZATION WITH ELECTIVE SINGLE EMBRYO TRANSFER IN A GOOD PROGNOSIS POPULATION? A. Schaffer,b D. McQueen,a J. Mathews,a J. Lieberman,a M. L. Uhlerb E. C. Feinberg,a “The University of Chicago, Chicago, IL; University of Illinois Chicago, Chicago, IL; Fertility Centers of Illinois, Chicago, IL; Reproductive Endocrinology and Infertility, Fertility Centers of Illinois, Warrenville, IL; Fertility Centers of Illinois, Highland Park, IL.

OBJECTIVE: Elective single embryo transfer (eSET) in a highly selected population offers excellent clinical pregnancy rates with low rates of multiple gestation. Preimplantation genetic screening (PGS) is increasingly utilized, but whether it is superior to eSET in a good prognosis population has yet to be determined. Our objective was to compare pregnancy outcomes in good prognosis patients who utilized PGS versus those who underwent a fresh IVF cycle with eSET.

DESIGN: Retrospective matched cohort study.

MATERIALS AND METHODS: IRB approval was obtained. Women <38yo undergoing autologous IVF with single embryo transfer between 2012-2015 were included. eSET was offered to women <38yo with <2 prior failed cycles and >1 high quality blastocyst on day 5. Outcomes with eSET were compared to outcomes with PGS followed by frozen transfer of a single euploid embryo (PGS/eSET). eSET patients were matched to PGS/eSET patients by age and date of embryo transfer with a 3:1 ratio. The primary outcome was ongoing pregnancy rate (OPR) at 20 weeks gestation. Odds ratios (OR) used eSET as the reference group.

RESULTS: 237 women were included: 172 (72.6%) eSET and 65 (27.4%) PGS/eSET. There were no significant demographic differences between groups (Table 1). There was no significant difference in clinical pregnancy rate (CPR) between PGS/eSET and eSET, 58.5% vs. 61.6%, OR 0.88 (95% CI 0.49-1.57). There was also no significant difference in OPR between PGS/eSET and eSET, 44.6% vs 55.8%, OR 0.64 (95% CI 0.36-1.13). There was a significantly higher spontaneous abortion rate with PGS/eSET compared to eSET, 23.7% vs. 7.5%, OR 3.80 (95% CI 1.34-10.74). In patients <35yo, there was a trend toward a lower CPR in PGS/eSET compared to eSET, 44.7% vs 62.3%, P=0.09. In patients 35-37 years old, the OPR was similar between groups, 44.4% vs 43.1%, P=0.92.

CONCLUSIONS: Outcomes with PGS/eSET were not superior to eSET in this population. In women <38yo who underwent fresh IVF with careful visual selection of the single best embryo on day 5, ongoing pregnancy rates were similar to women who underwent PGS/eSET with euploidy as guidance for embryo selection. Surprisingly, there was a significantly higher miscarriage rate in women <38 undergoing PGS/eSET, which needs to be examined in a larger study. While the use of PGS may confer other benefits, it was not found to increase ongoing pregnancy rates in a good prognosis population.

Table 1. Group Characteristics (N=237)

<table>
<thead>
<tr>
<th></th>
<th>PGS/eSET (n=65)</th>
<th>eSET (n=172)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Age yrs (SD)</td>
<td>33.4 (3.0)</td>
<td>33.1 (2.8)</td>
<td>0.47</td>
</tr>
<tr>
<td>Mean BMI kg/m² (SD)</td>
<td>25.1 (5.7)</td>
<td>25.5 (6.4)</td>
<td>0.66</td>
</tr>
<tr>
<td>Mean Day 3 FSH (SD)</td>
<td>8.4 (3.2)</td>
<td>8.2 (4.1)</td>
<td>0.72</td>
</tr>
<tr>
<td>Smoking</td>
<td>2/65 (3.1%)</td>
<td>13/172 (7.6%)</td>
<td>0.25</td>
</tr>
<tr>
<td>Clinical Pregnancy Rate (CPR)</td>
<td>38/65 (58.5%)</td>
<td>106/172 (61.6%)</td>
<td>0.76</td>
</tr>
<tr>
<td>Ongoing Pregnancy Rate (OPR)</td>
<td>29/65 (44.6%)</td>
<td>96/172 (55.8%)</td>
<td>0.16</td>
</tr>
<tr>
<td>Biochemical Loss Rate</td>
<td>8/46 (17.4%)</td>
<td>12/118 (10.2%)</td>
<td>0.29</td>
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<tr>
<td>Spontaneous</td>
<td>9/38 (23.7%)</td>
<td>8/106 (7.5%)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

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OBJECTIVE: Preimplantation genetic screening (PGS) attempts to maximize the proportion of euploid transfers thus increasing per transfer pregnancy rates while decreasing multiple gestations. However, false positive (FP) results lead clinics to discard euploid embryos. Women over 39 have few blastocysts available for transfer thus experiencing greater harm from discarding a euploid embryo from a false positive PGS. We have designed a decision analytic model and cost effectiveness analysis to compare the live birth rate and cost effectiveness of a fresh blastocyst transfer cycle versus a PGS cycle based on various FP rates for PGS.

DESIGN: Decision tree and cost-effectiveness analytic model.

MATERIALS AND METHODS: A model was built to conduct a head to head comparison of live birth rates per cycle of PGS versus fresh blastocyst transfer in women ages 39-40, 41-42, and 43-44. Point estimates were collected from peer reviewed manuscripts, publically available SART data and expert consensus when necessary. Based on available data we estimated the cost of an IVF cycle including medications to be $14,800 and that of a PGS cycle to be $20,300. The harmful effects of embryo biopsy and blastocyst freeze/thaw were assumed to be negligible. Miscarriage rates for blastocyst transfer were modeled as 22.6%, 36.7% and 45% for women ages 39-40, 41-42 and 43-44, respectively. Women undergoing PGS had miscarriage rates of 18.8%, 14.5% and 20% for ages 39-40, 41-42 and 43-44, respectively. A sensitivity analysis was conducted to support the robustness of the model. A range of values for FP for PGS between 4% and 16% were utilized. The primary outcome measures were live birth rate and cost-effectiveness per cycle of PGS versus fresh blastocyst transfer.

RESULTS: The live birth rates per cycle were lower for each group of women aged 39-44 with PGS versus conventional blastocyst transfer cycles (Table 1). Meanwhile, PGS was less cost effective than a fresh blastocyst cycle. Women 39-40 had a decreased cost per live birth of $37,015. The per cycle live birth rate of women aged 39-40 undergoing PGS varied between 18-26% with decreasing FP from 16% to 4%. CONCLUSIONS: Women above 39 undergoing PGS experience inferior live birth rates and worse cost effectiveness per cycle compared to women with a fresh blastocyst transfer. Across a range of possible false positives for PGS, our model demonstrated a decreased live birth rate. This model highlights the clinical imperative to evaluate PGS among older women who will produce few blastocysts for transfer.

MENTAL HEALTH

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OBJECTIVE: The purpose of this study was to assess the impact of psychological distress (depression, anxiety and stress), as assessed by both subjective and objective measures, on in-vitro Fertilization (IVF) outcome and to describe the pattern of psychological distress throughout the course of IVF treatment.

DESIGN: Prospective, controlled study with psychological data collected at four time points during IVF treatment: start of IVF; oocyte retrieval, embryo transfer and day of pregnancy test.

MATERIALS AND METHODS: Setting: Academic center for Reproductive Medicine & Infertility. Patients were divided in three groups: those who underwent IVF for the first time, those who underwent IVF having failed two or more times, and those who underwent IVF as oocyte donors. Stress Measures: Four self-report questionnaires and serum levels of cortisol, ACTH and IL-6. Main outcome measure: Clinical pregnancy as documented by an intrauterine pregnancy on ultrasound. One-way analyses of variance (ANOVA) were run for each of the four time points to compare the mean levels of anxiety, depression and infertility related stress among patients.

RESULTS: The sample consisted of 186 patients who underwent IVF between 1/2010 and 9/2013 for either primary or secondary infertility. Self-report measures of depression, anxiety and stress did not show any association to IVF outcome. These findings were further corroborated by the lack of an association between biological markers of stress and IVF outcome. Significant differences, however, were found in the pattern of psychological distress among the three groups. Higher levels of depression and stress were reported by both IVF treatment groups in comparison to donors at the start of treatment and at the time of retrieval. However, it was the donors who showed a more direct, acute HPA activation as seen by elevated cortisol level. At the time of oocyte retrieval and embryo transfer cortisol levels dropped significantly, especially among donors, despite the rise in reported stress. Between the time of embryo transfer and pregnancy, cortisol levels began to rise again to a similar degree in both IVF groups, but it was those with repeated IVF failures that reported the greatest degree of psychological distress.

CONCLUSIONS: Psychological distress did not affect pregnancy outcome. While it is important to reassure patients that their level of stress will likely not impact their chances of IVF success, it is also essential to be sensitive to the fact that infertile patients undergoing IVF do experience real psychological distress, especially during the period between embryo transfer and 1st pregnancy test. Reaching out to patients who, because of prior failed treatment attempts, are more psychologically vulnerable, may be an important tool in reducing the burden of treatment and ultimately decreasing patient drop out.

Supported by: Support: The study was supported by a grant from the NIH-funded Clinical and Translational Science Center at the Weill Cornell Medical College and New York Presbyterian Hospital

O-152 Tuesday, October 18, 2016 11:30 AM

BEATING BIOLOGY AND BUYING TIME: AN UPDATE SURVEY OF WOMEN’S EXPERIENCES AFTER OOCYTE CRYOPRESERVATION (OC) FOR DEFERRED REPRODUCTION. B. Hodes-Wertz, S. Druckenmiller, M. Smith, Y. G. Kramer, N. Noyes. NYU Langone Medical Center, New York, NY.

OBJECTIVE: To further understanding of how women who pursue OC for deferred reproduction think and act relative to reproduction and dating.

DESIGN: 2016 anonymous 39-question survey with comparison to our prior OC patient survey completed in 2012.

MATERIALS AND METHODS: From 2005-15, 1817 women underwent ≥1 OC treatment cycle at our facility; 866 (48%) agreed to post-treatment contact, and our survey was distributed to these patients.

RESULTS: There were 224 survey responses (rate: 26%). From 2012 to 2016, the percentage of women that froze at 33-35y increased (13 to 24%) while those 39-41y decreased (39 to 23%); 44% froze between 36-38y consistent with our clinical data also demonstrating a decrease in age at time of OC. 53% underwent OC in the last 2 years. As in 2012, 80% of respondents were Caucasian, and >70% were never married, reported lack of partner as the no. 1 reason for not yet having children and wished they had undergone OC earlier. The majority now feel the ideal age for egg freezing is 29-34y, with only 16% choosing ≥35y. Of note, more (25 vs. 16%) were in a relationship at time of OC with ½ stating the relationship was <1y. 77% reported difficulty finding someone with whom to co-parent at the time of OC. >80% currently report a desire to have children while <20% remain unsure as to whether they definitely want children in the future. Cost was the greatest obstacle to pursuing OC. 1/3 received

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financial support, mostly from family, with parents being the most common source. After OC, 30% admitted an attitude change toward parenting, mostly in a positive way (i.e. made it a priority or increased openness to alternative family-creating options). >60% also felt less embarrassed or biologically undefined. They were most often met with positive responses, though a sizable minority reported feeling feeling more focused, less desperate with more time to find the right partner. >60% admitted discussing OC while dating and 90% with family/friends. They were most often met with positive support. 96% would recommend OC to another. After undergoing OC, 22% got pregnant or had children without resorting to their frozen eggs (2/3 naturally; 1/3 ART; 4% adoption). 13% of respondents thawed eggs resulting in a 32% live birth rate. Of those not yet thawing, 1/2 cited lacking a suitable co-parent as the obstacle; 90% reported future intent to thaw.

CONCLUSIONS: Women are pursuing OC at younger ages, with the primary indication being lack of a suitable co-parenting partner; the latter was also the most common reason cited for not returning to use eggs sooner. Cost was prohibitive for many, with some relying on family finances. Most reported OC as a positive experience, improving views of parenting, inciting healthier dating practices, enhancing hope for future family and expanding acceptable options for achieving that goal.

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STRESS, DEPRESSION, AND THE DESIRE FOR SOCIAL SUPPORT AMONG MALE PATIENTS IN FERTILITY AND CANCER CLINICS. S. A. Miner,a D. M. Daumler,a F. Chan,a K. Lo,a A. Gupta,a Z. Rosberger,a P. Zelkowitz,a,b 1Department of Psychiatry, Jewish General Hospital, Montreal, QC, Canada; McGill University Health Center, Montreal, QC, Canada; 2Mount Sinai Hospital, University of Toronto, Toronto, ON, Canada; 3Princess Margaret Cancer Centre, University of Toronto, Toronto, ON, Canada; 4Psychology, Jewish General Hospital, Montreal, QC, Canada; 5Lady Davis Hospital for Medical Research, Jewish General Hospital, Montreal, QC, Canada.

OBJECTIVE: For women, the diagnosis of infertility has been shown to be as stressful as a cancer diagnosis; however, such relative stress levels have not been studied in men. This study compares male fertility and cancer patients’ self-reported mental health status and their relative desire for social support.

DESIGN: We conducted separate online surveys of male fertility patients (N = 242) and male cancer patients (N = 167) who were recruited in hospitals and clinics. Men were asked about their fertility concerns, mental health, and desire for social support.

MATERIALS AND METHODS: After combining the datasets for the two surveys, we performed a two-way analysis of variance (ANOVA) to evaluate the relationship between patient type and self-reported stress (PSS-4) and depression, separately. We also used a logistic regression analysis to assess the association between patient type and the desire for social support, controlling for age, self-reported mental health status, and other demographic characteristics.

RESULTS: We found that male cancer patients reported higher levels of stress (p < 0.001) and depression (p < 0.05), relative to male fertility patients. Although self-reported mental health status was associated with a greater willingness to use a social support network, cancer patients were less interested in accessing all forms of social support (p < 0.001), even after controlling for age, stress, and depression. Ultimately, patient type was the most significant predictor of men’s desire to use a social support network (p < 0.05) and a mobile health application (p < 0.01), controlling for stress, depression, and all demographic variables.

CONCLUSIONS: In contrast to previous research on women, our findings show that male cancer patients report worse mental health status than male fertility patients. Despite having lower levels of self-reported stress and depression, male fertility patients are more likely than male cancer patients to express a desire for social support. The increased need for support may be due to the lack of resources that are available to male fertility patients, as compared to those available to male cancer patients. An educational mobile health application with a built-in peer support network could address male fertility patients’ desire for information and resources.

References:

Supported by: The study was funded by a grant from Canadian Institutes of Health Research TE1-138296.

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AN INTERNET-BASED MIND/BODY INTERVENTION TO MITIGATE DISTRESS IN WOMEN EXPERIENCING INFERTILITY: A RANDOMIZED PILOT TRIAL. J. Clifton,a J. Parent,b G. Worrall,a M. Seehus,a M. Evans,b R. Forehand,a A. D. Domar,b 1Psychological Science, University of Vermont, Burlington, VT; 2College of Medicine, University of Vermont, Burlington, VT; 3Psychology, Middlebury College, Middlebury, VT; 4Domar Center for Mind/Body Health, Boston IVF, Waltham, MA.

OBJECTIVE: Heightened anxiety and depressive symptoms are often comorbid with infertility diagnoses. However, despite numerous studies which document the positive impact of group mind/body interventions on distress levels and pregnancy rates, most patients do not avail themselves of such services. Barriers include privacy, a fear of stigmatization, cost, and the time commitment. The current study translated an empirically validated in-person mind/body group program into an internet-delivered intervention. The need for such an intervention is supported by the data from this study. The primary goals of this pilot were to demonstrate that (1) the mind/body program developed for in-person implementation can be translated into an internet-based treatment; (2) participants will report appropriate levels of acceptance and readiness to engage in and complete this internet-based intervention; (3) participants will demonstrate reduction over the course of treatment in anxiety and depression symptom severity, and 4), the intervention is associated with increases in pregnancy rates.

DESIGN: This pilot project was a randomized controlled trial using a between groups repeated measures experimental design. Data are being reported at mid-point as the pilot study is still underway.

MATERIALS AND METHODS: The Mind/Body Program for Infertility was modified to an internet-based program. Seventy-one women were recruited and randomized to the intervention (internet-based intervention) or wait-list control group. Inclusion criteria were as follows: 2.25 years of infertility, as well as a current desire to become pregnant. Exclusion criteria included the presence of untreated depression or anxiety conditions. Additional inclusion criteria included self-reportedKnight depression, male fertility patients are more likely than male cancer patients to express the desire to use a social support network. Despite having lower levels of self-reported stress and depression, male fertility patients are more likely than male cancer patients to express a desire for social support. The increased need for support may be due to the lack of resources that are available to male fertility patients, as compared to those available to male cancer patients. An educational mobile health application with a built-in peer support network could address male fertility patients’ desire for information and resources.

References:

Supported by: The study was funded by a grant from Canadian Institutes of Health Research TE1-138296.

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BURDEN OF CARE IS THE PRIMARY REASON WHY INSURED WOMEN TERMINATE IVF TREATMENT. A. D. Domar,a K. Rooney,b C. Rich,c M. R. Hacker,d D. Sakkas,a L. E. Dodge,a 1Domar Center for Mind/Body Health, Boston IVF, Waltham, MA; 2Boston IVF, Waltham, MA; 3Obstetrics and Gynecology, Beth Israel Deaconess Medical Center, Brookline, MA; 4Obstetrics and Gynecology, Boston, MA.

OBJECTIVE: To determine the primary reason(s) why insured patients discontinue in vitro fertilization (IVF) treatment prior to achieving a live birth.

DESIGN: Cross-sectional study.
MATERIALS AND METHODS: A survey regarding treatment termination was sent to 905 women whose final IVF cycle was between January 1, 2010 and May 31, 2014, who did not achieve a live birth and who did not return for treatment for at least one year. The survey focused on an academically-affiliated IVF center was completed online or over the phone. Most residents of the state have six IVF cycles covered through an insurance mandate.

RESULTS: A total of 324 women completed the survey; the response rate was 36%. Of these, 268 (83%) had full or partial insurance coverage for IVF and were included in the analysis. Two thirds (66%) did not seek care elsewhere and discontinued all treatment. When asked for all the reasons why treatment was discontinued, the respondents indicated that further treatment was too stressful (41%), that they could not afford out of pocket costs (24%), that they lost insurance coverage (24%), that they had or were pursuing adoption (19%), that they were advised to stop treatment (11%), that they were pursuing childfree living (10%) or that they had moved on to egg or sperm donation (3%). The top three sources of stress included having already given IVF their best chance (64%), feeling too anxious or depressed to continue (51), and infertility taking too much of a toll on their relationship (39%). Interestingly, 23% of women reported that they conceived spontaneously. Of the remaining 34% of women who sought care elsewhere, the most common reason (60%) was wanting a second opinion. When participants were asked what could have made their treatment experience better, the most common suggestions were evening or weekend office hours (46%), easy and immediate access to a mental health professional (38%), more access to the physician (36%), more convenient location (35%), drop-in evening peer support groups (34%), written information on how to deal with stress (34%) and stress reduction classes (33%).

CONCLUSIONS: Psychological burden was the most common reason why insured patients reported discontinuing IVF treatment. Stress reduction strategies are desired by patients and could impact the decision to terminate treatment before achieving a live birth.

Supported by: This study was funded by the Domar Foundation.

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OBJECTIVE: Up until the point of retrieval, the patients’ requirements for oocyte freezing (OOF) and in vitro fertilization (IVF) are identical. Both require weeks of self-injection with fertility drugs, frequent office monitoring with transvaginal ultrasounds and surgery with anesthesia. However, the two groups of patients may experience different emotions or somatic manifestations of stress (1,2). The purpose of the study is to investigate the differences in attitudes and responses to fertility medications and treatment for women undergoing OOF versus IVF.

DESIGN: Prospective descriptive survey.

MATERIALS AND METHODS: Patients undergoing oocyte retrieval for OOF and IVF from February 1 to April 20, 2016 at a single institution were offered a voluntary, anonymous, and written questionnaire. The survey was adapted from a validated questionnaire, FertiQol, which assesses quality of life for patients with infertility. Demographic information and patients’ attitudes and responses to fertility medications and treatment for women undergoing OOF versus IVF.

RESULTS: For each semen variable (volume, sperm concentration, progressive motility, normal morphology) a significant proportion of HIV-1 infected patients had values below the 5th percentile of the WHO 2010 reference group (p < 0.05). The analysis of sperm DNA fragmentation showed that, in Group A, 35 patients (68.65%) had sperm DNA fragmentation > 30% whereas in Group B 9 patients (37.5%) showed sperm DNA fragmentation > 30% (P < 0.02). We did not observe any correlation between antiretroviral therapy and semen parameters.

CONCLUSIONS: Our study provides evidence that a significant proportion of HIV-1 infected patients have impaired semen parameters values below the 5th percentile of the WHO 2010 reference group and therefore a possible altered fertility. Oxidative stress, as a host response to HIV mitochondrial damage induced by HAART, and reactive oxidative species produced could damage sperm DNA and alter sperm quality. In addition, sperm nuclear fragmentation rate increases in HIV-1 infected patients receiving antiretroviral therapy when compared to HIV-1 infected patients who do not receive therapy. In the light of these results, reproductive counselling is strongly suggested for all couples with HIV-1 male partner who desire a pregnancy.

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HIV INFECTION AND ANTIRETROVIRAL THERAPY ON SEMEN PARAMETERS AND SPERM DNA INTEGRITY. V. Savasi, A. Laoreti, M. Oneta, P. Amoroso, I. Cetin. Obstetrics and Gynecology, Hospital, University of Milan, Milan, Italy; Obstetrics and Gynecology, Hospital ‘L’Sacco’, University of Milan, Milan, Italy.

OBJECTIVE: The use of antiretroviral drugs has provided a noteworthy improvement in both the quality and the expectancy of life of people infected with HIV and many couples with an HIV positive partner can consider pregnancy planning. The aims of this study were twofold: the first aim was to assess the effect of HIV-1 infection on semen parameters; the second one was to evaluate the effects of highly active antiretroviral therapy (HAART) on sperm DNA fragmentation comparing HIV-1 patients receiving HAART versus naive HIV-1 patients.

DESIGN: Observational study and Prospective study.

MATERIALS AND METHODS: For the first aim of the study, we analyzed semen samples obtained from 770 HIV-1 patients recruited between January 2005 and June 2015 in our Unit of Assisted Reproduction. Co-infections with HBV or HCV and genital tract infections represented exclusion criteria; all patients received HAART and had a CD4 count > 200 cells/mm3 Complete semen analysis was performed according to WHO 2010 recommendations, with each semen variable of the study population being compared with the WHO reference group. For the second aim of the study we performed a case-control prospective study including 75 HIV men infected: 51 of them receiving HAART (Group A) and 24 patients not receiving HAART (Group B). Sperm DNA fragmentation and semen analysis was performed using chromatin dispersion test (SCD) to evaluate the effect of HAART on sperm DNA fragmentation.

RESULTS: For each semen variable (volume, sperm concentration, progressive motility, normal morphology) a significant proportion of HIV-1 infected patients had values below the 5th percentile of the WHO 2010 reference group (p < 0.05). The analysis of sperm DNA fragmentation showed that, in Group A, 35 patients (68.65%) had sperm DNA fragmentation > 30% whereas in Group B 9 patients (37.5%) showed sperm DNA fragmentation > 30% (P < 0.02). We did not observe any correlation between antiretroviral therapy and semen parameters.

CONCLUSIONS: Our study provides evidence that a significant proportion of HIV-1 infected patients have impaired semen parameters values below the 5th percentile of the WHO 2010 reference group and therefore a possible altered fertility. Oxidative stress, as a host response to HIV mitochondrial damage induced by HAART, and reactive oxidative species produced could damage sperm DNA and alter sperm quality. In addition, sperm nuclear fragmentation rate increases in HIV-1 infected patients receiving antiretroviral therapy when compared to HIV-1 infected patients who do not receive therapy. In the light of these results, reproductive counselling is strongly suggested for all couples with HIV-1 male partner who desire a pregnancy.

O-158 Tuesday, October 18, 2016 11:30 AM
ANEUPLOIDY SCREENING AND GENOME PROFILING IN INFERTILE COUPLES. S. Cheung, T. Cuzzubbo, Z. Rosenwaks,
OBJECTIVE: Current assessment of the infertility male utilizes semen analyses, chromatin fragmentation, and fluorescent in situ hybridization (FISH) on spermatozoa. At least 15% of infertility cases are related to genetic disorders, such as chromosomal and single-gene alterations. To investigate whether all genome sequencing by estimating the involvement of specific genes can supplement standard tests used for patients undergoing infertility treatment and help profile the male genome.

DESIGN: Aneuploidy assessment on spermatozoa was carried out by 9 chromosome FISH analysis for 10 consenting men who were subdivided as fertile or infertile according to ART outcome. Two anonymous donors with proven fertility served as control. An all chromosomes analysis was then carried out by Next Generation Sequencing (NGS) and copy number variants (CNVs) were recorded to validate the chromosomal duplications and deletions. Genes with the highest CNVs were then noted for all chromosomally abnormal spermatozoa in each sample.

MATERIALS AND METHODS: FISH was performed on at least 1000 spermatozoa for each patient and controls, with a threshold of >1.6%. PCR-based random hexamer amplification from as few as 500 spermatozoa per sample yielded a DNA concentration of 447.8±198 ng/ul and quality of 1.7±1.0nm. CNVs were recorded using CASAVA and VarScan software.

RESULTS: In total, 10 men with an average age of 44.9±7.7yrs had a semen specimen concentration of 27.0±34x10⁶/ml, motility of 23.1±26.5%, and morphology of 1.5±2%. Three couples in 12 ART cycles achieved a clinical pregnancy of 75.0%, defining the fertile group. Seven couples treated in 18 cycles achieved a clinical pregnancy of 11.1% that all resulted in pregnancy loss and defined the infertile cohort. When average aneuploidy was assessed by FISH, there was no significant difference among the donor (0.1±1.0%), the fertile (0.5±0.6%) and the infertile cohorts (0.5±0.3%). Moreover, aneuploidy assessed by NGS evidenced a significant increase in aneuploidy between the fertile (5.4±1.7%) and infertile (8.2±0.6%) cohorts (P<0.00001). The incidence of duplications increased from the control at 2.3% to 7.0% for the fertile and to 9.0% for the infertile cohorts (P<0.00001). Deletions increased from the control at 4.4% to 5.9% in the fertile and to 89.7% in the infertile cohorts (P<0.00001). Additionally, NGS was unable to detect mutations in 14 genes related to the development of the normal male gamete. These mutated genes appeared to correlate to the complexity of the infertility treatment applied, such as DPY19L2 (acrosomal development) was prevalent in ICSI couples and a cohort of six genes (protein coding and RNA transport), required treatment by testicular biopsy and ICSI.

CONCLUSIONS: The utilization of NGS for analysis of spermatozoa can further optimize aneuploidy assessment and can allow for CNV detection to screen for gene mutations. NGS may help identify specific genes to provide insight into the etiology of unexplained male infertility and guide toward the appropriate treatment.

O-159 Tuesday, October 18, 2016 11:45 AM
RECONSIDERATION OF HUMAN ROUND SPERMATID INJECTION INTO THE OOCYTE (ROSI) USEFULNESS. A. Tanaka, M. Nagayoshi, Y. Takemoto. Saint Mother Hospital, Kitakyusyu, Japan.

OBJECTIVE: To date, the application of ROSI in clinical IVF has been disappointing due to difficulties in accurate identification of round spermatids among other round spermatogenic cells and insufficient oocyte activation. The existence of round spermatids has been believed to be associated with testicular spermatoozoan. That is, no testicular spermatids means no mature spermatozoa for each patient and controls, with a threshold of >1.6%. PCR-based random hexamer amplification from as few as 500 spermatozoa per sample yielded a DNA concentration of 447.8±198ng/ul and quality of 1.7±1.0nm. CNVs were recorded using CASAVA and VarScan software.

RESULTS: In total, 10 men with an average age of 44.9±7.7yrs had a semen specimen concentration of 27.0±34x10⁶/ml, motility of 23.1±26.5%, and morphology of 1.5±2%. Three couples in 12 ART cycles achieved a clinical pregnancy of 75.0%, defining the fertile group. Seven couples treated in 18 cycles achieved a clinical pregnancy of 11.1% that all resulted in pregnancy loss and defined the infertile cohort. When average aneuploidy was assessed by FISH, there was no significant difference among the donor (0.1±1.0%), the fertile (0.5±0.6%) and the infertile cohorts (0.5±0.3%). Moreover, aneuploidy assessed by NGS evidenced a significant increase in aneuploidy between the fertile (5.4±1.7%) and infertile (8.2±0.6%) cohorts (P<0.00001). The incidence of duplications increased from the control at 2.3% to 7.0% for the fertile and to 9.0% for the infertile cohorts (P<0.00001). Deletions increased from the control at 4.4% to 5.9% in the fertile and to 89.7% in the infertile cohorts (P<0.00001). Additionally, NGS was unable to detect mutations in 14 genes related to the development of the normal male gamete. These mutated genes appeared to correlate to the complexity of the infertility treatment applied, such as DPY19L2 (acrosomal development) was prevalent in ICSI couples and a cohort of six genes (protein coding and RNA transport), required treatment by testicular biopsy and ICSI.

CONCLUSIONS: The utilization of NGS for analysis of spermatozoa can further optimize aneuploidy assessment and can allow for CNV detection to screen for gene mutations. NGS may help identify specific genes to provide insight into the etiology of unexplained male infertility and guide toward the appropriate treatment.

O-160 Tuesday, October 18, 2016 12:00 PM
HEREDITARY RISK IN ICSI WITH SPERM FROM NON-MOSAIC KLINEFELTER SYNDROME PATIENTS. T. Miki, A. Tanaka, M. Nagayoshi, S. Watanabe. Saint Mother Hospital, Kitakyusyu, Japan; A. Tanaka, Y. Takemoto. Saint Mother Hospital, Kitakyusyu, Japan; A. Tanaka, Y. Takemoto. Saint Mother Hospital, Kitakyusyu, Japan.

OBJECTIVE: To verify the actual risk of hereditary Klinefelter Syndrome (KS) or incidental aneuploidy in ICSI treatment of KS patients, which has been warned in previous cytogenetic studies using testicular cells from KS patients.

DESIGN: Cyto genetic analysis in KS patients, their testicular cells and delivered babies.

MATERIALS AND METHODS: 1) 45 babies who were born by ICSI treatment of KS patients in our hospital underwent chromosomal analysis using amniocentesis or peripheral blood samples. 2) Fluorescent in-situ hybridization (FISH) analysis for sex chromosome constitution was carried out in morphologically normal metaphase cells or mature sperm which were identified and isolated from testicular cell suspension in 5 or 10 KS patients, respectively. 3) Using blood samples of 4 KS patients and their parents and 18 KS patients, the origin of the extra X chromosome was determined with X-chromosome haplotype markers, according to the method by Shrivastava et al. (2014). DNA was extracted from blood samples of KS patients and their parents with consent. Multiplexed PCR amplifications of the 12 X-STR loci were conducted using an kit X-12 QS Kit (Quigen). Electrophoresis was run on an ABI PRISM 3100 Genetic Analyzer for the PCR products. The data obtained was analyzed with GeneMapper ID software.

RESULTS: 1) No chromosomal abnormality was found in 45 KS patient’s babies examined. 2) In the most of 5 KS patient’s testes examined, spermatogonia showed XY and XXY mosaicism. However, the sex chromosome constitution of all primary spermatocytes and spermatids was normal, suggesting the possibility that XXY spermatogonia can not enter meiosis. In one case, there were no XXY spermatogonia. 3) X-chromosomal STR DNA profiles were compared among KS patient and their parents. In 3 of the 4 KS patients, both X chromosomes were maternal origin, showing that an extra X chromosome was left in an oocyte as a result of chromosomal non-disjunction at the 1st or 2nd meiotic division. In one patient, X-chromosomes were inherited from parents, suggesting that fertilization of XY-sperm is the cause of KS. In addition, it was surmised that 12 cases in 18 patients showed maternal origin and 6 in 18 patients were paternal. Although the sample number applied for X-chromosomal STR DNA profiling is not enough, the present data may indicate that contribution of XX oocyte to the production of XXY embryos is greater than XY sperm. Namely, a XX oocyte penetration by a Y sperm is the cause of KS.

CONCLUSIONS: All data indicates that the risk of KS baby resulting from ICSI treatment of KS patient couples may be a lot lower than expected from the previous studies. Cytogenetic analysis with smear of testicular cell mixture that was used in the studies may overestimate chromosomal abnormality. This finding encourages the opinion that we should strongly recommend vigorous treatment with ART for KS patients.
O-161 Tuesday, October 18, 2016 12:15 PM

ALTERED METHYLOME IN NORMOZOOSPERMIC MALES CONTRIBUTES TO POOR EMBRYOGENESIS. M. Denomme Tignanelli, B. R. McCallie, J. C. Parks, W. B. Schoolcraft, M. Katz-Jaffe. Colorado Center for Reproductive Medicine, Lone Tree, CO.

OBJECTIVE: Unexplained male factor (MF) infertility accounts for a significant proportion of in vitro fertilization (IVF) failures, with increasing evidence pointing to epigenetic alterations between the two embryo developmental groups (p < 0.05), 8,349 sites were enriched at key developmental loci that may significantly impact embryogenesis. Three distinct classes were identified: A) hypermethylated loci, B) hypomethylated loci, and C) variably methylated loci. Validation confirmed methylation array differences, including hypermethylated genes ARID3A (DNA binding protein), and KLF6 (transcriptional activator), hypomethylated genes HOXA11 (DNA-binding transcription factor) and SMARCD3 (transcription regulator by chromatin remodeling) and variably methylated genes GATA3 (negative regulator of transcription) and RASA3 (cellular proliferation and differentiation).

CONCLUSIONS: The results of this study confirm the presence of tightly regulated genes, both hyper- and hypomethylated, as well as loosely regulated genes with variable methylation in normozoospermic samples. Having eliminated female factor infertility, significantly altered methylation profiles enriched at developmental loci were observed in normozoospermic samples resulting in poor embryogenesis, reflecting a subset of unexplained MF infertility. Our data suggests that moderate epigenetic changes throughout the genome may have a cumulative effect on fertility and embryonic developmental capacity.

O-162 Tuesday, October 18, 2016 12:30 PM

WHEN TO REQUEST KARYOTYPE ANALYSIS IN INFERTILE MAN? A NEW PREDICTIVE MODEL. P. Capogrosso, E. Ventimiglia, F. Filippo, F. Montorsi, A. Salonia. IRCCS Ospedale San Raffaele, Milan, Italy; Division of Experimental Oncology/Unit of Urology, Milan, Italy.

OBJECTIVE: To retrospectively validate the EAU guidelines for KA in a cohort of white-European men presenting at the same academic outpatient clinic for unexplained infertility and to develop a novel nomogram capable of predicting karyotype alterations.

DESIGN: Retrospective study.

MATERIALS AND METHODS: Complete socio-demographic, clinical and hormonal data from 1169 consecutive infertile men seeking medical help for primary couple’s infertility were analysed. Health-significant comorbidities were scored with the Charlson Comorbidity Index (CCI; categorized 0 vs 1 vs 2). Testicular volume was assessed with a Prader orchimeter. Serum hormones were measured (8-10 am) in all cases. Hypogonadism was defined as total testosterone < 3ng/ml according to the Endocrine Society classification criteria. Karyotype analysis was requested for every patient. Semen analysis values were assessed based on 2010 World Health Organization reference criteria. EAU guidelines for karyotype analysis (sperm concentration <10 million/mL) were used to predict such alteration in our cohort and thus validated. Moreover, we developed a novel logistic regression based nomogram (considering patient BMI, FSH, testis size and sperm concentration) in order to predict karyotype alterations in our cohort and compared to EAU guidelines.

RESULTS: Overall, 742 (63.5%) patients would have deserved KA according to the EAU guidelines. Of those, 48 (6.9%) of the assessable patients (according to EAU guidelines) displayed any kind of alteration at KA. Conversely, hypothetically relying on the EAU criteria, 12 (20%) out of 60 patients with karyotype abnormalities would not have been candidate for the same genetic assessment. Of all, 694 (62.6%) patients would have been candidate to genetic workup despite having a normal karyotype. As a whole, the EAU guidelines sensitivity, specificity, and discrimination were 89%, 37%, and 59%, respectively. We developed a novel nomogram, with a 2% probability cut-off, which allows for a more careful detection of KA alterations.

CONCLUSIONS: The application of EAU guidelines for karyotype analysis does not ensure an adequate diagnostic process. At this regard, we propose a novel diagnostic tool to improve detection of alterations at karyotype analysis.

OVARIAN RESERVE

O-163 Tuesday, October 18, 2016 11:15 AM


OBJECTIVE: Diminished ovarian reserve (DOR), as determined by low antimullerian hormone (AMH) and high, early follicular phase follicle stimulating hormone (FSH) levels in serum, have been associated with earlier menopause and low egg yield in response to ovulation stimulation. Some studies suggest women with DOR have a lower probability of pregnancy after assisted reproductive technology. Thus, it is presumed that DOR is a cause of infertility. We sought to determine if measures of ovarian reserve would be significantly associated with infertility.

DESIGN: Prospective, time-to-pregnancy, cohort study.

MATERIALS AND METHODS: Women (n=755), 30-44 years old, with no history of infertility, who were trying to conceive for less than 3 months, were recruited from the community. They provided a serum and urine sample at enrollment on menstrual cycle day 2, 3, or 4. Women were followed using standardized pregnancy testing until pregnancy was detected or up to 12 months of attempt. Serum was analyzed for FSH (Immulite Siemens) and AMH (ELISA, Aush labs). Urine was analyzed for FSH and creatinine-corrected. Unadjusted cox analysis.

RESULTS: In this cohort of women 30-44 years of age, 86 (11.4%) were judged DOR by AMH (n=0.7 ng/ml) and 30 (4.1%) by serum FSH (>10 mIU/ml), and 73 (9.7%) by urinary FSH (>11.5 mIU/mg cr). Overall probability of infertility was 24%. Censor reason was not associated with AMH values (p=0.89). The probability of infertility among women with low AMH (20%, 95% confidence interval (CI): 10%-33%) did not differ from women with normal AMH values (0.7-5.0 ng/ml) (24%, 95% CI: 19%-28%, p=0.61). Probability of infertility also did not differ by serum FSH (>10 mIU/ml; 25%, 95% CI: 21%-29%, p=0.67) or urinary FSH (>11.5 mIU/mg cr: 33%, 95% CI: 20%-46%; ≤ 11.5 mIU/mg cr: 24%, 95% CI: 20%-28%; p=0.50). In women over 35 years of age, probability of infertility was lower with low AMH (24%, 95% CI: 10%-43%) compared to normal levels (40%, 29%-50%; p=0.63). However, among women 30-35 years of age, probability of infertility was higher with low AMH (27%, 13-43%) compared to normal AMH levels (19%-15-24%, p=0.28).

CONCLUSIONS: Measures of ovarian reserve, AMH and FSH, do not appear to predict the probability of infertility in a population of older, reproductive-age women with no known fertility problems. This suggests that diminished ovarian reserve, as measured by these biomarkers, may not be a cause of infertility.

Supported by: Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health (R21 HD060229 and R01 HD067683).

FERTILITY & STERILITY®
e65
ELEVATED SERUM LEVELS OF BIOLOGICALLY ACTIVE OMEGA-3 FATTY ACIDS ARE ASSOCIATED WITH BETTER OVARIAN RESERVE. M. E. Skaznik-Wikiel, A. M. Rudolph, D. C. Swindle, A. J. Polotsky. Obstetrics and Gynecology, University of Colorado School of Medicine, Aurora, CO; Endocrinology, Diabetes, and Metabolism, University of Colorado School of Medicine, Aurora, CO.

OBJECTIVE: Dietary omega-3 fatty acids (FA) delay ovarian aging, but it remains unclear if they affect ovarian reserve parameters. We sought to assess the relationship between the omega-3 FA and ovarian reserve in a mouse model, by evaluating essential FAs (linoleic and α-linolenic) and biologically active FAs (arachidonic acid, docosahexaenoic acid) in eicosapentaenoic acid (EPA)). We assessed significant correlations between the biologically active omega-6 to omega-3 FA ratio (AA/EPA+DHA) and primordial and growing (primary, preantral, antral) follicle count.

RESULTS: We evaluated oocyte number and quality in a mouse model, by evaluating essential FAs (linoleic and α-linolenic) and biologically active FAs (arachidonic acid, docosahexaenoic acid) and EPA. To assess correlation between FA levels and ovarian follicle numbers. P value < 0.05 was considered statistically significant.


Supported by: NIH ST32HD040135-13A National Training Program in Reproductive Medicine and ABOG/AAOGF Grant to M.S-W.

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MFR1 PREMUTATION CARRIERS ARE PREPARED TO POOR OOCYTE RESPONSE, BUT EXHIBIT NO DIMINUTION IN OVERAL OOCYTE EFFICIENCY, BLASTULATION RATE OR INCREASE IN ANEUPLOIDY. S. J. Morin, J. M. Fransasiak, C. J. Runear, M. D. Werner, J. Johnson, P. L. Pellier, R. T. Scott. Reproductive Medicine Associates of New Jersey, Basking Ridge, NJ; Department of Obstetrics & Reproductive Sciences, Yale School of Medicine, New Haven, CT; Instituto Valenciano de Infertilidad, Valencia, Spain.

OBJECTIVE: MFR1 premutation carriers (PMCs) are at an increased risk of premature ovarian aging and poor response to stimulation during IVF. However, less is known about how their oocytes and embryos perform after retrieval. The objective of this study was to compare overall oocyte efficiency and embryonic aneuploidy rates between PMCs and infertile patients with normal range alleles.

RESULTS: The mean age of the participants is 32.2 (±4.29) years and the mean BMI is 26.8 (±6.40) kg/m2. There was no relationship between PSQ and SF-36 in relation to ovarian reserve. A p value < 0.05 was considered statistically significant.

CONCLUSIONS: Current psychological stress is not associated with ovarian reserve measures in women with prolonged unexplained infertility enrolled in the AMIGOS trial.

Supported by: CREST (Clinical Research/Reproductive Scientist Training) Program, Eunice Shriver National Institute of Child Health and Human Development R25HD075737

O-164 Tuesday, October 18, 2016 11:30 AM


OBJECTIVE: While psychosocial stress in couples undergoing fertility treatments is associated with lower pregnancy rates, there is also evidence that psychosocial stress in women may up-regulate ovarian function, possibly increasing fecundability, a phenomenon known as “psychosocial acceleration”. This hypothesis has emerged from evolutionary life history theory, and posits that under unpredictable or stressful conditions, it may be advantageous to accelerate or increase reproductive readiness because delaying reproduction may be more costly and ultimately, lead to lower fitness. We sought to examine the relationship between psychological stress and ovarian reserve in women with unexplained infertility in the Assessment of Multiple Intrauterine Gestations after Ovarian Stimulation (AMIGOS) trial.

DESIGN: Cohort study

MATERIALS AND METHODS: Pretreatment psychological stress summary scores were derived from the FertiQoL, Patient Health Questionnaire (PHQ), 36-item short form health survey (SF-36) data for 845 women with unexplained infertility enrolled in the AMIGOS trial, a randomized clinical trial of letrozole, clomiphene or gonadotropins with insemination. Ovarian reserve measures included pretreatment anti-mullerian hormone (AMH), antral follicle count (AFC) and FSH and estradiol and were log-transformed and posited that under unpredictable or stressful conditions, it may be advantageous to accelerate or increase reproductive readiness because delaying reproduction may be more costly and ultimately, lead to lower fitness. We sought to examine the relationship between psychological stress and ovarian reserve in women with unexplained infertility in the Assessment of Multiple Intrauterine Gestations after Ovarian Stimulation (AMIGOS) trial.

RESULTS: The mean age of the participants is 32.2 (±4.29) years and the mean BMI is 26.8 (±6.40) kg/m2. There was no relationship between psychological stress summary scores from the FertiQoL and the ovarian reserve markers, AMH (β = 0.0008, p = 0.71), AFC (β = 0.001, p = 0.32), FSH (β = 0.0002, p = 0.84), and estradiol (β = 0.0006, p = 0.59). Similarly, non-significant results were observed for analyses using PHQ and SF-36 scores.

CONCLUSIONS: Current psychological stress is not associated with ovarian reserve measures in women with prolonged unexplained infertility enrolled in the AMIGOS trial.


Supported by: NIH ST32HD040135-13A National Training Program in Reproductive Medicine and ABOG/AAOGF Grant to M.S-W.
RESULTS: A total of 38 PMCs were identified. The reference database included 3,006 patients. Six PMCs (15.8%) had cycles cancelled during stimulation due to poor response. The IVF cancellation rate prior to retrieval in the reference population was 9.2%. However, in patients who proceeded to retrieval, 2PN and blastulation rate were not significantly different between PMCs and controls (Table). A subset of the highest risk patients (n=13), defined by an AMH of <1, also exhibited no decrease in 2PN or blastulation rate (86% and 56%, respectively). Furthermore, the aneuploidy rate was not significantly different between PMCs and controls (Table).

CONCLUSIONS: While FMR1 premutation carriers may exhibit an increased risk of cycle cancellation due to poor response to stimulation, their oocytes and embryos perform no differently overall in the laboratory once retrieved. This remains true of patients with low AMH, as well. Furthermore, there is no increased risk of aneuploidy in PMCs who proceed with CCS. These findings are important when planning treatment in PMCs, as a larger number of embryos are desired due to need for concomitant single gene analysis during IVF.

References:

O-167 Tuesday, October 18, 2016 12:15 PM
SPECIAL RESEARCH PRESENTATION: A ROLE FOR CHTF18 IN FEMALE FERTILITY AND OVARIAN AGING. B. Mukerji, A. Harris, F. Dia, T. Singh, K. Berkowitz. OBGYN, Monmouth Medical Center, Long Branch, NJ; Biochemistry and Molecular Biology and OB-GYN, Drexel University College of Medicine, Philadelphia, PA.

OBJECTIVE: Ovarian aging in women correlates with progressive loss of both quantity and quality of eggs, collectively known as ovarian reserve. When these processes occur early or are accelerated, their clinical correlates are diminished ovarian reserve and/or premature ovarian insufficiency. These conditions have important consequences for the reproductive and generative health of women, including fertility. Yet, little is known about the molecular basis of processes underlying ovarian aging. The ultimate objective of our work is to investigate the molecular mechanisms underlying ovarian aging and reserve.

DESIGN: We generated mice lacking Chtf18, an evolutionarily conserved gene that is crucial for fertility in the fruitfly and that is essential for the establishment of sister chromatid cohesion and accurate chromosome segregation in yeast. We demonstrated previously that Chtf18 is expressed throughout meiosis2. Currently, we examined the phenotype of Chtf18-null female mice.

MATERIALS AND METHODS: Mating trials were conducted to assess fertility. Histologic and morphometric analyses were performed on ovaries. Meiotic chromosome spreads were prepared from oocytes and examined with fluorescence microscopy. Oocytes were cultured up to the metaphase plate and kinetochore distances between sister chromatids. An in situ chromosome counting assay was used to score numbers of chromosomes in metaphase II oocytes. Statistical analyses were performed with the unpaired t-test and Chi square test.

RESULTS: Ovaries of Chtf18-null females were smaller and contained fewer ovarian follicles at all stages of development compared to wild-type mice; the decrease became more significant as females aged and Chtf18-null ovaries contained 50% fewer ovarian follicles by 6 months of age. Homologous chromosomes of Chtf18-null oocytes separated prematurely during prophase I and had fewer DNA crossovers. In addition, only 26% of Chtf18-null oocytes progressed to metaphase II and chromosomes were misaligned on the metaphase plate. Preliminary results also demonstrate increased kinetochore distances between sister chromatids and aneuploid metaphase II oocytes in Chtf18-null females.

CONCLUSIONS: Chtf18 has critical functions in female germ cell development and fertility. The phenotype of Chtf18-null mice resembles that of women with diminished ovarian reserve, and we posit that Chtf18 helps to maintain the quantity and quality of oocytes consistent with ovarian reserve in humans. Future studies will examine mouse strains unifying these defects and also explore a potential role for Chtf18 in women.

References:

Supported by: Commonwealth of Pennsylvania CURE Award, DeWitt Pettit Award, American Society of Reproductive Medicine 2013 Research Grant, and NIH R01GM106262.

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ANTI-MULLERIAN HORMONE (AMH) FOR PREVENTION OF TISSUE ACTIVATION AFTER VITRIFIED/THAWED OVARIAN CORTEX XENOTRANSPLANTATION. L. Detti,a N. M. Fletcher,b G. M. Saed,a R. A. Uhlmann,a A. M. Tobias,a L. J. Williams.a 1. Obstetrics and Gynecology, University of Tennessee Health Science Center, Memphis, TN; 2. Obstetrics and Gynecology, Wayne State University, Detroit, MI. 1. We sought to determine whether recombinant AMH could prevent post-transplant follicular tissue activation by inhibiting the same pathway, in vivo.

DESIGN: Experimental study on ovarietomized nude mice xenotransplanted with human vitrified/thawed ovarian cortex and treated with rAMH via infusion pump.

MATERIALS AND METHODS: Twelve nude mice were ovarietomized and Alzet pumps delivering 1.23 mcg rAMH/day to reach a serum concentration of 17.5 pg/mL (x5 physiologic AMH level in humans), or placebo, were inserted intraabdominally at the same time. Previously vitrified/thawed 2x2 mm ovarian cortex fragments were transplanted on day 7 and then harvested on day 14 after pump placement. All explanted fragments were flash-frozen for PCR analyses, which were executed in triplicates. We utilized real-time RT-PCR to determine mRNA levels for AMH, VEGF, GDF9, Oct-4, Sox2, and NANOG in ovarian cortex tissue. We used Mann-Whitney U tests to compare the placebo vs. the AMH-pump groups with a p<0.05 significance.

RESULTS: In mice treated with rAMH, ovarian cortex expression of all markers was lower in rAMH mice than in placebo except for NANOG, which was increased (Table 1).

CONCLUSIONS: In vivo administration of rAMH during the peri-transplant period caused downregulation of Oct-4, Sox2, GDF9, and VEGF, but not NANOG. Even though not all comparisons reached statistical significance, these results help our understanding of the inhibitory effects of AMH on follicular development and identify AMH as a useful ‘protectant’ of the ovarian cortex during the peri-transplant period.

References:

Supported by: University of Tennessee Departmental grant.

Table 1: mRNA expression of the study markers in the two treatment groups.

<table>
<thead>
<tr>
<th>Marker</th>
<th>Placebo (mean±SD)</th>
<th>rAMH (mean±SD)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMH (fg/μg RNA)</td>
<td>0.036±0.004</td>
<td>0.0001±0.00001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>VEGF (fg/μg RNA)</td>
<td>1.84±0.200</td>
<td>0.034±0.013</td>
<td>0.005</td>
</tr>
<tr>
<td>GDF9 (fg/μg RNA)</td>
<td>0.077±0.042</td>
<td>0.009±0.001</td>
<td>0.001</td>
</tr>
<tr>
<td>Oct-4 (fg/μg RNA)</td>
<td>2.36±0.465</td>
<td>0.72±0.053</td>
<td>0.048</td>
</tr>
<tr>
<td>Sox2 (pg/μg RNA)</td>
<td>0.17±0.063</td>
<td>0.02±0.007</td>
<td>0.048</td>
</tr>
<tr>
<td>NANOG (fg/μg RNA)</td>
<td>0.031±0.099</td>
<td>0.070±0.018</td>
<td>0.041</td>
</tr>
</tbody>
</table>

OBJECTIVE: Seg aneuploidy may be associated with reduced reproductive potential in human embryos. Recent data also suggest that the majority of seg errors arise during mitotic cell division, resulting in mosaicism within the blastocyst. This study will evaluate contemporary methods of comprehensive chromosome screening (CCS) for the ability to detect mosaic seg aneuploidy, and characterize their clinical predictive value when integrated with blastocyst transfer.

DESIGN: Prospective blinded non-selection study following cell line validation of preclinical accuracy.

MATERIALS AND METHODS: Phase I - Assay Validation: 6 cell mixtures of seg aneuploid and normal cell lines were prepared to model mosaic blastocyst biopsies. Performance for detecting mosaic seg aneuploidies was evaluated using SNP array and targeted next generation sequencing (tNGS) based CCS. Techniques were compared and thresholds for automated detection established. The protocol was part of 2 Clinical Predictive Value Studies. In prior prospective studies, embryos were selected for transfer on the basis of whole chromosomal euploidy with no evaluation for seg abnormalities. Once the final outcome occurred (failed cycle or delivery), the data were analyzed to determine if seg abnormalities were present in transferred embryos. These results were compared to embryos with no evidence of seg abnormalities. Infants born from embryos designated as having seg abnormalities underwent buccal swab testing to determine if this abnormality was present.

RESULTS: Phase I: tNGS was significantly more capable of detecting mosaic seg aneuploidy at 50% compared to SNP array technology when applied to control cell line mixtures (58% vs. 8% detection, p = 0.027). Phase II: SNP based assessment ofseg aneuploidy had no predictive value for clinical outcomes (seg abnormality 59/89; 62%; no abnormality 187/207; 63%; p = 0.57). In contrast, tNGS predicted seg aneuploid embryos displayed significantly reduced reproductive potential (13/39; 33%) compared to embryos with none (141/229; 62%)(p = 0.001).

CONCLUSIONS: Application of tNGS to identify seg abnormalities allows identification of a cohort of embryos whose reproductive potential is reduced by nearly half. In ongoing pregnancies, no evidence of seg aneuploidies was identified. Clinical swabs were used to confirm mosaicism, extrusion of cells with seg abnormalities within mosaic embryos, or potential extracellular signals of seg abnormalities. Infants born from embryos designated as having seg abnormalities underwent buccal swab testing to determine if this abnormality existed.

OBJECTIVE: To evaluate prognostic factors for live birth in fresh blastocyst transfer cycles in women of advanced age.

DESIGN: Retrospective cohort study conducted at a single academic center.

MATERIALS AND METHODS: Women aged 40-43 years who underwent fresh, non-donor, blastocyst transfer between January 2011 and June 2015 were included in the analysis. Embryos were cultured to the blastocyst stage and transferred on day 5. According to territorial law, a maximum of 2 blastocysts can be transferred in this age group. Women with >3 previous in vitro fertilization cycles were excluded. Logistic regression analysis of baseline demographic characteristics and ovarian stimulation parameters was performed to determine predictors of live birth. Data is presented as mean±SD. Continuous data was confirmed for normal distribution.

RESULTS: 337 women who underwent a total of 376 fresh blastocyst transfer cycles were included in the analysis. The mean female age was 41.0±0.9 years, the mean number of previous cycles was 0.8±0.9, the mean number of transferred blastocysts was 1.4±0.5, the live birth rate was 21%, and multiple birth rate was 8%. Women who had a live birth were more likely to have: lower gonadotropin stimulation (2835.4±1768IU, p = 0.007), more metaphase II oocytes collected (10.15±4.4 vs. 8.94±3.7, p = 0.017), more 2PN embryos developed (7.77±3.7 vs. 6.74±2.7, p = 0.006), blastocysts transferred in the expanded stage rather than the early stage (92% vs. 76%, p = 0.04) and cycles with supernumerary vitrified blastocysts (68% vs. 54%, p = 0.041). Female age at treatment (40.7±0.8 vs. 41±0.9 years, p = 0.22), day 3 follicle stimulating hormone level (7.4±2.4 vs. 6.3±2.2, p = 0.14), antral follicle count (13.6±9.4 vs. 11.9±9.7, p = 0.14) and number of transferred embryos (1.47±0.5 vs. 1.39±0.49, p = 0.23) were not predictive for live birth. Transferring 2 blastocysts versus 1 was associated with increased chance of multiple birth (16.6% vs. 0%, p = 0.008), but not live birth.

CONCLUSIONS: In women 40-43 years of age undergoing fresh blastocyst transfer, ovarian response to stimulation as reflected by the number of oocytes collected and quality of embryos was found to be the best predictor of live birth. Importantly, the number of blastocysts transferred did not predict live birth but only multiple birth rate, suggesting the practice of elective single blastocyst transfer should be expanded to women above the age of 39 years. Among women 40-43 years of age, when a blastocyst is obtained, age is not a predictor of live birth.
O-172 Tuesday, October 18, 2016 12:00 PM

OOCYTE AGING IS ASSOCIATED WITH ALTERED METABOLIC STRESS RESPONSE AND LOWER MITOCHONDRIAL DNA COPY NUMBER THAT CORRELATE WITH INTRACELLULAR NADH AND FAD MEASUREMENTS BY FLUORESCENCE LIFETIME IMAGING MICROSCOPY (FLIM). E. Babayev, T. Wang, T. Sanchez, K. Lowther, H. S. Taylor, D. Sakkas, D. Needleman, E. Seli. Department of Obstetrics, Gynecology and Reproductive Sciences, Yale School of Medicine, New Haven, CT; Harvard School of Engineering and Applied Sciences, Cambridge, MA; Boston IVF; Waltham, MA.

OBJECTIVE: Mitochondrial function is essential for reproduction. We hypothesized that the decreased viability of aging oocytes may be partly due to impaired mitochondrial function. We investigated key mitochondrial stress parameters in association with aging in mouse oocytes, and assessed mtDNA quantity and NADH/FAD fluorescence as potential invasive and non-invasive biomarkers of age-related changes, respectively.

DESIGN: Experimental study.

MATERIALS AND METHODS: Mature (metaphase II) oocytes from old (12 months) and young (9 weeks) C57BL/6J mice were compared. Metabolic stress was assessed by determining the levels of reactive oxygen species (ROS) under baseline conditions and following H2O2 treatment (using carbboxy-H2DCFDA fluorescent staining); and by quantifying expression of mitochondrial unfolded protein response (mt-UPR) genes (Clpp, DnaJq3, Hasp1, Haspe1) via qRT-PCR. Absolute mtDNA levels were quantitated via cloning of mitochondria specific gene (Cox3) as a standard, followed by qPCR analysis of individual oocytes (20 young and 20 old). Fluorescence lifetime imaging microscopy (FLIM) was used to obtain non-invasive measurements of intracellular NADH and FAD. FLIM measurements were performed on individual oocytes (19 young and 14 old) in an on-stage incubator system to avoid environmental effects. Oocytes assessed by FLIM also underwent mtDNA quantification as described above.

RESULTS: ROS levels in aged MII oocytes were higher following pre-treatment with H2O2 (p<0.05). The expression of mt-UPR gene Hasp1 was also elevated in aged MII oocytes (p<0.05). Oocytes from old mice had significantly less mtDNA compared to young ones (58,222 +/- 15,429 copies/oocyte vs. 162,106 +/- 19,302 copies/oocyte [mean +/- SEM; p<0.01]). FLIM analysis showed a weak but statistically significant correlation with age and mtDNA copy number (p<0.05).

CONCLUSIONS: Aging is associated with a significant increase in ROS levels in oocytes under stressful conditions and elevated expression of mitochondrial stress response gene Hasp1. Importantly, aged mouse oocytes have lower mtDNA levels that correlate with NADH/FAD levels detected by FLIM. Further delineation of mitochondrial changes associated with aging may help the development of diagnostic biomarkers and therapeutic tools in a prospective, blinded, non-selection setting.

DESIGN: Prospective blinded clinical study.

MATERIALS AND METHODS: mtDNA was assessed in trophoderm (TE) samples biopsied from 337 blastocysts that had been shown to be chromosomally normal. These were generated by 195 couples (average female age 36.7 years). All patients underwent IVF in a single clinic. Cytogenetic assessment occurred via next generation sequencing, whereas mtDNA quantification utilized quantitative PCR. The study took place in a blinded, non-selection manner - i.e. mtDNA quantity was not known at the time of single embryo transfer. The fate of the embryos transferred was subsequently compared to the mtDNA levels measured.

RESULTS: mtDNA assessment showed that 25/336 (7.4%) of embryos contained elevated mtDNA levels. At the time of writing, 159 of the blastocysts have been transferred. All transfers involved a single chronosomally normal blastocyst of good morphology. mtDNA amounts were not known at the time of transfer. 109 (69%) of these led to ongoing pregnancies, and all (100%) had mtDNA levels in the normal range. The remaining 50 (31%) blastocysts failed to implant. 8 (16%) of these non-viable embryos were found to have elevated quantities of mtDNA. This meant that the ongoing pregnancy rate for morphologically good, euploid blastocysts, with elevated mtDNA levels, was 0/8 (0%), a highly significant difference compared to the 72% pregnancy rate observed for similar embryos with normal levels of mtDNA (P<0.0001).

CONCLUSIONS: This is the first study to evaluate the clinical impact of increased mtDNA in a prospective blinded manner. Results confirm that embryos with elevated mtDNA rarely if ever implant, providing support for its use as a viability biomarker. 72% of euploid embryos with normal quantities of mtDNA implanted vs. 69% for the cohort as a whole. No embryos with elevated mtDNA levels implanted.

O-173 Tuesday, October 18, 2016 12:15 PM

CLINICAL APPLICATION OF MITOCHONDRIAL DNA QUANTIFICATION FOR EMBRYO VIABILITY ASSESSMENT: A BLINDED PROSPECTIVE NON-SELECTION STUDY. E. Fraguoli, K. Ravichandran, S. Munne, J. Grifo, C. McCaffrey, D. Wells. Repro-genetics UK, Oxford, United Kingdom; Reprogenetics, Livingston, NJ; NYU Langone Medical Center, New York, NY; ReproGenetics, Oxford, United Kingdom.

OBJECTIVE: Recent reports have suggested that the quantity of mtDNA in embryonic cells may serve as an indicator of embryo viability, higher levels being associated with reduced implantation potential. The current investigation represents the first evaluation of the predictive potential of mtDNA quantification in a prospective, blinded, non-selection setting.

DESIGN: Prospective blinded clinical study.

MATERIALS AND METHODS: mtDNA was assessed in trophoderm (TE) samples biopsied from 337 blastocysts that had been shown to be chromosomally normal. These were generated by 195 couples (average female age 36.7 years). All patients underwent IVF in a single clinic. Cytogenetic assessment occurred via next generation sequencing, whereas mtDNA quantification utilized quantitative PCR. The study took place in a blinded, non-selection manner - i.e. mtDNA quantity was not known at the time of single embryo transfer. The fate of the embryos transferred was subsequently compared to the mtDNA levels measured.

RESULTS: mtDNA assessment showed that 25/336 (7.4%) of embryos contained elevated mtDNA levels. At the time of writing, 159 of the blastocysts have been transferred. All transfers involved a single chronosomally normal blastocyst of good morphology. mtDNA amounts were not known at the time of transfer. 109 (69%) of these led to ongoing pregnancies, and all (100%) had mtDNA levels in the normal range. The remaining 50 (31%) blastocysts failed to implant. 8 (16%) of these non-viable embryos were found to have elevated quantities of mtDNA. This meant that the ongoing pregnancy rate for morphologically good, euploid blastocysts, with elevated mtDNA levels, was 0/8 (0%), a highly significant difference compared to the 72% pregnancy rate observed for similar embryos with normal levels of mtDNA (P<0.0001).

CONCLUSIONS: This is the first study to evaluate the clinical impact of increased mtDNA in a prospective blinded manner. Results confirm that embryos with elevated mtDNA rarely if ever implant, providing support for its use as a viability biomarker. 72% of euploid embryos with normal quantities of mtDNA implanted vs. 69% for the cohort as a whole. No embryos with elevated mtDNA levels implanted.

O-174 Tuesday, October 18, 2016 12:30 PM


OBJECTIVE: IVF and ET has been used successfully for almost 30 years and accounts for 1-4% of annual conceptions. There has been a longstanding association of adverse perinatal outcomes, such as low birthweight and prematurity, associated with IVF; a trend that has been attributed to the high proportion of multiple gestations associated with multiple embryos being transferred. Improvements in laboratory technology and clinical practice have allowed IVF to evolve into a safer, more effective and efficient treatment. This study examined changes in clinical and laboratory practice and their influence on neonatal birthweights over the past 11 years.

DESIGN: Retrospective

MATERIALS AND METHODS: Electronic records of neonates born from women who underwent IVF between 2004-2015, with ≥1 live born child were included. Patient and cycle demographics as well as trends in birth weights were analyzed. Student’s t-test was used for continuous variables.

Patient demographics, cycle characteristics and clinical outcomes
and the $X^2$ test was used for categorical variables. Significance was confirmed at $p<0.05$.

RESULTS: A total of 5782 cycles with birthweight reported were included. All patient demographics, cycle characteristics and clinical outcomes are shown in Table 1. Single ET cycles increased from 9.5% in 2004 to 60.0% in 2015. The average birth weight increased from 2869.1 ± 797.3 grams to 3126.8 ± 723.3 grams, a difference of +257.7 grams ($p<0.05$). The average days of gestation increased from 263.8 ± 23.2 to 269.6 ± 23.9, a positive difference of +6.2 days ($p<0.05$).

The proportion of neonates with Low Birthweight (<1000 grams) decreased from 31.9% to 28.0% to 15.7%. The proportion of neonates with Extremely Low Birthweight (<750 grams) decreased from 1.9% to 1.9%. The proportion of patients with a preterm delivery (32-37 weeks) decreased from 23.2% to 13.1%.

CONCLUSIONS: Current techniques including extended embryo culture, genomic embryo selection, and transfer of a single thawed euploid embryo into synthetically prepared endometrium have the potential to improve the social, medical, financial, and psychological aspects of IVF. Our longitudinal analysis of data study suggests that the reduction in number of embryos transferred is a major driver of the 8% overall increase in neonatal birthweight, decreased from 23.2% to 13.1%.

The proportion of patients with a preterm delivery (32-37 weeks) decreased from 23.2% to 13.1%.

CRYOPRESERVATION AND FROZEN EMBRYO TRANSFER

O-175 Tuesday, October 18, 2016 11:15 AM

CLOSED SYSTEM EMBRYO VITRIFICATION IS ASSOCIATED WITH A HIGHER BIRTHWEIGHT COMPARED TO FRESH EMBRYOS REPLACEMENT. E. Maris, A. Gala, T. Mullet, S. Hamamah. 1Département de Médecine de la Reproduction CHRU de Montpellier, Montpellier Cedex 5, France; 2CHU Montpellier, Montpellier, France; 3ART PDG Department, Montpellier, France; 4ART/PGD Department, Arnaud de Villeneuve Hospital, Montpellier, France.

OBJECTIVE: It is already known that children born after slow frozen embryo transfer have a significantly higher birthweight compared to children born after fresh embryo transfer. Same data have been published about embryo transfer after use of an open vitrification system. However, no available data relative to birthweight and the use of a complete closed vitrification system has been published. The objective of this study was to know if embryo closed vitrification system is associated with a higher birtweight compared to fresh embryo replacement.

DESIGN: This was a monocentric retrospective cohort study. 371 children were issued from fresh embryo replacement and 127 from vitrified embryo transfer.

MATERIALS AND METHODS: All singletons born after transfer of fresh or closed system vitrified embryos between January 2011 and April 2015 of which birthweight was known were included. Births from the vitrified and frozen ET of a euploid embryo, from December 2011 to March 2016, were included. Blastocysts were derived from fresh donor oocytes and underwent trophectoderm biopsy. Main outcome measures included implantation (IR), clinical pregnancy (CPR), early pregnancy loss (EPL) and multiple pregnancy rates (MPR). A sub-analysis involving only single ET (SET) only cycles was conducted. T-test, chi-square and logistic regression analysis was used.

RESULTS: Thirty-two screened donor oocyte embryos were transferred fresh (n=25 patients) and 46 were frozen-thawed and transferred (n=14 patients). Demographic, cycle characteristics and outcome data is shown in Table 1. The fresh cohort had significantly higher IR (80.0% vs. 65.1%, P<0.05), CPR (80.0% vs. 55.8%, P<0.05) and MPR (12.0% vs. 4.6%, P=NS) (Table 1). These outcomes were equivalent in the sub-analysis limited to SETs. After adjusting for the number of blastocysts transferred, recipient age and BMI and oocyte age, the odds of IR (OR 1.8 [95% CI 0.6-5.9], p=0.31), CPR (OR 2.7 [95% CI 0.9-8.6], p=0.09) and EPL (OR 4.0 [95% CI 0.1-2.0], p=0.29) did not differ among the fresh or frozen cohorts.

CONCLUSIONS: The transfer of a single, frozen-thawed, euploid blastocyst dramatically reduces the incidence of multiple gestations, while maintaining high implantation and pregnancy rates. Knowledge that the process of vitrification and thawing of preimplantation embryos, itself, does not affect cycle outcome should reassure patients and clinicians and further promote the strategy of embryo banking to facilitate successive single FETs.

Demographic, cycle characteristics and outcome data

<table>
<thead>
<tr>
<th></th>
<th>Fresh OD ET</th>
<th>Frozen OD ET</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient’s age at ET</td>
<td>43.4 ± 4.0</td>
<td>44.4 ± 4.0</td>
<td>NS</td>
</tr>
<tr>
<td>Oocyte’s age</td>
<td>26.9 ± 3.7</td>
<td>28.5 ± 4.5</td>
<td>NS</td>
</tr>
<tr>
<td>BMI</td>
<td>23.2 ± 3.6</td>
<td>23.0 ± 4.0</td>
<td>NS</td>
</tr>
<tr>
<td>Endometrial Thickness at transfer (mm)</td>
<td>8.8 ± 1.9</td>
<td>8.5 ± 1.7</td>
<td>NS</td>
</tr>
<tr>
<td>Peak E2</td>
<td>670.6 ± 440.9</td>
<td>760.3 ± 532.2</td>
<td>NS</td>
</tr>
<tr>
<td>Number of Embryos Transferred</td>
<td>1.28 ± 0.26</td>
<td>1.07 ± 0.26</td>
<td>NS</td>
</tr>
<tr>
<td>Number of SETs</td>
<td>18</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td>IR // SET IR</td>
<td>80.0% (20/25) // 77.8% (14/18)</td>
<td>65.1% (28/43) // 65.0% (26/40)</td>
<td>&lt;0.05 // NS</td>
</tr>
<tr>
<td>Clinical PR // SET clinical PR</td>
<td>80.0% (20/25) // 77.8% (14/18)</td>
<td>55.8% (24/43) // 55.0% (22/40)</td>
<td>&lt;0.05 // NS</td>
</tr>
<tr>
<td>MPR // SET MPR</td>
<td>12.0% (3/25) // 5.6% (1/18)</td>
<td>0.6% (2/39) // 5.0% (2/40)</td>
<td>NS // NS</td>
</tr>
<tr>
<td>EPLR // SET EPLR</td>
<td>12.0% (3/25) // 5.6% (1/18)</td>
<td>16.3% (7/43) // 15.0% (6/40)</td>
<td>NS // NS</td>
</tr>
</tbody>
</table>
COMPARISON OF AQUEOUS SUBCUTANEOUS VS VAGINAL PROGESTERONE IN FROZEN EMBRYO TRANSFER (FET) CYCLES. V. Arun Mathuvel N. Sanjeeva Reddy. Sri Ramachandra University, Chennai, India.

OBJECTIVE: This is the first study evaluating the use of subcutaneous (SC) aqueous progesterone (P4) preparation in FET cycle. The objective of this study was to compare aqueous SC progesterone with vaginal progesterone capsules in GnRH agonist suppressed FET cycle.

DESIGN: Prospective, randomized study

MATERIALS AND METHODS: The study was conducted between April 2015 to April 2016. A total of 119 FET cycles were studied. Age >37 years, history of genital tuberculosis, history of ≥3 IVF failures were excluded. All the patients underwent FET using hormone replacement therapy (HRT) after GnRH agonist downregulation. Patients were randomly allocated to either vaginal or SC group. In Group A, 25mg of aqueous P4 (Michelle,Akumentis) SC once a day was used and in group B, 3-4 days of micronized P4 capsules 3x200mg daily vaginally (Susten, Sun Pharma) was inserted. Embryo transfer was done on either the 4th or 5th day of P4, depending on which day following fertilization the embryo had been frozen. P4 supplementation was continued till 12 weeks in both the groups. Statistical analysis was performed with the use of SAS version 9.2. Significance was p <0.05.

RESULTS: Age, Body mass index (BMI), HRT duration, endometrial thickness, number of embryos transferred were similar in both the groups. Positive serum beta hCG rate in group A was higher compared to group B (38.2% vs 31.3%), ongoing pregnancy rate (27.3% vs 28.1%) and early pregnancy. The implantation rate (17.12% vs 13.80%), clinical pregnancy rate was continued till 12 weeks in both the groups. Statistical analysis was performed on either the 4th or 5th day of P4, depending on which day following fertilization the embryo had been frozen. P4 supplementation was continued till 12 weeks in both the groups. Statistical analysis was performed with the use of SAS version 9.2. Significance was p <0.05.

CONCLUSIONS: Luteal phase replacement of P4 with aqueous SC progesterone is a good alternative to vaginal P4 in FET cycles.

SUBCUTANEOUS AQUEOUS VS VAGINAL PROGESTERONE IN FET CYCLES

<table>
<thead>
<tr>
<th></th>
<th>Aqueous group (n=55)</th>
<th>Vaginal group (n=64)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>31 ± 4.84</td>
<td>30.84 ± 5.05</td>
<td>0.864</td>
</tr>
<tr>
<td>BMI (kg/m2)</td>
<td>26.4 ± 0.08</td>
<td>27.09 ± 3.93</td>
<td>0.348</td>
</tr>
<tr>
<td>HRT (days)</td>
<td>18.27 ± 5.33</td>
<td>18.06 ± 5.21</td>
<td>0.829</td>
</tr>
<tr>
<td>Endometrial thickness(mm)</td>
<td>9.767 ± 1.418</td>
<td>9.708 ± 1.4395</td>
<td>0.824</td>
</tr>
<tr>
<td>No of embryos transferred</td>
<td>2.67 ± .64</td>
<td>2.83 ± .490</td>
<td>0.145</td>
</tr>
<tr>
<td>Positive serum beta hCG rate</td>
<td>47.3% (26/55)</td>
<td>31.3% (20/64)</td>
<td>0.074</td>
</tr>
<tr>
<td>Clinical pregnancy rate</td>
<td>38.2% (21/55)</td>
<td>31.3% (20/64)</td>
<td>0.428</td>
</tr>
<tr>
<td>Implantation rate</td>
<td>17.12%</td>
<td>13.80%</td>
<td>0.469</td>
</tr>
<tr>
<td>Early pregnancy miscarriage rate</td>
<td>9.1% (5/55)</td>
<td>3.1% (2/64)</td>
<td>0.168</td>
</tr>
<tr>
<td>Ongoing pregnancy rate</td>
<td>27.3% (15/55)</td>
<td>28.1% (18/64)</td>
<td>0.918</td>
</tr>
</tbody>
</table>

O-177 Tuesday, October 18, 2016 11:45 AM

FREEZE-ALL POLICY IN NORMAL RESPONDERS. M. Roque, a M. Valle, a F. Guimaraes, a A. F. Kostolanska, b M. Sampaio, c S. Geber, a Reproductive Medicine, ORIGEN - Center for Reproductive Medicine, Rio de Janeiro, Brazil; b ORIGEN - Center for Reproductive Medicine, Rio de Janeiro, Brazil; c Clinica Origen, Rio de Janeiro, Brazil; d ORIGEN - Center for Reproductive Medicine, Belo Horizonte, Brazil; e Origen, Belo Horizonte, Brazil.

OBJECTIVE: The supra-physiological hormone levels observed during controlled ovarian stimulation (COS) may lead to morphologic and biochemical endometrial alterations. These changes may jeopardize embryo implantation during fresh embryo transfer cycles. With improvements in the cryopreservation techniques, the quality and potential of implantation of cryopreserved embryos remains similar to those from fresh cycles. Thus, although the fresh embryo transfer is the norm during in vitro fertilization (IVF) cycles, there is increasing interest in the elective frozen-thawed embryo transfer (freeze-all policy). The main objective of this study was to compare IVF outcomes between fresh embryo transfer and freeze-all policy in normal responders.

DESIGN: Prospective observational cohort study

MATERIALS AND METHODS: The study was conducted between January 2012 and December 2015. A total of 938 IVF cycles (fresh group - 523; freeze-all group - 415) submitted to COS with gonadotropin-releasing hormone (GnRH) antagonist protocol and cleavage stage embryo transfer were included. In the fresh group embryo transfers were performed only if progesterone levels were <= 1.5 ng/ml on the trigger day. The analysis was also performed in three sub-groups of patients based on the number of retrieved oocytes: group 1 (12-15 oocytes), group 2 (8-11 oocytes), and group 3 (4-7 oocytes). The main outcome measure was ongoing pregnancy rate. The secondary outcomes were implantation, pregnancy, and clinical pregnancy rates.

RESULTS: In general, there were a higher implantation (25.5% versus 19.3%, p=0.002) and ongoing pregnancy rate (41% versus 32%, p=0.004) in freeze-all group when compared to fresh group. The sub-group analysis is presented in Table 1. There was no statistical difference between fresh and freeze-all groups in ovarian reserve tests, days of stimulation, total dose of gonadotropin, and fertilization rates.

CONCLUSIONS: This is the largest study evaluating the freeze-all strategy and the first to evaluate sub-groups of normal responders based on ovarian response to ovarian stimulation. The results of this study show that although the freeze-all policy may be related to better IVF outcomes in normal responders, these potential advantages decrease with worsening ovarian response. Patients with poorer ovarian response don’t have benefit from the freeze-all strategy.
RESULT: One hundred forty eight SETs (fresh ET: n = 79; FET: n = 69) were identified. Baseline demographics, cycle characteristics and perinatal outcome are shown in Table 1. There was no significant difference in gestational age at delivery, infant birthweight or height in the fresh vs. frozen ET groups. After controlling for oocyte age, recipient age and BMI, the odds of preterm delivery (OR 1.3 [95% CI 0.6-2.8]), p = 0.56), low birthweight (OR 1.5 [95% CI 0.3-6.4]), p = 0.60), normal birthweight (OR 0.5 [95% CI 0.1-1.6]), p = 0.24) and macrosomia (OR 1.0 [95% CI 0.99-1.0]), p = 0.56) were similar among fresh vs. frozen ET.

CONCLUSIONS: Singleton live births from fresh and frozen donor-egg derived embryo transfers were similar in gestational age at delivery, infant size and birthweight. These findings reassure clinicians and patients that exposure of the screened blastocyst to the vitrification and thawing process has no effect on perinatal outcome. Furthermore, this finding suggests that the primary driver of reduced birthweight seen in infants conceived from fresh ET is the supraphysiologic hormonal milieu associated with controlled ovarian hyperstimulation.

ACCESS TO CARE 3

O-181 Wednesday, October 19, 2016 11:15 AM

PATIENT PREFERENCES REGARDING SOCIAL MEDIA USE IN AN REI PRACTICE. D. E. Broughton, K. M. Cipolla, E. Junghem, K. Omurtag. Obstetrics and Gynecology, Washington University, St. Louis, MO.

OBJECTIVE: To query patients regarding preferences for the use of social media platforms in their reproductive endocrinology and infertility (REI) practice.

DESIGN: Survey study of patients seeking care at a large university based REI practice.

MATERIALS AND METHODS: All patients checking in for an appointment at our REI practice were offered the opportunity to complete the anonymous survey from October 2015 to February 2016. Surveys were returned to the front desk upon completion.

RESULTS: A total of 40 patients filled out the survey, with 28 (70%) fully completing it. Of surveyed patients, 35% had previously undergone IVF. Patients with two or more miscarriages comprised 12.5% of the study population. A large majority of surveyed patients, 82.5%, felt that social media provided additional benefit to infertility patients. Of survey participants, 55% reported using Instagram compared with only 20% using Twitter. Only 12.5% of respondents reported being interested in using social media for reproductive endocrinology and fertility patients. The topics of interest to the largest majority of patients were “Education regarding fertility testing and treatment” (95%), “Myths and facts about infertility” (92.5%), “Meet the staff posts” (90%) and “Patient success stories” (90%). The topic of interest to the fewest patients was “You and your partner: when couples disagree” (60%). We then asked patients to rank the topics in order of interest, and the results are presented in Table 1. When asked if they would be interested in seeing newborn patients was ‘You and your partner: when couples disagree’ (60%). We then asked patients to rank the topics in order of interest, and the results are presented in Table 1. When asked if they would be interested in seeing newborn patients was ‘You and your partner: when couples disagree’ (60%).
completed, respectively. Most common causes of infertility were anovulation and tubal factor. The mean age of patients was 32.5 ± 3.6 years with reported 5.4 ± 3.8 years duration of infertility. IVF and lab outcomes are presented in Table 1. Number of oocytes retrieved ranged from 2.3 to 4.6, depending on the protocol used. An average of 1.1 embryos were transferred (range 1-2). Ongoing pregnancy rates in clomiphene/letrozole alone, sequential, flare, and low dose gonadotropin arms were 27% (6/22), 30% (3/10), 31% (15/48), and 0% (0/3), respectively. Ongoing pregnancy rate in frozen transfer cycles was 27% (8/30). Cancellation rate was 30.8%, due to single dominant follicle (54%), spontaneous ovulation (16%), or no response (30%). In the 83 cycles that went to retrieval, oocytes were retrieved in 94% and embryos were transferred in 88%. There was only a single instance of multiple gestation (twins). No complications were observed.

CONCLUSIONS: Use of mild stimulation protocols, simplified monitoring, and minimized laboratory-handling protocols achieved excellent pregnancy rates in a low resource, socioculturally diverse infertile population.

O-183 Wednesday, October 19, 2016 11:45 AM


OBJECTIVE: To determine factors associated with achieving pregnancy in HIV serodiscordant couples treated with sperm washing and intrauterine insemination (SW-IUI) when the male partner is HIV-infected and the female partner is treated with pre-exposure prophylaxis (PrEP) anti-retroviral therapy.

DESIGN: Retrospective cohort analysis.

MATERIALS AND METHODS: HIV serodiscordant couples (male HIV+) who have undergone SW-IUI at Columbia University from 6/2014 - 2/2016 were included. Male participants had CD4 counts >250 cells/mm³, undetectable HIV load for >3 months, medical clearance, were adherent to highly active antiretroviral therapy, and had a semen analysis (SA) within 3 months of initiating SW-IUI demonstrating a total motile count (TMC) of ≥ 10 million. Females were <40 years (yr) old (median 34, IQR 31.2 - 35 yrs) with patent fallopian tubes and normal ovarian reserve (anti-Müllerian hormone >1.0 ng/mL). Couples reported safe-sex practices with condoms. Women were prescribed PrEP (emtricitabine/tenofovir disoproxil fumarate) for 3 days (day before, during and after) the IUI. Demographics, female ovarian reserve, cycle type, and male baseline and post-washing SA results were compared in couples that achieved pregnancy to those with no resultant pregnancy. Mann Whitney U and Fischer’s exact tests were used. There was no difference in female age or ovarian reserve in couples that achieved pregnancy as compared to those that did not. For males, there was no difference in age or years since HIV diagnosis between the groups. Baseline SA revealed a greater TMC in couples that achieved pregnancy (145 million) as compared to those that did not (32.8 million, P<0.05).

RESULTS: Ten couples completed 24 cycles of SW-IUI. Overall fecundability rate was 5/24 (20.8%). All women who achieved pregnancy did so during the 1st or 2nd SW-IUI cycle. In comparing individual cycles resulting in pregnancy (n=5) to non-pregnant cycles (n=19), initial TMC was greater in the pregnancy group compared to those without resultant pregnancy [Table 1]. After sperm washing, there was a trend toward a higher TMC in samples that resulted in pregnancy. In cycles achieving pregnancy, women were more often in natural cycles compared to cycles empirically stimulated with clomiphene citrate. All women were HIV negative at follow-up testing.

CONCLUSIONS: SW-IUI appears to be a safe and effective method of conception for well-selected HIV serodiscordant couples. Initial SA TMC

### Table 1

<table>
<thead>
<tr>
<th>Stimulation Protocol</th>
<th>Age, years (SD)</th>
<th>Average dose of gonadotropins, IU (SD)</th>
<th>Average number of oocytes retrieved (SD)</th>
<th>Oocyte recovery rate, oocytes retrieved/ follicles ≥13mm (SD)</th>
<th>Total fertilization proportion, 2PN/oocytes retrieved (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clomiphene or Letrozole only (n=22)</td>
<td>32.6 (3.2)</td>
<td>NA</td>
<td>2.3 (2.5)</td>
<td>0.78 (0.52)</td>
<td>0.71 (0.33)</td>
</tr>
<tr>
<td>Sequential (n=10)</td>
<td>30.4 (4.3)</td>
<td>477.3 (260.4)</td>
<td>3.1 (2.2)</td>
<td>0.83 (0.65)</td>
<td>0.63 (0.38)</td>
</tr>
<tr>
<td>Flare (n=48)</td>
<td>33.3 (3.4)</td>
<td>719.7 (234.9)</td>
<td>4.6 (2.6)</td>
<td>0.97 (0.48)</td>
<td>0.59 (0.3)</td>
</tr>
<tr>
<td>Gonadotropins only (n=3)</td>
<td>32.4 (2.1)</td>
<td>1300 (567.9)</td>
<td>4.3 (3.2)</td>
<td>0.83 (0.15)</td>
<td>0.56 (0.1)</td>
</tr>
</tbody>
</table>
appears to be predictive of success. Couples who achieved pregnancy did so within two IUI cycles, regardless of whether or not ovarian stimulation was used.

O-184 Wednesday, October 19, 2016 12:00 PM


OBJECTIVE: To understand the barriers that HIV serodiscordant couples face in accessing risk reductive Assisted Reproductive Technology (ART) and infertility care.

DESIGN: “Secret shopper” methodology whereby investigators posed as patient and physicians in standardized, scripted phone calls to a sample of Society for Assisted Reproductive Technology (SART) registered fertility clinics.

MATERIALS AND METHODS: January to March 2016, a “patient” inquiring on behalf of his/her same patient population conducted scripted phone calls to a sample of 140 fertility clinics. We sampled 15 states with the highest HIV prevalence in the U.S. Call scripts consisted of simulated phone calls to fertility clinic(s) and use of FP have been tracked at this center.

RESULTS: Of the 140 sampled SART clinics across 15 states, both patient and physician callers reached greater than 90% of targeted clinics. 63% of physician callers were told that the clinic could offer services, as compared to only 40% of patient callers (p < .0001). Of the 55 clinics that denied services to the patient caller, 51% referred to other clinics that offered services, as compared to only 40% of patient callers (p < .0001). Of the 55 clinics that denied services to the patient caller, 51% referred to other clinics that offered services, as compared to only 40% of patient callers (p < .0001). Of the 55 clinics that denied services to the patient caller, 51% referred to other clinics that offered services, as compared to only 40% of patient callers (p < .0001). Of the 55 clinics that denied services to the patient caller, 51% referred to other clinics that offered services, as compared to only 40% of patient callers (p < .0001).

O-185 Wednesday, October 19, 2016 12:15 PM

INCREASE ACCESS TO FERTILITY PRESERVATION CARE USING A PATIENT NAVIGATOR MODEL. K. N. Smith, A. K. Lawson, S. Klock, M. Pavone. OB/GYN, Northwestern Medicine, Chicago, IL; Northwestern University, Chicago, IL; Obstetrics & Gynecology and Psychiatry, Northwestern Medicine, Chicago, IL.

OBJECTIVE: The main role of a fertility preservation patient navigator (PN) is to see reproductive aged patients in the comprehensive cancer center and other centers where gonadotoxic therapies are utilized. PN then reviews possible options for fertility preservation, helps facilitate consultations with reproductive specialists, and coordinates care between different specialties. Here we determine if the use of a Patient Navigator (PN) increases access to fertility preservation (FP) services and information.

DESIGN: Retrospective cohort

MATERIALS AND METHODS: An urban, academic medical center has employed a full time PN on campus since 2010. Previous years, a part time PN was employed. Oncology providers can page or call the PN directly to request same day consults for patient convenience. The PN can discuss the impact of treatment on fertility, FP options and triage patients appropriately to either REI or Urology as needed. New patient consults by the PN, referrals to fertility clinic(s) and use of FP have been tracked at this center.

RESULTS: The PN model has increased both the quantity of fertility preservation consults in REI and urology as well as the number of patients pursuing FP as shown in the table. In the first year of having a full-time PN present on campus, a 14% and 67% increase in consults and FP options pursued was seen in REI and urology, respectively.

CONCLUSIONS: Use of a PN in a medical center can increase access to FP care by increasing FP awareness and creating an easy referral system for healthcare providers and patients to access.
up front cost of COS/IVF may dissuade couples from attempting a cycle. We have utilized a modified natural cycle approach to IVF cycles (mnIVF) to offer patients good results at significantly decreased costs. We devised a decision analytic model to compare the live birth (LB) rate and cost effectiveness of mnIVF vs COS/IVF.

DESIGN: Decision tree and cost effectiveness analytic model

MATERIALS AND METHODS: Utilizing a decision tree and cost effectiveness analytic model, LB rates in mnIVF versus traditional COS/IVF in young (≤35 years) good prognosis infertile patients were compared. Based on available data, we estimated the total cost of COS/IVF cycle to be $12,364 and that of a mnIVF to be $8,197. Elective single embryo transfers were chosen in this young cohort to decrease multiple gestations. The likelihood of a frozen embryo transfer (FET) being available in COS/IVF was 90%, whereas it was 30% after mnIVF. Specific point estimates were collected from the literature, available SART data and expert consensus when necessary. A sensitivity analysis confirmed the robustness of the point estimates within our model. The primary outcome measure was cumulative LB of each treatment strategy. The secondary outcome measures were entry cost of treatment strategy, cost effectiveness, and cost per LB.

RESULTS: A head to head comparison as outlined in table 1 comparing six scenarios of mnIVF versus COS/IVF demonstrated decreased mean patient cost of all mnIVF models and superior cost effectiveness for three strategies of mnIVF over COS/IVF. Undergoing one mnIVF cycle (26% LB) versus one COS/IVF cycle (36% LB) represented a cost saving of $7,226 per LB in the mnIVF group. The most cost effective strategy was two cycles of mnIVF with two possible FETs ($22,042/LB) with an effectiveness of 40%. The break-even point of cost effectiveness was in comparing two mnIVF cycles with one possible FET versus one IVF cycle with two possible FETs ($22,490.6 vs $22,152 per LB).

CONCLUSIONS: Young, good prognosis patients undergoing mnIVF have good results in comparison to traditional COS/IVF while offering superior cost effectiveness to the patient. Our model demonstrates that mnIVF is an efficient way to optimize cost effectiveness, decrease entry cost and maintain good LB outcomes in comparison to COS/IVF.

**ASRM RESEARCH GRANT PRESENTATIONS**

**O-187** Wednesday, October 19, 2016 11:15 AM

**SPECIAL RESEARCH PRESENTATION: THE ASSOCIATION BETWEEN ANTIHYPERTENSIVES AND MALE INFERTILITY USING INSURANCE CLAIMS DATA.** M. Eisenberg, S. Li, Stanford University, Stanford, CA.

**OBJECTIVE:** As the age of paternity is rising in the US, an increasing number of prospective fathers have medical comorbidities. For most of the medications used to treat these medical conditions, the implications to male fertility is unknown. We sought to determine if medications used for the treatment of hypertension is associated with the incidence of infertility using modern pharmacovigilance techniques.

**DESIGN:** Retrospective cohort

**MATERIALS AND METHODS:** We identified subjects contained within the Truven Health MarketScan claims database from 2001 to 2009 taking an anti-hypertensive medication (ACE inhibitors, n=347,634; beta blockers, n=261,849; calcium channel blockers, n=190,903). This US database provides information of insurance claims filed for the care of privately-insured individuals with employment-based insurance through a participating employer. We limited the analysis to men with diagnosis or treatment codes provides information of insurance claims filed for the care of privately-insured men evaluated as employer. We limited the analysis to men with diagnosis or treatment codes gives information of insurance claims filed for the care of privately-insured men evaluated as employer. We limited the analysis to men with diagnosis or treatment codes validates information of insurance claims filed for the care of privately-insured men evaluated as employer. We limited the analysis to men with diagnosis or treatment codes.

**RESULTS:** No TRTed animals died, weights (241 to 244 g; P<0.05), whereas there were no differences in mean weight were similar among TRTs. Minimal (1 point) chronic inflammatory infiltrates and ovum morphologic changes were observed in all rodents. Mild (2 points) glomerular and tubular changes in kidneys and minimal (1 point) degenerative changes in the stifle joint were of similar proportion among TRTs. No toxicities were found in the small intestine, heart, uterus, bone marrow, skin, or hair. Degenerative follicles with apoptotic granulosa or cumulus cells, diminished numbers of granulosa cells and occasional luteinated un-fruited follicles were found in 89% of rTIMP1 TRT rats. Fewer rTIMP1+Ab TRT rats (70%) had ovarian anomalies as predicted; but suggesting a need for reassessing antibody dose. Analysis of variance
Levels of vitamin D (VD) in their circulation.4-10 AGEs also accumulate in their ovaries potentially altering ovarian function.11 We hypothesize that AGEs (sRAGE), and that VD previously shown that VD supplementation to VD-deficient women with AGEs contribute to the etiology of ovarian dysfunction in PCOS. We have and proteins. Women with PCOS commonly have elevated AGEs1-3 and low pro-inflammatory molecules that form following the glycation of lipids with endometriosis.

Wednesday, October 19, 2016 11:45 AM

OBJECTIVE: Advanced glycation end products (AGEs) are highly reactive pro-inflammatory molecules that form following the glycation of lipids and proteins. Women with PCOS commonly have elevated AGEs1-3 and low pro-inflammatory molecules that form following the glycation of lipids with endometriosis.

RESULTS: VD3 downregulated RAGE mRNA by 49% and RAGE protein significantly increased rAMH-induced SMAD 1/5/8 phosphorylation in CYP19A1, CYP17A1, CYP11A1, StAR, and 3 beta-hydroxysteroid dehydrogenase (HSD). RAGE protein was assessed by immunofluorescence staining in human cumulus granulosa cells (CCs).13 We further hypothesize that VD attenuates the AGE-induced ovarian dysfunction.

DESIGN: Translational research.

MATERIALS AND METHODS: Human CCs (n=6 participants) were cultured in media (control) or with human glycated albumin (HGA; 0.4 mg/mL) as a source of AGEs ± 1.25 dihydroxyvitamin D3 (VD3; 100 nM). mRNA was compared using RT-PCR for LH receptor (LHR), AMH, AMHR-II, RAGE (receptor for AGEs; proinflammatory cell membrane), CYP19A1, CYP17A1, CYP11A1, StAR, and 3 beta-hydroxysteroid dehydrogenase (HSD). RAGE protein was assessed by immunofluorescence and culture media was collected for estradiol (E2; pg/mL) and progesterone (P4; ng/mL) concentrations. In order to assess the effect of AMH signaling, KGN granulosa cells were treated with recombinant AMH (rAMH) with or without HGA ± VD3 after which immunofluorescence for phospho-SMAD 1/5/8 was assessed. Finally, follicular fluid (FF) of women (n=72) who underwent IVF was collected and tested for sRAGE, AGEs (pentosidine and N-carboxymethyllysine [CML]), 25 hydroxyvitamin D (25 OHD), VD binding protein (VDBP), testosterone (T), insulin, glucose, and SHBG.

REFERENCES: VD3 regulated RAGE mRNA by 49% and RAGE protein by 44% (p<0.05). Compared to controls, CCs treated with HGA had significantly higher LHR (59%), AMHR-II (52%), CYP17A1 (44%), CYP11A1 (93%), StAR (71%), and HSD (61%) mRNA levels (p<0.05). These changes were inhibited by VD3 (except for HSD). Changes in P4 in culture media did not differ between control CCs and CCs treated with HGA ± VD3. However, compared to control CCs where E2 in cell culture media significantly decreased between baseline and 48 h of culture, E2 in cell culture media where CCs were treated with HGA ± VD3 remained unchanged. HGA significantly increased RANKL-induced SMAD 1/5/8 phosphorylation in KGN cell line. This effect was also inhibited by VD3. In FF, sRAGE levels correlated positively with pentosidine, CML, 25 OHD, SHBG, and negatively with insulin and glucose (p<0.05). There was no correlation between sRAGE levels and VDBP or T (p>0.05).

CONCLUSIONS: AGEs alter the function of CCs in a pattern similar to that observed in PCOS. VD3 attenuates the action of AGEs. AGEs might contribute to the etiology of ovarian dysfunction in PCOS.

Supported by: Grants from ASRM and Ferring Pharmaceuticals Inc.


OBJECTIVE: Embryo aneuploidy is the most common genetic cause of early miscarriage and infertility. Although aneuploidy rates positively correlate with advanced maternal age (>35 years), there are individuals at the extremes for the aneuploidy phenotype at any given age suggesting that age alone cannot always predict the chance of producing an aneuploid embryo. The purpose of this study is to determine if genetic variants in Aurora kinase B (AURKB) and Aurora kinase C (AURKC) are associated with aneuploidy risk in female gametes.

DESIGN: Observational

MATERIALS AND METHODS: DNA from 192 female patients of European descent that are at the extremes of embryonic aneuploidy rates as determined by comprehensive chromosome screening for their age were used for sequencing AURKB and AURKC. These extreme groups included young patients with high aneuploidy levels (<35 years, >75% aneuploid concepti) and old patients with low aneuploidy levels (>35 years, <50% aneuploid concepti). Using two variant-calling pipelines (SAMtools and GATK), we identified two nonsynonymous mutations from Ampliseq data, one in each gene, and validated them by Sanger sequencing. By expressing these variants in mouse oocytes undergoing meiosis I in vitro, we assessed the biological significance of these variants.

RESULTS: The analysis revealed the presence of a non-synonymous mutation in AURKB in one patient and one in AURKC in another patient. The AURKC variant causes an isoleucine-to-valine substitution at amino acid position 79. To perform functional analysis of this variant, we expressed it in oocytes isolated from Aurkc knockout mice, and found no significant change in...
in function. The AURKB variant encodes a leucine-to-proline change at amino acid position 39. Expression of this variant in Aurbk knockout mouse oocytes revealed a change in its subcellular localization from chromosomes to spindle poles. The proline substitution identified in AURKB is conserved in the AURKA homolog, which normally localizes to spindle poles.

CONCLUSIONS: The variant encoding AURKC-I79V was identified in DNA from a young patient with high levels of aneuploid embryos. Because its activity is similar to wild-type AURKC it is likely not causative of embryo aneuploidy. The variant encoding AURKB-L39P was identified in an older patient who had lower than average rates of aneuploid embryos. This is the first indication that a variant in AURKB that alters its subcellular localization could be protective against maternal aneuploidy.

Supported by: This work was supported by an American Society for Reproductive Medicine Research grant and the Charles and Johanna Busch Memorial Fund at Rutgers.

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SPECIAL RESEARCH PRESENTATION: DIRECT CONVERSION OF HUMAN SOMATIC CELLS TO INDUCED GERM-LIKE CELLS BY GENETIC REPROGRAMMING.

J. V. Medrano,1-6 J. M. Miguez,7 I. Moreno,7 C. Simon,7-9 Fundación Instituto Valenciano de Infertilidad (FIVI), Paterna, Spain; 2Reproduction Unit, IIS La Fe, Valencia, Spain; 3Genomix S.L., Paterna, Spain; 4Department of Obstetrics and Gynecology, Stanford University, Stanford, CA.

OBJECTIVE: We sought to genetically reprogram human somatic cells to an induced germ-like cell (iGLC) phenotype in vitro.

DESIGN: A selected pool of key genes in germ line development was ectopically expressed in human male foreskin fibroblasts and bone marrow mesenchymal cells, which were cultured under conditions for spermatogonial stem cell proliferation.

MATERIALS AND METHODS: Consensus coding sequences (CCDS) for the genes PRDM1, PRDM14, LIN28A, NANOG, NANO3, DAZZ, BOLL, DAZL, DXD4, STRA8, DMC1, and SYCP3 were cloned into pLenti3.3/V5-DEST lentiviral expression vectors. Transduced cells were cultured in media with Leukemia Inhibitory Factor (LIF), Gliial cell Derived Neurotrophic Factor (GDNF), basic Fibroblast Growth Factor (bFGF), Stem Cell Factor (SCF), and Retinoic acid (RA) for up to 3 weeks. iGLCs were characterized by time-course qPCR, expression arrays, immunocytochemistry, methylation arrays, and bisulfite sequencing. Meiotic competence was assessed by immunocytochemistry, flow cytometry, Fluorescent In Situ Hybridization (FISH), Amelogenin PCR, and Comparative Genomic Hybridization (aCGH). iGLCs were xenotransplanted into the seminiferous tubules of chemically sterilized immunodeficient mice as a functional assay. Statistics were performed with one-way ANOVA, t-test pairwise comparisons, and Linear Models for Microarray data (LIMMA) test.

RESULTS: Screening among the initial 12 factors revealed that ectopic expression of PRDM1, PRDM14, LIN28A, DAZL, DAZ, and SYCP3 (6f) increased acquisition of a cell clump phenotype accompanied by significant upregulation of early primordial germ cell (PGC) specific markers (SOX17 and TFAP2L)19-25. PGC markers (CDH1 and STELLA), but also markers for meiotic progression (GFRA1, PWIL2, TP2P, and ACR). Meiotic-like patterns for SYCP3, SYCP1 and γH2A.X were observed in up to 2% of iGLCs19-25, and approximately 1% formed haploid cells. iGLCs displayed upregulation of the TET-mediated demethylation pathway with reduced methylation in the paternally imprinted gene H19 and increased in maternally imprinted SNRPN, PEG3, and KDM5R. Germ cell xenotransplant of iGLCs into mouse testes resulted in colonization of the testicular niche with an efficiency of 0.76 cells per 10^9 injected cells. CONCLUSIONS: Human male somatic cells can be directly converted to iGLCs by 6f through regulation exerted by DAZL and DXD4,8,19-24 on the pool of transcripts induced by PRDM1 and PRDM14, also up-regulated by LIN28A19-27. SYCP3 induction resulted essential for meiosis initiation in iGLCs.

References:

Supported by: Grant PI13/00546 from Instituto de Salud Carlos III (ISCIII), Government of Spain, and KY Cha Award 2014 from the American Society for Reproductive Medicine (ASRM).

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SPECIAL RESEARCH PRESENTATION: EGG FROM OVARIAN STEM CELLS DEVELOPS INTO EMBRYO.

S. Park,1 K. Marquis,2 A. H. DeCherney,3 E. F. Wolf.4 NICHHD, NIH, Bethesda, MD; 5Emuice Kenney Center, Shriver National Institute of Child Health and Human Development, NIH, Bethesda, MD; 6NICHHD, NIH, Bethesda, MD.

OBJECTIVE: Unlike male germ line stem cells including spermatogonial stem cells have been widely studied, existence and potency of female germ
line stem cells referred to ovarian-derived stem cells (OSC) were firstly reported only in 2009. Isolation of these cells was replicated by a small number of other groups in mouse, rat and extended to a human model. The objective of this study is to demonstrate the presence of OSC in non-human primates (NHPs), which can generate mature oocytes following transplantation into the ovary.

DESIGN: Eggs from ovarian stem cell transplantation were characterized and explored their fertilization potential.

MATERIALS AND METHODS: The ovarian cortex was digested with collagenase IV and DNase followed by FACs with the DDX4 antibody. The cells were expanded in culture, transfected with a GFP lentivirus, and transplanted into the remaining ovary of the rhesus monkey. Following transplantation, gonadotropins were used for ovarian hyperstimulation to isolate oocytes. Oocytes transplant derivations were assessed by fluorescence, PCR and nested PCR. True oocyte phenotype with appearance of intact zona pellucida and polar body was observed along with expression of oocyte specific genes. Intracytoplasmic sperm injection was performed with collected MII oocytes and fertilization and embryo development potential assessed.

RESULTS: Here we demonstrate, for the first time, the presence of adult stem cells in the primate ovary which form mature oocytes with fertilization capacity following orthotopic transplantation. Two out of 68 oocytes obtained by follicular aspiration were confirmed OSCs origin, whereas 17 out of 83 from microdissection. A mature oocyte originating from OSCs developed into 64-cells stage embryo.

CONCLUSIONS: Stem cells from NHP adult ovaries can be transplanted and give rise to new oocytes that fertilize and develop into an embryo, suggesting that these stem cells could be a novel approach to treating infertility.

MALE REPRODUCTION AND UROLOGY: CLINICAL 2

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OBJECTIVE: Recent military conflicts have resulted in a dramatic increase in genitalourinary trauma experienced by members of the United States Armed Forces. Penile transplantation has the potential to improve the quality of life of these men. Our objective was to characterize urologists’ attitudes towards penile transplantation and the perceived relative importance of penile functions.

DESIGN: Online survey

MATERIALS AND METHODS: An online survey was sent to members of the American Urological Association (AUA) using the SurveyMonkey platform. Respondents were asked if they are in favor of (1) organ transplantation for QOL? (2) transplantation of organs that improve quality of life (i.e. face), (3) transplantation of organs that improve quality of life of these men. Our objective was to characterize urologists’ attitudes towards penile transplantation and the perceived relative importance of penile functions.

RESULTS: Two hundred twenty eight urologists responded to the survey. Three quarters of the respondents were general urologists, 9.1% were specialists in genitourinary reconstruction, and 13.5% were specialists in andrology. The respondents were 88.5% male and 88.4% white, similar to the demographics of the AUA. Twenty percent of the respondents had been employed by the armed forces at some point in their life. At baseline, the participants were significantly less in favor of penile transplantation [mean (SD) 2.4 (1.2)], than other forms of organ transplant (Table). Age, race, and religion were factors that influenced participant attitudes toward penile transplantation and penis function (Table).

CONCLUSIONS: Urologists’ attitudes toward penile transplantation are more negative than other forms of organ transplantation. Various demographic differences in race and age are associated with attitudes toward penile transplantation and function.

Supported by: This project was supported by grant number T32HS000066 from the Agency for Healthcare Research and Quality. The content is solely the responsibility of the authors and does not necessarily represent the official views of the Agency for Healthcare Research and Quality. The project was also supported by The Frederick J. and Theresa Dow Wallace Fund of the New York Community Trust.

Participant Responses and Subset Differences

<table>
<thead>
<tr>
<th>Category</th>
<th>Overall Mean (SD)</th>
<th>p value</th>
<th>Subset 1: Mean (SD)</th>
<th>p value</th>
<th>Subset 2: Mean (SD)</th>
<th>p value</th>
</tr>
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<tbody>
<tr>
<td>In favor of penile transplantation? (Baseline)</td>
<td>2.4 (1.2)</td>
<td>Reference</td>
<td>White: 2.3 (1.1)</td>
<td>Non-white: 2.9 (1.5)</td>
<td>0.05</td>
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<tr>
<td>In favor of organ transplantation?</td>
<td>1.6 (0.9)</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>In favor of organ transplantation to prolong life?</td>
<td>1.2 (0.5)</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In favor of organ transplantation for QOL?</td>
<td>1.9 (0.9)</td>
<td>&lt;0.001</td>
<td>Jewish: 1.6 (0.7)</td>
<td>Non-Jewish: 2.0 (1.0)</td>
<td>0.029</td>
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<tr>
<td>In favor of penile transplantation insurance coverage?</td>
<td>2.2 (1.2)</td>
<td>0.290</td>
<td>Age &lt;55: 2.3 (1.3)</td>
<td>Age &gt;54: 2.0 (1.0)</td>
<td>0.047</td>
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<tr>
<td>Importance of penile social function</td>
<td>2.6 (1.1)</td>
<td>Reference</td>
<td>White: 2.1 (1.1)</td>
<td>Non-white: 2.9 (1.4)</td>
<td>0.009</td>
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<tr>
<td>Importance of penile reproductive function</td>
<td>2.3 (1.1)</td>
<td>0.025</td>
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<td>Importance of penile urinary function</td>
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<td>&lt;0.001</td>
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<td>Importance of penile erectile function</td>
<td>1.8 (0.8)</td>
<td>&lt;0.001</td>
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<tr>
<td>Importance of penis to gender identify</td>
<td>1.6 (0.8)</td>
<td>&lt;0.001</td>
<td>Jewish: 1.3 (0.4)</td>
<td>Non-Jewish: 1.7 (0.8)</td>
<td>&lt;0.001</td>
<td></td>
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<tr>
<td>Importance of penile sexual function</td>
<td>1.6 (0.8)</td>
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17.9% (28 - 35 maternal age), however, this study cohort evidenced a clinical pregnancy rate of just 3.2% still with maternal age ranging from 25-51 years. Men in this group presented with a TUNEL of 27.4±17% and SCSA DFI of 38.2±2.27%. Men with normal SFC were subsequently treated by in vitro intra-cytoplasmic and reported a pregnancy rate of 22.1%. Once we controlled for an eventual confounding female factor (female age ≤35yrs), a remarkably higher pregnancy rate of 36.6% (P < 0.001) was reached. On the other hand, couples with abnormal DFI were treated exclusively by ICSI yielding a higher pregnancy rate at 20.6%, and 28.7% with females ≤35yrs old (P < 0.001). For those patients that failed to establish a viable pregnancy with ICSI and ejaculated spermatozoa, after thorough counseling testicular sampling was offered. In 40 couples that consented testicular biopsy the SFC was 11.7±6%, remarkably lower than in their ejaculate, and a pregnancy rate of 25.6% (P < 0.001) was attained.

CONCLUSIONS: This study provides a DNA fragmentation-based algorithm that allows appropriate allocation of resources and guides patients towards the appropriate infertility treatment. IVF is successful in men with intact sperm chromatin; however, when sperm SFC is compromised in the ejaculate, ICSI is the most suitable insemination method. In men with high DNA fragmentation in their ejaculate and pursuant pregnancy failure, surgical sampling yielded spermatozoa with lower SFC and higher changes of pregnancy.

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SLEEP AND MALE FECUNDITY IN A NORTH AMERICAN PRE-CONCEPTION COHORT STUDY. L. A. Wise, a C. Mckinnon, a CONCEPTION COHORT STUDY. L. A. Wise, a C. Mckinnon, a

OBJECTIVE: To evaluate prospectively the extent to which duration and quality of sleep influences male fecundability. Sleep problems have been associated with lower sperm concentration, total sperm count, and percent normal sperm morphology, as well as decreased testosterone levels. No studies have been prospective in design.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: The Boston University Pregnancy Online Study (PRESTO) is a web-based prospective cohort study of couples residing in the United States and Canada. Male participants are aged 21 years or older; female participants are aged 21-45 years. At baseline, men reported data on their average nightly sleep duration and the frequency with which they had trouble sleeping in the previous two weeks (as assessed by the Major Depression Inventory). Male data were linked with those of their female partner, and follow-up questionnaires were completed by the female partner every 8 weeks for up to 12 months or until reported pregnancy, whichever occurred first. The analysis was restricted to 695 couples who had been attempting to conceive for 6 or fewer cycles at study entry. We used proportional probabilities regression models to estimate fecundability ratios (FR) and 95% confidence intervals (CI), controlling for male and female age, male and female BMI, intercourse frequency, male education, smoking, multivitamin use, unemployment status, average number of work-hours per week, and clinical depression.

RESULTS: We observed an inverted U-shaped relation between sleep duration and male fecundability. Relative to 8 hours/night of sleep, FRs for less than 6, 6, 7, and 9 or more hours/night of sleep were 0.69 (CI: 0.47-1.02), 1.08 (CI: 0.84-1.39), 0.97 (CI: 0.77-1.21), and 0.51 (CI: 0.27-0.99), respectively. Compared with men who had no trouble sleeping, FRs for men who had trouble sleeping “some of the time or slightly less than half of the time” and “slightly more than half of the time, most of the time, or all of the time” were 0.79 (CI: 0.53-1.17) and 0.57 (CI: 0.27-1.23), respectively. When we did not control for intercourse frequency or clinical depression, which are possible causal intermediates, there was little difference in these effect estimates. Further restriction of the cohort to those with fewer than 3 cycles of attempt time at baseline produced similar results.

CONCLUSIONS: In this cohort of pregnancy planners, short and long durations of sleep, as well as trouble sleeping at night, were associated with reduced male fecundability.

Supported by: This research was supported by NICHD (R21-HD072326).

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OBJECTIVE: Some vaginal lubricants and ultrasound gels can be detrimental to sperm function and therefore could negatively affect fertility. The toxic properties of substances coming into contact with human sperm can be screened using a sperm survival assay that provides a sperm motility index (SMI), where values <0.75 indicate sperm toxicity. The aim of this study was to test the SMI as a potential predictor of sperm toxicity in ultrasound gels and vaginal commercial lubricants.

DESIGN: Comparative prospective in vitro study.

MATERIALS AND METHODS: 20 normozoospermic washed ejaculates adjusted to 20 million/mL were used to evaluate the toxicity of two ultrasound gels (Kefus® and Aquasonic®) and five vaginal lubricants (Durex®, Vagine- sil®, K-Y Jelly®, Control® and Velastisa®). Three concentrations (1, 5 and 10%) of each lubricant were tested. Only 10% concentration was tested for ultrasound gels. An aliquot of sperm suspension served as control. A computer-assisted semen analyzer (CASA) assessed motility. The sperm toxicity was screened using SMI for each concentration at 0.5, 1, 2 and 24 hours. SMI was calculated by dividing the percent of progressively motile sperm in the test solution by that in control at specific times. Vitality was evaluated by HOS test. Multifactorial ANOVA analysis determined variance between groups.

RESULTS: There were significant differences in vitality and sperm motility following exposure to different preparations and incubation times (p < 0.01). Durex® had the higher vitality percentage at 24 hours (83.8% for a 5% and 71.6% for a 10%) and the lowest was Vaginez® (11% for a 5% and 8.4% for a 10%). Exposure to Durex® resulted in a significantly higher percentage of progressive motility spermatozoa compared with all other lubricants (~80% at 30 min concentration after 2 hours). However, Vaginez® dramatically decreased sperm motility after 0.5 hours of exposure at 1% and resulted toxic for all concentrations and incubation periods (SMI<0.12). Control® and Velastisa® did not present toxicity for any concentration and incubation period, K-Y Jelly® only showed toxicity at 10% from 1 hour incubation. Aquasonic® showed toxic effects after only 30 min (SMI 0.69). Though Kefus® was toxic after 120 min (SMI 0.69).

CONCLUSIONS: Coital lubricants and ultrasound gels contain traditionally harmless ingredients that could be detrimental for sperm function. The American Society for Reproductive Medicine Practice Committee consensus guideline Optimizing Natural Fertility urges physicians to discuss the importance of ultrasound gels and coital lubricants choice for couples who are trying to conceive.

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Management and Outcomes of Patients with Acute External Genital Trauma: A 12-Year Combined Institution Experience. M. C. Hehemann, I. Kashanian, A. M. Kandabarow, J. Tse, D. J. Mazur, G. Barton, A. Farooq, R. E. Brannigan. Loyola University Health Systems, Department of Urology, Maywood, IL; Department of Urology, Weill Cornell Medicine, New York, NY; Department of Urology, Loyola University Health Systems, Maywood, IL; Department of Urology, Northwestern University Feinberg School of Medicine, Chicago, IL.

OBJECTIVE: External genital trauma (EGT) often requires emergent urologic (GU) intervention. Reproductive and sexual outcomes in this population are poorly studied. We aim to characterize the presentation, management, and GU follow-up of patients with EGT. We hypothesize

| Table 1 |
|-----------------|-----------------|-----------------|-----------------|
| External Genital Trauma (n = 304) | GU Consultation Performed n = 176/304 (58%) | Surgical Management n = 88/176 (50%) | Non-Surgical Management n = 88/176 (50%) |
| Sclerot Trauma 208/304 (68%) | Sclerot 55/111 (50%) | 56/111 (50%) |
| Penile Trauma 76/304 (25%) | Penile 111/208 (53%) | 19/47 (40%) | 28/47 (60%) |
| Dual Trauma 20/304 (7%) | Dual 47/76 (62%) | 14/18 (78%) | 4/18 (22%) |

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that patients with EGfT have poor GU follow-up and that reproductive and sexual dysfunction in this group are poorly characterized.

DESIGN: Retrospective review

MATERIALS AND METHODS: Medical records of male patients presented with EGT to two urban academic Level I Trauma Centers were reviewed (2002-2014). Patient characteristics, EGT type, GU consultation, operative intervention, and follow-up were recorded. Chi-squared and Fisher’s Exact comparison analyses were performed.

RESULTS: 304 men presented with acute EGT. Table 1 details initial presentation and management characteristics (p<0.05). Dual trauma was managed surgically more often than scrotal or penile (p<0.05). Only 110/176 (63%) of men undergoing surgery followed up in GU clinic. Median follow-up was at 47 days. 66/68 (75%) patients receiving GU consultation and surgical management had GU follow-up vs 44/88 (50%) managed non-operatively (p<0.05). Only 46/110 (42%) patients with GU follow-up were counseled on reproductive and sexual dysfunction. Scrotal trauma patients (17/61;28%) were less likely to be counseled vs penile (20/34;59%) or dual trauma (9/15;60%) (p<0.05). 12/110 (11%) patients complained of new-onset erectile dysfunction in clinic (6/61 scrotal, 5/34 penile, 1/15 dual trauma). Overall, only 5/110 (4%) had serum testosterone labs; 1 of these 5 patients was hypogonadal. No patients reported new infertility, although clinician queries on this issue were limited.

CONCLUSIONS: Urologic follow up is poor in men with EGT. Reproductive and sexual outcomes are discussed with a minority returning for follow-up, despite a high rate (11%) of new sexual dysfunction among these men. Reproductive function is even more poorly characterized in this cohort. We recommend improved assessment and counseling regarding reproductive and sexual dysfunction in patients with EGT.

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ANTIMÜLLERIAN HORMONE IN PREPUBESCEN AND ADOLESCENT GIRLS. J. R. Ho,1 W. Houghton,1 W. Salem,2 L. Ma,2 A. Kumar,2 B. Kalra,2 M. Terry,1 F. Z. Stanczyk1 1University of Southern California, Los Angeles, CA; 2Columbia University, New York, NY; 3AnshLabs, Webster, TX.

OBJECTIVE: Anti-müllerian hormone (AMH) serves as a biochemical marker for ovarian reserve in adult women. There is still much to understand regarding its significance early in the reproductive lifespan, particularly during the pubertal transition. Previous studies are mixed, as some show a consistent rise in AMH from birth, while others show a slight decline with the onset of puberty. Body mass index (BMI) is thought to influence the timing of puberty. We sought to determine whether AMH levels varied based on BMI. We also examined differences in AMH levels by stages of pubertal development.

DESIGN: Cross-sectional analysis of a prospective study.

MATERIALS AND METHODS: Demographics and anthropometry were collected at the clinic in a cohort of girls recruited to the New York site of the LEGACY Girls Study: Using baseline serum samples, we measured levels of AMH using a validated ultrasensitive ELISA (AnshLabs, Webster, TX). We used linear regression to analyze the relation of log-transformed AMH with BMI percentile. We also compared AMH levels between girls at different breast and pubic hair Tanner Stages and between girls that did and did not reach menarche. Results are reported as means and standard errors (SE) in ng/mL.

RESULTS: In this pilot study, we included 90 girls ages 6-13 years old in our analysis. The mean age was 10 (standard deviation = 2.3) and the mean AMH was 4.39 (standard deviation = 1.9). Inter- and intra-assay coefficients of variation for AMH were 4.5% and 1.8%, respectively. A little over one quarter of girls (27.8%) were classified as overweight/obese (≥ 85th BMI percentile). There were no differences in AMH levels by BMI as mean levels were 4.3 (1.08) in girls between the 5th and < 85th percentiles and 4.66 (1.16) in overweight/obese girls (p=0.61). When examining puberty milestones, AMH levels were 4.53 (1.15) in girls with breast development and 4.18 (1.1) in girls without breast development (p=0.60). AMH levels were 4.57 (1.15) in girls with pubic hair growth and 4.26 (1.09) in girls without pubic hair growth (p=0.64). AMH levels were 4.22 (1.08) in girls who had not started menarche compared to 5.16 (1.17) in girls that had reached menarche (p=0.22).

CONCLUSIONS: In this study, we did not observe differences in AMH by pubertal development or body size. Based on our findings, AMH is not a predictive marker for thelarche, pubarche, or menarche in prepubertal and adolescent girls. Longitudinal studies are needed to measure AMH changes within the same individuals across the pubertal window.

Supported by: AnshLabs (Webster, TX), American Society for Preventative Oncology, Breast Cancer Research Foundation.
be affected by variables such as age, environment, and genetics. This study aimed to identify genetic variants that impact hormone signaling in women.

DESIGN: Retrospective

MATERIALS AND METHODS: Clinical variables, including AMH and day 2/3 FSH, estradiol (E2), and progesterone (P4), were collected for 407 women. Genotype information was collected for 18 single nucleotide polymorphisms (SNPs) across 9 genes that were previously found to have associations with fertility markers. Statistical tests were run to measure the association between 1 hormone level and 1 SNP. Mann-Whitney U-tests were run when women were divided into 2 groups based on genotype; Kruskal-Wallis was run when women were divided into 3 groups based on genotype. A total of 62 hormone-SNP comparisons were made, 44 of which were considered independent due to linkage disequilibrium. Adjusting for multiple hypothesis testing, a p-value of 0.001136 was considered significant. Informed consent was obtained.

RESULTS: We found the FSHR p.S680N (rs6166) to be significantly associated with FSH levels (see Table 1). No other hormone-SNP associations were found to be significant.

CONCLUSIONS: Our data confirmed the Ser allele leads to a less functional FSHR, resulting in a need for more FSH to have the same effect as FSHR with the Asn allele. Further, we see that the effect is dependent on how many copies of the 680Ser allele are present. This finding suggests a dose-dependent response. Future analyses in larger populations will be important for confirming the effect of 680Ser copies. This finding may help to refine treatment protocols for women pursuing ART treatments. However, the lack of other significant associations suggests the need for further analysis with larger sample size and more complex multivariate analysis.

O-201 Wednesday, October 19, 2016 11:45 AM

IMATINIB MESYLATE ACCELERATES FOLLICULAR DEATH AND IS NOT PROTECTIVE AGAINST CHEMOTHERAPY INDUCED DAMAGE IN HUMAN OVARY. G. Bildik,*, N. Akin,*, D. Urman,*, I. Keles,*, B. Balaban,*, B. Urman,*, O. Oktem,*. School of Medicine and the Graduate School of Health Sciences, Koc University, Istanbul, Turkey; Women’s Health Center Assisted Reproduction Unit, American Hospital, Istanbul, Turkey; *Obstetrics and Gynecology, Koc University School of Medicine, Istanbul, Turkey.

OBJECTIVE: Imatinib mesylate is an inhibitor of the oncopgenic tyrosine kinases BCR-ABL and c-kit. There is a controversy in the literature regarding its protective role against chemotherapy induced ovarian damage in the murine model (1-3) and no human data is available. We aimed to address this issue in the current study.

RESULTS: Treatment of the ovarian samples with imatinib alone caused massive follicle loss and significant reduction in their in vitro E2 and AMH productions in a dose-dependent manner. Its administration prior to or concurrent with Cyc or Cis did not prevent follicle loss (Table). Bizarre shaped primordial and secondary follicles with empty zona and unclassifiable small follicles possessing atretic oocytes without granulosa cells were exclusively observed in the samples exposed to imatinib and anti-CD177 but not in those treated with GNF-2, Cyc and Cis. Follicle numbers and hormone productions were preserved to a greater extent in the samples exposed to GNF-2 compared to imatinib and anti-CD177 (Table). The rate of apoptosis in the GV and MI oocytes was significantly increased from 2% of the controls to 78, 82 and 92% at 12 hr post-exposure to imatinib, cisplatin and cyclophosphamide, respectively. The co-administration of imatinib with chemo drugs did not rescue the oocytes from apoptosis. Exposure to Cyc and Cis resulted in increased expression of p-HH2AX, cleaved caspase-3 and PARP. But in contrast to the findings in the mouse ovary (1) it did not activate c-abi-TAp63 pathway in human oocytes and granulosa cells.

CONCLUSIONS: These results together with a case report of a woman who showed a severely compromised ovarian response to gonadotropin stimulation while on imatinib (4) heighten the concerns about its potential gonado-toxicity on human ovary and urger caution in its use in young female patients.

References:

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HIGH FOLLICLE-STIMULATING HORMONE (FSH) PROMOTES TUMOR ANGIOGENESIS OF BREAST CARCINOMA OF MENOPAUSAL WOMEN. 5. Shi. Zhejiang Normal University, Jinhua, China.

OBJECTIVE: The object of this study was to determine the follicle stimulating hormone receptor (FSHR) expression in microvessel endothelium of breast tumor and the role of FSH on angiogenesis of breast tumor of pre- and post-menopausal women. Through this study, whether or not high circulating FSH causes the higher severity of breast tumor of pre- and post-menopausal women than young women will be researched from a new perspective.

DESIGN: Cell experiment: to research the effect of FSH on the proliferation, migration, invasion and tube formation of human umbilical vein endothelial cells (HUVECs). Animal model: to research the effect of FSH on the angiogenesis and development of breast tumor implanted in the female nude mice. Clinical research: to research the correlation between FSH level and
microvessel density (MVD) of breast tumor of the pre- and post-menopausal women.

MATERIALS AND METHODS: Materials: Cells model: Blood vessel cells: human umbilical vein endothelial cells (HUVECs) Breast tumor cells: Bcap37 cells. Methods: 1. Female nude mice aged 6-8 weeks received subcutaneous injection of 30 mice in each group. 


RESULTS: 1. FSH receptor was expressed at a higher level on endothe-lium of breast tumor vessel than benign breast tissue vessel, and FSHR was expressed in HUVECs. 2. FSH promoted the angiogenesis on HUVEC in the following aspects: 1) stimulated the proliferation, migration, invasion and tube formation of HUVEC; 2) decreased the cell junctions of HUVEC and increased expression of matrix metalloproteinase; 3) activated calcium influx and the phosphorylation of a wide range of kinases and transcription factors. 3. Animal model research: nude mice were divided into three groups, sham (sham operation), OVX (ovariectomized) and OVX+FSH (ovariecto-mized mice treated with FSH). Bcap37 cells were injected into nude mice, and the results showed that the tumor size of the OVX group were larger than sham group, and OVX+FSH showed the significant larger tumor size than other two groups after 6 weeks. FSH had no effects on the proliferation of Bcap37. However, the immunohistochemical staining analysis of the MVD showed that FSH injection resulted in the highest level of MVD of OVX group. So the animal results showed that FSH can enhance the development of tumor implanted in the nude mice through stimulating the angiogenesis without stimulating the proliferation of breast tumor cells. 4. Clinical research: clinical investigation showed a linear positive correlation between FSH level and MVD of breast tumor.

CONCLUSIONS: High FSH promotes breast tumor development of pre- and post-menopausal women through stimulating tumor angiogenesis.

**O-203 Wednesday, October 19, 2016 12:15 PM**

**TIMING OF INITIATION OF HORMONE REPLACEMENT THERAPY AND COGNITIVE FUNCTION: A PROSPECTIVE STUDY**

S. Iliodromiti,a M. Magnus,b cTownsend deprivation index, smoking and history of cardio-vascular disease and diabetes did not modify the direction of the associations.

CONCLUSIONS: HRT use is associated with lower verbal reasoning and visual memory, but a shorter (i.e. better) reaction time. We found some evidence that age at initiation modifies some of the associations without evidence of a decrease in verbal reasoning and visual memory in women commencing HRT at the age of 50-60 years.

**O-204 Wednesday, October 19, 2016 12:30 PM**

**PLATELETS FOR ENDOMETRIAL REGENERATION: A NOVEL APPROACH**


OBJECTIVE: Asherman’s syndrome and a thin lining refractory to available therapy present significant challenges in ART practice. Autologous platelet rich plasma (PRP) is used to support tissue repair and growth in orthopedics, dentistry and other specialties. Herein we tested the hypothesis that PRP stimulates cellular processes involved in endometrial regeneration relevant to management of a thin lining or intrauterine scarring.

DESIGN: Laboratory-based study.

MATERIALS AND METHODS: PRP and platelet-poor plasma (PPP) were prepared using a double-spin method and activated with thrombin and calcium chloride. Human primary endometrial epithelial cells (eEC), endometrial mesenchymal cells (eMSC), bone marrow-derived mesenchymal stem cells (BM-MSC) and Ishi-kawa endometrial adenocarcinoma cells (IC) were cultured with and without 5% activated PRP, non-activated PRP, activated PPP and non-activated PPP. Effects of treatments were evaluated using *in vitro* assays for cell proliferation (WST-1), wound healing migration, and chemotaxis Transwell migration. Occurrence of mesenchymal-to-epithelial transition (MET) was evaluated by cytokeratin and vimentin immunofluorescence.

RESULTS: Activated PRP promoted the migration of human eEC, eMSC, BM-MSC, IC and eEC compared to non-activated PRP, PPP and vehicle controls, in both wound healing and chemotaxis assays, in a time-dependent manner (p < 0.05). The WST-1 assay showed increase in stromal and mesenchymal cell proliferation by activated PRP vs. non-activated PRP and PPP (p < 0.05), while epithelial cell proliferation was affected by both activated, but not non-activated, PRP and PPP (p < 0.05). Under the experimental conditions tested, PRP did not promote MET in eEC or eMSC as shown by expression of vimentin and absent cytokeratin immunoreactivity.

CONCLUSIONS: This is the first study to evaluate the effect of PRP on different human endometrial cells and on BM-MSC involved in regeneration. PRP enhanced migration and proliferation of all cells studied. These data provide an initial ex vivo proof of principle for the use of autologous PRP to promote endometrial regeneration in Asherman’s syndrome and a thin endometrial lining and warrant pre-clinical studies in animal models and subsequently in the clinical setting.

Supported by: IntegraMed Fertility 2016 Research Grant (LA), NIH NCTRI P50HD055764 (LCG).

**O-205 Wednesday, October 19, 2016 11:15 AM**

**INTEGRATED ANALYSIS OF MIRCORNAs (miR) AND MESSENGER RNA (mRNA) EXPRESSION PROFILES REVEALS MIR REGULATION IN SEX STEROID ACTIONS IN THE MOUSE UTERUS.**

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OBJECTIVE: To identify miRs involved in estradiol (E2) and progesterone (P4) actions in the mouse uterine epithelium and to explore miR-mRNA target pairs and their biological functions.

DESIGN: Controlled laboratory study.

MATERIALS AND METHODS: Ovariectomized CD1 mice were randomly assigned to receive oil (control), E2 alone (E2 group), or P4 for...
4 days and E2 on the last day (PE group). After sacrifice, uterine horns were removed, followed by epithelial cells isolation and RNA extraction. Affymetrix MoGene 2.0 arrays and miRNA sequencing (Illumina HiSeq2500) were employed to establish mRNA and miRNA expression profiles, respectively (n = 4). Expression of select miRs was validated in time course experiments in separate groups of mice by qRT-PCR. In situ hybridization (ISH) with miR probes allowed cellular localization of miRs in the uterine frozen sections. Targetscan and mirWalk prediction programs were used for miR-mRNA target pair predictions, while Ingenuity and DAVID were utilized for functional annotations and network analysis. Statistical significance level was set at False Discovery Rate <0.05 and P < 0.005.

RESULTS: Principal component and hierarchical clustering analysis appropriately segregated the E2 and PE samples into their respective groups. 994 miRNAs and 26 miRs were differentially expressed between the PE and E2 samples. MiR-138 showed the greatest increase in expression (5-fold) in the PE vs. E2 treated samples and demonstrated exclusive localization to the luminal and glandular epithelium. PE treatment induced increased expression of miR-31 and miR-204, similar to the findings of the human secretory phase endometrial epithelium. The time course experiments showed the greatest increase in the expression of miR138, miR-31 and miR-204 in PE vs. E2 samples 4 hours after the last hormone treatment, whereas the differential expression started to diminish at 9 hour time point. We discovered several known and predicted miR-mRNA target pairs with importance in endometrial physiology, including the cell cycle, cell adhesion and implantation.

CONCLUSIONS: Sex steroid status can be defined by miR expression in the mouse uterus epithelium. The analysis of miR-mRNA target pairs and networks suggests miR involvement in E2 and P4 regulation of the cell cycle and differentiation of the epithelium into its receptive state. Our mouse model provides feasible in vivo model for manipulative experiments to further unravel the role of miRs in the endometrium.

Supported by: U54 HD058155 (NIH) and AAOGF/ABOG.

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FRESH IVF CYCLES ARE ASSOCIATED WITH POTENTIALLY DELETEROUS CHANGES IN KEY MATERNAL SERUM FACTORS ASSOCIATED WITH ANGIogenesis AND VASCULOgenesis.


OBJECTIVE: Fresh IVF cycles are more likely to be affected by disorders of placentation, such as small for gestational age (SGA) and pre-eclampsia, than pregnancies resulting from frozen/thawed embryo transfer (FET). While these adverse perinatal outcomes have been linked to abnormal vasculogenesis and angiogenesis during implantation, the mediators responsible for these changes remain unclear. In this study we compare maternal serum levels of key angiogenic factors, maternal angiogenesis and fetal vasculogenesis between fresh and frozen IVF cycles and determine if changes in these factors are associated with adverse pregnancy outcomes.

DESIGN: Prospective cohort study

MATERIALS AND METHODS: Serum was banked from 156 patients with a positive hCG 10-20 days following embryo transfer: 90 fresh IVF cycles and 66 FET IVF cycles. Levels of VEGF, sFlt-1, and PIGF were measured in maternal serum using commercially available ELISA kits. Pregnancy outcomes were followed to delivery. Associations between serum levels (log-transformed), cycle type, and pregnancy outcome were estimated with Wilcoxon Rank Sum test, multivariable linear or logistic regression as appropriate.

RESULTS: There were no significant differences in maternal age, race, or gestational age (GA) at blood draw between patients having fresh or frozen embryo transfers. After adjusting for GA, fresh IVF cycles had significantly higher maternal serum VEGF levels compared to FET cycles (Median Fresh: 261.2 pg/mL [IQR 183.3-357.4] vs. FET 206.3 pg/mL [IQR 123.6-324.2] p = 0.004). Maternal serum sFlt-1 levels and PIGF levels were significantly lower in fresh IVF cycles, (sFlt-1 Median Fresh: 78.6 pg/mL [IQR 54.5-112.9] vs. FET 103.5 pg/mL [IQR 56.8-184.9] p = 0.02; PIGF Median Fresh: 15.5 pg/mL [IQR 12.9-18.5] vs. FET 17.9 pg/mL [IQR 13.4-22.5] p = 0.03). As sFlt-1 binds circulating PIGF and VEGF and limits these factors’ bioavailability, we examined sFlt1:PIGF and sFlt1:VEGF as measures of bioavail-

able PIGF and VEGF. While there was no difference in the sFlt1:PIGF ratio between fresh and FET cycles, maternal serum from fresh cycles had a significantly lower sFlt1:VEGF ratio when compared to serum from FET cycles (Fresh 0.27 [IQR 0.15-0.52] vs. FET 0.52 [0.26-1.01] p < 0.0001). Finally, for fresh and FET cycles together, the ratio of sFlt1:VEGF was positively associated with increased risk of SGA as well as a composite outcome of disorders of placentation (SGA: OR 3.35 [CI 1.08-10.44] p = 0.04, composite outcome: OR 2.41 [CI 1.12-5.2] p = 0.025).

CONCLUSIONS: Ovarian stimulation during fresh IVF cycles results in changes in maternal serum levels of members of the VEGF family including significantly more bioavailable VEGF during the critical period of early implantation, angiogenesis, and vasculogenesis. These, seemingly paradoxical, changes may explain the increased risk of adverse perinatal outcomes observed in fresh IVF cycles, and highlight the critical role of the peri-implantation environment in the establishment of normal placentation.

References:


Supported by: NIH 5K12HD001265 (SS), ASRM Research Grant (MM), P50-HD068157 (CC, MM).

O-207 Wednesday, October 19, 2016 11:45 AM

EXCESS PROVISION OF NUTRIENTS IN CULTURE MEDIUM REDUCES BLASTOCYST QUALITY.

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OBJECTIVE: Metabolomic analysis has revealed that embryos use only a limited amount of the substrates provided to them in vitro. Our objective was to determine the efficacy of reducing nutrient (carbohydrates, amino acids, vitamins and EDTA) concentrations in culture medium to optimize embryo quality.

DESIGN: Research Study

MATERIALS AND METHODS: In vivo matured IVF mouse zygotes were cultured in sequential, defined medium (OEC1/OEC2) containing 100%, 75%, 50%, and 25% nutrient concentration (5 replicates, ≥147 embryos/trt). Next, EDTA, glucose, alanyl-glutamine, and pyruvate (P) lactate (L) were individually added to 25% OEC1/2 (reduced; OEC1/2) at 50% concentration (4 replicates, ≥99 embryos/trt). In the third experiment, zygotes were placed into four OEC1 treatments: rOEC; rOEC1 + 50% PL; rOEC1 + 50% NEAA; rOEC1/2 + 50% PL + 50% NEAA (PLNEAA); all treatments were cultured in rOEC2 + 50% PL (3 replicates, ≥135 embryos/trt). Last, to further refine OEC, zygotes were cultured in rOEC1 + 50% PL, and either rOEC2 or rOEC2 + 50% PL.

RESULTS: Blastocyst development at 96 h was significantly lower in 25% compared to 50%, 75%, and 100% (39.8±3.4%, 61.7±3.9%, 63.4±4.0%, 61.2±4.0%), as well ICM cells hatching (43.2±3.5%, 63.8±4.0%, 61.9±4.0%, 62.6±4.0%). Blastocysts developing in 25% tended (p=0.08) to have a higher percentage of ICM cells than those in 100% (12.1±1.4%, 9.1±0.7%). Only the addition of PL to rOEC1/2 significantly increased (p<0.05) development, both to blastocyst (68.7±4.7%, 29.4±4.1%), and hatching blastocyst (63.6±4.9%, 28.6±4.0%). Supplementation of PL significantly increased blastocyst cell number (115.0±8.2) compared to rOEC (86.5±11.3), as well ICM cells (15.8±1.4, 10.5±1.4). Development to the blastocyst stage was not different in NEAA and PLNEAA compared to rOEC; PL again improved development (p=0.03). PL increased (p<0.03) blastocyst cell number (150.9±6.0) compared to rOEC (130.6±8.0) and NEAA (128.7±7.0). Embryos cultured in rOEC1/2 + 50% PL had an improved ICM:TE ratio (1.6:2) compared to standard (100%) OEC (1.9:8). Inclusion of PL in rOEC in only the first
STEP OF CULTURE SIGNIFICANTLY IMPROVED ICM CELL NUMBER (rOEC1+50% PL/rOEC2+50% PL 14.9±1.0).

CONCLUSIONS: Nutrient concentrations of just 25% can successfully support embryonic development when pyruvate and lactate alone are restored to 50% concentration in the first step of culture. Supplementation with additional nutrients can be detrimental to embryo quality. These results suggest that embryos cannot simply choose from available nutrients in the culture environment, but rather benefit from particular concentrations of specific energy substrates.

This approach may hold the key to improving in vitro embryo viability.

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DEVELOPMENTAL POTENTIAL OF OOCYTES WITH SMOOTH ENDOPLASMIC RETICULUM CLUSTERS AND THEIR BEHAVIOR OBSERVED BY TIME-LAPSE RECORDING SYSTEM. C. Mizoguchi, a K. Iwata, a M. Tsuneto, a K. Yumoto, a Y. Mio. a Reproductive Centre, Mio Fertility Clinic, Yonago, Japan; b Mio Fertility Clinic, Yonago, Japan.

OBJECTIVE: We previously reported that oocyte morphology was associated with embryo quality and viability, suggesting that controlled assessment of oocyte morphology is useful to predict human embryo quality. During intracytoplasmic sperm injection (ICSI), we occasionally observe oocytes with smooth endoplasmic reticulum clusters (sERC) (Otsuki et al, 2004), which are thought to disappear after fertilization and be closely associated with poor prognosis in achieving pregnancy. This study aimed to investigate the developmental potential of oocytes with sERC and their behaviors using time-lapse recording system.

DESIGN: Research study

MATERIALS AND METHODS: We collected the data of 6,765 matured oocytes retrieved after controlled ovarian hyper-stimulation from August 2010 to September 2015. During ICSI, three experienced embryologists noticed oocytes containing vacuole-like structures, which were defined as sERC by their disappearance at the zygote stage. These embryos were incubated and imaged by either high-resolution time-lapse cinematography or EmbryoScope®. Developmental velocity, rate of clinical use in embryo transfer or cryopreservation, and achieving pregnancy were compared between oocytes with [sERC(+)] and without [sERC(−)].

RESULTS: Of the 6,765 mature oocytes, 46 (0.7%) showed sERC(+). The developmental velocity of embryos derived from sERC(+)-oocytes was significantly higher than that of sERC(-)-oocytes, including the time of 2nd polar body (PB) extrusion, pronuclei (PN) formation, and syngamy from the ICSI procedure (in h: 2.5±0.6 vs. 2.9±1.0, 7.6±2.4 vs. 9.9±5.9, and 20.7±2.2 vs. 23.7±4.5, respectively; P<0.05). The sERC all disappeared by 4.3±1.2 h after ICSI in the period from 2nd PB extrusion to PN formation. The rate of clinical use of sERC(+) oocytes was 80.4% (37/46), of which 6 underwent fresh embryo transfer and 31 were cryopreserved. In total, 15 embryos were transferred (6 fresh embryos, 9 frozen/thawed embryos), the pregnancy rate was 40% (6/15), and miscarriage rate was 33.3% (2/6). Moreover, the live birth rate was 50% (3/6) and one is still ongoing. Healthy babies were born from oocytes with sERC(+).

CONCLUSIONS: This study demonstrated that oocytes with sERC could develop into good quality embryos and achieve successful pregnancy resulting in healthy babies. Further follow-up of the children are clearly needed, and mechanisms of the emergence of sERC and its impact on embryonic development are still under investigation. Detailed studies with molecular biological methods are necessary.

O-209 Wednesday, October 19, 2016 12:15 PM

STEM CELL MARKERS DESCRIBE A TRANSITION FROM SOMATIC TO PLURIPOTENT CELL STATES IN A RAT MODEL OF ENDOMETRIOSIS. E. R. Othman, a F. Y. Meligy, a A. A. Sayed, a M. A. Elmokhtar, a A. M. Elrefaey, a OB-GYN, Center of Excellence of Stem Cells and Regenerative Medicine CESRM, Assiut University, Assiut, Egypt; b Histology Department, Assiut University, Assiut, Egypt; c Medical Biochemistry Department, Assiut University, Assiut, Egypt; d Microbiology and Immunology, Assiut University, Assiut, Egypt; e Pathology Department, Assiut University, Assiut, Egypt.

OBJECTIVE: To study Thy1 as a fibroblast marker, SSEA1 as a marker of intermediate pluripotency and Oct4 as a marker of established pluripotency in rat model of endometriosis.

DESIGN: In vivo animal study

MATERIALS AND METHODS: Endometriosis was induced in 20 albino female rats through autologous transplantation of one uterine horn to mesentery of intestine. Other 20 rats had their horn removed without transplantation (controls). Rats were sacrificed 4 weeks after induction surgery. Ectopic, eutopic and control endometria were harvested from endometriosis and control animals respectively. Quantitative syber green based RT-PCR was used to detect expression of Thy1 (CD90), FUT4 (SSEA1), POU5F1 (Oct4) genes in tissues. Relative expression was normalized to that of β actin. In addition, Thy1, SSEA1 and Oct4 protein expression were detected by immunohistochemistry. Immunoscores were calculated by averaging number of positive cells in 10 non-overlapping high power fields in each section.

RESULTS: Ectopic endometrium expressed significantly higher mRNA of Oct4 and SSEA1 as compared to control endometrium. Expression levels of OCT4 and SSEA1 were comparable between eutopic and eutopic endometria and between eutopic and control endometria. Thy1 (CD90) gene expression level was comparable among eutopic, eutopic and control endometria (table 1). Oct4 immunoscore were significantly higher in eutopic (6.6±0.91) than eutopic (2.5±0.78) or control endometrium (3.7±0.1) (P value 0.02). Thy1 and SSEA1 immunoscores were comparable among all three types of endometria.

CONCLUSIONS: Using rat model of endometriosis, ectopic endometrium showed significantly higher Oct4, SSEA1, but similar Thy1 gene expression to that of control endometrium. This indicates increased transition from somatic to pluripotent cell states in ectopic endometrium which may play a role in endometriosis pathogenesis.


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O-210 Wednesday, October 19, 2016 12:30 PM

MYELOPEROXIDASE AND ACTIVATED MACROPHAGES ALTER METAPHASE II MOUSE OOCYTE QUALITY BY DISASSEMBLY OF MICROTUBULE ORGANIZING CENTER. S. Khan, a F. Shaeib, a R. Jeelani, a M. Thakur, a H. Abu-Soud, a Wayne State University, Detroit, MI; b OB/GYN-Physiology, Wayne State University/Medical School, Detroit, MI; c REI, Wayne State University, Royal Oak, MI; d Division of Reproductive Endocrinology, Department, Wayne State University/Detroit Medical Center, Detroit, MI.

OBJECTIVE: Macrophages, ubiquitous inflammatory cells, are major cellular producers of myeloperoxidase (MPO) and inflammatory mediators, such as cytokines and reactive oxygen species (ROS). Recently we have shown that MPO and ROS from various sources negatively affect oocyte quality, and we hypothesize that disturbance of pericentrin, a key scaffold protein of the microtubule organizing center (MTOC), plays a crucial role in these alterations and may serve as a predictor for oocyte quality. By monitoring changes in pericentrin after exposure to MPO, activated macrophages (AM), and ROS we seek to determine the inflection point at which oocyte quality and functionality are compromised and the mechanisms underlying these changes.

Relative expression of Thy1, SSEA1, and Oct4 genes in ectopic, eutopic, and control endometrium

<table>
<thead>
<tr>
<th>Gene</th>
<th>Ectopic endometrium</th>
<th>Eutopic endometrium</th>
<th>Control endometrium</th>
<th>P value/ Ectopic versus eutopic endometrium</th>
<th>P value/ Ectopic versus control endometrium</th>
<th>P value/ Eutopic versus control endometrium</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oct4</td>
<td>2.26</td>
<td>2.22</td>
<td>1.98</td>
<td>0.8</td>
<td>0.004*</td>
<td>0.13</td>
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<tr>
<td>SSEA1</td>
<td>1.53</td>
<td>1.50</td>
<td>1.44</td>
<td>0.5</td>
<td>0.5*</td>
<td>0.2</td>
</tr>
<tr>
<td>Thy1</td>
<td>1.47</td>
<td>1.48</td>
<td>1.38</td>
<td>0.8</td>
<td>0.25</td>
<td>0.25</td>
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</tbody>
</table>
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OBJECTIVE: To examine the frequency of incidental findings in expanded carrier screening - diseases where carriers may also have clinical health implications (CHI).

DESIGN: Expanded carrier screening (ECS) identifies couples at risk for transmitting a genetic condition to their offspring. Patients may be counseled during the informed consent process that carriers of recessive conditions usually do not experience symptoms. Yet, there are several conditions on ECS panels where carriers may have CHI. We analyzed Counsyl laboratory’s experience of over 346,790 expanded carrier screens to calculate this frequency.

MATERIALS AND METHODS: Individuals were tested for carrier status in up to 108 genes by either targeted genotyping (TG) of up to 417 sites or next-generation sequencing (NGS) of the exons and selected introns of the chosen genes. Carrier frequencies for each condition were calculated as the higher of TG or NGS frequencies.

Five autosomal recessive diseases were identified for their association with CHI: Nijmegen breakage syndrome (NBN) for cancer risk; ataxia-telangiectasia (ATM) for breast cancer risk; pseudocholinesterase deficiency (BCHE) for increased risk for prolonged period of breathing paralysis; and factor XI deficiency (F11) for risk for bleeding problems. Carriers for each condition were tabulated per ethnic group, and carrier frequencies for each condition were calculated per ethnic group.

RESULTS: 346,790 patients indicating ‘routine carrier testing’ as the reason for testing were selected from a total population of 430,584 (all indications). From this subset, 308,668 (89%) received TG and 38,122 (11%) received NGS test.

The carrier frequencies for each condition were 1/280 (ATM), 1/24 (BCHE), 1/109 (DPYD), 1/150 (F11), and 1/560 (NBN). This summates to an overall frequency of 6.2% for CHI on ECS. BCHE accounted for 67% of the frequency of CHI and is more common in individuals of Ashkenazi Jewish (4.5%) and European descent (4.9%) than those of African (1.0%) or Asian descent (1.2%).

CONCLUSIONS: 6.2% of individuals (1 in 16) screened for these diseases will have an incidental finding - where carriers identified may experience CHI. Pre-test counseling, informed consent, reporting, and post-test counseling should educate patients and providers regarding this possibility.

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OBJECTIVE: To document and report the relevance and implications of incidental findings identified during PGD in an effort to bring awareness and emphasize the need for implementing a standard operating protocol to report such findings to patients and their physicians.

DESIGN: Incidental findings identified in couples undergoing PGD for gene disorders were recorded and reported from July 2015 to March 2016.

MATERIALS AND METHODS: During the 9 month period, 269 cases were prepared through utilization of single nucleotide polymorphism (SNP) arrays (Karyomapping; Illumina, USA). DNA samples were obtained from couples and family members for test preparation purposes. During evaluation of sample quality, review of the SNP array profiles was completed. All incidental findings were reported to the physician and patient and recommendation for follow-up microarray testing was provided.

RESULTS: Incidental findings were identified in 10/269 PGD test preparations, affecting chromosomes 4, 14, 15, 16, 22, and X. Nine were microduplications and 1 was a microdeletion. The size of microduplications detected ranged from 0.18 megabases (Mb) to 3.5 Mb. Interestingly, three of the microduplications detected (4q35.2, 15q11.2, and 16q23.3) were each seen in 2 separate cases, accounting for 6/10 cases. The microdeletion identified (located on chromosome X) was determined to be of considerable size at 28Mb, potentially associated with health implications in the carrier female. Follow-up microarray analysis was pursued in 7 of the cases, as 1 of the patients declined further evaluation. Three of the incidental findings were reported as variants of uncertain significance (VUS), and 3 were reported as normal population variants. Results are still pending on 1 case. One patient elected to pursue PGD for the microduplication. Results from 2 PGD cycles for this patient with a total of 9 embryos, revealed 3 embryos free of the microduplication, but a total of 1 embryo available for transfer as the other 2 were affected with the single gene disorder and/or aneuploidy.

CONCLUSIONS: With the implementation of new and advanced methodologies in clinical practice, it is becoming progressively more common to incidentally obtain information that is additional to the requested test but may have significant health implications to the patient, other family members and/or future children. It is vital to acknowledge and address this issue in the clinical laboratory setting and a standard operating procedure has to be in place to handle such situations.
syndrome and other chromosome abnormalities was a significantly higher motivation in Oregon (81%, N = 38) than in South Dakota (45%, N = 5). The most cited reasons to decline PGS were cost, not finding a personal benefit in testing, and perceived risks to the embryos. One hundred percent of participants who met with a genetic counselor (N = 75) found the session helpful in making their decision. Helpful components included education about the risks, limitations, and benefits of PGS and discussion of psychosocial issues.

CONCLUSIONS: To the authors’ knowledge, this is the first study to examine the role of genetic counselors in the PGS decision. Patients have many motivations behind this decision, including the desire to improve pregnancy chances and reduce miscarriages. Utilizing genetic counselors in this setting may help patients to understand the benefits, limitations and risks of the test as well as address psychosocial issues.

Supported by: Funded in part by the National Society of Genetic Counselors ART/Infertility Special Interest Group 2016 Grant Award.

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INCREASED FETAL CHROMOSOME DETECTION WITH THE USE OF OPERATIVE HYSTEROSCOPY DURING EVACUATION OF PRODUCTS FOR MISCARRIAGE. A. Cholkeri-Singh,a O-214

OBJECTIVE: To determine if incorporation of hysteroscopy reduced maternal cell contamination when evaluating products of conception for chromosomal abnormalities as a cause of miscarriage.

DESIGN: Retrospective chart study.

MATERIALS AND METHODS: Setting: Private, minimally invasive surgery and infertiltiy practice with academic-community hospital affiliation.


Interventions: Suction curettage, diagnostic hysteroscopy with curettage or hysteroscopic biopsy with or without curettage followed by chromosomal analysis of products of conception for determination of fetal genetics.

RESULTS: A total of 243 charts were analyzed. Patients were categorized based on surgery performed: Group 1 (n=136) - suction curettage only; Group 2 (n=23) - diagnostic hysteroscopy followed by suction curettage; Group 3 (n=84) - hysteroscopy, biopsy of gestational sac, chorionic villi and/or fetus followed by suction curettage. No significant differences were detected between the groups for BMI, ethnicity, gravidity, parity, primary infertility, secondary infertility, spontaneous conception, singleton or multiple gestation, and surgical complications. All miscarriages were diagnosed in the first trimester with ultrasound.

Maternal contamination was significantly less in Group 3 (14.3%) versus Group 1 (30.1%) and Group 2 (34.8%), p=0.016. Removing all cases of maternal contamination and chromosomal analysis not performed, the fetal chromosome detection rate was significantly higher in Group 3 (84.4%) versus Group 1 (66.6%) and Group 2 (61.9%), p=0.009. Table 1 shows the comparison between the Groups with chromosome detection.

CONCLUSIONS: Obtaining fetal genetics can be useful when planning for a future successful pregnancy. Maternal contamination occurred at a higher rate when all products of conception were evacuated with curettage despite use of diagnostic hysteroscopy to identify intracavitary products of conception. The addition of operative hysteroscopy to biopsy the gestational sac, chorionic villi and/or fetus significantly decreased the risk of maternal contamination and increased the detection of fetal chromosomes for genetic analysis without increasing the risk of surgical complications.

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OBJECTIVE: To study the impact of test indications and family member availability on single gene validation studies and its influence on probe development and test design.

DESIGN: Retrospective study.

MATERIALS AND METHODS: A review was performed of 270 SGD analysis plans corresponding to 209 individual cases that were initiated from Oct. 2013 to Mar. 2016. Test indications were divided into three subgroups: routine carrier screening (RCS), expanded carrier screening (ECS), and personal/family history. Diseases categorized as RCS included cystic fibrosis, fragile X syndrome, spinal muscular atrophy and hemoglobinopathies. Test designs were categorized as follows: direct mutation with linkage-family members, direct mutation with linkage-embryos, linkage analysis only and direct mutation analysis only.

RESULTS: Out of a total of 270 SGD plans, 78.9% (213/270) of probe strategies were developed using family member samples. Of these plans, 75.1% (160/213) were initiated due to personal/family history, while 24.9% (53/213) were initiated following RCS (39 cases) or ECS (14 cases). In contrast, 21.1% (57/270) of probe strategies were designed without additional family member samples, 70.2% (40/57) of which were initiated following RCS or ECS, and 9.8% (17/57) were initiated due to personal/family history. The distribution between RCS vs. ECS was almost evenly divided; 22 and 18 cases respectively. To date, 1,041 embryos from 209 patients have been tested. Of these, 425 embryos have been identified as negative for the genetic disorder in question. Related pregnancy data has been summarized elsewhere.

CONCLUSIONS: In our study, approximately 1 out of 5 probe strategies were developed without the use of additional family member samples. Almost one-third of these cases were referred due to personal/family history and, in many of these instances, additional family member testing was not possible due to de novo inheritance, germline mosaicism or death of affected family members. Over two-thirds of these cases were initiated due to RCS or ECS, and these numbers are expected to increase as the uptake of RCS and ECS heightens. As such, there is a growing need to develop testing strategies for patients that are not able or do not wish to include family members in the development of linkage probes. A probe strategy that targets the mutation in question without a requirement of samples from other family members allows for the option of SGD PGD to be made available to a broader spectrum of patients.

## Table 1: Comparison of surgical groups for chromosome detection
(all p-values)

<table>
<thead>
<tr>
<th>Chromosomes</th>
<th>G1 vs G2</th>
<th>G1 vs G3</th>
<th>G2 vs G3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>0.972</td>
<td>0.351</td>
<td>0.545</td>
</tr>
<tr>
<td>Abnormal</td>
<td>0.699</td>
<td>&lt;0.001*</td>
<td>0.013*</td>
</tr>
<tr>
<td>Maternal contamination</td>
<td>0.656</td>
<td>0.008*</td>
<td>0.025*</td>
</tr>
<tr>
<td>Not Performed</td>
<td>0.627</td>
<td>0.127</td>
<td>0.372</td>
</tr>
<tr>
<td>Chromosome Detection</td>
<td>0.349</td>
<td>0.004*</td>
<td>0.006*</td>
</tr>
</tbody>
</table>

Probe Strategies Stratified by Indication

<table>
<thead>
<tr>
<th>Direct Mutation with Linkage Family Members</th>
<th>Linkage Analysis Only</th>
<th>Direct Mutation with Linkage Embryos</th>
<th>Linkage Analysis Only</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Personal/Family History</td>
<td>40.7%(110/270)</td>
<td>18.5%(50/270)</td>
<td>5.2%(14/270)</td>
<td>1.1%(3/270)</td>
</tr>
<tr>
<td>RCS</td>
<td>8.5%(23/270)</td>
<td>5.9%(16/270)</td>
<td>8.1%(22/270)</td>
<td>0%(0/270)</td>
</tr>
<tr>
<td>ECS</td>
<td>4.1%(11/270)</td>
<td>1.1%(3/270)</td>
<td>6.7%(18/270)</td>
<td>0%(0/270)</td>
</tr>
<tr>
<td>Total</td>
<td>53.3%(144/270)</td>
<td>25.6%(69/270)</td>
<td>20.0%(54/270)</td>
<td>1.1%(3/270)</td>
</tr>
</tbody>
</table>

OBJECTIVE: PGS is used clinically to enhance embryo selection in patients of advanced maternal age (AMA) and those with recurrent pregnancy loss (RPL) or recurrent IVF failure. We sought to understand if patients’ motivations for pursuing PGS are consistent with these established indications.

DESIGN: Anonymous quantitative and qualitative survey.

MATERIALS AND METHODS: Anonymous survey emailed confidentially to all patients who underwent their first cycle of IVF with PGS between 1/2014 and 3/2015 (n=395). Responses are reported as percentage (%).

RESULTS: 80 patients completed the survey; 7 respondents underwent PGD/PGS for single gene disorders and were excluded. The majority identified as Caucasian (77%) or Asian (19%). 26% had no insurance coverage and 18% had < 50% of expenses covered. The majority of patients identified with the following religions: Christianity (25%), Judaism (19%), Catholicism (15%) or none (16%). 86% were married. The majority were AMA (18% ages 35-37y, 32% ages 38-40, 15% ages 41-42 and 16% over age 42), but nearly 20% were <35y. The vast majority (64%) had not heard of PGS prior to their fertility consultation, 23% were referred from an outside physician, and 7% from a friend. A minority of patients pursued PGS for the indications of recurrent IVF failure (12% with > 2 prior IVF cycles) or RPL (26% had > 2 SAB). 64% of patients had not done a previous IVF cycle and 17% had been trying to conceive for under one year. 51% had zero previous miscarriages, 23% only 1 miscarriage and 33% already had 1 living child. The most common infertility diagnosis was unexplained infertility (36%). When asked the primary motivation for PGS, the most common response was “to maximize IVF efficiency and have a baby sooner” (36%). Only 26% cited their primary indication as previous miscarriage, 12% wanted to decrease the chance of miscarriage but had not yet had a miscarriage, 11% reported multiple failed attempts at IVF, and 14% chose PGS electricly and were young, undergoing their first IVF cycle, and without prior miscarriage. 15% (n = 11) reported ‘other,’ with reasons including family balancing and ‘to reduce the number of unknowns.’ 27% of patients agreed that they may be more likely to pursue pregnancy with donor eggs if unable to conceive from IVF with PGS. Overall, 94% of patients were happy they pursued PGS, regardless of their outcome, as the information they obtained was deemed valuable.

CONCLUSIONS: Beyond the standard indications of advanced maternal age, recurrent IVF failure, and recurrent pregnancy loss, an increasing number of patients are using PGS as part of routine IVF to improve efficiency, reduce miscarriage and decrease the time to pregnancy. Understanding these motivations will help providers deliver appropriate support and counseling.

ART: CLINICAL 3

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OBJECTIVE: To investigate whether fresh double blastocysts transfer (DBT) improve the live birth rate compared to fresh elective single blastocyst transfer (eSBT) and subsequent vitrified-warmed single blastocyst transfer (FBT) in women 40-43 years of age.

DESIGN: Retrospective cohort study conducted at a single academic center.

MATERIALS AND METHODS: Women aged ≥ 40 years, who underwent fresh eSBT where supernumerary blastocysts were available for cryopreservation and women who underwent fresh DBT between January 2011 and June 2015 were included in the study. Women with >3 previous in-vitro fertilization (IVF) cycles were excluded. Embryos were transferred on day 5. Remaining embryos of good quality (≥3BB) were cryopreserved. According to our guidelines, up to 2 blastocysts can be transferred in this age group. The decision regarding the number of transferred blastocysts was made by the treating physician and couple. Outcomes of fresh and FBT cycles were analyzed. Chi-squared tests and logistic regression controlling for confounders were used.

RESULTS: 267 women were included, 146 underwent eSBT and 121 underwent DBT. Women with eSBT were significantly younger (40.7 ± 4.6 years vs. 41.0 ± 8.0 years, p < 0.01), had significantly fewer previous IVF cycles compared to women with DBT (0.5 ± 0.8 vs. 1.1 ± 1.02 cycles, p < 0.001). eSBT and DBT had comparable: peak stimulated serum estradiol levels (7414 pmol/l vs. 7447 pmol/l, p = 0.26), number of metaphase II oocytes collected (9.7 ± 4 vs. 9.6 ± 4, p = 0.17). The live birth rate (20% vs. 26%, p = 0.20) was similar for eSBT and DBT respectively, although favoring the latter. After failed fresh eSBT, 82 women returned for a total of 91 FBT cycles. Average blastocyst quality for the eSBT, DBT and FBT did not differ. The live birth rate per cycle was (15% vs. 26%, p = 0.001) for eSBT plus FBT versus DBT respectively. However, the cumulative live birth rate did not differ between eSBT plus FBT as compared to fresh DBT (25% vs. 26%, p = 1.0) respectively. There were 6 twin deliveries after DBT and none from eSBT plus FBT (19% vs. 0%, p = 0.02) respectively.

CONCLUSIONS: The practice of eSBT and subsequent vitrified-warmed blastocyst transfer in women aged 40-43 years reduces the per cycle live birth

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rate while minimizing the multiple birth rate and results in similar cumulative live birth rates, when compared to fresh DBT. Outcome implications should be discussed with patients and individualized. Given the added risk of multiple pregnancies in this age group, eSBT is preferential in women 40-43 years of age.

**O-219** Wednesday, October 19, 2016 11:45 AM

**METHOTREXATE TREATMENT OF ECTOPIC PREGNANCY DOES NOT IMPACT OVARIAN RESERVE OR CLINICAL OUTCOME, REGARDLESS OF THE DURATION OF TIME SINCE EXPOSURE.** L. Sekhon,1 a J. Rodriguez-Purata, a J. A. Lee, a M. C. Whitehouse, a A. B. Copperman.1 a Reproductive Medicine Associates of New York, New York, NY; aObstetrics, Gynecology & Reproductive Science, Icahn School of Medicine at Mount Sinai, New York, NY.

**OBJECTIVE:** Methotrexate (MTX) is a minimally invasive treatment for ectopic pregnancy. As it targets rapidly dividing cells, there is concern it may affect proliferating germinal cells in the ovary, ovarian reserve. Most centers recommend patients wait 2-3 months before attempting subsequent fertility treatment. It is not known whether recent MTX exposure increases the incidence of meiotic error within oocytes, contributing to embryonic aneuploidy. We sought to investigate the effect of MTX treatment and the interval of time from its administration to subsequent fertility treatment on ovarian reserve and IVF outcome.

**DESIGN:** Retrospective cohort study, case control study

**MATERIALS AND METHODS:** All patients who received MTX in a prior cycle and underwent subsequent IVF ± ET from 2003-2016 were included. The interval of time from administration to the start of their subsequent cycle was calculated. Paired t-test compared ovarian reserve markers (day 3 FSH) and cycle parameters pre- and post-MTX. Linear and binary logistic regression were performed to identify if interval since MTX modified implantation and early pregnancy loss.

**RESULTS:** A total of 491 patients received MTX and underwent subsequent COH (n=339) with fresh ET (n=279) or frozen-thawed (FET) (n=198). The interval from MTX to subsequent cycle start, cycle characteristics and clinical outcome of COH and ET cycles are shown (Table). After controlling for the increase in patient age, FSH, egg yield and fertilization, total gonadotropin dose required and blastocyst count were similar among pre- and post-MTX COH cycles. Intercycle variation in these parameters was not correlated with MTX interval. Odds of failed implantation (OR 1.0 [95% CI 1.0-1.0], p=0.3) and pregnancy loss (OR 1.0 [95% CI 0.9-1.0], p=0.8) were not influenced by MTX interval.

**CONCLUSIONS:** In agreement with the existing literature, these results suggest ovarian reserve and IVF outcomes are not compromised by MTX treatment of ectopic pregnancy. The interval of time from MTX did not impact cycle outcome or the incidence of aneuploidy. To date, this is the only study to assess embryonic aneuploidy following MTX exposure. Though the results are reassuring regarding MTX safety, large-scale, multicenter studies are required to confirm these findings.

**O-220** Wednesday, October 19, 2016 12:00 PM

**IMPACT OF THE OXYTOCIN RECEPTOR ANTAGONIST (ATOSIBAN) ADMINISTERED SHORTLY BEFORE EMBRYO TRANSFER ON PREGNANCY OUTCOME AFTER INTRACYTOPLASMIC SPERM INJECTION (ICSI).** S. A. Heibisha, a B. A. Aboelazm, a H. M. Adel, a A. I. Ahmed, a Gynecology, Alexandria University - Faculty of Medicine, Alexandria, Egypt; aObstetric and Gynecology, MFM Division, Department of Medical Genetics, Wayne State University, Detroit, MI.

**OBJECTIVE:** To evaluate the impact of the oxytocin receptor antagonist (Atosiban) administered shortly before embryo transfer on implantation and pregnancy rates in patients undergoing intracytoplasmic sperm injection (ICSI) using long agonist protocol.

**DESIGN:** Randomised controlled trial.

**MATERIALS AND METHODS:** one hundred and eighty two women, prepared for intracytoplasmic sperm injection for male or tubal factor infertility, using long agonist protocol were divided randomly into two groups; Group A (n=91) who received 7.5 mg Atosiban by slow IV injection and Group B (n=91) who received placebo as sodium chloride 0.9% solution also by IV injection 20 minutes before embryo transfer (blastocyst stage ET). Pregnancy and implantation rates were compared among the two study groups.

**RESULTS:** Pregnancy rate was significantly higher in group A (atosiban group) (58/91) compared to group B (44/91) (63.7% vs 48.4% respectively, p=0.037*). Also, implantation rate was significantly higher in group A (atosiban group) compared to group B (45.20%, vs 34.69% respectively, P=0.045*). All of the intermediate cycle parameters were also comparable.

**CONCLUSIONS:** Atosiban in the given dose and regimen improved both implantation and ongoing pregnancy rates in patients undergoing ICSI using blastocyst stage embryo transfer.

**References:**
Comparison between the two studied groups according to implantation and pregnancy rates

<table>
<thead>
<tr>
<th>Group A (n=91)</th>
<th>Group B (n=91)</th>
<th>test of significance</th>
<th>p value</th>
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</thead>
<tbody>
<tr>
<td>ET</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Min-Max.</td>
<td>1.0 - 2.0</td>
<td>1.0 - 2.0</td>
<td></td>
</tr>
<tr>
<td>Mean± SD</td>
<td>1.60 ± 0.49</td>
<td>1.62 ± 0.49</td>
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</tr>
<tr>
<td>Total no. of ET</td>
<td>146.0</td>
<td>147.0</td>
<td></td>
</tr>
<tr>
<td>Implantation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Min-Max.</td>
<td>0.0 - 2.0</td>
<td>0.0 - 2.0</td>
<td></td>
</tr>
<tr>
<td>Mean± SD</td>
<td>0.74 ± 0.66</td>
<td>0.55 ± 0.58</td>
<td></td>
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</tbody>
</table>

**ET**

**Maternal Endometrial Secretions 24 Hours Prior to FET**

Wednesday, October 19, 2016 12:15 PM

O-221

**OBJECTIVE:** It is well known that successful implantation is dependent on an intricate dialogue between a competent embryo and a receptive endometrium. On the maternal side, specific biological changes in adhesion need to occur for attachment, while tight regulation of signaling pathways are crucial for the embryo. The objective of this study was to examine the uterine fluid in association with implantation outcome 24 hours prior to, and at the time of euploid embryo transfer.

**DESIGN:** Research study.

**MATERIALS AND METHODS:** Infertile patients (n=48) were recruited with IRB consent prior to a frozen embryo transfer (FET) with euploid blastocysts. Uterine secretions were collected by aspiration (~2-5ul), either 24h prior to, or at the time of FET. Uterine secretome analysis was performed blinded of implantation outcome using qPCR for miRNA analysis (n=12) and mass spectrometry (n=36) for metabolite (UHPLS-MS, Thermo) and protein analysis (LC-MS/MS, Thermo). MiRNA profiles were analyzed by REST® statistical software. MS data was converted with MassMatrix and processed with Maven (Princeton Univ). MS/MS data was examined using Mascot™ (v. 2.2) and Scaffold (v. 2.06). Validation of target genes was performed using qPCR on endometrial biopsies (n=14) and cryopreserved blastocysts (n=14) donated with patient consent.

**RESULTS:** A notable uterine secretome profile of miRNA, metabolites and proteins was significantly associated with a negative, toxic environment both 24hrs prior to, and at the time of embryo transfer (P<0.05, >2 fold change). Specifically, 6 maternal miRNAs showed increased expression with negative implantation, including miR-17 (P<0.05). A known target gene for miR-17 through negative regulation of VEGFA, a signal protein essential for fertilization and secretion by the receptive endometrium as well as the developing embryo. Validation of VEGFA expression was confirmed in endometrial cells and individual blastocysts. A total of 12 amino acids displayed decreased quantities in the uterine secretome associated with negative implantation (P<0.05, >2 fold change) including arginine, essential for blastocyst activation and trophoectoderm motility. Additionally, the MUC protein family were observed at increased levels with implantation failure (P<0.05). MUCIN proteins are epithelial cell surface proteins that have considerable effect on endometrial function, creating a barrier to implantation.

**CONCLUSIONS:** Aberrant maternal uterine miRNA and molecular secretions allow for the characterization of implantation failure both 24hrs prior to, and at the time of FET. This compromised embryo-endometrial dialogue further impacts the transcription levels of key signaling molecules, resulting in significantly lower implantation success. Predicting the maternal molecular microenvironment ahead of embryo transfer may allow for fine tuning of procedures for IVF patients thereby improving implantation outcomes.

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**MATERNAL ENDOMETRIAL SECRETIONS 24 HOURS PRIOR TO FROZEN EMBRYO TRANSFER IS PREDICTIVE OF IMPLANTATION OUTCOME.**

**OBJECTIVE:** It is well known that successful implantation is dependent on a tight regulation between a competent embryo and a receptive endometrium. On the maternal side, specific biological changes in adhesion need to occur for attachment, while tight regulation of signaling pathways are crucial for the embryo. The objective of this study was to examine the uterine fluid in association with implantation outcome 24 hours prior to, and at the time of euploid embryo transfer.

**DESIGN:** Research study.

**MATERIALS AND METHODS:** We analyzed 8,588 autologous IVF cycles in women under 38 that included an SET in cycle 1. 3,727 of these cycles failed and were followed by a successive IVF cycle with SET (n=1,815) or DET (n=1,912). Cycles with pre-implantation genetic screening (PGS) were excluded. Multivariate logistic regression models were used to evaluate the odds of ongoing pregnancy and multiples. Predictors were refined using least absolute shrinkage and selection operator (LASSO).

**RESULTS:** We observed that SET was performed in 36.9% of first cycles in women under 38 that involved an SET in cycle 1. The odds of success with the first versus second SET cycle (P<0.16). Further, our models showed that first cycle outcome (e.g. miscarriage) had no significant impact on second cycle ongoing pregnancy rates. Evaluation of multiples rates found much higher risk for DET compared to SET (P<0.001). Cycles with pre-implantation genetic screening (PGS) were excluded. Multivariate logistic regression models were used to evaluate the odds of ongoing pregnancy and multiples. Predictors were refined using least absolute shrinkage and selection operator (LASSO).

**CONCLUSIONS:** We found that patients that have failed an SET cycle have no reduction in odds of ongoing pregnancy when performing a second SET attempt. We also found that those that choose to do a DET are at a significantly higher risk for multiples.

**Supported by:** Celmatix Inc.
PLANNING Eeva™-DMX MARKERS TO IMPROVE TIME-LAPSE EMBRYO CLASSIFICATION

B. Aparicio-Ruiz,a N. Basile,b L. Romany,c T. Viloria,d R. G. Ferreira,e M. L. Sánchez, a e90 ASRM Abstracts

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PROSPECTIVE STUDY OF AUTOMATED VS. MANUAL ANNOTATION OF Eeva™ TIME-LAPSE MARKERS. D. J. Kaser,a D. L. V. Farland,a,1 S. A. Missmer,a,2 C. Racowsky,a "Dept of Obstetrics & Gynecology, Brigham & Women’s Hospital, Harvard Medical School, Boston, MA; 2Dept of Epidemiology, Harvard Chan School, Boston, MA.

OBJECTIVE: To compare automated time-lapse annotation (Eeva™) to manual annotation performed by embryologists certified in measuring durations of the 2-cell (P2) and 3-cell (P3) stages.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: Embryos cultured in the Eeva™ system from 8/2014 to 2/2016 were assigned a blastocyst prediction score of High (H), Medium (M), Low (L), or scored as not rated (NR) by Eeva™ version 2.2 according to P2 and P3. An embryologist then manually annotated each embryo; if manual annotation changed the final score, a second embryologist independently repeated the annotation to reach consensus. Proportions of discordant results were determined, along with performance characteristics (sensitivity, specificity, PPV and NPV) of each method for blastocyst prediction. Factors associated with discordance were investigated.

RESULTS: 1,477 embryos were imaged. Eeva™ was more likely than an embryologist to score an embryo as NR (11.1 vs. 3.0%, P<0.0001), leading to higher proportions of patients with at least one NR embryo (41.1% vs. 17.9%; P<0.0001), or all NR embryos (2.0% vs. 0.0%; P<0.009). The distribution of H, M and L scores differed by automated vs. manual method (P<0.0001). Discordance occurred in 30.0% (443/1,477) of all embryos, with 82.6% (366/443) upgraded from a lower to a higher score by manual annotation. The proportion of discordant embryos varied by automated score (H: 9.8%; M: 19.1%; L: 40.2%; NR: 30.9%; P<0.0001). Neither abnormal cleavage nor day 3 conventional morphology grading was associated with discordance. Embryos located in the ten outer wells of the Eeva™ dish were more likely to be discordant than embryos in the two central wells (31.2% vs. 23.8%; P<0.02). The NPV and sensitivity of Eeva™ for blastocyst prediction of H or M was lower than manual annotation, while neither the PPV nor specificity were different (Table).

CONCLUSIONS: Discordance between the two annotation methods occurred in nearly one-third of embryos; the majority of which were ‘overcalled’ as having a lower score by the automated software. Factors associated with discordance included an automated score of L or NR, and outer well location. Manual annotation increased the likelihood of an embryo being assigned a score, and likewise improved the sensitivity and NPV of the test. These findings suggest that manual annotation may be superior to automated annotation for these early time-lapse markers, underscoring the importance of the Manual Update feature available on current Eeva™ software available outside of the United States.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Quartile 1</th>
<th>Quartile 2</th>
<th>Quartile 3</th>
<th>Quartile 4</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnancy Loss</td>
<td>20.6%</td>
<td>24.7%</td>
<td>24.5%</td>
<td>28.5%</td>
<td>0.01</td>
</tr>
<tr>
<td>Mean Blast Expansion Grade</td>
<td>5.48</td>
<td>5.51</td>
<td>5.46</td>
<td>5.51</td>
<td>NS</td>
</tr>
</tbody>
</table>

Supported by: Progyny, Inc.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Automated annotation</th>
<th>Manual annotation</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>56.1</td>
<td>68.4</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Specificity</td>
<td>68.3</td>
<td>64.9</td>
<td>0.15</td>
</tr>
<tr>
<td>Positive predictive value</td>
<td>77.4</td>
<td>78.5</td>
<td>0.52</td>
</tr>
<tr>
<td>Negative predictive value</td>
<td>44.6</td>
<td>52.3</td>
<td>&lt;0.0001</td>
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Supported by: Progyny, Inc.
RESULTS: Patients where no HIGH embryos were transferred (n=75) had an ongoing pregnancy rate (OPR) of 46.70% and those patients where at least one HIGH embryo was transferred (n=109) significantly increased OPR to 67% (p=0.009). Those patients where no A ASEBIR embryos were transferred (n=108) presented an OPR of 60.20%, while patients with at least one A ASEBIR embryo (n=81) was 59.30% (p=0.098). Combining both categorizations: Patients where no A or HIGH embryos were transferred had an OPR of 60.0% while those without a ASEBIR but at least one HIGH had 71.20% (p=0.025). Patients where at least one embryo was A but no one was HIGH had 60% (p=0.084). In the logistic regression analysis we observed whether at least one of the embryos is labelled as HIGH, OPR is 2.567 (CI95%:1.305-5.632) times higher than a cycle where no HIGH embryos are transferred (p=0.006). In the multivariable model no effect is observed when at least one embryo categorized as A ASEBIR is transferred (OR=0.563; CI95%:0.182-1.182) or according to day of transfer (OR=0.795 0.244-2.597).

CONCLUSIONS: To our knowledge, this is the largest data set of patients which embryos were evaluated by the Eeva system. Our results demonstrated a significant increase in the chances of achieving an OPR when Eeva is selecting a HIGH embryo for transfer showing higher accuracy than standard morphology for embryo selection.

Supported by: Spanish Ministry of Economy and Competitiveness (PI14/00523) through the Instituto de Salud Carlos III program.

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EFFECT OF STRICT SPERM MORPHOLOGY ON INTRAUTERINE INSEMINATION PREGNANCY SUCCESS: A SYSTEMATIC REVIEW AND META-ANALYSIS. T. P. Kohn, a S. A. Shabtaie, b INSEMINATION PREGNANCY SUCCESS: A SYSTEMATIC REVIEW AND META-ANALYSIS.

DESIGN: Systematic review and meta-analysis.

MATERIALS AND METHODS: Systematic search of MEDLINE, EMBASE, and Clinicaltrials.gov for studies evaluating semen morphology using the strict criteria and IUI success rates (measured by clinical pregnancies per cycle of IUI) published through April 2016. Studies were eligible for inclusion if they were published in peer-reviewed literature and assessed IUI pregnancy success rate for strict sperm morphology either >4% and ≤4% or ≥1% and <1%, and followed the WHO 2010 guidelines. Two separate meta-analyses were performed: the first to assess threshold of strict sperm morphology between >4% and ≤4% for pregnancy success with IUI. The second was to examine the threshold of morphology between ≥1% and <1% for IUI pregnancy successes. Estimates were pooled using random-effects meta-analysis. Differences by study-level characteristics were estimated using meta-regression.

RESULTS: Data were extracted from 30 trials involving 16,915 IUI cycles. A total of 28 trials reported IUI results with sperm morphology >4% and ≤4%, and 9 trials reported IUI results with sperm morphology ≥1% and <1%. Average IUI pregnancy success rate for couples with a sperm morphology >4% was 15.0% [95% CI: 12.9% to 17.4%; I²=88.9%, p < 0.0001] and was higher compared to couples with sperm morphology ≤4%: 10.5% [95% CI: 8.2% to 13.4%; I²=80.3%, p < 0.0001]; between-group difference, Q = 2.57, p = 0.016. No significant difference, however, was seen between the average pregnancy success for couples with a sperm morphology ≥1%: 14.0% [95% CI: 12.0% to 16.26%; I²=77.9%] compared to the pregnancy success for couples with sperm morphology <1%: 11.0% [95% CI: 6.59% to 17.99%; I²=28.1%]; between-group difference, Q = 0.79, p = 0.373. A within-group difference was noted in sub-analysis that controlled for a potential confounder of minimum total motile sperm count for strict morphology <1% (p = 0.025). This indicates that total motile count plays an important role in IUI pregnancy success rate when strict morphology is <1%. For all other groups, potential confounders, such as minimum IUI total motile count and average study year, were found to be insignificant (p > 0.05 for all comparisons). A significant limitation was that no studies reported female age as a function of successful and non-successful pregnancies for sperm morphology >4% and ≤4%.

CONCLUSIONS: While successful pregnancy was higher in couples with sperm morphology >4% compared to ≤4%, it is important to note that up to 10.5% of cycles with morphology ≤4%, including men with sperm morphology <1%, achieved a successful pregnancy. Thus for couples with abnormal morphology, IUI ought to be attempted prior to proceeding with in vitro fertilization - a much more expensive route.

References:


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DYSREGULATION OF THE HIPPO PATHWAY IN SELECTIVE THECA CELL PHOSPHATASE AND TENSIN HOMOLOG (PTEN) MUTANT MICE EXHIBITING A POLYCYSTIC OVARIAN SYNDROME (PCOS)-LIKE PHENOTYPE. K. A. Ehlers, B. Lin, X. Li, K. Pagidas, Z. Lei. OB/GYN and Women’s Health, University of Louisville Health Sciences Center, Louisville, KY.

OBJECTIVE: Genome-wide association studies of patients with PCOS in multiple ethnic groups have consistently identified single-nucleotide polymorphisms of Yes-associated protein (YAP), a central player of the Hippo pathway, implicating that YAP may play a role in the pathophysiology of PCOS. The Hippo signaling pathway regulates cell growth and organ size through a kinase cascade that influences the activity of the transcriptional regulator YAP. Disruption of the Hippo pathway leads to the activation of YAP by reducing its phosphorylation leading to nuclear translocation. Our previous unpublished studies demonstrated that tPtenMT mice exhibit phenotypic features of human PCOS such as androgen excess, prolonged diestrus, enlarged ovaries, ovulation dysfunc-

tion, and early loss of the fertile female phenotype. The objective of this study is to determine if the Hippo pathway is dysregulated in tPtenMT mice by evaluating YAP phosphorylation and the expression of target genes in the ovary.

DESIGN: Laboratory study using a conditional gene knockout mouse model.

MATERIALS AND METHODS: Ovaries from tPtenMT and wild type (WT) mice were collected at 2.5 months of age. Tissue was prepared to examine protein levels, phosphorylation status, and subcellular location of YAP by Western Immunoblotting and immunohistochemistry (IHC), respectively. Granulosa cells were then isolated from sexually immature tPtenMT and WT mice and cultured for 24 to 48 hours in vitro with and without the YAP-specific inhibitor verteporfin. Total RNA was isolated from the treated and untreated cells and used to evaluate the expression of known YAP downstream targets and gonadotropin receptors using real-time polymerase chain reaction (PCR) and reverse transcription-PCR.

RESULTS: Phosphorylation of YAP at both serine 127 and 397 sites was significantly decreased in tPtenMT ovaries, but total YAP protein was unchanged. IHC localized YAP to ovarian granulosa cells with more abundant nuclear immunostaining in granulosa cells of tPtenMT ovaries. YAP downstream targets Ccn5 and Birc1, and compelling PCOS candidate genes, luteinizing hormone/choriogonadotropin receptor (Lhcg) and follicle stimulating hormone receptor (Fshr), were markedly elevated in purified granulosa cells of tPtenMT mice compared to WT controls. Moreover, the expression of these genes was significantly attenuated in a dose and time dependent manner by verteporfin.

CONCLUSIONS: These results suggest that selective deletion of Pten in theca cells disrupts the Hippo pathway and leads to over-activation of YAP in granulosa cells, which in turn leads to Lhcg and Fshr granulosa cell over-expression. Dysregulation of the Hippo pathway in tPtenMT mice via YAP may contribute to the PCOS-like phenotype in these mice.

Supported by: Kentucky Science and Engineering Foundation Grant: KSEF-2791-RDE-016.

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INITIAL EXPERIENCE WITH FLUORESCENCE ACTIVATED CELL SORTING OF SPERMATOZOA FROM TESTIS TISSUE: A NOVEL METHOD FOR SPERM ISOLATION AFTER TESE. S. Mittal, A. Mielenk, A. Bolyakov, P. N. Schlegel, D. Paduch. Urology, New York Presbyterian / Weill Cornell Medicine, New York, NY; Urology, Weill Cornell Medical College, New York, NY; Weill Cornell Medicine, New York, NY; Dept of Urology, Weill Cornell Medical College, New York, NY.

OBJECTIVE: Non-obstructive azoospermia (NOA) is a cause of male infertility secondary to genetically driven defects in spermatogenesis. Testicular sperm extraction (TESE) is successful in identifying a small number of sperm in 50% of men with NOA. Traditionally, sperm are iso-

lated from testicular tissue using a combination of standard light microscopy, enzymatic digestion and significant time by embryologists analyzing the specimens in hope to isolate rare spermatozoa. Here we discuss our preliminary results utilizing fluorescence-activated cell sorting (FACS) of testis tissue to increase the efficiency in the isolation of spermatozoa.

DESIGN: Using fluorescence activated cell sorting we attempt to isolate and collect spermatozoa from testicular tissue from men with and without NOA.

MATERIALS AND METHODS: Testicular tissue was obtained from 5 patients: 2 cadaveric specimens that have normal spermatogenesis on histology and 3 specimens from wasted testicular tissue from micro-

TESE. Of these 3 specimens, 2 patients had an unsuccessful TESE. First, the specimens were prepared by sharp cutting with sterile scissors followed by mechanical disaggregation with a Medimachine (BD Bio-

sciences, USA). The specimens were passed through a 50-micron fol-

lowed by a 30-micron filter. The specimens were then fixed, permeabilized and stained with the DNA-stain To-Pro-3(ThermoFischer, USA) and incubated at room temperature for 20 mins. Sperm from a normal semen sample was also stained with To-Pro-3 and used as con-

trols for gating during flow cytometry based on the spermatozoa cell size (forward-scattered light, FSC), cell density and complexity (side-scatter-

ed light, SSC) and relative fluorescence of the haploid cell. Then, cell sorting was completed using a FACSArria II (BD Biosciences, USA) to isolate spermatozoa. Finally, each collected specimen was centrifuged at 800g for 5 minutes and underwent standard light micro-

scopy to identify spermatozoa.

RESULTS: This technique, spermatozoa were successfully isolated and recovered in 4 of 5 patients. This included successful isolation in 1 of 2 patients who underwent TESE that failed to recover sperm using standard tis-

sue processing techniques.

CONCLUSIONS: Our initial experience using fluorescence-activated cell sorting for rare spermatozoa isolation from testicular tissue proves the technical feasibility of this process. As this research continues to be refined, the use of novel, membrane permeable, nucleic acid stains will allow us to isolate living sperm and better understand the effects FACS may have on the motility and DNA-fragmentation of the spermatozoa. The clinical application of this technique has the potential to increase the rate of successful TESE to isolate spermatozoa.
OBJECTIVE: To evaluate the effect of elagolix, an oral, non-peptide gonadotropin-releasing hormone antagonist, on the quality of life (QoL) in women with moderate/severe endometriosis-associated pain (EAP).

DESIGN: These were two similar, double-blind, randomized, placebo-controlled, multicenter, 6-month, phase 3 studies (Studies 1 [North America] and 2 [global]) evaluating two doses of elagolix (150 mg once daily [QD] or 200 mg twice daily [BID]). Each study has an ongoing 6-month extension study.

MATERIALS AND METHODS: Participants were 18-49 year-old women with surgically diagnosed endometriosis and moderate/severe EAP. Following a screening period, 871 and 815 women in Studies 1 and 2, respectively, were randomized to receive placebo, elagolix 150 mg QD or 200 mg BID and treated for 6 months. The Endometriosis Health Profile (EHP-30) is a self-administered questionnaire used to measure health related QoL in women with endometriosis (scale of 0 [never] to 4 [always]). In this study, all 5 dimensions (pain, control and powerlessness, social support, emotional well-being, and sexual intercourse) of the core component, and 1 (sexual intercourse) from the modular component were assessed at baseline and months 1, 3 and 6 during the treatment period. The effect of elagolix on change from baseline of the 6 dimension scores was analyzed using an analysis of covariance model while controlling for baseline values.

RESULTS: In each of the 6 EHP-30 dimensions, each dose of elagolix showed greater reductions from baseline (greater improvements in health status) than placebo at months 1, 3 and 6 in a dose-dependent manner (Table, month 6 only). Compared to placebo, these changes were significantly different for elagolix 200 mg BID for all EHP-30 dimensions, whereas the changes were significantly different for elagolix 150 mg QD for all dimensions except self-image and sexual intercourse dimension in both studies (Table).

CONCLUSIONS: Over the course of 6 months, treatment with elagolix resulted in significant, dose-dependent improvements in QoL, based on the EHP-30 questionnaire.

Supported by: AbbVie Inc. funded these studies and participated in the study design, research, analysis, data collection, interpretation of data, reviewing, and approval of the publication.

EHP-30 Dimension Mean Scores at Baseline and Mean Change from Baseline to Month 6 in Studies 1 and 2

<table>
<thead>
<tr>
<th>EHP-30 Dimension</th>
<th>STUDY1</th>
<th>STUDY2</th>
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<tbody>
<tr>
<td></td>
<td>Elagolix</td>
<td>Elagolix</td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td>150 mg QD</td>
</tr>
<tr>
<td>Change from BL to M6</td>
<td>N=374</td>
<td>N=249</td>
</tr>
<tr>
<td>Pain</td>
<td>57.6; -15.4</td>
<td>58.1; -28.0***</td>
</tr>
<tr>
<td>Control and Powerlessness</td>
<td>66.9; -21.2</td>
<td>70.3; -34.7***</td>
</tr>
<tr>
<td>Emotional Well-being</td>
<td>47.4; -13.0</td>
<td>50.2; -20.0***</td>
</tr>
<tr>
<td>Social Support</td>
<td>51.3; -12.8</td>
<td>55.7; -20.3**</td>
</tr>
<tr>
<td>Self-image</td>
<td>48.7; -11.3</td>
<td>51.9; -15.4</td>
</tr>
<tr>
<td>Sexual Intercourse</td>
<td>64.3; -11.6</td>
<td>62.8; -16.3</td>
</tr>
</tbody>
</table>

EHP=Endometriosis Health Profile; BL = baseline; M = month; LS = least squares. The Ns in the treatment group header represent the number randomized and treated; the Ns for change from BL at M6 of each treatment group vary for each dimension and will be reported in the presentation. Decreases in the mean change from BL reflect improvements in QoL on the given dimension. Statistical significance on the mean change from BL to M6 vs. placebo was analyzed by an ANCOVA model and indicated by two-sided P-values of P ≤ 0.05 (*), P ≤ 0.01(**), P < 0.001 (***)
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NEW PROCEDURE FOR THE ENDOMETRIOSIS DIAGNOSIS. X. Santamaria, J. Vallve. IVI Barcelona, Barcelona, Spain.

OBJECTIVE: Previous studies revealed that when endometrial cells from GFP (Green Fluorescent Protein) mice were introduced into peritoneal cavity of RFP (Red Fluorescent Protein) mice to induce a murine model of endometriosis, GFP+ cells epithelial cells were aberrantly found in the stromal compartment of the eutopic endometrium of RFP mice two, three and four months after surgery. Arrays and immunofluorescence (IF) of these aberrant cells showed that GFP+ cells co-expressed cytokeratin (CK, epithelial marker) and LGR5, a stem-cell rich Repetition Containing G protein-Coupled Receptor 5 (LGR5, stem cell marker of the intestine). The aim of this study was to prove wether this procedure occurs in the human endometrium of patients affected with endometriosis and to characterize this type of cells in order to is to develop a non-invasive diagnostic test for this disease.

DESIGN: Experimental case-control study.

MATERIALS AND METHODS: Uterine Aspirates from women with endometriosis (n=26) and healthy donors (n=11) were collected from women undergoing surgery for endometriosis or ovum pick-up for donation. Endometriotic patients were divided in ovarian endometriosis (n=9), pelvic endometriosis (n=3), Deep Infiltrating Endometriosis (n=9) and Adenomyosis (n=4). Samples were aspirates was washed with 1x PBS and placed into 4% formaldehyde for fixation and paraffin embedding. Paraaffin-embedded fixed samples were sectioned for hematoxylin and eosin (H&E) staining to determine the stage of the menstrual cycle and for immunofluorescence experiments. Dating of phases of the menstrual cycle was determined by two pathologists according to the criteria of Noyes.Subsequently Immunofluorescence (IF) staining was performed to co-localize LGR5 with E-Cadherin and LGR5 with Citokeratine in the epithelial and stromal compartment. Additionally LGR5+ cells were isolated through cell sorting and mRNA sequencing.

RESULTS: IF analysis on paraffin embedded tissue of mice confirmed that GFP+ cells co-localize with LGR5 and E-cadherin (ECAD, epithelial marker). LGR5+ cells in epithelium and stroma of human eutopic endometrium from patients and donors in order to identify a genetic signature of the disease and its subgroups.

CONCLUSIONS: An aberrant expression of epithelial cells was found in the eutopic endometrium of women affected with endometriosis compared to healthy women. These aberrant cells were isolated and their expression was compared to healthy endometrium and each different subtype of endometriosis revealing that each type have a characteristic genetic signature that may led us to potentially establish an new and less invasive diagnostic tool for the diagnosis of endometriosis.

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THE EFFECT OF ELAGOLIX ON THE ENDOMETRIUM: SAFETY RESULTS FROM TWO RANDOMIZED, PLACEBO-CONTROLLED STUDIES IN WOMEN WITH ENDOMETRIOSIS-ASSOCIATED PAIN. M. P. Diamond,1 J. Simon,2 B. A. Lessey,3 H. S. Taylor,4 J. P. Rowan,4 K. Chwalisz,4 B. Schwefel,4 J. W. Thomas,4 R. I. Jain,5 L. A. Williams,6 Augusta University, Augusta, GA;7 Women’s Health and Research Consultants and George Washington University, Washington, DC; 8Obstetrics and Gynecology, Reproductive Endocrinology and Infertility, Greenville Health System, Greenville, SC; 9Yale School of Medicine, New Haven, CT; 10AbbVie Inc., North Chicago, IL.

OBJECTIVE: To evaluate the effect of elagolix, an oral, non-peptide gonadotropin-releasing hormone antagonist, on endometrial morphology and thickness after treatment for 6 months in women with moderate/severe endometriosis-associated pain (EAP).

DESIGN: These were two similar, double-blind, randomized, placebo-controlled, multicenter, 6 months, phase 3 studies (Studies 1 [North America] and 2 [global]) evaluating two doses of elagolix (150mg or 200mg daily) compared to placebo.

MATERIALS AND METHODS: Study participants (Study 1, n=871; 2, n=815) were premenopausal, 18-49 year-old women with surgically diagnosed endometriosis. Endometrial biopsies were performed at baseline and month 6 in Study 1, and not in Study 2. Endometrial thickness was measured via trans-vaginal ultrasound at baseline (day 2-8 of menstrual cycle) and at month 6 in both studies.

RESULTS: Based on the endometrial biopsies of 867 participants at baseline and 644 at treatment month 6 in Study 1, there was a dose-dependent reduction in proliferative and secretory patterns, an increase in quiescent/minimally stimulated endometrial patterns, and no findings of endometrial hyperplasia after 6 months of treatment with elagolix (Ta-Ble). At baseline in Study 1, the mean endometrial thickness was 6.8 mm for placebo and 6.5 mm in each elagolix group; the mean (SD) change from baseline to month 6 was 0.6 (3.4) mm at 150 mg QD and -1.4 (3.2) mm at 200 mg BID, which was statistically significant at 200 mg BID (p<0.001) compared to placebo (mean [SD] change from baseline to month 6=1.0 [3.3] mm). At baseline in Study 2, the mean endometrial thickness was 6.3 mm for placebo and 6.5 mm for elagolix 150 mg QD and 6.4 mm for elagolix 200 mg BID. The mean (SD) change from baseline to month 6 was 0.4 (3.7) mm at 150 mg QD and -0.8 (3.5) mm at 200 mg BID, which was statistically significant at 200 mg BID (p<0.001) compared to placebo (mean [SD] change from baseline to month 6=1.0 [3.3] mm). There were no adverse endometrial findings in these studies.

CONCLUSIONS: In women with EAP, elagolix treatment suppressed endometrial proliferation in a dose-dependent manner after 6 months of treatment with no evidence of endometrial hyperplasia, consistent with its mechanism of action.
EMBRYO-ENDOMETRIAL DIALOGUE IS ALTERED IN ENDOMETRIOSIS PATIENTS THROUGH MICRORNA REGULATION. L. N. Henry, J. C. Parks, B. R. McCallie, W. B. Schoolcraft, M. Katz-Jaffe. Colorado Center for Reproductive Medicine, Lone Tree, CO.

OBJECTIVE: MicroRNAs (miRNAs) are pivotal post-transcriptional regulators playing an important role in morphological and biochemical modifications for endometrial receptivity, the establishment and maintenance of early pregnancy, and disease pathologies such as endometriosis. The aim of this study was to investigate the impact of endometriosis on embryo-endometrial miRNA dialogue during the window of implantation.

DESIGN: Research study.

MATERIALS AND METHODS: Surplus, cryopreserved, good quality blastocysts were donated from endometriosis patients (n=12) and oocyte donor cycles (n=12) with IRB consent. Individual blastocysts were warmed for coculture on a monolayer of endometrial epithelial cells to simulate an in vivo like environment from endometrial biopsies of endometriosis patients (n=12) and normal controls (n=12). Exosomes were isolated from coculture supernatant for microRNA expression using qPCR. Blastocyst and endometrial cell transcription was assessed for target gene validation using qPCR. Statistical analysis was performed with REST® statistical software (Qiagen).

RESULTS: Isolated exosomes from supernatant collected after co-culture of endometrial epithelial cells with blastocysts from endometriosis patients revealed an altered miRNAome compared to controls. Specifically, 6 miRNAs showed significant decreased expression (P<0.05), including miR-106a, a miRNA suspected to contribute to endometrial-embryo cross talk. MiRTarBase target gene analysis of miR-106a identified 29 strong evidence based target genes, including CDKN1A, E2F1 and RUNX1. Validation analysis confirmed increased expression of E2F1 and RUNX1 in endometriosis epithelial cells compared to controls (P<0.05). CDKN1A is controlled by tumor protein 53 and mediates cell cycle arrest in response to stress. Target gene validation analysis confirmed increased expression of E2F1 and RUNX1 in endometriosis epithelial cells compared to controls (P<0.05). E2F1 is a transcription factor that plays a crucial role in the control of the cell cycle and can mediate apoptosis. RUNX1 is also a transcription factor when over expressed increases apoptosis.

CONCLUSIONS: This study has shown compromised miRNA embryo-endometrial dialogue in endometriosis patients. Altered miRNAs impacted target genes that increased apoptosis and cell cycle arrest. Embryo implantation is an intricate physiological process with changes to this delicate embryo-endometrial dialogue significantly impacting the potential for success.

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PERIOPERATIVE TREATMENT WITH BETA-BLOCKER AND ANDROGROPHOLIDE ABROGATES SURGERY-INDUCED ACCELERATION OF ENDOMETRIOSIS DEVELOPMENT IN MOUSE. X. Liu, Q. Long, S. Guo. **Gynecology, Shanghai OB/GYN Hospital, Fudan University, Shanghai, China; aResearch Institute, Shanghai OB/GYN Hospital, Fudan University, Shanghai, China.**

OBJECTIVE: Women tend to receive substantially more surgeries than men due mainly to gynecological and cosmetic surgeries. Despite its cosmetic, therapeutic or even life-saving benefits, surgery is reported to increase the cancer risk and promotes cancer metastasis. We have recently shown that surgical stress activates the adrenergic signaling pathway, induces angiogenesis and accelerates the growth of pre-existing endometriotic lesions in mouse. We also have shown that such a facilitory effect of surgery can be completely abrogated by β-blockade. Our hospital-based case-control study also indicates that past open abdominal surgery increases the risk of developing endometriosis by over 3 folds. This study was undertaken to investigate whether perioperative administration of β-blocker and andrographolide (Andro), an NF-κB inhibitor, can abrogate such a facilitory effect.

DESIGN: A prospective and randomized mouse experimentation.

MATERIALS AND METHODS: Fifty-nine female adult Balb/C mice were used for this study, 20 of them serving as donors of endometrial tissues. Three days after the induction of endometriosis by intraperitoneal injection of endometrial fragments after a baseline evaluation of hotplate latency, mice were randomly divided into 4 groups of roughly equal sizes, one served as control receiving saline only, and the Andro group that was administrated with Andro, the Prop group that received Propranolol, a non-specific β-blocker, and the Andro+Prop group that received both Prop and Andro treatment. One hour after the drug administration, a simulated open abdominal surgery was performed. One day after the surgery, all mice received the second treatment. Two weeks after the surgery, all mice were sacrificed, their lesion size and hotplate latency evaluated and endometriotic tissue samples harvested for immunohistochemistry analysis of β2-adrenergic receptor (ADRB2), phosphorylated cAMP responsive element-binding protein (p-CREB), vascular endothelial growth factor (VEGF), CD31-positive microvessels, and proliferating cell nuclear antigen (PCNA).

RESULTS: Perioperative administration of β-blocker completely abrogated the facilitory effect of surgery on lesion growth and the generalized hyperalgesia. Andro showed some inhibitory effect, but the results did not reach statistical significance. Both Prop and Andro significantly reduced the expression of ADRB2, p-CREB, VEGF, and PCNA and the microvessel density in endometriotic lesions.

CONCLUSIONS: Our data indicate that perioperative administration of β-blocker, and perhaps Andro as well, can abrogate the surgery-induced acceleration of endometriosis development in mouse. These findings warrant clinical studies of β-blockade in patients undergoing various surgery in order to forestall the development of endometriosis and perhaps also to reduce the recurrence risk, in endometriosis.

Supported by: This study was supported by grants 81270676, 81471434, 81530040, 81070470 and 81370695 from the National Natural Science Foundation of China, and grant 2013ZYJB0019 from Shanghai Municipal Commission of Health and Family Planning.

FIBROIDS

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RESULTS OF THE ASTEROID (ASSESS SAFETY AND EFFICACY OF VILAPRISAN IN PATIENTS WITH UTERINE FIBROIDS) 1 STUDY: A PHASE 2, PLACEBO-CONTROLLED DOSE FINDING STUDY. L. Bradley, X. Ren, E. Grootrup-Wolfers, K. Petersdorf, C. Seitz. *Cleveland Clinic, Cleveland, OH; 1Bayer HealthCare, Beijing, China; 2Bayer Pharma AG, Berlin, Germany.

OBJECTIVE: Selective progesterone receptor modulators (SPRMs) in women with uterine fibroids (UFs) reduce heavy menstrual bleeding
(HMB) and tumor size. We report the results of ASTEROID1, examining the efficacy and safety of the novel SPRM, vilaprisan, in women with UF.

**DESIGN:** In this multicenter, randomized, double-blind, placebo-controlled, parallel-group study, women were randomized to oral placebo or vilaprisan 0.5 mg, 1 mg, 2 mg, or 4 mg, once daily. Treatment began during the first week of the menstrual cycle and continued for 12 weeks, with a 24 week follow-up. The primary efficacy variable was amenorrhea.

**MATERIALS AND METHODS:** HMB was assessed using a daily bleeding diary, alkaline hematin method (except in Japan), and menstrual pain diary. UF was assessed using transvaginal/abdominal ultrasound, and pelvic magnetic resonance imaging. Fibroid related symptoms and health-related quality of life (HRQoL) were assessed. Safety parameters included adverse events (AEs), laboratory evaluations, and endometrial biopsies to assess progesterone receptor modulator-associated endometrial changes (PAECs). Statistical analyses were performed using Statistical Analysis Software (SAS Institute Inc, Cary, NC, USA). All variables were analyzed consistent with their type using descriptive statistics methods.

**RESULTS:** 309 women were randomized equally to the 5 study arms; 286 women completed treatment. At doses ≥1 mg, controlled bleeding (<80 ml in all subsequent 28-day intervals) was achieved within 3 days in the majority of patients; 97-100% of patients achieved controlled bleeding by the end of the treatment course; amenorrhea (<2 ml/28 days) was achieved in 87%-92% of patients by the end of the treatment course. Dose-dependent reductions in fibroid volume were seen with vilaprisan, up to approximately 40% at the highest dose. Fibroid related symptoms and HRQoL scores improved in all groups. The number of patients with treatment-emergent AEs was similar between the active and placebo groups, with no dose-dependent pattern. Laboratory parameters did not indicate any safety signal. No treatment-emergent critical endometrial findings were found in biopsies. PAECs were observed in 40% of patients at the end of treatment and their frequency returned to baseline levels during follow up.

**CONCLUSIONS:** In ASTEROID1, vilaprisan 1-4 mg effectively stops HMB, shrinks UF, and improves quality of life. Vilaprisan was well tolerated. Expected PAECs were observed and were reversible after treatment. Further long-term studies of efficacy and safety are warranted.

Supported by: This study was funded by Bayer Pharma AG.

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**DESIGN:** We recently demonstrated that early life exposure to environmental estrogens can permanently alter adult myometrium; yet, to-date there is no such data available regarding progesterone-regulated genes. In this study, we investigate the expression of progesterone-regulated genes (PRGs) in human myometrial cells from normal uterus (MyoN) versus fibroid uteri (MyoF).

**OBJECTIVE:** To examine the expression of PRGs in normal and fibroid myometrial cells.

**MATERIALS AND METHODS:** Human primary myometrial cells were collected from menopausal patients with structurally normal uteri (no fibroids or other myometrial pathologies). Samples were also collected and used from a comparative group with fibroids (P(MyoF)). Isolated tissues were excised at least 2 cm from the closest fibroid lesion(s). Progesterone receptor (PR) expression was assessed using quantitative PCR.

Expression levels of 12 PRGs using RT q-PCR in MyoN and MyoF primary cells treated with different concentrations of progesterone were also assayed.

**RESULTS:** Semi-quantitative PCR analysis revealed higher expression levels of PR in MyoF as compared to MyoN primary cells. Furthermore, we compared the expression patterns of 12 PRGs (specifically selected due to their importance in UF pathogenesis) in MyoN and MyoF primary cells in response to progesterone hormone treatment. We demonstrated that three PRGs including FOXO1A, CNP56 and MT1E exhibited significant progesterone-hyper-responsiveness in human MyoF primary cells as compared to MyoN primary cells, in a dose-dependent manner (P<0.05). Importantly, these genes play crucial roles in cell proliferation, apoptosis, cell cycle, tissue remodeling and tumorigenesis in the development of UF.

**CONCLUSIONS:** These data substantiate the pivotal role progesterone-related pathogenesis plays in the development of UF. Importantly, these findings support the notion that myometrium from uteri fated to develop UF has been reprogrammed to a pro-UFs phenotype, possibly due to adverse events related to early life environmental exposure.

Supported by: Augusta University startup package, the National Institute of Health grant HD04622811.
OBJECTIVE: To assess the usefulness of 3-month therapy with UPA prior to laparoscopic myomectomy (LM) of large uterine myomas.

MATERIALS AND METHODS: The study included premenopausal women who underwent LM because of myomas with the following characteristics: main myoma FIGO type 3, 4 or 5 with diameter ≥ 10 cm; presence of ≤ 3 myomas; main diameters of the other myomas (FIGO type 3, 4, 5 or 6) ≤ 5 cm and ≤ 3 cm. Patients underwent either direct surgery (group S) or received 3-month preoperative therapy with UPA (5 mg/day orally, Esmya; Gedeon Richter; group UPA). Patients who underwent surgery prior to UPA approval and those who refused preoperative treatment with UPA were included in group S. The pictorial blood-loss assessment chart (PBAC) was used to estimate uterine bleeding.

RESULTS: 34 women were included in group UPA and 43 patients in group S. The two groups were similar in demographic characteristics, pretreatment menstrual blood loss and characteristics of the myomas. Prior to treatment with UPA, the two study groups had similar main diameter of the largest myoma, volume of the largest myoma and total myoma volume. In the UPA group, all patients completed the 3-month hormonal treatment. At the end of the 3-month treatment, 70.6% of the patients were amenorrheic; 20.6% of the patients had controlled uterine bleeding (PBAC 28-days score < 75) and 12.5% of the patients had PBAC 28-days score < 100. The 3-month UPA treatment caused a mean (± SD) 31.8% (± 10.9%) vs. 95% C.I. 28.1%-35.4% decrease in the volume of the largest myoma (p = 0.04) as well as a 15.5% decrease in the major diameter of the largest myoma, a 31.8% (± 10.7%) vs. 95% C.I. 28.2%-35.4% decrease in the total myoma volume. Hemoglobin levels significantly increased after UPA treatment (p<0.001). Because of the preoperative treatment with UPA, at surgery, patients included in group UPA had lower diameter of the largest myoma (p<0.001), lower volume of the largest myoma (p<0.020), lower total myoma volume (p = 0.015) and higher hemoglobin levels (p<0.001) than patients included in group S. No patient required conversion to laparotomy. The operative time was shorter in group UPA than in group S (p<0.001); the suturing time was similar in the two study groups (p=0.076). Both the intraoperative blood loss (p=0.012) and the hemoglobin drop (p=0.034) were lower in group UPA than in group S. Six patients in group S and no patient in group UPA required postoperative blood transfusion (p=0.031). The incidence of complications was similar in the two study groups (p=0.726).

CONCLUSIONS: This study shows that a 3-month preoperative treatment with UPA prior to laparoscopic excision of large uterine myomas decreases the intraoperative blood loss, the hemoglobin drop, the need of postoperative blood transfusion and the length of surgery.
RESULTS: Gross inspection of the transplanted areas revealed that the 3D cultures and tissue transplants measured 1.5-2 mm in size. Each appeared as distinct, palpable masses that were adherent to the under-surface of the mouse skin and closely associated with a dense network of blood vessels. No obvious gross signs of necrosis were present. Histologically, the transplants 6-8 weeks post transplantation appeared viable as demonstrated by hematoxylin and eosin staining. Nuclei were normal in size, absent of karyopyknosis. Tissue xenografts demonstrated preservation of tissue tumor architecture. ECM production was observed for each subcutaneous intervention analyzed. 3D cultures and tissue transplants stained positively for fibronectin and smooth muscle cell actin proteins.

CONCLUSIONS: Transplanted 3D cultures, human leiomyoma cells and tissue remain healthy at least to 8 weeks post transplantation, and as such are a renewable source of materials for the study of human leiomyogenesis in a mouse xenograft model.

Supported by: Uniformed Services University of the Health Sciences, Pilot Study R085298815.

HEALTH DISPARITIES

O-241 Wednesday, October 19, 2016 11:15 AM

COMPARISON OF GENETIC ETHNICITY BETWEEN AMERICAN AND EUROPEAN FERTILITY PATIENTS: IMPLICATIONS FOR CLINICAL PRACTICE. N. Kumar,1 S. Yarmall,2 R. Shraga,3 S. Ghadir,4 J. Grifo: Recombine, New York, NY; 2Southern California Reproductive Center, Beverly Hills, CA; 3NYU Langone Medical Center, New York, NY.

OBJECTIVE: The recent recognition of increased genetic admixture and advances in technology advances have caused a shift to broader acceptance of pan-ethnic expanded carrier screening (ECS) panels. However, ECS has not been widely accepted across Europe. The resistance is partially due to a belief that the US is genetically diverse from years of admixture while the European population is genetically homogeneous, making pan-ethnic screening unnecessary. We sought to determine if this difference in admixture was present.

DESIGN: Retrospective.

MATERIALS AND METHODS: Genomic data from an ECS panel was analyzed for 7544 participants, 6297 from US clinics and 1247 from European clinics. For all participants, genetic ancestral origin was predicted by a statistical model based on 672 SNPs validated using samples from the 1000 Genomes Project, and admixture proportions were calculated for 6 ancestral populations (European, Oceania Native, Native American, East Asian, Sub-Saharan African, and South Asian). A comparison of the resulting predicted admixture proportions was made between patients in Europe against patients in the US. Consent to use de-identified genomic data was obtained for all participants.

RESULTS: For comparison, the European and American patients were further subdivided into four groups, based upon which ethnicity they self-reported on test requisition forms: European, Mediterranean, Latin American, or African. Across all four comparison groups, our results showed similar average admixture proportions. For example, European patients who self-identified as Mediterranean were genetically predicted to be an average of 86% European, and 5% Sub-Saharan African. American patients who self-identified as Mediterranean were genetically predicted to be an average of 81% European and also 5% Sub-Saharan African. European patients who self-identified as African were predicted to be an average of 78% African and 16% European, which was strikingly similar to the predictions for American patients who self-identified as African (78% African and 12% European). This similarity in admixture proportions was also seen between European and American patients who self-identified as European and Latin American.

CONCLUSIONS: These results demonstrate that on a genetic level, both European and American patients demonstrate equal degrees of admixture. The European patient population may not be as genetically homogeneous as previously believed. Pan-ethnic carrier screening panels could prove to be effective at identifying carriers in a European population, who would otherwise be missed.
The impact of race and ethnicity on assisted reproductive technology (ART) outcomes: A retrospective cohort study. E. L. McClennen, a K. S. Richter, b K. Moon, c I. Sasson, d L. A. Bishop, e Ob/Gyn, Lankenau Medical Center, Philadelphia, PA; f Research, Shady Grove Fertility Reproductive Science Center, Rockville, MD; g Shady Grove Fertility, Washington, DC; h Shady Grove Fertility of PA, Wayne, PA; i Shady Grove Fertility Reproductive Science Center, Rockville, MD.

OBJECTIVE: The aim of this study was to investigate the relationship between race and ART outcomes at a large fertility practice.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: All fresh autologous ART cycles performed from 2004 through 2014 were reviewed. Patient and cycle parameters among African American, Asian, and Latino populations were compared to the majority reference group of Caucasians by t-test or chi-square as appropriate. Clinical pregnancy, pregnancy loss, and live birth outcomes were compared using generalized estimating equations (GEE) analysis to account for multiple cycles per patient and adjust for age, BMI, and diagnoses.

Table 1. Group Characteristics (N=474)

<table>
<thead>
<tr>
<th></th>
<th>Caucasian (N=14,534)</th>
<th>African American (N=3,522)</th>
<th>Asian (N=6,272)</th>
<th>Latino (N=2,674)</th>
<th>p-value</th>
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</thead>
<tbody>
<tr>
<td>Number of Patients</td>
<td>14,534</td>
<td>3,522</td>
<td>6,272</td>
<td>2,674</td>
<td>1,006</td>
</tr>
<tr>
<td>Number of Cycles</td>
<td>25,917</td>
<td>5,795</td>
<td>6,272</td>
<td>2,674</td>
<td>1,659</td>
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<tr>
<td>Age (years)</td>
<td>35.4</td>
<td>36.3*</td>
<td>35.7*</td>
<td>35.8*</td>
<td></td>
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<tr>
<td>Body Mass Index (BMI)</td>
<td>25.1</td>
<td>28.1*</td>
<td>23.7*</td>
<td>25.4</td>
<td></td>
</tr>
<tr>
<td>Serum Estradiol at Trigger (pg/mL)</td>
<td>2156</td>
<td>2377*</td>
<td>2435*</td>
<td>2274*</td>
<td></td>
</tr>
<tr>
<td>Follicles &gt;14mm at Trigger</td>
<td>8.5</td>
<td>8.7</td>
<td>8.7</td>
<td>8.5</td>
<td></td>
</tr>
<tr>
<td>Oocytes Retrieved</td>
<td>13.6</td>
<td>13.6</td>
<td>12.6*</td>
<td>12.6*</td>
<td></td>
</tr>
<tr>
<td>Fertilization % (2pn/oocyte)</td>
<td>57.0%</td>
<td>52.2%*</td>
<td>55.9%</td>
<td>56.3%</td>
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<tr>
<td>Clinical Pregnancy per Transfer</td>
<td>49.1%</td>
<td>42.9%*</td>
<td>44.5%</td>
<td>50.7%</td>
<td></td>
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<tr>
<td>Live Birth per Transfer</td>
<td>40.3%</td>
<td>31.9%*</td>
<td>35.8%</td>
<td>40.4%</td>
<td></td>
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<tr>
<td>Clinical Pregnancy Loss per Clinical Pregnancy</td>
<td>18.0%</td>
<td>25.6%*</td>
<td>19.5%</td>
<td>20.4%</td>
<td></td>
</tr>
</tbody>
</table>

*Calculated by ANOVA  aCalculated by Fisher’s exact test  bCalculated by Chi-square test  c*p<0.05 referenced to White

CONCLUSIONS: Black women undergoing oocyte donation had a reduced likelihood of achieving pregnancy and a trend toward a reduced live birth rate. Asian and Hispanic women undergoing oocyte donation did not have reductions in clinical pregnancy rates or live birth rates compared to White women. This suggests that uterine factors may contribute to worse outcomes in Black women. Further studies are needed to better understand the pervasiveness of racial disparity in IVF outcomes.

References:

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Racial Disparities: In Vitro Fertilization (IVF) Outcomes in Donor Oocyte Recipients. X. Zhou, a D. McQueen, b A. Schufreider, a M. L. Uhler, c E. C. Feinberg. d The University of Chicago, Chicago, IL; e University of Illinois Chicago, Chicago, IL; f Reproductive Endocrinology and Infertility, Fertility Centers of Illinois, Warrenville, IL; g Fertility Centers of Illinois, Highland Park, IL.

OBJECTIVE: Several studies have shown that Black and Asian women undergoing fresh autologous IVF have decreased live birth rates (LBR) compared to White women. Oocyte donation cycles provide a unique opportunity to further pinpoint the etiology of disparity as the processes of oocyte retrieval and embryo transfer can be examined independently. Our objective was to evaluate the impact of race on LBR in recipients of donor oocytes.

DESIGN: Retrospective analysis.

MATERIALS AND METHODS: IRB approval was obtained. All donor oocyte recipients who underwent a fresh embryo transfer at Fertility Centers of Illinois from 2010-2012 were included. The first embryo transfer per subject occurring within this timeframe was included. Race was self-reported. Outcomes in each racial group were compared to White women. This suggests that uterine factors may contribute to worse outcomes in Black women. Further studies are needed to better understand the pervasiveness of racial disparity in IVF outcomes.

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The Impact of Race and Ethnicity on Assisted Reproductive Technology (ART) Outcomes: A Retrospective Cohort Study. E. L. McClennen, a K. S. Richter, b K. Moon, c I. Sasson, d L. A. Bishop, e Ob/Gyn, Lankenau Medical Center, Philadelphia, PA; f Research, Shady Grove Fertility Reproductive Science Center, Rockville, MD; g Shady Grove Fertility, Washington, DC; h Shady Grove Fertility of PA, Wayne, PA; i Shady Grove Fertility Reproductive Science Center, Rockville, MD.

OBJECTIVE: The aim of this study was to investigate the relationship between race and ART outcomes at a large fertility practice.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: All fresh autologous ART cycles performed from 2004 through 2014 were reviewed. Patient and cycle parameters among African American, Asian, and Latino populations were compared to the majority reference group of Caucasians by t-test or chi-square as appropriate. Clinical pregnancy, pregnancy loss, and live birth outcomes were compared using generalized estimating equations (GEE) analysis to account for multiple cycles per patient and adjust for age, BMI, and diagnoses.
RESULTS: A total of 39,643 cycles by 22,668 patients were available for analysis. Mean age for each minority group was higher than Caucasians. Mean BMI was higher for African Americans and lower for Asians. African Americans were more likely to be diagnosed with diminished ovarian reserve, tubal and uterine factors, and less likely to be diagnosed with endometriosis, male factor, or ovulatory dysfunction, and Asians were more likely to be diagnosed with diminished ovarian reserve (P<0.0001 for each). The number of embryos transferred and cryopreserved were similar among all four groups. The significantly lower pregnancy and birth rates per transfer for the African American and Asian groups persisted after adjusting for age, BMI and diagnoses in the GEE analyses, as did the higher pregnancy loss rate for African Americans (p<0.0001 for each).

CONCLUSIONS: This is the largest single practice study evaluating the association between race and ART outcomes. The significantly lower pregnancy and birth rates among African Americans and Asians, and the increased pregnancy loss rate among African Americans, when compared to Caucasians, could not be explained by differences in age, BMI, or infertility diagnoses that existed among these groups. Explanations for the poorer ART outcomes observed among these two groups require further study.

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GAPS IN KNOWLEDGE IN DIAGNOSIS AND MANAGEMENT OF POLYCYSTIC OVARY SYNDROME. S. Saini,1 M. Gibson-Helm,1 L. Cooney,1 H. Teede,2 A. Dokras.1 1Obstetrics and Gynecology, University of Pennsylvania, Philadelphia, PA; 2Monash Centre for Health Research and Implementation, Monash University, Melbourne, Australia.

OBJECTIVE: There is significant dissatisfaction amongst women with PCOS regarding their diagnosis and treatment experience. Australian and European data show inconsistent health professional approaches in diagnosis and treatment1,2. We conducted a survey aiming to identify the gaps in PCOS knowledge and treatment amongst reproductive endocrinologists (REI) and gynecologists (OBGYN) in North America.

DESIGN: Online survey conducted through ASRM and ACOG.

MATERIALS AND METHODS: The survey included questions regarding physician demographics, PCOS diagnostic criteria, key features associated with PCOS, and treatment and management practices. Pearson chi-square test was used to compare differences between groups.

RESULTS: Of the 630 surveys completed by physicians residing in North America, 70.1% were OBGYN physicians (n=442), 65.9% were females, and 83.1% were over the age of 35 years. The REI physicians were significantly younger, (37.4 vs 35.3 years in C vs SA, respectively, p<0.01). The majority of responders (30.0%) were REI physicians (67% versus 29.4%, p<0.01). Overall, 50% of physicians estimated the prevalence of PCOS to be between 1-5%. The commonest reason for a woman with PCOS to visit the REI physician was infertility (80.4%) and to visit the OBGYN was menstrual irregularity (80.4%). Only 69.4% of REI and 41.4% of OBGYN physicians used the Rotterdam criteria to establish the diagnosis of PCOS (p<0.0001), while 32.1% of OBGYN compared to 2.2% of REI reported that they did not know the criteria they used to establish the diagnosis (p<0.001). However, >86% of all physicians were aware that irregular menses, high androgens, hirsutism and acne were associated with PCOS. Over one-third of physicians associated ‘cysts on ovaries’ with PCOS (35% REI versus 68% OBGYN, p<0.01). The majority of responders (>85%) were aware of the comorbidities associated with PCOS, however fewer OBGYN physicians were aware of associated depression (49% versus 80%), anxiety disorders (23% versus 49%) and reduced quality of life (51% versus 75%) compared to REI physicians (p<0.001). Overall, less than 15% reported that women were seeing them for complaints of obesity, despite this being the number one health concern for women with PCOS. Oral contraceptive pills, lifestyle modifications and metformin were commonly recommended non-fertility treatments by all physicians however, few physicians prescribed anti-androgens or recommended laser therapy (<31% REI, <15% OBGYN, p<0.001).

CONCLUSIONS: Our survey, conducted in response to patient concerns, highlights several opportunities for both REI and OBGYN physician education in improving the diagnosis of PCOS and offering more comprehensive care by increasing knowledge of internationally accepted Rotterdam diagnostic criteria, associated psychosocial co-morbidities and weight-related concerns in women with PCOS.

References:

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PRELIMINARY RESULTS FOR ANEUPLOIDY SCREENING IN SOUTH ASIAN WOMEN COMPARED TO CAUCASIANS UNDERGOING PGs. F. Sharara,1,2,3 M. Goodwin,1,2 G. A. Abdo,1,2 1Virginia Center for Reproductive Medicine, Reston, VA; 2Ob/gyn, George Washington University, Washington, DC; 3Virginia Center for Reproductive Medicine, Reston, VA.

OBJECTIVE: Previous studies have shown lower pregnancy rates following blastocyst transfers in South Asian women compared to Caucasians despite a younger age in South Asians (Shahine 2009, Sharara 2012). No clear hypothesis has been able to explain this difference. We investigated whether such disparities existed when embryo euploidy was controlled for.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Outcomes of autologous IVF cycles performed at a private ART center between 1/2014 and 4/2016 were reviewed. All patients underwent day 5 trophoectoderm biopsy (Genesis Genetics, Detroit, MI), and a subset had fresh day 6 ET.

RESULTS: There were 85 cycles included in this analysis: 55 cycles in Caucasians (C) and 30 cycles in South Asians (SA). South Asians were significantly younger, (37.4 vs 35.3 years in C vs SA, respectively, P=0.003) and had higher AMH levels (2.3 vs 4.38 ng/ml in C vs SA, respectively, P=0.006) and lower gonadotropin use (3045 vs 2495 IU in C vs SA, respectively, P=0.041). There were no differences in the number of oocytes retrieved (10.6 vs 12.8 in C vs SA, respectively, P=0.15), MII oocytes retrieved (8.1 vs 9.6 in C vs SA, respectively, P=0.18), fertilization rates (91.4 vs 90.4 % in C vs SA, respectively, P=0.72), or peak progesterone (0.86 vs 0.90 ng/ml in C vs SA, respectively, P=0.53) or peak estradiol (1417 vs 1615 pg/ml in C vs SA, respectively, P=0.44) on the day of HCG administration. A larger proportion of embryos developed to the blastocyst stage and were biopsied in Caucasians compared to South Asians (52.3 vs 36.2 % in C vs SA, respectively, P=0.001), and a trend was noted toward a higher incidence of aneuploid embryos in Caucasians (54.1 vs 41.2 % in C vs SA, respectively, P=0.09). There was, however, no difference in the proportion of embryos that yielded no result (9.0 vs 12.1 % in C vs SA, respectively, P=NS). In 41 cycles with fresh day 6 ET (27 in C and 14 in SA), Caucasians tended to have more embryos transferred (1.37 vs 1.13 in C vs SA, respectively, P=0.083) and a higher clinical pregnancy rate than South Asians (69.2 vs 28.6 % in C vs SA, respectively, P=0.014). There were significant differences in top quality blastocysts (3-6 AA) between the 2 groups: 20/27 (74.1%) in Caucasians compared to 7/16 (43.75%) in SA (P=0.047).

CONCLUSIONS: As far as we know, this is the first study comparing outcomes between South Asian and Caucasian women undergoing PGs for aneuploidy screening followed by fresh day 6 ET. While significantly younger with higher AMH levels and requiring less gonadotropins, South Asian women produced fewer biopsied blastocysts, had a lower number of top quality embryos, resulting in a lower clinical pregnancy rate compared to Caucasians. In this study, both embryo euploidy and endometrial receptivity were accounted for, however embryo quality was the main difference in success rates. Larger studies are needed to confirm or refute our findings, and FET outcomes need to be evaluated. Our study is ongoing.

References:
**MATERNAL FAT INTAKE DURING PREGNANCY IN RELATION TO IGF2 AND H19 METHYLATION IN NEWBORNS.** A. J. Gaskins,7 H. Laue,5 K. Moley,5 A. Baccarelli,1,3 M. W. Gillman,3 J. E. Chavarro,3 1Department of Nutrition, Harvard T.H. Chan School of Public Health, Boston, MA; 2Department of Environmental Health, Harvard T.H. Chan School of Public Health, Boston, MA; 3OB/GYN, Washington University in St. Louis, St. Louis, MO; 4Environmental Health Sciences, Columbia Mailman School of Public Health, New York, NY; 5Department of Population Medicine, Harvard Medical School and Harvard Pilgrim Health Care Institute, Boston, MA.

OBJECTIVE: To determine the association between maternal fat intake during pregnancy and DNA methylation profiles in the offspring at the differentially methylated regions (DMRs) of the imprinted Insulin-like Growth Factor 2 (IGF2) and H19 genes, which are associated with early growth regulation.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: Within Project Viva, a prospective pre-birth cohort study in Massachusetts, we included a random sample of 96 pregnancies 40-42 weeks duration and free of major complications. We assessed maternal diet during pregnancy with validated food frequency questionnaires during the late first and second trimesters. We measured methylation patterns as %5-methyl cytosines at specific CpGs in the two DMRs, IGF2 and H19, by bisulfite pyrosequencing in DNA extracted from umbilical cord blood cells.

RESULTS: Our cohort was, on average, 32.8 years old, 86% white, 5% current smokers, and had a pre-pregnancy BMI of 24.0 kg/m². At the IGF2 and H19 DMR, the mean (standard deviation) methylation was 56.3% (3.9%) and 44.6% (1.9%), respectively. After adjusting for several maternal and newborn characteristics in linear mixed models, maternal fat intake during the first trimester was inversely associated with IGF2 methylation: a 10% increase in percent of calories from fat (at the expense of carbohydrate) was associated with -1.46% (95% CI -2.88, -0.04 lower methylation at the newborn’s IGF2 DMR. Maternal fat intake during the second trimester, however, was not associated with IGF methylation. Maternal fat intake during either the first or second trimester was not associated with H19 DMR methylation.

CONCLUSIONS: Higher intake of fat in early pregnancy was associated with lower offspring DNA methylation in cord blood. Maternal fat intake during early pregnancy may influence the offspring’s future health status.

Supported by: NIH grants 1U54CA155626, P30DK046200, and R37HD034568.

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INTENSIVE LIFESTYLE INTERVENTION INCLUDING EMOTIONALLY-FOCUSED COUPLES THERAPY LEADS TO MORE PREGNANCIES AND WEIGHT LOSS IN OBESE INFERTILE COUPLES. A. K. Moore, 1, 5 R. Rasmussen,1 J. Sandberg, 1, 3 Hitchcock, Lebanon, NH; 2University of Colorado, Aurora, CO.

OBJECTIVE: Obesity adversely affects both male and female fertility. Mood disorders and relationship stressors, common features of both obesity and infertility, may lead to lifestyle change very difficult in the midst of rigorous infertility treatments. We hypothesized that, by addressing the self-reinforcing challenges of obesity and psychosocial stress through intensive lifestyle intervention (LI), including emotionally-focused couples therapy (EFT), that infertile couples would lose more weight and be more likely to achieve pregnancy than with standard weight loss counseling.

DESIGN: Clinical Trial.

MATERIALS AND METHODS: Infertile couples in which the female partner was oligo-oophoristic and both partners were obese were enrolled in a 6-month EFT-LI program that consisted of a very low calorie diet and exercise program with weekly physician visits and group sessions and 2) bi-weekly emotionally-focused couples therapy sessions. EFT is an empiric humanistic psychodynamic therapy that addresses relationship attachment traumas to enhance pair bonding. A site-specific control group received standard weight loss counseling and low cost counseling at regular office visits with a nutritionist. All couples were encouraged to delay fertility treatment until 6 months of weight loss effort was complete. Fasters Exact test and Student t tests were used to analyze data.

RESULTS: 15 couples enrolled in the study, 11 in the treatment group, and 4 in the control group for a total of 30 participants. No baseline differences in groups were detected for age, duration of infertility or BMI. After 11 months of follow up, the EFT-LI group was more likely to achieve pregnancy (73% vs 0%, p = 0.03). Of 8 pregnancies conceived, 4 were spontaneous, 2 were with Letrozole and 2 with Letrozole/IUI. Intention-to-treat analysis demonstrated that the EFT-LI group lost significantly more weight than the control group (33.9 +/- 7.4 lb vs -2.0 +/- 3.8 lb, p < 0.01).

CONCLUSIONS: This is the first study to include both male and female overweight infertile partners together in a lifestyle intervention or to utilize EFT to enhance behavior change in an infertile population. The results show weight loss 2- to 4-fold higher than average published data in this population and demonstrate rarely seen improvements in pregnancy despite a relatively small pilot study. Psychometric, metabolic and andrology data will be reported.

Supported by: 1) Interdisciplinary grant from Brigham Young University School of Family Life, Provo, UT and 2) Meal replacements provided at reduced cost by Health Management Resources, Boston, MA.

O-249 Wednesday, October 19, 2016 11:45 AM

LOWER AMH IS ASSOCIATED WITH LOWER OOCYTE YIELD AND LIVE BIRTH RATE AMONG OBESE WOMEN: ANALYSIS OF 36,334 IVF CYCLES. W. Vittek, 1 S. Jin, 3 V. L. Baker, 2 A. K. Styer, 4 M. S. Christianison, 5 J. E. Stern, 6 A. J. Polotsky, 7 1University of Rochester Medical Center, Rochester, NY; 2Yale University, New Haven, CT; 3Division of REI, Department of Obstetrics and Gynecology and Health Policy, Stanford University, Stanford, CA; 4Massachusetts General Hospital/Harvard Medical School, Boston, MA; 5Gynecology and Obstetrics, Johns Hopkins University School of Medicine, Lutheville, MD; 6Obstetrics and Gynecology, Dartmouth-Hitchcock, Lebanon, NH; 7University of Colorado, Aurora, CO.

OBJECTIVE: Anti-mullerian hormone (AMH) is produced by small antral follicles and reflects ovarian reserve. Several studies have demonstrated that obesity is associated with lower serum AMH. It is unclear whether lower AMH in obese women is a sign of diminished ovarian reserve or is due to a separate physiologic mechanism. We sought to determine whether the association of AMH with fertility outcomes is affected by obesity.

DESIGN: Retrospective cohort of US women in SART CORS.

MATERIALS AND METHODS: Data from 17,541 obese women and 18,793 normal weight women undergoing IVF from 2012-2014 were analyzed. Obesity was defined as BMI ≥ 30 kg/m² and subjects were stratified as Class 1 obesity (BMI 30.0-34.9), Class 2 obesity (BMI 35.0-39.9) and Class 3 obesity (BMI ≥ 40). Baseline characteristics were compared using t-tests or Chi-square tests. Multivariable modeling was used to assess oocyte yield and odds of live birth. All models were adjusted for age, AMH and BMI.

RESULTS: In comparison to normal weight women, obese women were older (35.1 ± 4.8 vs. 35.3 ± 4.8, p = 0.001), more likely to be smokers (4.4% vs. 7.0%, p < 0.001) and more likely to be diagnosed with diminished ovarian reserve (21.7% vs. 25.5%, p < 0.001) or polycystic ovary syndrome (PCOS) (11.8% vs. 24.1%, p < 0.001). After excluding PCOS women, obese women had lower AMH levels (2.1 ± 2.0 vs. 1.8 ± 2.0, p < 0.001). Women with Class 3 obesity had lower AMH levels than women with Class 2 and Class 1 obesity (2.3 ± 2.6 vs. 2.6 ± 3.0 and 2.6 ± 3.0, p = 0.029). Obese women were more likely to undergo stimulation using an antagonist protocol (p < 0.001), receive higher FSH dosages (p < 0.001), undergo longer...
stimulation (p<0.001), experience a higher rate of cancellation (p<0.001) and have fewer oocytes retrieved (13.4 ± 8.1 vs. 12.8 ± 7.8, p<0.001). Obese women had a similar rate of transfer and number of embryos transferred, but had fewer embryos cryopreserved (2.7 ± 4.2 vs. 2.4 ± 3.7, p<0.001). After excluding PCOS women and adjusting for age and BMI, lower AMH was associated with a lower number of eggs retrieved (β=0.068, SE=0.003, p<0.001) and lower live birth rate (OR 0.96, 95% CI 0.92-0.997, p<0.035). CONCLUSIONS: Lower AMH in non-PCOS obese women was associated with lower oocyte yield and lower likelihood of live birth. Our data suggest that lower AMH among non-PCOS obese women is predictive of ovarian reserve and ART success.

Supported by: CREST (Clinical Research/Reproductive Scientist Training) Program Eunice Shriver National Institute of Child Health and Human Development R25HD075737.
metabolites derived from microbial sources (e.g., p-cresol sulfate, indolepro- pionate, and 3-indoxyl sulfate) were altered in the HFD group Plasma and placenta which confirms that changes in diet can lead to profound changes in the body’s microbiota and these changes may be transmitted to the fetal compartment.

CONCLUSIONS: Metabolomic profiling reveals that placental lipid abundance and utilization are altered in response to diet-induced obesity. The presence of increased sphingolipids may impact offspring health directly through passage to the fetal compartment as they have been shown to be involved in the development of metabolic syndrome or indirectly by impacting placental structure and function given their role in cell growth and de novo lipogenesis. Additionally, maternal serum profiles confirm that diet-induced obesity alters microbiome function and the alterations in metabolites derived from microbial sources are present in the placenta and therefore may be sensed in the fetal environment and impact offspring phenotype. Given the critical role of the placenta in determining the fetal nutrient environment, these findings could provide mechanistic insight into the disrupted offspring growth and metabolism associated with maternal obesity.

Supported by: 2K12HD000849 (KO).

O-253 Wednesday, October 19, 2016 11:15 AM
ENDOMETRIAL GENE EXPRESSION OF WOMEN WITH RECUR- RENT PREGNANCY LOSSES AND INFERTILITY. L. Wu, D. Katukurundage, N. Sung, M. D. Salazar Garcia, A. M. Skariah, S. V. Dambaeva, A. Gilman-Sachs, K. Beamam, J. Kwak-Kim, Rosalind Franklin University of Medicine and Science, Vernon Hills, IL; Reproductive Medicine Center, Anhui Provincial Hospital Affiliated to Anhui Medical University, Hefei, Anhui, China; Clinical Immunology Laboratory Rosalind Franklin University, North Chicago, IL.

OBJECTIVE: While the relationship between the various gene expression and immune effectors in endometrium remains unknown, the expression of these genes could be utilized as a biomarker for of optimal uterine receptivity with a history of recurrent pregnancy losses (RPL) and infertility (INF).

DESIGN: A prospective controlled study.

MATERIALS AND METHODS: This study was carried out in women with ≥2 RPL (n=15) and INF (n=14). Endometrial biopsy is performed during mid luteal phase and endometrial gene expression was investigated with quantitative RT-PCR for T helper 17 (Th17) related cellular factors, such as IL-6, TGF-β, IL-21, IL-17, IL-23, RORγT, and IFN regulatory factor 4 (IRF-4). Treg cells related factors, including Foxp3, and CTLA-4, and angiogenesis related factor such as CSF-R, GM-CSF and NF-κB. Peripheral blood Th1/Th2 cell ratios, NK cell levels and cytotoxicities were also investigated by flow cytometric analysis.

RESULTS: Patients with RPL had a 2 or more fold higher gene expressions for Th17 cells related factors such as IL-17, IL-23, RORγT, TGF-β and IRF-4 as compared with those of INF. These factors are positively correlated with each other (P<0.001 respectively). Meanwhile, patients with RPL also have 3 fold higher expression of Treg cell related factor such as Foxp3 but not CTLA-4. These two genes have a significant positive correlation (r=0.654, P<0.001). The ratio of RORγT/Foxp3 gene expression in RPL group was 9.7 times higher than that of INF group. The gene expression of CSF-R was 9 fold higher but GM-CSF expression was not different as compared with INF group. Signal pathway gene NF-κB had a 6 fold higher gene expression than INF group, and NF-κB gene expression have a positive correlation with Th17 related factors such as IL-17, IL-23, IL-6, IRF-4, TGF-β (P<0.001, respectively). However, these gene expressions were not correlated with Foxp3 and CTLA-4 gene expressions. NK cell level and cytotoxicity have positive correlations with Th17 cells related factors, such as IL-17, IL-23, IL-6, IRF-4, and TGF-β (P<0.001, respectively), but not with Foxp3 expression. Th1/ Th2 ratio has a positive correlation with Th17 related factors including IL-17, RORγT but not with Treg related factors such as Foxp3 and CTLA-4.

CONCLUSIONS: Women with RPL have up-regulated Th17 related gene expressions in endometrium and increased ratios of RORγT/Foxp3 gene expression as compared with those of women with INF. In women with RPL, both inflammatory genes and anti-inflammatory genes are up-regulated as compared to INF group, which may favor for implantation, but not be beneficial to maintain pregnancy.

Supported by: Clinical Immunology Laboratory at Rosalind Franklin University of Medicine and Science, North Chicago, IL.

O-254 Wednesday, October 19, 2016 11:30 AM
KISSEPTEIN AS NEW SERUM BIOMARKER TO DISCRIMINATE MISCARRIAGE FROM VIABLE INTRAUTERINE PREGNANCY. C. S. Sullivan-Pyke, D. J. Haisenleder, M. D. Sammel, S. Senapati, L. O. Nicolais, E. Eisenberg, K. Barnhart; OB-GYN, University of Pennsylvania, Philadelphia, PA; Center for Research in Reproduction, University of Virginia, Charlottesville, VA; Biostatistics and Epidemiology, University of Pennsylvania, Philadelphia, PA; Reproductive Medicine Network, NICHD, Bethesda, MD.

OBJECTIVE: To validate the ability of serum kisspeptin-54 to discriminate between first trimester viable pregnancies and miscarriage.

DESIGN: Case-control.

MATERIALS AND METHODS: Serum was collected from women between 8-12 week gestation with a viable intrauterine pregnancy (IUP, n=20), miscarriage (SAB, n=20), or from women who were not pregnant (NP, n=19). Conceptions were without medical assistance. IUP viability was determined by evidence of fetal cardiac activity beyond 20 weeks. SAB was determined by ultrasound evidence of anembryonic gestation or fetal demise. Kisspeptin-54 was measured in serum using a commercial ELISA (Peninsula Lab International, Inc.; San Carlos, CA). The assay was validated for non-extracted serum samples by spiking a commercial human serum pool (Sigma Chemical; St Louis, MO) with various concentrations of recombinant human Kisspeptin-54 (provided by the kit manufacturer), and demonstrating parallelism to the assay standard curve. Differences in serum biomarker levels by pregnancy outcome were assessed via Kruskal-Wallis or Wilcoxon rank-sum test. Kisspeptin levels were correlated with serum human chorionic gonadotropin (hCG) levels to assess applicability in the context of current standard of care. Data were log transformed for analysis and linear regression was used to estimate the association between serum kisspeptin and hCG in IUPs and SABs.

RESULTS: The limit of detection was 0.024 ng/ml; intra-assay and interassay coefficients of variation were 5.1% and 8.6%, respectively. Kisspeptin assay coefficients of variation were 5.1 % and 8.6%, respectively. Kisspeptin levels were associated with serum human chorionic gonadotropin (hCG) levels to assess applicability in the context of current standard of care. Data were log transformed for analysis and linear regression was used to estimate the association between serum kisspeptin and hCG in IUPs and SABs.

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Supported by: 5R01HD076279, U10 HD027049 Cooperative Multicenter Reproductive Medicine Network.

Supported by: 5R01HD076279, U10 HD027049 Cooperative Multicenter Reproductive Medicine Network.
eSET with 1 embryo frozen | No. Live births | Unadjusted live birth rate (%) | DET with 0 embryos frozen | No. Live births | Unadjusted live birth rate (%) | Relative Risk (RR) (95% CI) | Adjusted relative risk (aRR) (95% CI)
---|---|---|---|---|---|---|---
<35 (n=769 transfers) | 337 | 43.8 | <35 (n=9007 transfers) | 3708 | 41.2 | 1.06 (0.97-1.17) | 0.95 (0.87-1.03)
35-37 (n=258) | 82 | 31.8 | 35-37 (n=4637) | 1593 | 34.3 | 0.92 (0.77-1.10) | 0.81 (0.68-0.96)

| eSET with 2 embryos frozen | No. Live births | Unadjusted live birth rate (%) | DET with 1 embryo frozen | No. Live births | Unadjusted live birth rate (%) | Relative Risk (RR) (95% CI) | Adjusted relative risk (aRR) (95% CI)
---|---|---|---|---|---|---|---
<35 (n=963) | 491 | 51.0 | <35 (n=2318) | 1175 | 50.7 | 1.00 (0.93-1.08) | 0.93 (0.86-1.00)
35-37 (n=302) | 122 | 40.4 | 35-37 (n=1168) | 544 | 46.6 | 0.87 (0.72-1.04) | 0.81 (0.67-0.97)

| eSET with 3 or more embryos frozen | No. Live births | Unadjusted live birth rate (%) | DET with 2 or more embryos frozen | No. Live births | Unadjusted live birth rate (%) | Relative Risk (RR) (95% CI) | Adjusted relative risk (aRR) (95% CI)
---|---|---|---|---|---|---|---
<35 (n=4468) | 2349 | 52.6 | <35 (n=9961) | 5664 | 56.7 | 0.92 (0.89-0.96) | 0.88 (0.84-0.91)
35-37 (n=987) | 449 | 45.5 | 35-37 (n=3774) | 1940 | 51.4 | 0.88 (0.81-0.96) | 0.83 (0.76-0.91)

**O-255** Wednesday, October 19, 2016 11:45 AM

**LIVE BIRTH AND MULTIPLE BIRTH RATES IN WOMEN UNDER AGE 38 BY ELECTIVE SINGLE EMBRYO TRANSFER (ESET) VERSUS DOUBLE EMBRYO TRANSFER (DET) IN UNITED STATES IVF CLINICS.** A. Mancuso, S. Boullet, E. H. Duran, E. M. Munch, D. M. Kissin, B. J. Van Voorhis, Obstetrics and Gynecology, University of Iowa Hospitals and Clinics, Iowa City, IA; bDivision of Reproductive Health, Centers for Disease Control and Prevention, Atlanta, GA.

**OBJECTIVE:** To compare live birth and multiple birth rates for cycles using eSET versus DET among women under age 38.

**DESIGN:** Retrospective cohort study.

**MATERIALS AND METHODS:** Data were collected on all autologous fresh IVF cycles performed in 2013 and reported to the National Assisted Reproductive Technology Surveillance System (NASS). Cycles using preimplantation genetic diagnosis or screening were excluded. Analysis was stratified by patient age (<35, 35-37, 38). Adjusted and unadjusted risk ratios for the association between eSET and DET groups. Analysis was further stratified by patient age (<35, 35-37, 38). Models were adjusted for day of transfer, infertility diagnosis, parity, prior ART cycles, number of oocytes retrieved, assisted hatching, and ICSI. Adjusted and unadjusted risk ratios for the association between eSET and outcomes were calculated using log-binomial models.

**RESULTS:** There were 6,200 eSET cycles and 21,286 DET cycles analyzed for patient age <35 and 1,547 eSET cycles and 9,579 DET cycles for patient age 35-37. There was a marked reduction in multiple births with eSET compared to DET (1.7% versus 39.4% for age <35 and 1.7% versus 32.0% for age 35-37). Adjusted live birth rates were slightly higher with DET for age 35-37 and for age <35 with four or more embryos available for transfer but were similar for age <35 with two or three embryos available for transfer (Table). CONCLUSIONS: Although adjusted live birth rates tended to favor DET for patients aged 35-37, for patients <35 this was only seen when 4 or more embryos were available to transfer. Multiple birth rates were much lower with eSET for both age groups, supporting the recommendation for younger patients to transfer one embryo at a time.

**O-256** Wednesday, October 19, 2016 12:00 PM

**RISK OF MATERNAL MORBIDITY IN IVF AND NON-IVF BIRTHS: A US STUDY IN FIVE STATES.** B. Luke, M. B. Brown, L. G. Spector. Obstetrics, Gynecology, and Reproductive Biology, Michigan State University, East Lansing, MI; bBiostatistics, University of Michigan, Ann Arbor, MI; cPediatrics, University of Minnesota, Minneapolis, MN.

**OBJECTIVE:** To evaluate the risk of maternal morbidity due to IVF, plurality, and maternal age.

**DESIGN:** Longitudinal case-control cohort study

**MATERIALS AND METHODS:** IVF cycles from the Society for Assisted Reproductive Technology Clinic Online Reporting System were linked to birth certificates of singletons and twins in CA (2004-09), and PA, MI, NY, TX (2004-10) (IVF births); a 10:1 sample of non-IVF births were controls. Maternal morbidity was identified from six items on the birth certificate (see below). Using logistic regression, the risk of each morbidity was modeled by maternal age, IVF versus non-IVF conception, and plurality (twin versus singleton), separately for each mode of delivery. Parity was included in the model for perineal laceration.

**RESULTS:** The study population included 53,053 IVF births (37,193 singletons and 15,860 twin births) and 576,880 non-IVF control births (567,856 singletons and 9,024 twin births). Regardless of mode of delivery, older maternal age was associated with an increased risk of unplanned hysterectomy and unplanned operations; twins were at increased risk of maternal morbidity at delivery; IVF versus non-IVF conception; and plurality (twin versus singleton), separately for each mode of delivery. Parity was included in the model for perineal laceration.

**CONCLUSIONS:** The risks of maternal morbidity at delivery are increased with IVF, twin pregnancy, and older maternal age. Supported by: NIH Grant R01 CA151973.
HUMAN CHORIONIC GONADOTROPIN RISE IN EARLY PREGNANCY DIFFERS BY VALUE AT PRESENTATION. K. Barnhart, W. Guo, K. Chung, P. Takacs, S. Senapati, M. D. Sammel, OB-GYN, University of Pennsylvania, Philadelphia, PA; Biostatistics and Epidemiology, University of Pennsylvania, Perelman School of Medicine, Philadelphia, PA; USC Keck School of Medicine, Los Angeles, CA; Eastern Virginia Medical School, Norfolk, VA.

OBJECTIVE: To reduce the number of women falsely classified as nonviable by assessing if factors at clinical presentation affect the expected minimal rise of serum human chorionic gonadotropin (hCG) used to predict a viable intrauterine pregnancy.

DESIGN: Cohort MATERIALS AND METHODS: Serum from 285 women with first-trimester symptoms of pain, with or without bleeding and a pregnancy of unknown location for whom a normal intrauterine pregnancy was ultimately confirmed, was collected at 3 U.S. sites. The rise in serial hCG values were modeled using a non-linear, mixed effects regression assuming a random subject shift in intercept.

RESULTS: The hCG rise in symptomatic women with ongoing IUP differs by patient risk factors, demographics and level at presentation. African American women had a faster hCG rise (p < 0.001) compared to non-African American women. Variation in hCG curves was associated with prior miscarriage (p = 0.014), bleeding (p < 0.001), and maternal age > 34 years (p < 0.001). The 2-day minimum (1st percentile) rise in hCG for an IUP was faster when presenting hCG values were low and slower when presenting hCG value was high. For initial hCG values of <1500, 1500-3000 and >3000 mIU/mL, the predicted 2-day minimal (1st percentile) rise was 49%, 40% and 33%, respectively.

CONCLUSIONS: The minimal change in hCG for an ongoing intrauterine pregnancy is influenced by initial IUP and patient factors. A single cut off value cannot be used to determine potential viability when evaluating a woman with a pregnancy of unknown location. Changes in hCG rise related to race should not affect clinical care. However, when initial hCG values are >1500, >3000, a more conservative cut off (slower rise) is needed to avoid interruption of a potential desired IUP.

Supported by: Grant ROI R01 HD076279 (KB, MS).

EMBRYO BIOLOGY 2

O-257 Wednesday, October 19, 2016 12:15 PM

LEVELS OF TROPHOECTODERM MITOCHONDRIAL DNA DO NOT PREDICT THE REPRODUCTIVE POTENTIAL OF HUMAN BLASTOCYSTS. N. R. Treff,a Y. Zhan,a X. Tao,a M. Olcha,a M. Han,b J. Rajchel,b L. Morrison,b S. Morin,c R. T. Scott,a RMANJ, Rutgers-RWJ, Basking Ridge, NJ;bTEC, Basking Ridge, NJ.

OBJECTIVE: Recent data suggest that mitochondria (mtDNA) content in the blastocyst may be predictive of its reproductive potential. However, prior validation compared outcomes between patients, which is not how the test will be applied. Given that the test will be used to distinguish between embryos from a single cohort of an individual patient, it is important that validation be done in a paired fashion where two embryos from within the same cohort are compared to see if their mtDNA content prognostics differences in implantation and delivery rates. To address this, the present study determines whether mtDNA content could predict which sibling embryo implanted after double embryo transfer (DET) and singleton delivery.

DESIGN: Blinded non-selection.

MATERIALS AND METHODS: DNA from transferred sibling euploid embryos (one male and one female) were evaluated using qPCR for 3 mtDNA targets and normalized to an Alu nuclear DNA target for relative quantitation (n = 374). Newborn gender was used to determine which of the two embryos was successful in the event of a singleton delivery (n = 69).

To determine if mtDNA content provided additional selection criteria, a paired t-test was used, and was powered to detect a 1.18 fold change difference. Additional parameters such as maternal age were evaluated with a simple linear model.

RESULTS: In analysis of all embryos in the study, there was no correlation between reproductive potential and mtDNA content (p = 0.53). Furthermore, when specifically evaluating DETs that led to a singleton delivery, there was no difference in mtDNA content between successful and unsuccessful sibling embryos (p = 0.40). As expected, the maternal age of the embryos displayed a significant correlation with mtDNA content (p = 0.007).

CONCLUSIONS: This well controlled study demonstrates that mtDNA quantitation provides no additional selection advantage between euploid sibling embryos in a DET model. Furthermore, our findings confirm that mtDNA content is associated with variables known to influence reproductive potential such as maternal age. Thus, prior studies which indicated the putative utility of evaluating mtDNA content in SETs between different patients were likely influenced by these associations. These findings illustrate the importance of adequate control over patient specific variables when assessing the predictive value of any diagnostic tool for reproductive competence.

O-258 Wednesday, October 19, 2016 12:30 PM

IS BLASTOCYST TRANSFER ASSOCIATED WITH A SIGNIFICANTLY LOWER INCIDENCE OF ECTOPIC PREGNANCY? A STRICTLY CONTROLLED RETROSPECTIVE COHORT STUDY BASED ON MORE THAN 30,000 FROZEN EMBRYO TRANSFER CYCLES. T. Du, Q. Chen, Q. Lyu, Y. Kuang, Department of Assisted Reproduction, Shanghai Ninth People’s Hospital, Shanghai, China.

OBJECTIVE: To analyze the incidence of ectopic pregnancy (EP) in blastocyst transfer cycles compared with cleaved embryo transfer cycles of in vitro fertilization (IVF)/intracytoplasmic sperm injection (ICSI).

DESIGN: Strictly controlled retrospective cohort study.

MATERIALS AND METHODS: Women undergoing 31,871 frozen-thawed embryo transfer (FET) cycles of IVF/ICSI in the period between March 2003 and May 2015 were enrolled, and those with uterine abnormalities, uterine disorders or disorder history, uterine or uterine cavity surgery and other conditions that were not suitable for matching were excluded. After that, those undergoing cleaved embryo transfer cycles and those undergoing blastocyst transfer cycles were strictly matched by age, number of cycles, number of prior full-term births, type of infertility, presence of Fallopian tubal diseases, previous Fallopian tubal surgery, previous EP, polycystic ovary syndrome, endometriosis and male factor infertility, type of endometrial preparation, number of embryos transferred and endometrial thickness on embryo transfer (ET) day, and then divided into two groups according to the stage of embryos transferred: cleaved embryo transfer group (n = 3,003 FETs) and blastocyst transfer group (n = 3,003 FETs). Statistical analyses were carried out by SPSS version 19.0. The normality of quantitative data was tested both by Kolmogorov-Smirnova test and Shapiro-Wilk test, and the Mann-Whitney U test, Chi-square test or Fisher’s exact test were applied to obtain group comparisons as appropriate. P < 0.05 was considered statistically significant.

RESULTS: Main baseline characteristics including age, body mass index, number of cycles, number of prior full-term births, profiles of type of infertility, indications for IVF/ICSI and preexisting conditions including previous Fallopian tubal surgery and previous EP, and FET characteristics including profile of type of endometrial preparation, number of embryos transferred and endometrial thickness on ET day had no statistically significant differences between cleaved embryo transfer group and blastocyst transfer group. As for pregnancy outcome, the clinical pregnancy rate (52.2% vs. 40.9%, p < 0.001), multiple pregnancy rate (25.2% vs. 19.8%, P = 0.001), live birth delivery rate (32.9% vs. 26.0%, p < 0.001) were statistically significant higher in blastocyst transfer group than in cleaved embryo transfer group. Meanwhile, blastocyst transfer group had a statistically significant lower EP rate than cleaved embryo transfer group (1.0% vs. 3.2%, p < 0.001, relative risk reduction: 68.8%, 95% confidence interval: 34.4%-103.1%).

CONCLUSIONS: Blastocyst transfer is associated with a significant lower incidence of EP when compared with cleaved embryo transfer in FET cycles of IVF/ICSI.

Supported by: National Natural Science Foundation of China.
from 10 litters), pups resulting from embryo transfers into the SO environment had significantly smaller than those transferred into a hormonally physiologic milieu. The objective of this study was to study the effect of the peri-implantation environment on vasculogenesis and fetal blood flow in the term placenta in a mouse model.

**DESIGN:** Laboratory research.

**MATERIALS AND METHODS:** Mice were superovulated, mated and 2-pronuclear embryos were collected and cultured to the blastocyst stage. Ten blastocysts were transferred into each pseudopregnant female created through either natural mating (NAT) to a vasectomized male or following superovulation (SO) and mating to a vasectomized male. Near term, on day E17.5, the pregnant mice were evaluated with a high frequency linear 40 MHZ ultrasound probe by a single, blinded, experienced sonographer. Assessment of umbilical artery Doppler flow was performed on each pup at the segment of cord insertion to the fetal abdomen and three recordings were made for each vessel. Peak systolic velocity (PSV) and end diastolic velocity (EDV) were measured and resistance index (RI) was calculated as PSV/EDV. On E18.5, the pregnant mice were sacrificed and the placental vasculature were isolated and fixed for histology. Placental endothelial cells were stained with an antibody to MECA32. Microvascular density in the placenta was measured and resistance index (RI) was calculated as PSV/EDV/PSV . On E18.5, the pregnant mice were sacrificed and the placental vasculature were isolated and fixed for histology. Placental endothelial cells were stained with an antibody to MECA32. Microvascular density in the placenta was measured and resistance index (RI) was calculated as PSV/EDV/PSV .

**RESULTS:** There was no difference in litter size between NAT (n=15 litters) and SO (n=13 litters) hosts. As previously demonstrated, pups from the SO recipients were significantly smaller than mice from the NAT recipients. Pups resulting from embryo transfers into the SO environment had significantly higher umbilical artery RI compared to pups resulting from transfer into NAT recipients [0.917 SO (n=16 from 6 litters) vs. 0.896 NAT (n=30 from 10 litters), p=0.02]. Immunohistochemistry demonstrated significantly lower microvascular density in the placentas resulting from the SO recipients compared to the NAT recipients [1.24x10^3 vessels/μm² SO (n=14) vs. 1.46x10^3 vessels/μm² NAT (n=15), p<0.05].

**CONCLUSIONS:** In a mouse model of ART, the peri-implantation hormonal milieu following superovulation has a significant effect on umbilical artery resistance and microvascular density in the placenta. Our data strongly suggest that the peri-implantation hormonal milieu following superovulation leads to altered vasculogenesis in the developing placenta, resulting in altered fetal growth and an increase in disorders of placentalation.

**References:**

**O-261 Wednesday, October 19, 2016 11:45 AM**

**ANEUPLOIDY RATES ARE NOT INCREASED IN PATIENTS WITH RECURRENT PREGNANCY LOSS.**

**OBJECTIVE:** To evaluate the expression and function of a mitochondrial progesterone receptor (PR-M) in oocytes, cleavage-stage embryos and blastocysts in humans and non-human primates.

**DESIGN:** Laboratory research study.

**MATERIALS AND METHODS:** Oocytes were collected from Rhesus monkeys after controlled ovarian hyperstimulation. MII oocytes were used directly or inseminated with thawed sperm from Rhesus monkeys via intracytoplasmic sperm injection and cultured to cleavage-stage. MII oocytes were examined for mitochondrial abnormalities by transmission electron microscopy and total RNA was isolated from normal blastocysts. PR-M transcript levels were determined in oocytes and embryos to be genetically abnormal by pre-implantation genetic screening (PGS). PR-M transcript levels were determined in oocytes and embryos with realtime RT-PCR using RPL32 housekeeping gene as a control. Immunofluorescent analysis was performed with antibodies directed to the N-terminus or hormone-binding domain (HBD) of PR along with mitochondrial staining. Embryos were cultured in media containing 10^-6 M P4 or vehicle followed by JC-1 staining to determine mitochondrial membrane potential (Ψm). Realtime RT-PCR and Ψm assays

**Table 1**

<table>
<thead>
<tr>
<th>Non-RPL</th>
<th>RPL</th>
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<tr>
<td># of Patients (n=119)</td>
<td>n= 64</td>
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<tr>
<td># of Cycles (n=161)</td>
<td>n= 75</td>
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<td>Age</td>
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<td>Day FSH</td>
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<td>AMH</td>
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<td>Oocytes retrieved</td>
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<td>Aneuploidy Rate</td>
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<td>Clinical Pregnancy Rate</td>
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**O-262 Wednesday, October 19, 2016 12:00 PM**

**THE EFFECT OF PROGESTERONE ON EARLY EMBRYO METABOLISM.**

**OBJECTIVE:** To determine the effect of progesterone on early embryo metabolism.

**DESIGN:** Retrospective cohort analysis.

**MATERIALS AND METHODS:** Couples with a female partner aged ≤35 years who underwent a fresh autologous IVF cycle with pre-implantation genetic screening (PGS) (trophectoderm bx) from January 2010 through March 2016 were included. Cohorts were segregated into RPL and Non-RPL. RPL was defined as a patient experiencing ≥2 failed clinical pregnancies. Main outcomes included number of embryos biopsied and aneuploidy rates. Student’s t-test was used for continuous variables, and the X² test was used for categorical variables. Significance was confirmed at p<0.05.

**RESULTS:** A total of 139 patients who underwent 161 cycles met the inclusion criteria. All demographic characteristics are shown in Table 1. Overall, all variables analyzed were similar between groups except the average day 3 FSH level (6.4±2.7 vs. 5.4±2.8, p<0.05). The average number of embryos biopsied per cycle (5.9±3.5 vs. 6.6±5.0), proportion of aneuploid embryos (32.6% vs. 33.6%, OR 1.01 [95% CI 0.8 - 1.4]) and clinical pregnancy rate was similar between non-RPL and RPL cohorts (57.6% vs. 58.3%, OR 0.97 [95% CI 0.5 - 1.9]).

**CONCLUSIONS:** This study suggests that RPL in couples with a female partner ≤35 yo is not influenced by embryo aneuploidy. This study’s results are reassuring; RPL patients ≤35 who seek treatment with PGS have similar chances of achieving a pregnancy as to non-RPL counterparts.
were completed using mouse cleavage and blastocyst embryos as a control.

RESULTS: Immunofluorescent staining with a HBD-directed antibody showed non-nuclear staining partially co-localizing with mitochondrial stained (No reaction was seen with the N-terminal antibody in Rhesus). No staining was seen with either antibody in the mouse. Realtime RT-PCR detected PR-M transcript in oocytes and embryos in both humans and rhesus monkeys but interestingly did not detect nuclear progesterone receptor transcripts. PR-M transcripts were expressed at the same level in oocytes and embryos when controlled for RPL3. PR-M transcript was not found in the mouse. Rhesus embryos treated with progesterone had a higher $\Psi_m$ compared to vehicle ($p = .005$). No change in $\Psi_m$ was seen with mouse embryos.

CONCLUSIONS: PR-M is expressed in human and non-human primate oocytes and embryos, whereas nuclear progesterone receptor (PR A&B) is not. Progesterone treatment yields significant increases in mitochondrial membrane potential suggestive of increased cellular respiration. Mouse embryos neither express PR-M nor show a mitochondrial response to progesterone. These findings provide a mechanism whereby progesterone may enhance mitochondrial activity to provide cellular energy necessary for early embryo development.

Supported by: Research funded by a grant from the Foundation for Embryonic Competence.

**O-263 Wednesday, October 19, 2016 12:15 PM**


OBJECTIVE: Both Seq and Mono culture media formulations are widely utilized. Seq media consists of two phases designed to mimic in vivo conditions while Mono media is a single formulation. Mono formulations require less manipulation and are less expensive. Both formulations have attained good outcomes, with no difference in blastulation, ploidy or delivery rates. To date there has been no comparison of delivery outcomes after euploid blastocyst transfer in regards to the culture media utilized.

DESIGN: Prospective.

MATERIALS AND METHODS: Patients with normal ovarian reserve were recruited and half of the patient’s zygotes were cultured in Seq media (Quinn’s Advantage Cleavage Medium, Sage then Blast Assist, Origo) and the other half in Mono media (Continuous Single Culture; Irvine Scientific). All embryos were cultured to the blastocyst stage and trophectoderm biopsies performed with CCS. Patients underwent either a single (SET) or double embryo transfer (DET) of the morphologically best euploid embryo(s). In the case of a DET, the morphologically best embryo from both culture groups was transferred. Delivery outcomes were then assessed, including birth weight and DNA fingerprinting of children was used to link each embryo to a definitive outcome. Outcomes were compared using Student’s t-tests in singleton deliveries and paired t-tests in twins. This study had an 80% power to detect a difference of 340.4g in birth weight.

RESULTS: 50 patients had a singleton delivery and 18 patients delivered twins. Of the 23 patients who delivered a singleton after monophasic culture the average birth weight was 3334.2 ± 392.4g. Of the 27 patients who delivered a singleton after sequential culture the average birth weight was 3439.0 ± 449.3g. There was no statistical difference between groups ($p=0.5226$). Of patients who delivered twins, there was no statistical difference in birth weight ($p=0.90$).

CONCLUSIONS: This is the first analysis of delivery outcomes after the transfer of euploid embryos cultured in sequential vs. monophasic media. This study demonstrates that there is no significant difference in birth weight after culture in the different media formulations and should provide reassurance, although further study is needed.

**Reference:**

**Supported by:** Irvine scientific provided Mono media.

**L-CARNITINE IMPROVES THE HUMAN BLASTOCYST DEVELOPMENT. T. Tanaka, M. Satoh, S. Hashimoto, Y. Nakao, Y. Morimoto. IVF Namba Clinic, the Centre for Reproductive Medicine and Infertility, Osaka, Japan; HORAC Grand Front Osaka Clinic, Osaka, Japan.**

OBJECTIVE: It has been shown that L-Carnitine (LC) improve the development of the blastocyst in mice and decrease the apoptosis in blastocyst. However, it remains unclear the effect of LC on the development of human embryos. In this study, we investigated the effect of LC on the development of human embryos.

DESIGN: Prospective clinical study.

MATERIALS AND METHODS: This study was carried out using 1,308 zygotes at pronuclear stage donated from 107 patients who were treated with controlled ovarian stimulation between April and July 2015, and then were randomized more than five fertilized ova, and informed consent. The zygotes obtained from each patient were randomly divided into two groups and cultured in SAGE 1-Step*O (Origo) with or without 1 mM LC from Day 1 to 6. All embryos were assessed the embryo quality on Day 3. In some cases, embryo transfer and/or vitrification were performed and the remaining embryos were continued the culture until Day 6. To evaluate the effect of LC, the rate of good quality embryo on Day 3, the blastulation on Day 5, good quality blastocyst on Day 5 and clinical outcome after embryo transfer were analyzed. The clinical outcome was assessed in the case of single embryo transfer of fresh and frozen embryos. Moreover, to investigate the age related effect of LC, we examined the effect of LC $< 40$ and $\geq 40$ years groups.

RESULTS: There was no difference in the rates of cleavage, good quality embryo on Day 3 and blastulation on Day 5 between embryos cultured with and without LC in all ages. However, the rate of good quality blastocyst of embryos cultured with LC was significantly higher than that of embryos without LC (14.2% (74/521) vs. 8.5% (42/492), $p<0.05$). In the $< 40$ years group, the rate of good quality blastocyst was also significantly higher in LC than control (15.1% (64/425) vs. 9.6% (38/395), $p<0.05$). There was no difference in the implantation rate between two groups (LC: 52.7% (36/69) vs. control: 32.5% (25/77)). Embryos cultured with LC developed to healthy babies ($n = 8$, April 27, 2016).

CONCLUSIONS: LC improved the development of human embryos to morphologically-good blastocyst especially in the $< 40$ years group. The safety of the LC-supplementation was confirmed. The data of the present study suggest that LC is effective in vitro culture of human embryos.

**ACCESS TO CARE**

P-1 Tuesday, October 18, 2016

**WIDENING ACCESS TO INFERTILITY CARE BY OFFERING AFFORDABLE IVF PROTOCOLS: THE MEXICAN EXPERIENCE.** A. Davila. Reproductive Medicine and Andrology, Instituto para el Estudio de la Concepcion Humana, Monterrey, Mexico.

OBJECTIVE: Despite considering procreation a human right, it is a harsh reality that access to assisted reproductive techniques (ART) constitutes a privilege among couples suffering infertility. Among the many barriers the cost and the availability of IVF clinics willing to provide affordable services are the major obstacles for the provision of treatments. In an effort to make ART more accessible our institute began offering 2 major variants for in vitro fertilization and here are the summary of outcomes.

**DESIGN:** Prospective and descriptive study.

**MATERIALS AND METHODS:** The two variants offered were In Vitro Maturation of oocytes (IVM) and clomiphene citrate stimulation for in vitro fertilization (CCS IVF), performed between January 2011 and August 2015. Patients included for either protocol had to have regular menstrual cycles, tubal factor or mild male factor or unexplained infertility. The choice for IVM or CCS-IVF depended on patient’s needs, whereas IVM was performed in patients with tubal factor or mild male factor. In the CCS-IVF, the doses were between 100 to a max of 150 mg/daily for 5 days. Cycles were considered canceled due to absent oocytes, no fertilization, and no embryo cleavage.

RESULTS: Sixty-tree cycles were included for IVM (group 1) and 56 cycles for the CCS IVF (group 2). The mean age was 31.9±3.2 for group 1 and 33.1±4.0 for group 2. In group 1, 18 cycles were canceled (33%) and in group 2, 23 cycles were canceled (41%). Fertilization rate was 77% and cleavage rate was 62%. Embryos were transferred on day 3 of development. The clinical pregnancy rate was 28.0% (12/41) and the ongoing/delivered rate was 22%. For group 2, 13 cycles were canceled.
DESIGNING EDUCATIONAL MATERIALS TO IMPROVE ATTITUDES ABOUT IN VITRO FERTILIZATION. D. M. Fankhauser,1 J. B. Corwin,1 C. M. Skabitz.2 President, Fertility Within Reach, Newton Highlands, MA; 1Health Communication, Emerson College, Boston, MA; 2Communication, Emerson College, Boston, MA.

OBJECTIVE: A study was designed to investigate knowledge and current attitudes about In Vitro Fertilization (IVF) in the US adult population and across demographic groups. Research results were used to develop educational materials designed to promote positive attitudes, reduce stigma, increase knowledge, and increase interpersonal communication about IVF. Ultimately, this project aimed to gain support for IVF and insurance benefits.

DESIGN: A combination of data from a web based survey, insights gained from expert interviews, and review of the published literature was used to inform a finalized communication strategy. The Theory of Reasoned Action (Ajzen & Fishbein, 1975), was used as a framework for the study design and for the development of education materials.

MATERIALS AND METHODS: The survey responses addressed research questions and hypotheses to measure variables of interest. Participants included: 608 adults (189 men, 419 women) aged 18-77 (Mean = 36.6, Standard Deviation = 15), from 43 states. Several instruments designed the survey to measure prevailing norms about IVF, knowledge about infertility, and attitudes about IVF. Demographics, and personal experiences with infertility/IVF. The survey included both open-ended and closed-ended questions, Likert scale items, and semantic differential scale items.

RESULTS: Data examined 5 groups of interest: all participants, gender, age (younger adults under age 34 and older adults age 34 and older), experience with infertility, and experience with IVF. All groups incorrectly reported the rate of infertility in U.S. (76% incorrect) and were unaware infertility is recognized as a disability (91.4% unaware). Results indicate high and accurate knowledge of infertility did not necessarily mean participants felt positively about IVF. Participants were asked to list reasons someone would feel favorable and unfavorable about IVF. Reported reasons were coded into 13 categories for unfavorable and 11 categories for favorable. The predominant reasons for feeling unfavorable included: high cost, IVF is unnatural, and IVF is expensive or unnecessary. The most commonly reported favorable reasons included: success rate, natural and family building. Additionally, expert interviewees recommended communication materials about IVF must avoid offensive language; address the emotional tolls of infertility patient’s, while carefully not perpetuating the stigma surrounding infertility.

CONCLUSIONS: Society could benefit from education materials to increase knowledge about infertility and bolster reasons for people to feel favorable about IVF. A video script, including a narrative and images, was developed and pre-tested with three target audience members. This research and resulting education material provides insight on how to improve access to services for those seeking treatment and improve quality of life for those experiencing infertility.

P-4 Tuesday, October 18, 2016

ABSTRACT WITHDRAWN

P-5 Tuesday, October 18, 2016

CONTRIBUTION OF THIRD PARTY REPRODUCTION TO THE BIRTH COHORT FOLLOWING ART IN THE USA. V. A. Kushner,1,2 D. H. Barad,1 S. Darmon,1 D. Albertini,1 N. Gleicher2 Center for Human Reproduction, New York, NY; 1Wake Forest School of Medicine, Winston-Salem, NC; 2Albert Einstein College of Medicine, Bronx, NY; 3University of Kansas Medical Center, Kansas City, KS; 4Rockefeller University, New York, NY.

OBJECTIVE: To examine the contribution of third party reproduction to the birth cohort in the USA following ART.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: To explore trends in third party reproduction use among different ethnic and racial groups, we reviewed ART data reported to the Society for Assisted Reproductive Technology (SART) on donor oocyte, sperm, embryo and gestational carrier cycles performed in the USA between 2004 and 2013. Routine ART cycles, which did not involve third parties, performed over the same time period served as reference group.

RESULTS: The data includes a total of 1,349,874 ART cycles which resulted in 421,526 live birth. Third party ART accounted for 16% of all cycles and 20.4% of all live birth (Table). The most common third party reproduction techniques were oocyte donation followed by sperm donation. Both routine and third party ART annual cycle volume and live birth rates gradually increased over the study period. Live birth rates were highest in cycles which utilized multiple third party modalities followed by oocyte donation.

CONCLUSIONS: Third party ART utilization and efficacy have increased over the past decade. Because third party ART modalities led to higher live birth rates than routine ART, children conceived with assistance of third parties make up more than 20% of the birth cohort following ART.

Supported by: Intramural funds from The Center for Human Reproduction and grants from The Foundation for Reproductive Medicine.
CONCLUSIONS: Utilization of third-party ART reflects similar racial/ethnic disparities previously observed in the use of in vitro fertilization (IVF).

Supported by: Intramural funds from The Center for Human Reproduction and grants from The Foundation for Reproductive Medicine.

P-6 Tuesday, October 18, 2016

PARTNERSHIP FOR FAMILIES PROGRAM: A NON-PROFIT MODEL FOR ACCESS TO IVF. T. Segal; S. Thakore; G. Collins; J. M. Goldfarb; Reproductive Endocrinology & Infertility, University Hospitals Case Medical Center, Beachwood, OH; Case Western Reserve University, Cleveland, OH; University Hospitals Fertility Center, Beachwood, OH; Reproductive Endocrinology and Infertility, Case Western Reserve University, Cleveland, OH.

OBJECTIVE: The cost of in vitro fertilization (IVF) is on average $12,000 in the United States. Unlike many diseases where the most effective and safe treatment is covered by insurance, patients with infertility must cover their own costs. As a consequence, this can result in cost saving procedures that can lead to multiple gestations or no pregnancies at all. Beyond infertility, IVF has many other indications such as fertility preservation in cancer patients and preventing transmission of genetic diseases to offspring. Through generous donations from the community, the Partnership for Families Program provides full grants to patients who could not otherwise afford IVF.

DESIGN: Partnership for Families is a 501(c)(3) non-profit organization that provides financial assistance to qualifying patients at University Hospitals Fertility Center.

MATERIALS AND METHODS: Initially Partnership for Families provided grants to patients who had paid for an IVF cycle, had not conceived and could not afford a second IVF cycle. With the program expanded to include patients who need fertility preservation and then patients needing pre-implantation genetic diagnosis (PGD) because they have had, or are at risk of having, babies with lethal genetic conditions. Most recently the program has been expanded to give grants for Veterans with VA insurance that does not cover IVF. Initially grants were awarded to those in the above categories with incomes less than $70,000. Over the years the income limit has been raised to $120,000.

RESULTS: Over a 9 year period, the Partnership for Families Program has provided 325 grants – 242 for infertile couples to have a second IVF cycle, 61 fertility-sparing procedures for cancer patients, 20 cycles with preimplantation genetic diagnosis, and 2 cycles for veterans. This has resulted in 134 ongoing or delivered pregnancies.

CONCLUSIONS: The Partnership for Families Program has changed lives. It can be started at any fertility location with the help and organization of a passionate community, especially those who have experienced infertility first hand and are willing to give back.

P-7 Tuesday, October 18, 2016

FACTORS AFFECTING CANCER PATIENTS’ DECISION TO PROCEED WITH FERTILITY PRESERVATION (FP) TREATMENTS AND THEIR RELATION TO DELAY IN CHEMOTHERAPY. M. A. Clapp, E. H. Illions, E. Buyuk. Albert Einstein College of Medicine/Montefiore M, Bronx, NY.

OBJECTIVE: Patients with a cancer diagnosis may face barriers to preserve their fertility, such as cost or the possibility that fertility treatments may delay chemotherapy. These barriers can affect their decision whether or not to proceed with FP. The primary objective of this study was to determine whether FP treatment in cancer patients delays the initiation of chemotherapy and/or surgery and to determine whether race or socioeconomic level are associated with patients’ decision to proceed with treatment.

DESIGN: Retrospective cohort study in an academic setting.

MATERIALS AND METHODS: Women evaluated for an outpatient FP consult for an oncologic diagnosis from 2012 to 2015 were included in the study. Demographics, clinical parameters including oncologic data, and treatment modalities (oocyte cryopreservation, embryo cryopreservation, and ovarian tissue cryopreservation) were collected. The primary outcome was the time (days) from the initial Reproductive Endocrinology and Infertility (REI) consult to the first day of chemotherapy. Descriptive statistics were computed. Bivariate analysis was performed using Student’s t, Pearson’s chi-squared, Fisher’s exact, and Wilcoxon rank sum tests as appropriate. P<0.05 was considered significant. Stata 14 was used for statistical analysis.

RESULTS: A total of 60 patients were included in the study with 33 participants in the no FP treatment group and 27 participants in the FP treatment group. Demographic and clinical parameters were similar between the two groups, except for health insurance status, a surrogate for socioeconomic level. Patients electing to undergo FP treatment more often had private than Medicaid insurance (77.8% vs. 22.2%) compared to patients who did not undergo FP treatment (51.5% vs. 48.5%)(p=0.04). Race was not statistically significantly different between the two groups. Of note, when race was further categorized as Caucasian and other, 77.8% of Caucasians compared to 40.8% of the other race category elected for FP treatment (p=0.07). The time from consultation to chemotherapy was 21.1 days in the no FP treatment group compared to 35.5 days in the FP treatment group (p=0.03). On average, the chemotherapy was delayed by 2 weeks in patients undergoing fertility treatments.

CONCLUSIONS: Patients with private health insurance may be more likely to proceed with FP treatment secondary to financial reasons. However, this is associated with a delay in their chemotherapy. Further studies are needed to determine whether this delay affects their cancer prognosis.

P-8 Tuesday, October 18, 2016

WHAT DOES A SINGLE SEMEN SAMPLE TELL YOU? IMPLICATIONS FOR THE DIAGNOSIS OF MALE FACTOR INFERTILITY. Y. Chiu; R. Edifor; F. Nassan; A. J. Gaskins; L. Miguez-Alarcon; P. Williams; C. Tanrikut; R. Hauser; J. E. Chavarro; Nutrition, Harvard T.H. Chan School of Public Health, Boston, MA; Global Health and Population, Harvard T.H. Chan School of Public Health, Boston, MA; Environmental Health, Harvard T.H. Chan School of Public Health, Boston, MA; Department of Nutrition, Harvard T.H. Chan School of Public Health, Boston, MA; Biostatistics and Epidemiology, Harvard T.H. Chan School of Public Health, Boston, MA; Urology, Massachusetts General Hospital, Boston, MA; Harvard Chan School of Public Health, Boston, MA; Department of Nutrition, Harvard School of Public Health, Boston, MA.

OBJECTIVE: In clinical practice, a second diagnostic semen sample is generally requested only when one or more parameters of the first sample are abnormal according to the World Health Organization (WHO) standards. It is unclear, however, to what extent this practice may result in underdiagnosis of male factor infertility.

DESIGN: Longitudinal study at a fertility clinic.

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MATERIALS AND METHODS: 197 men from couples presenting for infertility provided 596 semen samples (range: 2-9 samples/man) between 2005 and 2014. Ejaculate volume, sperm concentration, total sperm count, motility and morphology were clinically assessed according to WHO standards. To evaluate the accuracy of classification based on the 2010 WHO reference limits, we calculated positive (PPV), negative predictive value (NPV) and false negative rate (FNR) by comparing the agreement in classification based on the first sample only versus each man’s long-term average.

RESULTS: Men in this study provided 2 (47%), 3 (23%), 4+ (30%) semen samples collected, with median of 94 days apart for the consecutive samples. Using a single sample to classify men according to WHO semen quality standards resulted in low NPV for some semen parameters. Specifically, 44% of men classified as having a normal semen analysis on their first sample had at least one semen parameter below WHO reference limits when they were classified based on their long-term average. When individual parameters were separately examined, the FNR for the first semen sample ranged from 5% for sperm concentration to 48% for progressive motility. On the other hand, among men who had all semen parameters above the reference in their first two semen samples, the FNR was decreased considerably (range: 0% for sperm count and concentration to 8.6% for progressive motility). An average of two semen samples was needed to achieve high PPV (range: 86-100%) and NPV (range: 91-100%).

CONCLUSIONS: Nearly half of men classified as having a normal semen analysis in their first sample would be classified as having at least one semen parameter below the 2010 WHO reference limits if repeat samples were obtained, possibly contributing to the under-diagnosis of male factor infertility.

References:

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P-9 Tuesday, October 18, 2016
ABSTRACT WITHDRAWN

P-10 Tuesday, October 18, 2016

IMPROVED PATIENT CARE THROUGH LAWSUIT PROTECTION AND PREVENTION. G. Mangelson. American Society for Asset Protection, Las Vegas, NV.


DESIGN: This course teaches proven and effective strategies to prevent and protect against lawsuits.

MATERIALS AND METHODS: Sources of lawsuits physicians are exposed to and how to protect against them: failure/delay to diagnose, failure/delay to refer, negligence by staff/employees, premise liability, etc. How physicians can protect 100% of their professional and personal assets from lawsuits. How physicians should structure their practice. How physicians can protect their practice, property, and personal assets in the event of a judgment in excess of liability insurance or an exclusion in a policy. How to avoid the most common asset protection mistakes made by physicians and their advisors, such as putting assets into a spouse’s name. How physicians can avoid the serious problems that can result from operating as a sole proprietor. How physicians can minimize vicarious liability for the acts of other professionals and staff.

RESULTS: You will have the peace of mind necessary to focus on improved patient care.

CONCLUSIONS: You will learn lawsuit protection strategies most advisors are unaware of.

P-11 Tuesday, October 18, 2016

INFERTILITY AS A WOMEN’S HEALTH ISSUE. J. S. Place. Physiology and Health Science, Ball State University, Muncie, IN.

OBJECTIVE: Around 11% of women ages 15-44 have an impaired ability to get pregnant or carry a baby to term. Despite infertility being a significant concern, we hypothesized that there is limited discussion on infertility in the peer-reviewed women’s health literature.

DESIGN: We conducted a systematic review to assess the quantity and content of articles on infertility from peer-reviewed, scientific women’s health journals.

MATERIALS AND METHODS: Two undergraduate students searched article archives between years 2000 and 2015 of Journal of Women’s Health, Healthcare for Women International, Women and Health, and Women’s Health Issues. They evaluated all article titles published in each volume.
for each year to determine if infertility was addressed. The terms infertility, assisted reproduction technology, in vitro fertilization, fertility preservation, fecundity, embryo transfer, premature ovarian failure, oocyte recipients/donors, and fertility treatment were used to assess relevance. If relevance could not be ascertained through the title, the abstract was accessed in order to make a determination. If infertility was mentioned only as part of background information and was not central to the article’s topic, it was not included. We used a Google spreadsheet to record all relevant articles on infertility. We excluded articles if they were considered a book review, news, or letter to the editor.

RESULTS: Out of 4,894 eligible articles from selected women’s health journals for the past 15 years, 54 addressed infertility as a main topic, which is around 1% of articles. Among the 54 articles, most addressed infertility in light of psychological distress, environmental or biological risk factors, cancer, treatment availability or treatment-seeking, or physiology. Very little research focused on gamete donation, impact of infertility on future health, or infertility in light of diseases other than cancer.

CONCLUSIONS: Given the increasing number of infertile women in the United States, it is concerning that the quantity of peer-reviewed research published in women’s health journals on infertility does not reflect this problem. Furthermore, public awareness on infertility is low. Concerted effort to publish and disseminate research on infertility within women’s health journals could enhance the public’s understanding.

P-12 Tuesday, October 18, 2016
EXPANDING SAME-SEX COUPLES’ ACCESS TO ASSISTED REPRODUCTION. S. Daneshmand,1,2 C. E. Bedient,1,3 F. Garner,1,3 B. S. Shapiro.1 1Fertility Center of Las Vegas, Las Vegas, NV; 2University of Nevada School of Medicine, Las Vegas, NV.

OBJECTIVE: Same-sex couples are routinely excluded from insurance coverage for assisted reproduction in many countries, and the oocyte donation and gestational surrogacy services they may require are often not covered by insurance or not allowed by law. We therefore describe methods for expanding access for same-sex couples to assisted reproduction, particularly in countries where the treatment options are not funded, provided, or allowed.

DESIGN: Retrospective cohort study at one private fertility center.

MATERIALS AND METHODS: Efforts included education/advocacy, identification/recruitment of all parties (intended parents, oocyte donors, gestational carriers), coordination with agencies and a spectrum of health care advocacy and legal professionals, medical and psychological screening, multi-lingual staffing, consultation, financial counseling, travel coordination, third-party coordination, and medical procedures. We created a financial aid program to assist same-sex couples in affording third-party assisted reproduction.

RESULTS: Education of all parties initially consisted of numerous broad-based presentations, interviews, question/answer sessions, and hand-outs provided at special-interest sessions and symposia in 20 countries, followed by individualized consultation for prospective intended parents, typically using video technologies. In 2015, we provided 217 cycles to intended parents from 37 countries, including 168 international cases. Despite being advised against double-blastocyst transfer so that both males could have a chance of pregnancy, same-sex couples frequently insisted on double-blastocyst transfer so that both males could have a chance for biological parenthood without the expense of a second gestational carrier cycle.

CONCLUSIONS: Advocacy and education improve access to treatment. We were able to help 217 intended parents to access assisted reproduction procedures. The current high cost of using a gestational carrier remains a barrier to some same-sex couples and understandably encourages others to transfer two embryos.

P-13 Tuesday, October 18, 2016
SMARTPHONE FERTILITY APP USE AMONG COUPLES OF REPRODUCTIVE AGE: POTENTIAL USE OF BIG DATA TO IMPROVE FERTILITY CARE AND ADVANCE REPRODUCTIVE HEALTH RESEARCH. A. Lange,1 J. Yeh,1 C. Messerlian,2 R. Hauser,3 J. E. Chavarro,4 A. J. Gaskins,5 T. L. Toth.6 Massachusetts General Hospital Fertility Center, Boston, MA; 2Environmental Health, Harvard T.H. Chan School of Public Health, Boston, MA; 3Harvard Chan School of Public Health, Boston, MA; 4Department of Nutrition, Harvard School of Public Health, Boston, MA; 5Department of Nutrition, Harvard T.H. Chan School of Public Health, Boston, MA; 6OB/GYN, Massachusetts General Hospital, Boston, MA.

OBJECTIVE: Smartphone applications (apps) are used by a significant proportion of the reproductive age population. Fertility apps have gained popularity in recent years as more women attempting pregnancy have become interested in real-time interactive features that respond to individual level information provided by users and aim to increase the probability of identifying the optimal fertile window. This bidirectional relationship between the app and its users results in a continuous inflow of data and provides an opportunity to capture a large number of observations across a diverse population, making big data a new avenue of fertility research. We received access to user-entered data from a widely used fertility app and sought to describe parameters of this database.

DESIGN: Analysis of a large, self-selected sample of female fertility app users across the United States attempting pregnancy.

MATERIALS AND METHODS: A fertility app company granted the investigators of this study access to questions posed to women and the de-identified self-reported data collected by the app. Data included in the analysis was collected from March 2014 through April 2016. Descriptive analysis was performed to delineate the parameters of the database.

RESULTS: A total of 1,014,647 women used the fertility app during the study period. The questions posed in the app included demographic information, time to conception, and 708 questions related to medical history, social history, health symptoms, such as stress and mood, and daily activities. Over 200,000 women recorded a pregnancy while using the app.

CONCLUSIONS: Our analysis includes one of the largest available databases of de-identified user-entered fertility information on over 1,000,000 women attempting to achieve pregnancy. This big database has the potential to generate important population based information regarding fertility in a broad US population.

P-14 Tuesday, October 18, 2016
THE DOCTOR WILL TWEET YOU NOW: EXPANDING ACCESS TO CARE THROUGH SOCIAL MEDIA ENGAGEMENT. S. H. Chen,1 S. Sehnert,2 W. Ash,3 N. Kumar,4 S. Foster,5 S. Yarnall,6 I. Carlsson.7 1Gynecology and Obstetrics, IRMS at Saint Barnabas, Livingston, NJ; 2Recombine, New York, NY; 3Today’s Business, Pine Brook, NJ; 4Medical Affairs, Recombine, New York, NY.

OBJECTIVE: Our aim was to assess the utility of social media as a platform for increasing access to fertility information and care. The ultimate goal of increased engagement and education through social media is greater exposure to, understanding of, and access to available fertility services.

DESIGN: Retrospective analysis.

MATERIALS AND METHODS: Retrospective analysis of uptake and engagement with social media outreach was performed for an academically-associated fertility practice with 7 clinical centers within the tri-state area. A variety of social media sites, including Facebook and Twitter, were utilized as platforms for sharing educational content. The target population included individuals of both genders, with varying ages and sexual orientations who are seeking information regarding fertility, infertility diagnoses and treatment, and/or fertility preservation. Analyzed measures included: page “like” and follower data; post reach, likes, shares, and comments; patient reviews; volume and source of website traffic; and time spent on website.

RESULTS: The clinic studied had 8,929 Facebook page likes and 1,432 Twitter followers. A sample Facebook post by the clinic which linked to an article about Polycystic Ovarian Syndrome (PCOS) was seen by 7,294 people, was liked 94 times, was shared to users’ personal pages 30 times, and was commented on four times by individuals sharing their experience or story. Of visitors to the clinic’s website who came to the site from a social media platform, 81% were new viewers who had not previously visited the site. Overall, site visitors arriving via social media spent twice as much time on the clinic website as compared with any other source.

CONCLUSIONS: All analyzed measures demonstrated high engagement and response to clinic outreach via social media. Social media may help to erase the stigma of infertility or assisted reproductive technologies by providing an open-forum and sense of community for individuals to find information and be heard. For individuals who otherwise might struggle to obtain information or care, such as the LGBT community, the use of social media could lower barriers. Furthermore, when patients comment and share their experience, the clinic has the opportunity
to respond and offer support and resources. With minimal effort, direct and personalized engagement between clinic and audience may lead to increased awareness and education, as well as better communication with patients. Both of these factors ultimately contribute to bettering patient care. The examples shown here demonstrate the utility of social media as a platform for education and patient engagement, and thus increased access to care.

**CONTRACEPTION/FAMILY PLANNING**

**P-15 Tuesday, October 18, 2016**

**EVALUATION OF TUBAL PATENCY WITH HYSTEROALGINOGRAPHY (HSG) IN BABOONS: EFFECT OF MENSTRUAL CYCLE PHASE.** J. Jensen,a C. Hanna,a S. Yao,a O. D. Slayden,a bDepartment of OB/GYN, OHSHU, Portland, OR; bDivision of Reproductive and Developmental Sciences, Oregon National Primate Research Center, Beaverton, OR.

**OBJECTIVE:** Functional obstruction at the utero-tubal junction may affect the quality of tubal imaging and success of transcervical permanent contraception procedures. We evaluated whether menstrual cycle phase influences visualization of tubal patency by HSG in baboons.

**DESIGN:** Descriptive nonhuman primate study.

**MATERIALS AND METHODS:** Female baboons (n=86) underwent serum sampling for estradiol and progesterone before undergoing an evaluation for tubal patency by a HSG. Of these, 23 underwent a second, and 3 a third examination for a total of 111 HSG studies. Tubal patency (bilateral patent, unilateral patent, bilateral obstruction) and vascular filling were noted, and correlated with serum estradiol (E2) and progesterone (P4) levels. Data was dichotomized as E2 ≥ 60 pg/mL and E2 < 60 pg/mL. The Fisher Exact and McNemar test were used to compare the proportion of exams with bilateral patent tubes in the overall population and in repeated exams respectively. Histologic evaluation was performed in cases where tubal patency was not observed on repeat HSG examination.

**RESULTS:** Overall, bilateral tubal patency was observed in 81/112 (72.3%) HSG studies. Bilateral occlusion was identified in 17.9%, and unilateral patency in 10.7%. A bilateral patent HSG result was significantly more likely when the exam was performed on females with serum E2 ≥ 60 (23/26, 88%) compared to those with E2 < 60 (58/66, 69%; p = .045). Including females with E2 levels < 60 during the luteal phase (P4 > 1.0 ng/mL) in the higher estrrogen group strengthened the association (88% vs 65% bilateral patency, p = .013). Fifteen females had an exam during a cycle with E2 <60 and E2 ≥ 60; in 8 of these pairs bilateral patency was observed during the exam with the higher estrogen level (p = .045 McNemar test). In all but three females that received confounding treatments, the cause of the tubal obstruction observed at HSG was determined to be functional rather than a true anatomic blockade by either repeat HSG exam or histologic evaluation that showed normal tubes.

**CONCLUSIONS:** In baboons, examination in the early follicular phase of the menstrual cycle was associated with an increased risk of failure to demonstrate bilateral tubal patency by HSG. Timing of tubal imaging and permanent contraception procedures toward midcycle may improve the likelihood of success.

**Supported by:** Support: Bill and Melinda Gates Foundation OPP1025233, NIH P51OD011092, P51 OD011133, U54-055744-07.

**P-17 Tuesday, October 18, 2016**

**ETHNIC AND RACIAL DIFFERENCES IN THE UTILIZATION OF INFERTILITY SERVICES: NATIONAL SURVEY OF FAMILY GROWTH (NSFG).** A. Janitz,a J. D. Peck,a L. B. Craig,a,bSection of REI; Dept of Ob/Gyn, OU Health Science Center, Oklahoma City, OK; bSection of REI; Dept of Ob/Gyn, OU Health Science Center, Oklahoma City, OK.

**OBJECTIVE:** Clinical and population-based comparisons of the racial/ethnic burden of infertility have identified disparities in infertility care. The objective of this study was to evaluate utilization of infertility services in the U.S. population by race/ethnicity by analyzing pooled data from the NSFG, a nationally representative sample of men and women aged 15-44 years.

**DESIGN:** Secondary analysis of existing cross-sectional data from the NSFG, a US population-based survey collecting data on infertility and receipt of infertility service.

**MATERIALS AND METHODS:** We analyzed female respondent data from the pooled NSFG cycles 2002, 2006-2010 and 2011-2013. Racial/ethnic groups were categorized as 1) Non-Hispanic (NH) white; 2) NH black; 3) NH other, or 4) Hispanic. Respondents reported use of any medical services to help get pregnant and specific types of evaluation and treatment [e.g., advice, testing, drugs, surgeries, intrauterine insemination (IUI), in vitro fertilization (IVF), etc.]. We compared the prevalence of receiving any infertility services across race/ethnicity groups using logistic regression. Weighted prevalence odds ratios (POR) and 95% confidence intervals (CI) were adjusted for income, education, metropolitan residence, treatment for infertility, history of infertility, and history of infertility. Reported odds ratios and 95% CI were calculated using the Rao-Scott Chi-Square test. We estimated 80% power to detect a minimum POR of 1.4 for comparisons of infertility service utilization among all women.

**Supported by:** Intramural program, NIDDK, National Institutes of Health.
RESULTS: Overall, 8.7% of all women (n=25,270) reported ever using infertility services of any kind. Hispanics (POR: 0.79, 95% CI: 0.64, 0.98) and NH blacks (POR: 0.57, 95% CI: 0.46, 0.70) had a lower adjusted odds of using infertility services compared to NH whites, with a higher odds in NH others (POR: 1.16, 95% CI: 0.85, 1.57). Use of specific infertility services differed by race/ethnicity, with statistically significant differences (p < 0.05) observed for use of drugs to induce ovulation, infertility testing on female or her partner, advice, IUI, IVF or other assisted reproduction, and surgery or drug treatment for endometriosis or uterine fibroids. No differences were observed for surgery to correct blocked tubes (p=0.46).

CONCLUSIONS: Understanding potential racial/ethnic disparities in infertility and differential access to infertility treatments is necessary to eliminate reproductive health disparities and barriers to health care access and assure equality of care for all patients. These disparities in infertility service utilization may be attributed to the cost of care and lack of health insurance for affordable diagnostic testing and treatment, which are barriers to infertility care that may disproportionately affect minorities.

Supported by: This project is supported by the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services (HHS) under I R40MC29449-01-00. Support is also provided by Oklahoma Shared Clinical and Translational Resource Institute NIGMS US5 GM104938. The information, content and/or conclusions are those of the authors and should not be construed as the official position or policy of nor should any endorsements be inferred by HRSA, HHS or the U.S.

P-18 Tuesday, October 18, 2016

AN EX VIVO MODEL FOR ASSESSING ACUTE EFFECTS OF TRANSCERVICAL POLIDOCANOL FOAM IN THE MACAQUE FALLOPIAN TUBE. S. Yao,a C. Hanna,a O. D. Slayden,a J. Jensen.b aDivision of Reproductive & Developmental Sciences, Oregon National Primate Research Center, Beaverton, OR; bDepartment of OB/GYN, OHSU, Portland, OR.

OBJECTIVE: To develop a model to evaluate candidate agents to create tubal occlusion for nonsurgical permanent contraception

DESIGN: Descriptive nonhuman primate study.

MATERIALS AND METHODS: Reproductive tracts were collected from rhesus macaques (n=10) at necropsy. Tubal patency was assessed by passing a small balloon catheter transcervically into the uterine cavity, and infusing foam until it was observed to pass freely from the fimbriae end of the fallopian tubes. The specimens were infused with 5% polidocanol foam (PF), 3% PF, or methylcellulose (control) foam (10mL). Following the foam infusion, the specimen was incubated at 37°C for 15 minutes, and then a solution of 8mL of 4% paraformaldehyde was delivered through the same catheter to rinse out the tube. The tract was then dissected to the cornua, isthmic, ampulla, and fimbriae portions and then embedded in paraffin, sectioned, and stained with hematoxylin and eosin for histologic evaluation.

RESULTS: Controls treated with inert methylcellulose foam displayed normal tubal epithelium. In contrast, treatment with PF led to varying degrees of epithelial cell damage progressing in severity from patchy epithelial disruption to complete epithelial exfoliation, and lumen dilation confined to the intramural zone. Mcuosal damage after 5% PF was more marked and consistent than the effect of 3% PF.

CONCLUSIONS: Transcervical perfusion of the reproductive tract PF results in acute epithelial damage to the fallopian tubes. Previous studies report that PF treatment results in permanent tubal occlusion. Effects of PF reported here represent the initial events in this process. These results support the use of ex vivo experiments to evaluate novel sclerosing agents prior to nonhuman primate in vivo experiments.

Supported by: Support: Bill and Melinda Gates Foundation.

P-19 Tuesday, October 18, 2016

DIGITAL WOMEN'S HEALTH BASED ON WEARABLES AND BIG DATA. P. Stein,a L. Falco,a F. Kuebler,a S. Annaheim,a A. Lenkaddem,a R. Delgado-Gonzalo,a C. Verjus,a B. Leeners,a aAva AG, Zurich, Switzerland; bEMPA - Swiss Federal Laboratories for Materials Science and Technology, St. Gallen, Switzerland; cCSEM - Centre Suisse d'Électronique et de Microtechnique, Neuchâtel, Switzerland; dUniversity Hospital Zurich - Clinic for Reproductive Endocrinology, Zurich, Switzerland.

OBJECTIVE: Currently available options for family planning are often cumbersome and imprecise. Moreover, women's demand for insights into their cycles has increased due to older age at pregnancy and the need for better planning of life and career. The goal of the presented research project was to develop data of physiological data measured at the wrist allows for natural family planning.

DESIGN: Observational study. The study received approval by the Ethical Commission of the Canton of Zurich. 41 healthy women between 20 and 40 were recruited and kept anonymous throughout the study. Once trained about the proceedings of the study, subjects were able to conduct all measurements at home. 180 menstrual cycles were documented.

MATERIALS AND METHODS: In a collaboration of scientists from the field of gynecology, physiology, sensor technology, and data science, a new solution for family planning was developed. It consists of a wrist worn sensor bracelet and intelligent algorithms. The bracelet contains various sensors which measure cardiovascular, movement, thermal, skin, and sleep parameters during sleep at night. The smart sensor bracelet was tested in a trial conducted by University Hospital Zurich and referenced with hormonal measurements. Daily surveys were filled out by the subjects to document confounding parameters.

RESULTS: In a first step, skin temperature and pulse rate readings were analyzed. Both show significant differences between follicular and luteal phase. Minimum average resting pulse rate occurs in the follicular phase with 55.5 beats per minute and maximum resting pulse rate in the luteal phase with 59.3 beats per minute. Wrist skin temperature follows the same pattern with 34.3 degrees Celsius respectively 34.7 degrees Celsius. Alcohol intake in the evening decreased skin temperature non-significantly and increased pulse rate readings throughout the night significantly. Further confounding parameters and physiological parameters like breathing rate and sleep will be analyzed soon.

CONCLUSIONS: The results show that wrist-based measurements allow for measuring parameters which correlate with the changes throughout the menstrual cycle. Compensating confounding parameters will be key for achieving precise information about the status of the menstrual cycle. Further analysis of the measured parameters will be conducted.

Supported by: Swiss Commission for Technology and Innovation CTI, Einsteinstrasse 2, 3003 Bern, Switzerland

P-20 Tuesday, October 18, 2016

SHARED MEDICAL APPOINTMENTS FOR VASECTOMY CONSULTATION: PROSPECTIVE ASSESSMENT OF PATIENT SATISFACTION AND COUNSELING EFFECTIVENESS. E. Chan,a D. J. Mazur,a J. Kahanian,a W. C. Choi,a J. Moss,a R. E. Bramnigan.a aDepartment of Urology, Northwestern University Feinberg School of Medicine, Chicago, IL; bDepartment of Urology, Weill Cornell Medicine, New York, NY.

OBJECTIVE: While a large number of publications support the use of shared medical appointments (SMA), to date no studies have assessed the utility of this approach for men seeking evaluation for vasectomy. The purpose of this study was to compare shared medical appointments (SMA) vs individual medical appointments (IMA) for men pursuing vasectomy consultation.

DESIGN: Prospective, IRB-approved, questionnaire-based cohort study of men presenting for vasectomy consultation in both SMAs and IMAs.

MATERIALS AND METHODS: At the time of vasectomy consultation scheduling, men were permitted to choose the SMA or IMA setting. All were then given pre- and post-appointment questionnaires assessing their satisfaction, preferences, and knowledge about vasectomy. At the time of the vasectomy procedure, men were given a 3rd questionnaire also assessing satisfaction, preferences, and retention of knowledge.

RESULTS: A total of 119 men presented for vasectomy consultation (51% SMA vs 49% IMA). 76% of men completed the post-consultation questionnaire, and 71% presented for vasectomy and completed the third
questionnaire. Baseline demographics were similar between the SMA and IMA groups. Importantly, there was no difference between SMA and IMA groups regarding patient satisfaction post consultation, and only 6% of men who completed the SMA consultation reported being dissatisfied with the group setting. 88% of men who participated in the SMA reported that their individual concerns were addressed at the time of consultation, and 90% of men felt that their questions about the procedure were adequately answered. 88% of men reported that SMA was an effective method of medical consultation. Interestingly, regarding knowledge-based questions, men in the SMA group initially scored higher than men in the IMA group after their consultation (p<0.05). However, at the time men presented for their vasectomy procedure, there was no difference between groups.

CONCLUSIONS: To our knowledge, this is the first study assessing the utility of SMA in the setting of vasectomy. Patients selecting SMAs report similar satisfaction and retention of vasectomy knowledge when compared to those undergoing IMAs. SMAs appear to be an effective setting and result in high patient satisfaction for appropriately selected patients.

MENTAL HEALTH

P-21 Tuesday, October 18, 2016

PREDICTORS OF DECISION REGRET FOLLOWING PREIMPLANTATION GENETIC SCREENING (PGS). K. N. Goldman, a J. K. Blakemore, a Y. G. Kramer, a A. K. Lawson, a J. Grifo. a New York University, New York, NY; bNorthwestern University, Chicago, IL.

OBJECTIVE: We sought to identify predictors of self-reported decision regret and anxiety following 24-chromosome aneuploidy screening and euploid embryo transfer.

DESIGN: Anonymous cross-sectional survey at a university-based fertility center.

MATERIALS AND METHODS: Patients who underwent their first cycle of IVF with 24-chromosome aneuploidy screening (PGS) between 1/2014 and 3/2015 (n=395) were invited to complete an anonymous internet-based survey containing three validated questionnaires: the Brinhaut Decision-Regret Scale (DR), short-form State-Trait Anxiety Inventory (STAI-6), and health literacy scale. Patients who underwent preimplantation genetic diagnosis for single gene disorders were excluded. The Shapiro-Wilk test was used to assess normality of distribution and the Mann-Whitney-U test and Chi-square tests were used for data analysis (GraphPad Prism 6.0). Data are presented as median (range) or %, p<0.05. The DR score is based on a 0-100 scale.

RESULTS: 80 surveys were returned and 73 met criteria for analysis. The majority (80%) of respondents were >35 years old, and the most common reason for PGS was ‘to maximize the efficiency of IVF’ (36%). 94.5% of respondents demonstrated adequate health literacy. The overall mean regret score was 8.2 (scale 0-100). Respondents who completed euploid embryo transfer (E) and had ≥1 euploid (E) embryo(s) (n=61) were compared to respondents with no euploid (NE) embryos after PGS (n=10). DR scores were similar between E and NE groups [0 [range 0-55] vs. 15 [range 0-50] p=0.07]. However, when dichotomizing respondents with a DR score=0 (no regret) compared to DR score >0 (any regret), twice as many respondents in the NE group expressed regret compared to the E group (70% vs. 34%, p<0.05). All respondents who underwent embryo transfer ET (n=54) were then compared. Those with an ongoing/delivered pregnancy after euploid ET (n=42) had significantly less decision regret compared to those with a negative pregnancy test or miscarriage (n=11) [0 [range 0-35] vs. 15 [range 0-55], p=0.0005]. Those with an ongoing/delivered pregnancy also had significantly lower STAI-6 scores compared to those with a negative pregnancy test or miscarriage (32.7 [range 16.7-60] vs. 46.7 [range 26.7-56.7], p=0.002).

OBJECTIVE: To understand medical students’ knowledge, intentions and attitudes towards egg freezing and the impact of employer coverage of fertility preservation on their decision making process.

DESIGN: Cross-sectional survey.

MATERIALS AND METHODS: An online survey was distributed to 280 female medical students at an urban university to assess their knowledge, attitudes and intentions towards elective egg freezing. Demographics, data on fertility knowledge, aging and fertility, egg freezing, whether they would consider elective egg freezing and what factors would influence their decision making were assessed via a self-reported multiple choice questionnaire.

RESULTS: A total of 84 surveys were completed. The average age of respondents was 25 ±2.5 years (mean ±SD). Most respondents were heterosexual (94%), not married (90%), did not have any children (99%). 91% wanted to have children in the future. Results show that 72% of participants correctly identified the age at which fertility significantly declines. 47% and 33% correctly estimated the likelihood of pregnancy following one year of unprotected intercourse in a <35 year old and a 35-40 year old female respectively. 41% consider themselves as potential egg freezers, while 24% would not consider the procedure and 35% were unsure. 79% of participants would not delay childbearing due to employer coverage of egg freezing and 66% did not view employer coverage as a form coercion to delay child bearing. Factors influencing decision making in potential freezers were the absence of a suitable partner (91%), likelihood of success (94%), financial reimbursement (97%) and health of offspring (100%). Knowledge about the low chance of pregnancy per oocyte (6-10%) would influence decision making in only 31% of potential freezers.

CONCLUSIONS: In this population of well-informed women, most would consider elective egg freezing. While financial reimbursement would make it easier to pursue and be a facilitator in potential freezers, employer coverage does not influence decision making and is not viewed as coercive by the majority of women. Additionally, accurate knowledge of the likelihood of success played a limited role in decision making. This is compelling information in light of certain industries offering coverage for egg freezing to its female employees.

P-22 Tuesday, October 18, 2016

KNOWLEDGE OF EGG FREEZING AMONG MEDICAL STUDENTS AND THE IMPORTANCE OF EMPLOYER COVERAGE OF ELECTIVE EGG FREEZING ON DECISION MAKING. D. E. Ikhen, a R. Confino, a N. J. Shah, b A. K. Lawson, b S. Klock, b M. G. Pavone. a Obstetrics and Gynecology, Prentice Women’s Hospital, Northwestern University Feinberg School of Medicine, Chicago, IL; bNorthwestern University - Feinberg School of Medicine, Chicago, IL; cObstetrics and Gynecology, Northwestern Medicine, Chicago, IL; dObstetrics & Gynecology and Psychiatry, Northwestern Medicine, Chicago, IL.

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P-23 Tuesday, October 18, 2016

FOLLOW UP OF MEXICAN EGG DONORS EXPERIENCES AND REACTIONS. A. Braverman, a C. Palachi Cohen, a C. Chapa, a J. C. Rosales, a R. Santos, a P. Diaz. a Obstetrics & Gynecology, Thomas Jefferson University, Philadelphia, PA; bCentro de Fertilidad IECH, Monterrey, Northen Mexico; cREI, Centro de Fertilidad IECH, Monterrey, Mexico; dCentro de Fertilidad IECH, Monterrey, Mexico; eCentro de Fertilidad IECH, Monterrey N.L., Macao.

OBJECTIVE: To explore the influences on Mexican ovum donors’ attitudes, reactions and emotional concerns after donation and up to 4 years following their donation.

DESIGN: A retrospective survey of ovum donors who donated from January 2011- January 2015 at a large urban ART center in Northern Mexico.

MATERIALS AND METHODS: A post ovum retrieval study utilizing Likert scale questions was developed to inquiry about donors’ experiences with all aspects of donation. 122 donors were identified of which 89 emails were available. and sent; 15 came back undeliverable and 26 were returned for analysis for a 35% response rate. Descriptive statistics were derived for all data.
RESULTS: About half the donors reported that they rarely think about being a donor and 60% rarely/never think about if there was a child. Overall, donors felt the medical and emotional aspects of donation were good or very good and they were well prepared. Donors preferred to know there was a pregnancy. 80% of donors did not regret donating their eggs and 20% were neutral. Donors felt proud, happy about donating; only 16% would not donate again. 84% of donors shared their experience with friends; 52% with family. Motivation to donate again was predominantly altruistic and secondarily financial. Time and logistical demands (64%) were the reasons for not wanting to donate again but also physical aspects concerned 46%. Physical side effects were bloating (52%), changes in menstrual cycle (22%), and none (44%). Medical complications were ovarian hyperstimulation (16%), infection (16%), and ovarian cysts (16%). Emotional side effects were mood changes (32%) and depression (8%); 48% described none. Only 1 donor attempted to get pregnant in the year after donation. Donors trend toward being favorable to meeting offspring at age 18. 48% of donors would consider registering on a website connecting them with donor conceived offspring but 32% would not. Several donors wrote that they felt donor-conceived offspring would do well emotionally as they were desired by the parents; only 4 wrote that they felt the offspring would feel negatively.

CONCLUSIONS: Donors felt prepared and felt neither worse nor better than what they anticipated post donation. Donors felt happy about donating with the majority willing to donate again. Logistics and time demands were the main reason for choosing not to donate again. Donors did not have physical side effects and some medical complications. Donors felt they should be told the outcome. Many Mexican donors may be willing to meet with offspring in the future and would consider being a part of an online registry.

P-24 Tuesday, October 18, 2016
FERTILITY PRESERVATION COUNSELING: DECISION MAKING AND REGRET
A. Lawson, A. Mendoza, K. N. Smith, E. Confino, E. E. Marsh. Obstetrics and Gynecology, Feinberg School of Medicine-Northwestern University, Chicago, IL.

OBJECTIVE: To examine the frequency and causes of disparities in fertility preservation counseling (FPC) by an oncologist in adult female cancer patients as well as decision regret among those who received FPC.

DESIGN: Cross-sectional questionnaire study.

MATERIALS AND METHODS: Women of reproductive age (ages 18-45) between 2011 and 2014 with a new diagnosis of cancer were identified via electronic medical records at an urban academic medical center. Study participants were mailed a consent form and questionnaire to meet with offspring in the future and would consider being a part of FPC. Results of improved FPC was warranted among cancer patients of reproductive age.

Supported by: The study was funded by the NIH Women’s Reproductive Health Research Scholars Award (EEM); Robert Wood Johnson Foundation (EEM), Friends of Prentice (EEM, AKL, and EEC) and the Evergreen Invitational (EEM).

P-25 Tuesday, October 18, 2016
ANXIETY SYMPTOMS AS PREDICTORS OF FERTILITY TREATMENT OUTCOMES
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OBJECTIVE: Systematic reviews and some recent studies have suggested that anxiety plays a role in reducing chances of becoming pregnant, although the literature is not yet settled. The primary goal of this study was to further explore trait anxiety as a predictor of fertility treatment outcome in patients seeking treatment at an academic reproductive clinic serving a rural population in the northeastern United States.

DESIGN: This is a prospective cross-sectional study.

MATERIALS AND METHODS: Anxiety symptomatology was assessed through self-report using the Brief Symptom Inventory (BSI) subscales Phobic Anxiety (PA, e.g., ‘Feeling uneasy in crowds, such as shopping or at a movie’), Anxiety (A, e.g., ‘Feeling tense or keyed up’), and Obsessive-Compulsive (OC, e.g., ‘Having to check and double-check what you do’). Fertility treatments are defined as ovulation induction and IVF. Fertility treatment outcomes (i.e., positive pregnancy test at two weeks following intervention) were obtained through medical chart review. Thirty-three women were recruited and assessed during their first appointment to the clinic.

RESULTS: After controlling for age, body mass index (BMI), and insurance coverage for reproductive care, anxiety symptomatology significantly predicted fertility treatment outcomes. This model explained a significant proportion of variance in outcomes, R² = .42, F(2, 26) = 3.17, p = .018. All three anxiety subscales - PA (β = -.75, p = .001); A (β = .79, p = .01); OC (β = -.47, p = .05) had a negative predictive value for a successful treatment. More broad analyses of clusters of symptomatology underlying anxiety disorders, demonstrate that an increase in anxiety symptoms, specifically phobic and obsessive-compulsive symptomatology, is related to a decrease in pregnancy rates following fertility treatment.

CONCLUSIONS: Results of this study further support the body of research that trait anxiety plays a predictive role in the outcome of fertility treatment and suggest that identifying and treating anxiety in patients undergoing fertility treatment could improve outcomes. In addition to improving fertility treatment outcomes, early screening and intervention for anxiety could also benefit more long term outcomes such as maternal well-being and birth outcomes.

Reference:

P-26 Tuesday, October 18, 2016
DISTRESS AND EARLY DECISIONAL CONFLICT AND SATISFACTION IN WOMEN CONSIDERING FERTILITY PRESERVATION PRIOR TO CANCER TREATMENT
A. Bradford, L. Covarrubias, T. L. Woodard. aGynecologic Oncology and Reproductive Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX; bHealth Services Research, The University of Texas MD Anderson Cancer Center, Houston, TX; cObstetrics and Gynecology, Baylor College of Medicine, Houston, TX.

OBJECTIVE: The aim of this study was to determine the extent to which psychological distress is associated with decisional conflict and satisfaction in women considering fertility preservation prior to cancer treatment.
DESIGN: Descriptive analysis of baseline data from a clinical trial of a decision support and distress management intervention for young women considering fertility preservation.

MATERIALS AND METHODS: Twenty-two women completed self-report measures immediately after a fertility preservation consultation with a reproductive endocrinologist. Measures included the Brief Symptom Index-18 (composed of subscales for anxiety, depression, and somatization), Intolerance of Uncertainty Scale, Decisional Conflict Scale, Satisfaction with Decision Scale, and Reproductive Concerns Scale. Descriptive statistics and Spearman’s rho correlations were generated to assess baseline levels of distress and to test relationships between variables. We predicted that greater anxiety and intolerance of uncertainty would be associated with greater conflict and lower satisfaction related to initial decisions about fertility preservation, whereas we predicted that depression would be associated with reproductive concerns (fertility-specific distress). We also sought to determine whether the pre-existing reproductive health context (parity, prior history of fertility problems) was associated with distress and decision-making outcomes.

RESULTS: Contrary to predictions, neither anxiety nor intolerance of uncertainty was associated with decisional conflict or satisfaction. Decisional conflict and satisfaction were not correlated with any other variables including reproductive history, although very few women reported a history of fertility problems. Reproductive concerns were strongly correlated with depression (Spearman’s rho = -0.55, P = 0.01) and intolerance of uncertainty (Spearman’s rho = -0.63, P < 0.01).

CONCLUSIONS: Although general measures of distress and intolerance of uncertainty are associated with fertility-specific distress in women with cancer, they did not appear related to conflict or satisfaction with early decisions about fertility preservation immediately following consultation with a reproductive endocrinologist.

Supported by: This research was supported by a Young Investigator Award from the National Comprehensive Cancer Network.

P-27 Tuesday, October 18, 2016

PROVIDER PERCEPTION OF PSYCHOLOGICAL CONDITIONS AND INFERTILITY. H. S. Hoff, a N. M. Crawford, b J. E. Mersereau. c

aReproductive Endocrinology and Infertility, University of North Carolina, Chapel Hill, NC; bObstetrics and Gynecology, University of North Carolina, Chapel Hill, NC; cREI, UNC, Chapel Hill, NC.

OBJECTIVE: To determine if reproductive specialists are screening new patients for depression or anxiety, explore possible reasons why providers are not screening, and assess physician’s views about the impact of mental health disorders on fertility.

DESIGN: Cross sectional study.

MATERIALS AND METHODS: All members of the Society for Reproductive Endocrinology and Infertility received an email with a link to an internet based survey. Practicing infertility physicians were asked to complete the survey. Twenty questions (multiple choice or Likert scale responses) were generated with the objective of evaluating provider screening for psychologic conditions, provider perception of mental health disorders and infertility, and barriers to screening or recommending further evaluation for these illnesses. The survey also included questions regarding demographic information (location and type of practice, years in practice, number of IVF cycles per year, etc.). Descriptive statistics were generated for all variables and bivariate analysis was conducted using student’s t-test and Pearson’s chi square for continuous and categorical variables, respectively.

RESULTS: Eighty-six physicians filled out the 20 question survey. Although the majority of infertility providers believe psychological conditions negatively impact pregnancy success (75%), most providers are not formally screening patients for depression or anxiety. Formal screening for anxiety and depression is reported by only 28% of these fertility physicians. Of those providers who didn’t screen for mental health disorders, 36% reported this was due to a lack of time during the appointment and 18% stated uncertainty about recommendations if a patient is anxious or depressed. Providers who did not screen for depression were most likely to be uncomfortable assessing patients for mental health disorders and to work in a private practice setting. Interestingly, there was no correlation between screening formally for mental health disease and the belief that psychological conditions negatively impact pregnancy success.

CONCLUSIONS: This is the first study to evaluate providers’ screening practices and attitudes toward psychological disorders and infertility.

Satisfaction with Decision Scale, and Reproductive Concerns Scale. Descriptive statistics and Spearman’s rho correlations were generated to assess baseline levels of distress and to test relationships between variables. We predicted that greater anxiety and intolerance of uncertainty would be associated with greater conflict and lower satisfaction related to initial decisions about fertility preservation, whereas we predicted that depression would be associated with reproductive concerns (fertility-specific distress). We also sought to determine whether the pre-existing reproductive health context (parity, prior history of fertility problems) was associated with distress and decision-making outcomes.

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OBJECTIVE: To determine if reproductive specialists are screening new patients for depression or anxiety, explore possible reasons why providers are not screening, and assess physician’s views about the impact of mental health disorders on fertility.

DESIGN: Cross sectional study.

MATERIALS AND METHODS: All members of the Society for Reproductive Endocrinology and Infertility received an email with a link to an internet based survey. Practicing infertility physicians were asked to complete the survey. Twenty questions (multiple choice or Likert scale responses) were generated with the objective of evaluating provider screening for psychologic conditions, provider perception of mental health disorders and infertility, and barriers to screening or recommending further evaluation for these illnesses. The survey also included questions regarding demographic information (location and type of practice, years in practice, number of IVF cycles per year, etc.). Descriptive statistics were generated for all variables and bivariate analysis was conducted using student’s t-test and Pearson’s chi square for continuous and categorical variables, respectively.

RESULTS: Eighty-six physicians filled out the 20 question survey. Although the majority of infertility providers believe psychological conditions negatively impact pregnancy success (75%), most providers are not formally screening patients for depression or anxiety. Formal screening for anxiety and depression is reported by only 28% of these fertility physicians. Of those providers who didn’t screen for mental health disorders, 36% reported this was due to a lack of time during the appointment and 18% stated uncertainty about recommendations if a patient is anxious or depressed. Providers who did not screen for depression were most likely to be uncomfortable assessing patients for mental health disorders and to work in a private practice setting. Interestingly, there was no correlation between screening formally for mental health disease and the belief that psychological conditions negatively impact pregnancy success.

CONCLUSIONS: This is the first study to evaluate providers’ screening practices and attitudes toward psychological disorders and infertility.

Satisfaction with Decision Scale, and Reproductive Concerns Scale. Descriptive statistics and Spearman’s rho correlations were generated to assess baseline levels of distress and to test relationships between variables. We predicted that greater anxiety and intolerance of uncertainty would be associated with greater conflict and lower satisfaction related to initial decisions about fertility preservation, whereas we predicted that depression would be associated with reproductive concerns (fertility-specific distress). We also sought to determine whether the pre-existing reproductive health context (parity, prior history of fertility problems) was associated with distress and decision-making outcomes.

RESULTS: Contrary to predictions, neither anxiety nor intolerance of uncertainty was associated with decisional conflict or satisfaction. Decisional conflict and satisfaction were not correlated with any other variables including reproductive history, although very few women reported a history of fertility problems. Reproductive concerns were strongly correlated with depression (Spearman’s rho = -0.55, P = 0.01) and intolerance of uncertainty (Spearman’s rho = -0.63, P < 0.01).

CONCLUSIONS: Although general measures of distress and intolerance of uncertainty are associated with fertility-specific distress in women with cancer, they did not appear related to conflict or satisfaction with early decisions about fertility preservation immediately following consultation with a reproductive endocrinologist.

Supported by: This research was supported by a Young Investigator Award from the National Comprehensive Cancer Network.

P-27 Tuesday, October 18, 2016

PROVIDER PERCEPTION OF PSYCHOLOGICAL CONDITIONS AND INFERTILITY. H. S. Hoff, a N. M. Crawford, b J. E. Mersereau. c

aReproductive Endocrinology and Infertility, University of North Carolina, Chapel Hill, NC; bObstetrics and Gynecology, University of North Carolina, Chapel Hill, NC; cREI, UNC, Chapel Hill, NC.

OBJECTIVE: To determine if reproductive specialists are screening new patients for depression or anxiety, explore possible reasons why providers are not screening, and assess physician’s views about the impact of mental health disorders on fertility.

DESIGN: Cross sectional study.

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Supported by: This research was supported by a Young Investigator Award from the National Comprehensive Cancer Network.
following the study, 83% indicated they would not discard the unused embryos.

CONCLUSIONS: Internet-based education that addresses alternative options to long-term frozen embryo storage fills a gap in current clinical practice efforts associated with helping individuals and couples make challenging disposition decisions.


**NURSING**

P-29 Tuesday, October 18, 2016

**HOW CAN WE MAKE A GOOD EXPERIENCE EVEN BETTER: WAYS TO ENHANCE THE FERTILITY JOURNEY.** R. Kudesia,1,2 D. Bhasin,1,2a J. A. Lee,3 C. Briton-Jones,3 M. Daneyko,3 B. Collura,2 A. B. Copperman,1,2 aReproductive Medical Associates of New York, New York, NY; bObstetrics, Gynecology and Reproductive Science, Icahn School of Medicine at Mount Sinai, New York, NY; cRESOLVE: The National Infertility Association, McLean, VA.

OBJECTIVE: To assess the infertility patient experience in the U.S. DESIGN: Survey.

MATERIALS AND METHODS: A 52-item survey, relating to demographics and treatment experience, of those undergoing fertility treatment. Each of 6 domains included a series of structured questions, pooled for analysis, and also allowed for open-ended feedback. Kruskal Wallis, Pearson’s chi-squared and Spearman’s correlation were used.

RESULTS: Four hundred and ninety-nine females of reproductive age (91.8% aged 25-40) responded. Seventy-eight percent had been trying to conceive for over a year prior to consultation, with 52.3% trying for 1-2 years. The majority (56.8%) had been receiving care for 1-3 years, and 50.4% were going forth or had completed at least one in vitro fertilization (IVF) cycle. Length of time prior to treatment had a weak negative correlation with pregnancy (r = 0.19, p = 0.0001), and time in treatment had a positive correlation (r = 0.1, p = 0.04), and time in treatment had a positive correlation (r = 0.1, p = 0.04), but neither were significant. The majority (84.7-90.9%) were satisfied with scheduling, phone calls, monitoring and confidentiality, though only 37.3% agreed that the office provided information for infertility support services. Though the majority (56.1-66.0%) agreed the finance team was courteous, only 33.4% agreed that they were informed of options to reduce their financial burden. A majority (75.2-85.7%) were also satisfied with their nurse care, though only 29.4% agreed that their nurse mentioned resources for emotional support. In terms of physician interaction, 64.9-75.9% agreed that their physicians spent enough time with them, offered appropriate explanations and treatment alternatives, and were sensitive. The majority (74.8-87.1%) were satisfied with their care. Finally, the majority (71.7%) used some form of complementary treatment, most frequently acupuncture (45.0%). These options were most frequently found online (27.1%), through advocacy groups (26.7%), or through a physician referral (22.9%). No significant associations were noted between demographics, pregnancy outcome or treatment satisfaction.

CONCLUSIONS: Though infertility patients are generally satisfied with their care and have overall positive perceptions regarding each team within their practice, a majority also utilize complementary services and express a need for greater awareness of external support. This survey identifies room for improvement in the delivery of reproductive care, namely helping patients identify financial, emotional and complementary medical resources. Along with providing top-quality medical care, which many patients felt they did receive, this enhancement of patient experience can help minimize the psychological trauma to those undergoing fertility treatments.

P-30 Tuesday, October 18, 2016

**THE PSYCHO-EMOTIONAL IMPACT OF WOMEN RECEIVING DONOR EGGS AND THE INFLUENCE ON DECISION TREATMENT.** C. T. Kimati,4 H. L. Montagnini,4b T. C. Bonetti,4d P. C. Serafini,4d E. Motta,6,7 T. S. Domingues,6,7 aNursing, Huntington Medicine Reproductive, Sao Paulo, Brazil; bPsychology, Huntington Medicine Reproductive, Sao Paulo, Brazil; cGynecology, Universidade Federal de Sao Paulo, Sao Paulo, Brazil; dScientific, Huntington Medicine Reproductive, Sao Paulo, Brazil; eDiscipline of Gynecology, Hospital das Clinicas, Un, Sao Paulo, Brazil; fClinical Head, Huntington Medicine Reproductive, Sao Paulo, Brazil; gHuntington Medicine Reproductive, Sao Paulo, Brazil.

OBJECTIVE: The demand for donated oocytes has been on the rise worldwide to overcome infertility. However, there is a concern for the psychological impact of oocyte recipients regard to the lack of a genetic link to the child. The aim of this study was to evaluate the psychological condition of oocyte recipients in an egg bank program.

DESIGN: This is a retrospective descriptive study conducted from July to December 2014 in a private IVF center. The infertile women screened for the egg bank program are routinely evaluated by a psychologist regarding their emotional condition before they underwent an IVF treatment with donor eggs.

MATERIALS AND METHODS: This study included 60 recipient women who were in donor egg selection process, to carry out IVF cycles. Infertile women were scheduled for a consultation with the psychologist, where the data collection was held by semi-structured interview lasting about 60 minutes. After the interviews, the patients were classified according to their emotional condition to accept the oocyte donation as: patients emotionally stable, accepting the egg donation and feeling that the genetic relationship were not essential to maternity (group A, n = 18), patients presenting emotional questions about the overall treatment, independently of the egg origin (group B, n = 28), and patients presenting marital conflict, or emotional conflicts to accept egg donation, feeling afraid of do not have a link with the offspring due to lack of genetic association (group C, n = 14).

RESULTS: All patients in groups A and B underwent the IVF with egg donation. From those, 10/18 (55.6%) in the group A and 17/28 (60.7%) in the group B had live birth babies. In the group C, in spite of patients presented emotional conflicts 13/14 (92.9%) realized the IVF treatment with donated eggs and 9/13 (69.2%) had live birth babies.

CONCLUSIONS: The findings of this study show that egg donors recipients decide to undergo the egg donor treatment independently of their emotional stability, believing in the desire to have a baby overriding the lack of genetic link with the offspring. Also, in spite of some patients were not emotionally confident to receive an egg donation, that attitude indicate that women deny their emotional conflicts and decide for undergo the treatment, and had a satisfactory live birth rates. The findings based on our casuistic must be carefully generalized, as emotional aspects of women regards to egg donation can be highly influenced by cultural aspects. The following up of those patients has been done to investigate the emotional condition after the babies.


P-31 Tuesday, October 18, 2016

**PATIENT AND NURSE EVALUATION OF THE IMPROVED FOLLITROPIN ALFA PEN INJECTOR FOR INFERTILITY TREATMENT.** J. Schertz,1 B. Felding,2 H. Worton.1 2EMD Serono, Billerica, MA; 1Acquus Research, London, United Kingdom.

OBJECTIVE: This international study evaluated patient and nurse experiences with the recently improved prefilled, ready-to-use follitropin alfa (Gonal-f® Pen [jGFP]) multi-dose pen injector.

DESIGN: Structured simulated training and questionnaire interview.

MATERIALS AND METHODS: 86 women of reproductive age with recent or current infertility requiring ART and 30 fertility nurses from four European countries participated in the study. 65 women had recently/were currently in treatment while 21 were naive to ART treatment. Training on correct iGFP use was performed using the Instructions for Use
They were then asked to complete a questionnaire assessing their experience and comparing this to either known (nurses) or previously used (women) fertility injection devices, if applicable. Nurses received initial training and then trained an average of 2.9 patients (range 2-5). Descriptive data are summarized.

RESULTS: Following training and use, all 30 (100%) nurses agreed or strongly agreed that the iGFP was easy to learn and 28 (93%) felt it would be easy to teach. After training patients, all 30 nurses evaluated the overall process of teaching patients how to self-administer as easy or very easy; 27 (90%) nurses felt that teaching the overall process of self-administering was easier or much easier than their expectations.

Of the 13 nurses with experience training patients on Bemfola® in the previous 6 months, 11 (85%) felt that the iGFP was easier or much easier to teach. Of the 28 nurses with Puregon® training experience in the previous 6 months, 22 (79%) felt that the iGFP was easier or much easier to teach. All of these nurses felt that the iGFP would minimize dosing errors compared with Bemfola (n=12; one nurse did not correctly complete this question) or Puregon (n=28). Almost all, 83 out of 86 (97%) patients, found the iGFP easy or very easy to learn to use. In particular, setting the iGFP dose was considered easy or very easy by 84 (98%) patients. Following training and use, 75 (90%) patients agreed or strongly agreed that they would recommend the iGFP to friends and family if they needed IVF treatment. Of the 30 nurses, 29 agreed or strongly agreed that they would recommend the iGFP to fellow fertility nurses.

CONCLUSIONS: The improved version of the prefilled, ready-to-use follitropin alfa multi-dose pen injector (Gonal-f® Pen) is easy to learn and easy to teach for fertility nurses and easy to use for women recently/currently receiving or requiring ART. Over 90% of nurses and patients in this study would recommend the improved pen.

Supported by: This study was supported by Merck.

COMPARISON OF FERTILITY QUALITY OF LIFE BETWEEN URBAN AND RURAL INFERTILE COUPLES. Y. Donga F. Zhou. aReproductive Medicine, Zhengzhou, China; bThe First Affiliated Hospital of Zhengzhou University, Zhengzhou, China.

OBJECTIVE: To determine whether the fertility quality of life differs between infertile couples from urban and rural areas in China.

DESIGN: A cross-sectional prospective study consisting of 670 infertile couples in assisted reproduction clinic of the First Affiliated Hospital of Zhengzhou University was conducted.

MATERIALS AND METHODS: Among all participants, 358 infertile couples (31.22 years for women and 32.58 years for men) were urban residents and 312 (29.79 years for women and 30.77 for men) were from rural areas. Male and female counterparts completed the FertiQoL questionnaire independently. Paired t-test was utilized to explore the differences of fertility quality of life (QoL) between urban and rural infertile couples. Whether and to what extent various characteristics contribute to the differences regarding fertility QoL was assessed by multiple stepwise regression analysis.

RESULTS: For all patients, women obtained significantly lower FertiQoL questionnaire scores compared with male counterparts, indicating lower fertility quality of life. Infertile couples resided in rural areas had considerably lower FertiQoL scores than those from urban residents. Coping style, cognition of children, family monthly net income, employment status, educational level and social support were risk factors predicting the differences in the fertility quality of life between urban and rural infertile couples.

CONCLUSIONS: The results show the fertility QoL significantly differs between infertile couples from urban and rural areas. According to different characteristics of coping style, cognition of children, family monthly net income, employment status, educational level and social support, targeted measures should be taken to resolve the difference, especially for rural women.
OBJECTIVE: Insulin-like growth factors (IGFs) are important regulators of follicle development and steroidogenesis in the ovary; however, their source, regulation and role in the primate follicle are unclear. The current study examined the production of IGF-2, the predominant IGF in primates, and its regulation by ovarian steroid hormones (androgen, estrogen and progesterone) in macaque follicles during 3-dimensional culture.

DESIGN: Nonprimate human model; randomized, controlled study.

MATERIALS AND METHODS: Follicles from young adult rhesus macaques (n=24 follicles/group x 3-4 animals/experiment) were encapsulated in alginate and cultured individually at 37°C in 5% O2 for 5 wks [1]. Treatment groups included 1) control (CTRL, no additives), 2) tri- lostane (TRL, a steroid-synthesis inhibitor, 250 ng/ml), 3) TRL + dihydrotestosterone (DHT, 50 ng/ml), 4) TRL + 17β estradiol (E2, 1 ng/ml), and 5) TRL + progesterone (P4, 100 ng/ml). All media contained 44 ml/ml FSH. Levels of IGF-2 and anti-Müllerian hormone (AMH) were measured in culture media of surviving follicles (n=9-19 follicles per group) using ELISA. The assays have been validated for macaques. Surviving follicles were categorized based on their wk 5 diameter: no-grow (<250 mm), slow-grow (250-500 mm) and fast-grow (>500 mm). Statistical differences (p<0.05) over time and treatment, and correlations between parameters, were determined using SPSS and SigmaPlot.

RESULTS: At week 5, media IGF-2 concentrations were higher (p<0.05) in fast-grow (2.1±0.5 ng/ml), compared to no-grow (undetectable, <0.21 ng/ml) and slow-grow (0.4±0.3 ng/ml) follicles. For fast-grow follicles, IGF-2 levels were highest during wk 5 (2.1±0.5 ng/ml), compared to wks 1 (undetectable) and 3 (0.3±0.2 ng/ml). A positive correlation (r=0.43, p<0.05) was observed between IGF-2 level and follicle diameter at wk 5. Steroid ablation reduced (p<0.05) IGF-2 levels (0.06±0.06 ng/ml, TRL, wk 5), but these were restored to the CTRL levels with DHT (0.8±0.3 ng/ml, TRL+DHT) and P4 (5.5±1.6 ng/ml, TRL+P4) replacement. A trend (r=0.20, p=0.1) towards a positive correlation between peak IGF-2 (wk 5) and AMH (wk 3) levels was evident.

CONCLUSIONS: This is the first report demonstrating IGF-2 production and its regulation by steroid hormones in primate follicles. IGF-2 levels increased as follicles developed to the small antral stage (wk 5), and are correlated with antral follicle diameter (wk 5) and peak AMH levels. In addition, IGF-2 production appears regulated by androgen and P4, but not E2. Thus, the results are consistent with the hypothesis that IGF-2 is a local factor regulating primate folliculogenesis and has implications for its role in abnormal follicle development during hyperandrogenemia [2] and polycystic ovarian syndrome.

REFERENCES:

Supported by: NIH 5P50HD071836, 8P51OD011092, K12HD043488 (BRCWH)

OVARIAN FUNCTION

P-34 Tuesday, October 18, 2016

INSULIN-LIKE GROWTH FACTOR-2 (IGF2) PRODUCTION AND REGULATION IN MACAQUE PREANTRAL FOLLICLES DURING 3-DIMENSIONAL CULTURE. O. Tkachenko,a A. Y. Ting,a J. Xu,b R. L. Stouffer. c Reproductive and Developmental Sciences, ONPRC, OHSU, Beaverton, OR; bDivision of Reproductive & Developmental Sciences, Oregon National Primate Research Center, Beaverton, OR; cOregon Health & Science University, Beaverton, OR.

OBJECTIVE: The total number of pregnant mice was 15 (75%) in the exercise group, which was significantly higher than 5 (25%) in the control group (P<0.05). The mean number of offspring was also significantly higher in the exercise group (9.2) than the control group (6.3) (P<0.05). The mean number of one-cell embryos retrieved and blastocyst formation rate were 12.6 and 43.8% in the exercise group and 10.8 and 8.1% in the control group with a significant difference (P<0.05). Ovarian VEGF and ENOS expression was increased, but ovarian apoptosis was decreased in the exercise group.

CONCLUSIONS: This study demonstrates that regular exercise induced by illumination with incandescent lights in aged mice improves their reproductive outcomes by improving ovarian function and oocytes quality. The beneficial effect of an optimal exercise on fertility may be associated with the activation of ovarian angiogenesis by increasing ovarian eNOS and VEGF expression.

P-36 Tuesday, October 18, 2016

ADIPOCYT AND FETAL FOLLICULAR DEVELOPMENT: AN ASSOCIATION BETWEEN LEPTIN AND CORD BLOOD AMH. S. Butts,a S. Senapati,b C. Coutifaris,b M. S. Bartolomei.a aObstetrics and Gynecology, Perelman School of Medicine, Philadelphia, PA; bObstetrics & Gynecology, Reproductive Endocrinology, University of Pennsylvania, Philadelphia, PA; cUniversity of Pennsylvania, Philadelphia, PA; dUniversity of Pennsylvania Perelman School of Medicine, Philadelphia, PA.

OBJECTIVE: While the developmental origins of adult disease hypothesis proposes a link between environmental exposures in utero and risk of subsequent cardiometabolic disease, few studies have investigated such a relationship with measures of female reproductive potential. We hypothesize that umbilical cord blood AMH reflects an association between measures of specific fetal exposure (adipocity) and early follicular development.

MATERIALS AND METHODS: Subjects ultimately achieving pregnancy were enrolled preconception. At delivery, umbilical cord blood measurements of AMH, insulin, IGF1, IGF2, IGFBP3 and leptin were performed (log transformed for analysis). Associations between variables were tested with Spearman correlations, simple regression, Wilcoxon Rank Sum tests, and multivariable linear regression as appropriate.

RESULTS: Thirty women (19 IVF conceptions, 11 unassisted conceived) had cord blood samples for assessment. Median (Interquartile range). IQR) cord blood AMH was 0.1 ng/mL (0.06, 0.69), median (IQR) BMI was 24.3 kg/m² (22.1, 30.6), median (IQR) maternal AMH was 1.2 ng/mL.

Correlation with Cord Blood AMH

<table>
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<th>Variable</th>
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<tr>
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<td>Maternal Preconception AMH</td>
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<td>p = 0.8</td>
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</table>

FERTILITY & STERILITY®
Adiposity with diminished AMH in adults and provides evidence of early weight, cord blood leptin has a strong, negative relationship with cord blood AMH. Studies of the inhibitory effects of AMH on follicular development and BRCA2 expression in human ovarian cortex. These results help our understanding of the role of nutrition and genomic factors in these processes is becoming relevant.

DESIGN: The study was designed to examine the possible changes in the nutrient ovarian environment and how these could eventually affect the quality of the ovum. We therefore looked at specific nutrients like zinc, copper, iron, L-carnitine and acetyl-L-carnitine on the process of fertility and reproduction in an animal model of superovulation.

RESULTS: The mean number of oocytes in groups 2 and 4 was 32.4 and 31.3 respectively and was significantly higher (p<0.01, Student test) compared to the control group: 24.5. The number of degraded oocytes was 29.1% (p<0.05) and 19.3% (p<0.01) (group 2 and 4) versus 34.3% (control). The IVF experiments to establish numbers of fertilized eggs and developed embryos showed that, despite the treated groups had a minor percentage of 2-cells embryos versus control group, the major part of them reach the blastocyst stage (86% versus 60%).

CONCLUSIONS: These results support the evidence that carnitines and micronutrients are important for embryos development and may have some beneficial effect in both genesis and ovulation process. This study shows the wider implications and effects of critical nutrients on ovulation and in particular on oocyte quality which could determine fertilization potential. Further experiments are ongoing to examine the ability of the oocytes to be fertilized and gene expression after metabolic and nutrient treatment and to measure further parameters of ovum quality such as ability to be fertilized, chromosomal stability (aneuploidy) embryo development and pregnancy success.

Supported by: This preclinical research study was partly funded by Sigma-Tau HealthScience.

EFFECT OF ANTI-OXIDANT AND METABOLIC NUTRIENTS ON OOCYTES DEVELOPMENT IN IVF MODEL IN MICE. A. Virmani. Innovation, Research and Development, Sigma Tau HealthScience, Utrecht, Netherlands.

OBJECTIVE: The reproductive process is acutely sensitive to the nutritional state of the mother and even the grandmother. Studies show that nutrients affect the ovulation process and oocyte maturation as well as the whole pregnancy. There is growing consensus that egg quality declines with age and in conditions such as diabetes and polycystic ovary syndrome (PCOS). The role of nutrition and genomic factors in these processes is becoming relevant. The critical processes underlying ovulation and oocyte quality such as energy status, oxidative stress, inflammatory status and the mothers hormonal cycle are all affected.

DESIGN: The study was designed to examine the possible changes in the nutrient ovarian environment and how these could eventually affect the quality of the ovum. We therefore looked at specific nutrients like zinc, copper, iron, L-carnitine and acetyl-L-carnitine on the process of fertility and reproduction in an animal model of superovulation.

MATERIALS AND METHODS: Female 8 weeks old CD1 mice were divided into four groups of eight each. Treatment was daily for 3 weeks by intragastric gavage. Group 1 - Control only vehicle; Group 2 - Carnitines (L-carnitine 0.4 mg and acetyl-L-carnitine 0.12 mg per mouse); Group 3 - Microelements (Zinc: 4 ng, Copper: 0.8 ng, Iron: 7 ng per mouse); Group 4 - Microelements plus Carnitines (compounds of both group 2 and 3).

RESULTS: The mean number of oocytes in groups 2 and 4 was 32.4 and 31.3 respectively and was significantly higher (p<0.01, Student test) compared to the control group: 24.5. The number of degraded oocytes was 29.1% (p<0.05) and 19.3% (p<0.01) (group 2 and 4) versus 34.3% (control). The IVF experiments to establish numbers of fertilized eggs and developed embryos showed that, despite the treated groups had a minor percentage of 2-cells embryos versus control group, the major part of them reach the blastocyst stage (86% versus 60%).

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Supported by: This preclinical research study was partly funded by Sigma-Tau HealthScience.

P-37 Tuesday, October 18, 2016

ANTI-MULLERIAN HORMONE (AMH) REGULATES BRCA1 AND BRCA2 GENE EXPRESSION IN AN OVARIAN CORTEX TRANSPLANTATION MODEL. L. Detti,a N. M. Fletcher,b G. M. Saed,b R. A. Uhlmann,a M. Christiansen,d L. J. Williams.e aObstetrics and Gynecology, University of Tennessee Health Science Center, Memphis, TN; bObstetrics and Gynecology, Wayne State University, Detroit, MI; cObstetrics and Gynecology, Wayne State University School of Medicine, Detroit, MI; dThe University of Tennessee Health and Science Center COM, Memphis, TN; eOB/GYN, University of Tennessee Health Science Center, Memphis, TN.

OBJECTIVE: Decline in double strand DNA repair function, at least in part, explains diminished ovarian reserve and earlier menopause in women with BRCA mutations. [1,2] In fact, the BRCA1/2 mutation was associated with a significantly earlier age at natural menopause. [3] Expression of BRCA1, but not BRCA2, declines in mouse and human oocyte and ovarian reserve is determined by serum concentrations of anti-Mullerian hormone which is impaired in young women with BRCA1 mutations. We determined whether recombinant AMH could prevent post-transplant BRCA1/2 RNA expression in human ovarian cortex.

DESIGN: Experimental study on ovariectomized nude mice xenotransplanted with human vitrified/thawed ovarian cortex and treated with rAMH via infusion pump.

MATERIALS AND METHODS: Twelve nude mice were ovariectomized and Alzet pumps delivering 1.23 mcg rAMH/day to reach a serum concentration of 17.5 ng/mL (5x physiologic AMH level in humans), or placebo, were inserted infraabdominally at the same time. Previously vitrified/thawed 2x2 mm ovarian cortex fragments were transplanted on day 7 and then harvested on day 14 after pump placement. All explanted fragments were flash-frozen for PCR analyses, which were executed in triplicates. We utilized real-time PCR analyses, which were executed in triplicates. We utilized real-time RT-PCR to determine mRNA levels for AMH, BRCA1 and BRCA2 in ovarian cortex tissue. We used Mann-Whitney U test to compare the placebo vs. the AMH-pump groups with a p<0.05 significance.

RESULTS: In mice treated with rAMH, AMH, AMH-R2 and BRCA1 expression was lower in rAMH mice than in controls, while BRCA2 expression was not significantly affected (27.2). Number of degraded oocytes was 29.1% (p<0.05) and 19.3% (p<0.01) (group 2 and 4) versus 34.3% (control). The IVF experiments to establish numbers of fertilized eggs and developed embryos showed that, despite the treated groups had a minor percentage of 2-cells embryos versus control group, the major part of them reach the blastocyst stage (86% versus 60%).

CONCLUSIONS: These results support the evidence that carnitines and micronutrients are important for embryos development and may have some beneficial effect in both genesis and ovulation process. This study shows the wider implications and effects of critical nutrients on ovulation and in particular on oocyte quality which could determine fertilization potential. Further experiments are ongoing to examine the ability of the oocytes to be fertilized and gene expression after metabolic and nutrient treatment and to measure further parameters of ovum quality such as ability to be fertilized, chromosomal stability (aneuploidy) embryo development and pregnancy success.

Supported by: NIH U54HD068157
Telomeropathies, such as Dyskeratosis Congenita, provide a natural experiment to test the Telomere Theory of Reproductive Aging in women. This study attempts to extensively characterize the reproductive function in women with telomeropathies for the first time.

**DESIGN:** Blood samples, cumulus cells, and arrested embryos were collected following the cycle of A 30 year old woman with a precocious aging syndrome and aplastic anemia, attributed to a telomeropathy (AMH=0.3 and AFC=8). She underwent, controlled ovarian stimulation with E2 prime protocol and 600 IU/day of gonadotropin, using mixed protocol and GnRH antagonist for 18 days.

**MATERIALS AND METHODS:** Monochrome multiplex quantitative polymerase chain reaction (qPCR) assay (Cawthon 2009) measured telomere length in leukocytes extracted from whole blood as well as, cumulus cells stripped from retrieved follicles. Telomere (T) amplification was normalized to a single copy gene (S), resulting in a T/S ratio proportional to average telomere length in the population. Single-Cell Amplification of Telomere Repeats (SCATR) PCR (Wang 2013) was used to measure telomere length in discarded embryo blastomeres. Telomere (T) amplification was normalized a reference gene (R), producing a T/R ratio . One-Way ANOVA test was used to determine statistical significance.

**RESULTS:** Hyperstimulation resulted in only 7 oocytes and 1 euploid blastocyst. Over the treatment course, leukocyte telomere length increased from T/S ratio = 0.192±0.157 to 0.234±0.0306 and there was a statistically significant (p = .0256) linear increase during the treatment. Further, telomere length in a retrieved parthenogenetic, 2-cell embryo was (T/R average = 169±47) and that in cumulus cells (T/S = 0.586±0.147). Telomere lengths in all assayed cell types were shorter than those from age matched controls.

**CONCLUSIONS:** Young woman with reduced ovarian reserve, poor response to ovarian stimulation and a high percentage of arrested embryos and aneploid embryos was still able to generate one euploid blastocyst with high dose controlled ovarian stimulation, demonstrating the promise of ART for fertility preservation in women with telomeropathies. Intriguingly, controlled ovarian hyperstimulation increased her leukocyte telomere length. Presumably, the supraphysiologic levels of estrogen activated telomerase activity, consistent with prior studies reporting an estrogen response element in the TERT gene. Future studies should examine whether women with telomeropathies may benefit from estrogen supplementation.

**References:**

**Supported by:** Stanley Kaplan Research Endowment, NYU Langone Medical Center.

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**OVARIAN RESERVE**

**P-40 Tuesday, October 18, 2016**

**INCREASED TISSUE OMEGA-3 TO OMEGA-6 FATTY ACID RATIO RESULTS IN IMPROVED MARKERS OF OVARIAN RESERVE AND ALTERED SYSTEMIC CYTOKINES.** M. E. Skaznik-Wiktel, a D. C. Swindle, a T. K. Soderborg, a J. E. Friedman, b A. J. Polotsky, cDepartment of OB/GYN, University of Colorado School of Medicine, Aurora, CO; Department of Pediatrics, University of Colorado School of Medicine, Aurora, CO.

**OBJECTIVE:** Omega-3 fatty acid (FA) supplementation is often used as a strategy to improve oocyte quality but the mechanisms are not well understood. We hypothesized that anti-inflammatory action plays a role. The objective was to determine if transgenic increase in tissue omega-3/omega-6 FA ratio results in improved ovarian reserve in female mice.

**DESIGN:** Prospective laboratory animal study.

**MATERIALS AND METHODS:** We used Fat-1 transgenic mouse model which is capable of endogenously converting omega-6 to omega-3 FA. The Fat-1 mice have an increased tissue levels of omega-3 FA without any change in dietary omega-3 or omega-6 FA intake, which promotes an “anti-inflammatory state.” In our experiment wild-type (WT) and Fat-1 C57BL/6J female mice were maintained on chow diet and sacrificed at 15 weeks of age. Ovaries were collected for assessment of resting (primordial) and growing (primary, secondary, antral) follicles and serum was collected for anti-mullerian hormone (AMH) and cytokine levels (pro-inflammatory and anti-inflammatory). Body weight was recorded and percentage of body fat was measured at the time of ovary collection by quantitative magnetic resonance (qMRI). Statistical significance was determined using Student t-test.

**RESULTS:** The mean body weight (20.9 ± 1.3g vs 21.4 ± 0.9g) and percentage of body fat (12.1 ± 0.9% vs 11.3 ± 1.6%) were similar between Fat-1 and WT mice (p = 0.77; p = 0.73). More primordial and primary follicles were observed among Fat-1 mice than in WT animals. The numbers were 24/9 ± 239 vs 141 ± 136, p = 0.009 (primordial follicles) and 473 ± 42 vs 296 ± 58; p = 0.05 (primary follicles) in Fat-1 and WT animals, respectively. Secondary and astral follicle numbers were similar between the two groups. Significantly higher AMH levels were observed in Fat-1 mice (51.2 ± 11.9 ng/ml) than in WT animals (17.9 ± 3.5 ng/ml; p = 0.03), consistent with increased number of small growing follicles in the Fat-1 group. Fat-1 mice had lower serum level of IL-8 (pro-inflammatory cytokine) and higher level of G-CSF (anti-inflammatory cytokine). The levels of other cytokines were similar between the groups.

**CONCLUSIONS:** Increase in tissue level of omega-3/omega-6 FA ratio results in better ovarian reserve, as demonstrated by increased primordial and primary follicle numbers, and a higher AMH level. Altered levels of some pro-inflammatory and anti-inflammatory cytokines may mediate this effect.

**References:**

**Supported by:** NIH ST32HD04135-13A National Training Program in Reproductive Medicine and ABOG/AAGOF Grant to M.S.W.

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**P-41 Tuesday, October 18, 2016**

**EVALUATION OF THE PERFORMANCE OF THE NEW AMH ASSAY AND ITS PRINCIPAL APPLICATIONS.** K. Lukaszuk, a,b J. Zabierska, a,b G. Kloss, a I. Malinowska, a G. Jakiel, a,c A. Lukaszuk, a,b “INVICTA Fertility and Reproductive Center, Gdansk, Poland;” Department of Obstetrics and Gynecological Nursing, Faculty of Health Sciences, Medical University of Gdansk, Gdansk, Poland; “Department of Obstetrics and Gynecology, Center of Postgraduate Education, Warsaw, Poland.

**OBJECTIVE:** To compare performance of the new automated antimullerian hormone (AMH) assay - VIDAS AMH (bioMérieux) by ELFA (Enzyme Linked Fluorescent Assay) to the existing automated Elecsys AMH (Roche) by ECLIA (Electrochemiluminescence assay).

**DESIGN:** Prospective assay evaluation was conducted at the Invicta Fertility and Reproductive Centre.

**MATERIALS AND METHODS:** 48 serum samples of patients beginning their in vitro fertilization treatment in April and May 2016 were analyzed to determine AMH level by both VIDAS AMH and Elecsys AMH assay. Statistical analysis was performed, after exclusion of three oulying values, using MedCalc 12.1.40.

**RESULTS:** We obtained very similar results for both methods with medians: VIDAS = 2.610 ng/ml with 95% CI =1.3437 to 3.4870 and
AFC was strongly correlated with AMH levels obtained with the 3 assays—a phenomenon that tended to be improved in the low AFC group. Furthermore, AMH; 4.3% between AMH Gen II and Elecsys AMH; and 2.8% between interval in Bland-Altman plots (4.7% between AMH Gen II and Access AMH) limited amount of AMH values situated outside the Access AMH (-16%) and Elecsys AMH (-20%) than with AMH Gen II. The regression.

P-43 Tuesday, October 18, 2016

APOTOPSIS OF GRANULOSA CELLS AND CLINICAL OUTCOMES BETWEEN NORMAL AND POOR OVARIAN RESERVE PATIENTS UNDERGOING IVF/ICSI. Y. Fan, L. Wei, Y. Shi, J. Chen, X. Liang. Reproductive Medical Center, The Sixth Affiliated Hospital of Sun Yat-sen University, Guangzhou, China.

OBJECTIVE: To investigate apoptosis of granulosa cells and clinical outcomes in patients undergoing in-vitro fertilization (IVF)/intracytoplasmic sperm injection (ICSI).

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: A total of 78 women undergoing IVF/ICSI cycle, were divided into three groups according to their age and antral follicle count (AFC) before controlled ovarian hyperstimulation (COH). 58 women under 35 years old with normal ovarian reserve, AFC<6, were in group A; while 9 women under 35 years old with poor ovarian reserve, AFC 6 were in group B; and 11 over 37 years old, AFC 6 were in group C. All patients were followed prospectively and their cycle outcomes recorded. Serum AMH levels were detected before controlled ovarian hyperstimulation (COH). Follicular fluid (FF) samples were obtained from mature follicles during oocyte retrieval for IVF/ICSI. FF AMH and serum AMH levels were measured with the same automated AMH assay (Roche, Elecsys). Estrodiol (E2), progesterone (P), testosterone (T) concentrations in FF were also measured by automated electrochemiluminescence immunoassay (Roche, Elecsys). Granulosa cells were isolated from follicular fluid after oocyte retrieval. Apoptosis of granulosa cells was assessed with Annexin V-FITC/PI double staining by flow cytometry.

RESULTS: Significant differences were presented between group A and C, A and B regarding age, abortion times, BMI, serum AMH level, number of retrieved oocytes and top quality embryos (p<0.05). Group C was associated with higher percentage of early apoptotic events (annexin V+, PI-) and late apoptotic events (annexin V+, PI+) in granulosa cells when compared with group A and group B respectively (p<0.05). While there were no significant differences between group A and B (p=0.05) in apoptosis of granulosa cells.

CONCLUSIONS: This study suggests that women aged>37 with poor ovarian reserve were associated with higher apoptosis of granulosa cells in FF. And the FF P levels show a lower tendency in poor ovarian reserve patients. However, poor ovarian reserve women under 35, though not as good as the normal reserve women, may have lower granulosa cells apoptosis than those aged>37 with poor reserve.

Supported by: This study was supported by the National Natural Science Foundation of China (NSFC). (No. 81471507).

OBJECTIVE: Unlike the infertility setting, many women who present for elective oocyte freezing cycles are taking long-term (>1 year) combined hormonal contraceptives (OCP). Based on the hypothesis that long-term OCP use may cause ovarian suppression, we routinely recommend a break from OCP use prior to ovarian stimulation in women with low Antral Follicle Count (AFC).

DESIGN: Case-control.

MATERIALS AND METHODS: Women who presented for elective oocyte cryopreservation between 2012 and 2015 with an initial AFC in the lowest 25th percentile, adjusted for age, were included in the study. Those with a low AFC who were taking OCP at the time of initial egg cryopreservation evaluation were asked to take a break from OCP use prior to ovarian stimulation. We compared cases who took a break from OCP prior to ovarian stimulation (OCP Break) to controls who were not on OCPs prior to ovarian stimulation (No OCPs). Each OCP Break patient had a minimum of two AFC measurements. Among OCP Break, ovarian stimulation was initiated with a significant AFC rise or after the 3rd measurement if there was a plateau. Every patient underwent antagonist IVF cycle and egg retrieval. Paired t-tests, unpaired t-tests, and linear models were used as appropriate.

RESULTS: 96 women presented for elective egg cryopreservation and had an age-adjusted AFC < 25th percentile on their intake ultrasound. Average age was 35.7 +/- 3.5 years. 31 women (32%) were on OCP and were advised to take an OCP break for an average of 4 months (range 1 to 11 months). 65 women who had not taken OCP and had an AFC < 25th percentile were used as a control. Average initial AFC was similar between the OCP break and No OCP groups (6.2 vs. 6.6, p=0.47). After the OCP break, AFC increased significantly (initial AFC 6.2 vs post-break AFC 12.4, p<0.0001). Final oocyte yield was 50% higher in the OCP break group (9.5 vs 14.7, p=0.003). The difference in oocyte yield among cases and controls remained significant after adjustment for age.

Antral Follicle Count and Oocyte Yield Among Cases and Controls

<table>
<thead>
<tr>
<th>OCP Pre-stimulation</th>
<th>Oocyte yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>AFC (months)</td>
<td></td>
</tr>
<tr>
<td>No OCPs (controls)</td>
<td>6.6 +/- 2.5</td>
</tr>
<tr>
<td></td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>6.6 +/- 2.5</td>
</tr>
<tr>
<td></td>
<td>9.5 +/- 6.2</td>
</tr>
<tr>
<td>OCP Break (cases)</td>
<td>6.2 +/- 3.1</td>
</tr>
<tr>
<td></td>
<td>4 +/- 2.5</td>
</tr>
<tr>
<td></td>
<td>12.4 +/- 6.7</td>
</tr>
<tr>
<td></td>
<td>14.7 +/- 9.4</td>
</tr>
<tr>
<td>P-value</td>
<td>0.47</td>
</tr>
<tr>
<td>AFC</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>0.003</td>
</tr>
</tbody>
</table>

CONCLUSIONS: AFC may not retain its accuracy for predicting ovarian reserve in women using long-term OCP. Women with a lower-than-expected AFC who are taking OCP may have at least a 50% improvement in oocyte yield if a break from OCP is undertaken prior to ovarian stimulation.

P-45 Tuesday, October 18, 2016

LOW ANTI-MÜLLERIAN HORMONE (AMH) IS A BETTER PREDICTOR OF RESPONSE TO CONTROLLED OVARIAN HYPERSTIMULATION (COH) THAN ANTRAL FOLLICLE COUNT (AFC) IN WOMEN WITH DISCORDANT MARKERS OF OVARIAN RESERVE. V. Menasha, R. Alvero, Y. Zhang, Y. Huang, S. Wang, OB GYN/Division of Reproductive Endocrinology and Infertility, Women & Infants Hospital, Providence, RI; 3Biostatistics, School of Public Health, Brown University, Providence, RI.

OBJECTIVE: To assess the prognostic value of AMH by determining: 1) whether AMH is a predictor of clinical pregnancy outcome, 2) if a threshold exists for successful clinical pregnancy, and 3) whether low AMH is predictive of clinical pregnancy likelihood in young patients.

DESIGN: Retrospective analysis.

MATERIALS AND METHODS: Retrospective chart review of 448 IVF cycles at an academic center. IRB approval was obtained prior to study initiation. AMH values of women undergoing IVF from January 1st 2014 to March 18th 2016 were evaluated. All AMHs were performed at our hospital lab with the Ansh Labs Ultra-Sensitive AMH assay. Patients without AMH or whose AMH was obtained at an outside lab were excluded. Clinical pregnancy was defined as presence of fetal cardiac activity on ultrasound between 6-9 weeks gestation. Statistical modeling was performed using R programming to generate area-under-curve (AUC) ROC and spline curves to determine the association of AMH with clinical pregnancy outcome. Positive predictive values (PPV) and negative predictive values (NPV) were calculated at fixed AMH intervals to determine the AMH cutoff value for optimal PPV and NPV. Patients were then stratified by age into <35 and ≥35 to further examine the role of AMH in predicting pregnancy outcomes.

RESULTS: AMH is a significant predictor of clinical pregnancy probability across all age groups (AUC=0.656), for women <35 (AUC=0.57), and for women ≥35 (AUC=0.648). When assessed among all women, an AMH of 2.1 ng/mL or higher confers an approximately 41% PPV of clinical pregnancy. Above an AMH of 2.1 ng/mL, no significant increase in PPV is seen. When AMH is stratified among young women <35, values as low as 0.7 ng/mL confer a PPV of 44.6% for clinical pregnancy, however, values above 2.1 ng/mL do not significantly increase the PPV. Among older women ≥35, higher AMH values are associated with slightly increased clinical pregnancy probability, with the highest PPV reaching 36.4% at an AMH of 2.5 ng/mL.

CONCLUSIONS: We propose that among all reproductive age patients, an AMH of 2.1 ng/mL should be considered a cutoff value in predicting clinical pregnancy likelihood. For women ≥35, AMH is a positive predictor of clinical pregnancy until AMH equals 2.5 ng/mL; beyond this AMH value, the PPV does not improve. In young women <35, AMH as low as 0.7 ng/mL offers high PPV for clinical pregnancy. Thus our results suggest that the PPV for clinical pregnancy is higher in young women with low AMH compared to older women with the same or higher AMH.

References:
AFC, and NOR. Women were further categorized by whether or not they had discordance between AMH and AFC. Discordance was defined by having a two or more quintile difference between AMH and AFC. We looked at two groups with discordance—one group with women who had higher AFC than AMH, the other women with higher AMH than AFC. Spearman’s correlation co-efficient was calculated for AMH, AFC and NOR in each group. Receiver operator characteristic curves were also created to determine the ability of AMH and AFC to predict high oocyte yield (HOY) (defined as having oocytes in the highest quintile, 20 oocytes in this cohort). We also applied these methods to women with obesity and discordance as obesity is known to negatively impact AMH values as well as response to COH.

RESULTS: 65 women had discordant markers of ovarian reserve—33 with higher AFC than AMH by quintile, and 32 with higher AMH than AFC. Among the women with higher AFC, Spearman’s correlation coefficient for NOR with AMH and with AFC was 0.49 and 0.36 respectively (p less than 0.05). For women with higher AMH, the values were 0.52 and 0.47 (p less than 0.05). Investigating AMH and AFC as predictors of HOY ROC curves showed that neither AMH nor AFC were sensitive or specific markers for HOY among women with high AMH levels whereas AMH was a sensitive and specific predictor of HOY in women with high AFC values (area under the curve 0.81, 95% CI: 0.653-0.973, p=0.012). An AMH value of 2.02 was both sensitive (86%) and specific (91%) for hyperresponse among these women.

CONCLUSIONS: For women with discordant AMH and AFC values, AMH correlated better with NOR than AFC, regardless of whether the AFC or AMH was higher. For women with discordance and high AFC values, an AMH of 2 or more was sensitive and specific for predicting hyperresponse. Thus, if a patient has discordance between AMH and AFC, AMH correlates better with NOR. AMH above 2 is associated with a high response in women with high AFC but lower AMH values.

P-47 Tuesday, October 18, 2016

DO DIMINISHED OVARIAN RESERVE MARKERS NECESSARILY REFLECT LOWER OOCYTE QUALITY IN YOUNG PATIENTS? THE EFFECT OF ANTRAL FOLLICLE COUNT. S. Behbehani, M. Padmanabhan, W. Buckett, Y. Son, Y. Hasson. McGill University, Montreal, QC, Canada; MUHC Reproductive Center, Montreal, QC, Canada.

OBJECTIVE: To compare clinical pregnancy rates of single blastocyst transfers in young patients (age ≤35) with low ovarian reserve markers (baseline antral follicle count (AFC) ≤7) and controls with normal ovarian reserve (baseline AFC of 10-15).

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Among 2160 fresh single blastocyst transfer cycles performed at our center between the years 2013-2015, 132 transfer cycles were in women with baseline AFC ≤7. Out of those, 54 were in patients who were 35 years or younger. The control group was selected from the same cohort, and included all patients who were 35 years or younger but with baseline AFC of 10-15 (n=127). Comparison between the study groups was performed by t-test and Chi-square tests where applicable.

RESULTS: Baseline characteristics of Body Mass Index and smoking rates were comparable between the groups. Patients with baseline AFC ≤7 were slightly older than controls (32.9 ± 2 vs 32.1 ± 2.4 years, p=0.02). As expected, these patients required significantly more days and higher dose of gonadotropins for stimulation (days: 10 ± 2.2 vs 8.9 ± 1.8, p=0.0003; E2 dose: 3551 ± 1580 IU vs 2097 ± 929 IU, p<0.01). They also had significantly less oocytes collected and less blastocysts available for transfer (8.2 ± 5.5 vs 10.4 ± 5.3, p=0.01; 2.3 ± 1.6 vs 2.9 ± 2.0, p=0.02, respectively). On the other hand, markers of oocyte quality were similar between the groups: fertilization rate (80±% vs 76±%, p=0.22), and rate of good quality embryos (defined as Gardner classification 3aa and above: 57.4% vs 66.9%, p=0.22). Clinical pregnancy rates (defined as the presence of fetal heart activity by ultrasound at 6-7 weeks of gestation) were similar (37% vs 44%, p=0.37). There was also no difference in the level of first beta HCG drawn 11 days after the transfer.

CONCLUSIONS: Young patients with low ovarian reserve markers, reflected by low AFC, who have an embryo transferred at a blastocyst stage, have similar clinical pregnancy rates as patients of similar age with normal AFC. This is despite lower numbers of collected oocytes and fewer available blastocysts to transfer. These results suggest that in young patients with low ovarian reserve markers, age may be a better predictor of pregnancy. Although the response to ovarian stimulation may be diminished, oocyte quality may not necessarily be compromised and these patients still have good quality embryos and reassuring pregnancy rates.

P-45 Tuesday, October 18, 2016

THE DEGREE OF COMPARABILITY OF TWO COMMERCIALLY AVAILABLE AMH IMMUNOASSAYS VARIES ACROSS CLINICAL POPULATIONS IN REPRODUCTIVE MEDICINE. H. Huddleston, M. P. Diamond, M. C. C. Sanders, N. Santoro, R. S. Legro, D. J. Haisenleder. University of California at San Francisco School of Medicine, San Francisco, CA; Augusta University, Augusta, GA; Reproductive Medicine Network, Bethesda, MD; Obstetrics, Gynecology and Reproductive Sciences, University of California, San Francisco, San Francisco, CA; Obstetrics and Gynecology, University of Colorado School of Medicine, Aurora, CO; Penn State University College of Medicine, Hershey, PA; Medicine, University of Virginia, Charlottesville, VA.

OBJECTIVE: AMH continues to be widely used in the clinical setting despite on-going controversy regarding assay performance and lack of studies demonstrating comparability of existing assay systems. Our objective was to compare the performance of two commercially available assays for serum anti-mullerian hormone (AMH) in two populations: unexplained infertility (UI) and polycystic ovary syndrome (PCOS).

DESIGN: Cross-sectional cohort study.

MATERIALS AND METHODS: A randomly determined subset of patients enrolled in the Reproductive Medicine Network (RMN) multi-center trials for UI (AMIGOS, n=245) and PCOS (PPCOS II, n=338) had AMH tested by two assay systems: Gen II (Beckman Coulter) and Ultrasensitive (Ansh Labs). Measurements exceeding the assay ranges (25 ng/ml for GenII and 20 ng/ml for Ansh were re-run in dilution). Linear regression analyses were performed.

RESULTS: The assays were strongly correlated with one another (GenII vs PPCOS II: r=0.8827, p=0.00001 and PPCOS II vs AMIGOS: r=0.9071, p=0.0001). However, systematic bias between the assays was detected: results for regression models describing the relationship between assays demonstrated statistically significant slope and constant terms (Table 1). Further, the regression equations for each population (AMIGOS or PPCOS II) differed from each other. This finding may relate to assay differences that occur at higher AMH measurements. Regression models of the difference in AMH levels between assays (y-x) compared to mean AMH (y+x) confirmed proportional bias (p<0.01), with Bland Altman plots demonstrating increasing variability between assays with increasing mean values.

CONCLUSIONS: The clinical use of AMH may have outpaced our understanding of how currently utilized assays perform relative to one another and in different clinical populations. Our findings suggest conversion equations between Ultrasensitive and Gen II vary between unexplained infertility and PCOS subjects, likely due to differences in assay performance at higher AMH levels. As a result, the application of a single regression equation across a heterogeneous population would be likely to yield inaccurate results.

Regression describing relationship of AMH results by GenII and Ultrasensitive Slope Constant p value (slope,constant)

<table>
<thead>
<tr>
<th>Trial</th>
<th>Slope</th>
<th>Constant</th>
<th>p value (slope,constant)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMIGOS</td>
<td>1.9</td>
<td>0.8</td>
<td>(&lt;0.0001,&lt;0.0001)</td>
</tr>
<tr>
<td>PPCOS II</td>
<td>1.4</td>
<td>0.8</td>
<td>(&lt;0.0001,&lt;0.0001)</td>
</tr>
</tbody>
</table>

FERTILITY PRESERVATION

P-49 Tuesday, October 18, 2016


OBJECTIVE: This study aims to examine the mechanism of ovarian follicle over-activation by cisplatin in the ovary and to look into the synergic effect of melatonin and ghrelin for preserving primordial follicle pool during chemotherapy.

DESIGN: Experimental study using animal model.

MATERIALS AND METHODS: Five-week-old female ICR mice were randomly divided to five groups (n=10). Melatonin, a scavenger of reactive oxygen species (ROS); 30 mg/kg, and ghrelin, a suppressor of follicle
RESULTS: The assessment of sections between Group1 and Group2, it was observed that Group1 had statistically high value according to the antral follicles counts(p<0.001). In the comparison between Group2 and Group3 in terms of both the secorder and antral follicles, Group 2 was ascertained statistically significant(p=0.018 ve p<0.001). There was observed high value and statistically significance in administrated of silymarin group(Group 4) compared with cyclophosphamide administrated group(Group 2) in regard to the antral follicles counts. AMH levels did not show any significant difference in any group(p>0.05). (Table I).

CONCLUSIONS: It is reported that cyclophosphamide is caused by antral follicles atresia through oxidative pathway. In our study, the same results were observed. No changes in hormone levels could be explained that AMH was produced from only growing follicles. Silymarin’s positive effect on antral follicles during follicular stimulations was reported. In our study, we observed that cyclophosphamide has toxic effects on antral follicles in the late phase of the ovulation and administration of silymarin is reduced its toxicity in terms of antral follicles.

Table I

<table>
<thead>
<tr>
<th>Group</th>
<th>Seconder follicles counts</th>
<th>Antral follicles counts</th>
<th>AMH (ng/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1(n=12)</td>
<td>28(23-58)</td>
<td>23(12-41)</td>
<td>3.84(2.18-11.92)</td>
</tr>
<tr>
<td>Group 2 (n=12)</td>
<td>23(9-41)</td>
<td>10(5-17)</td>
<td>4.91(1.24-5.58)</td>
</tr>
<tr>
<td>Group 3 (n=6)</td>
<td>39(27-44)</td>
<td>19(15-30)</td>
<td>7.39(3.03-25.78)</td>
</tr>
<tr>
<td>Group 4 (n=5)</td>
<td>32(22-34)</td>
<td>19(15-21)</td>
<td>6.03(3.66-10.53)</td>
</tr>
<tr>
<td>Group 5 (n=6)</td>
<td>38(28-50)</td>
<td>22(15-29)</td>
<td>5.64(0.25-78)</td>
</tr>
<tr>
<td>P value</td>
<td></td>
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<td>&lt;0.001</td>
</tr>
<tr>
<td>G1/G2</td>
<td></td>
<td></td>
<td>0.291</td>
</tr>
<tr>
<td>G2/G3</td>
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<td></td>
<td>0.329</td>
</tr>
<tr>
<td>G4/G5</td>
<td></td>
<td></td>
<td>0.234</td>
</tr>
<tr>
<td>G2/G4</td>
<td></td>
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<td>&lt;0.001</td>
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</tbody>
</table>

References:

P-51 Tuesday, October 18, 2016

POLYMORPHISM IN MTFR IN 677 C>T AND 1298 A>C IN PATERNAL SPERM DNA IS ASSOCIATED WITH INCREASED RISK OF RETINOBLASTOMA IN INDIAN CHILDREN. S. Bisht,a B. Chawla,b R. Dada. Laboratory for Molecular Reproduction and Genetics, All India Institute of Medical Sciences, New Delhi, India; AIIMS, New Delhi, India; Anatomay, Lab For Molecular Reproduction and Genetics, New Delhi, India.

OBJECTIVE: Retinoblastoma (RB) is the most common childhood intraocular malignancy and its incidences has increased by 30% in the past 5 years
which is believed to be due to the effect of environmental factors which cause oxidative stress and can induce methylation alterations. Oxidative DNA damage in the male germ line impairs global sperm DNA methylation which can have adverse clinical outcomes in the next progeny including neuropsychiatric disorders, imprinting disorders and childhood cancers including RB. Methylene tetrahydrofolate reductase (MTHFR) is a key folate-metabolizing enzyme which may affect directly or indirectly the quality of sperm. The present study was planned with an aim to analyse polymorphism in two essential MTHFR SNPs 677 C>T and 1298 A>C in fathers of children affected with RB.

DESIGN: A case control study of 60 fathers of children affected with RB and 60 fathers of healthy children. Semen sample was obtained from all the cases and controls.

MATERIALS AND METHODS: Polymorphism in two essential SNPs of MTHFR gene, i.e., 677 C>T and 1298 A>C was studied in sperm DNA via PCR-Restriction Fragment Length Polymorphism (RFLP) technique using site specific restriction enzyme HinI and MboII for MTHFR SNPs 677 C>T and 1298 A>C respectively. Study was initiated after ethical clearance and informed consent was obtained from cases and controls.

RESULTS: The mean ages of cases and controls were 33.17 ± 11.2yrs and 31.52 ± 4.54yrs respectively. For MTHFR C677T polymorphism, T allele frequency in RB fathers was 0.16% and in controls 0.082%. For MTHFR A1298C polymorphism, C allele frequency in RB fathers was 0.13% and in controls 0.098%. We found significant differences in the frequency of SNP at 677 (X2 = 2.29, 95% CI = 1.323-3.9658, p < 0.05) and SNP 1298 AC (X2 = 8.237, OR = 2.90, 95% CI = 1.2029-4.052, p < 0.05) between RB fathers and controls. None of the cases showed the mutant genotype TT and CC in SNP 677 C>T and 1298 A>C respectively.

CONCLUSIONS: The present results showed a significant association between polymorphism in MTHFR SNPs 677 C>T and 1298 A>C in paternal sperm DNA and increased risk of RB in Indian children. Therefore, we can conclude that oxidative stress affects epigenetic regulation involving methylation via MTHFR in the paternal sperm DNA which may have adverse clinical outcomes in the next progeny including childhood cancers.

P-52 Tuesday, October 18, 2016

EFFECTS OF ACREOLIN AND MESNA ON FERTILIZATION OF MOUSE OOCYTE. R. Jeehan, F. Sheeib, S. Khan, F. Qadri, R. Morris, H. M. Abu-Soud. REI, Wayne State University, Detroit, MI; OB/GYN-Physiology, Wayne State University/Medical School, Detroit, MI; OB/GYN, Wayne State University, Detroit, MI; OB/GYN, Wayne State University, Detroit, MI; REI, Wayne State University, Detroit, MI; Ob/Gyn, Wayne State University, Detroit, MI.

OBJECTIVE: Cyclophosphamide (CP) is a well-known chemotherapeutic agent used to treat many gynecological cancers as well as autoimmune disorders such as lupus and rheumatoid arthritis. CP is metabolized in the liver to give two stable toxic compound one of which is Acrolein, a highly electrophilic, α, β-unsaturated aldehyde, which ultimately collects and gets excreted through the bladder. Mesna (sodium-2-mercaptoethane sulfonate) is primarily used to prevent CP-induced toxicity by binding to CP. Previous studies have established that CP, its major metabolite: acrolein and mesna affect female fertility through deterioration of oocyte quality by generation of reactive oxygen species (ROS). However, the effects of mesna and acrolein on fertilization of these oocytes remain unknown.

DESIGN: A prospective study.

MATERIALS AND METHODS: We used metaphase II mouse oocytes with cumulus cells (n = 240), retrieved from 3week old super ovulated hybrid mice (B6C3F1). Acrolein (5 μM, 10 μM, and 25 μM) and mesna (5 μM, 10 μM, and 50 μM) were added and incubated for 45 minutes (time of maximum plasma peak drug levels). These oocytes were then inseminated in vitro with capacitated mouse sperm (one million sperm/ml) obtained by epididymal extraction from male mice (B6D2F1). A control group was used to compare after the same incubation time. Outcomes of oocyte fertilization, cleavage rate, and development to the morula and blastocyst stages were compared at 24, 48, 96, and 120 hours after insemination occurred.

RESULTS: Our results showed that after 24 hours post insemination, majority of the oocytes exposed to acrolein and mesna failed to fertilize. However, the cleavage rate 24 hours post-fertilization was not statistically significant in the two treatment groups as compared to the control. Embryo development rate at 48 hours was significantly lower in oocytes exposed to acrolein (~2.4%) and mesna (~4%) when compared to control (~38%). Of note, majority of the zygotes had fragmented and had large perivitelline space. After 96 hours post-insemination, the rates of expanded blastocysts were significantly lower in both treatment groups; acrolein (~2.8%) and mesna (~2.4 %) in comparison to controls (~47%), respectively. At the 120 hour mark same trend was observed as compared to controls. At this stage the arrested embryos were highly fragmented and atretic.

CONCLUSIONS: Acrolein and mesna alter the spindle structure and chromosomal alignment due to ROS overproduction. We now show that this can result in poor oocyte cleavage and blastocyst development rate resulting in poor fertilization rate. Combination of acrolein with mesna should be investigated to see if the same deterioration in oocyte quality and fertilization occurs.

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OBJECTIVE: The survival rates for pediatric and adolescent patients with various types of malignancies have dramatically improved with advances in chemotherapeutic treatments. In male cancer survivors, the restoration of fertility and achievement of pregnancy have become important concerns, however, at diagnosis, patients with such serious diseases are often not concerned with reproductive issues.

DESIGN: A retrospective study in a reproductive center.

MATERIALS AND METHODS: We evaluated sperm retrieval survival rate (SRR) of microdissection TESE (micro TESE), two pronuclei (2PN) oocyte rates, blastocyst development rates, good-quality blastocyst (Grade 3BB and above on day 5 by the Gardner scoring rates), and clinical pregnancy rates per embryo transfer (ET) in 32 cases with post chemotherapy NOA patients (including 6 patients with bone marrow transplantation (BMT)). 254 cases without past history (unexplained NOA; not including after orchidectomy, Klinefelter syndrome, cryptozoospermia, mumps orchitis, etc), and 18 cases with obstructive azospermia (OA) between September 2013 and February 2016. The cancer types included testicular cancer, colon cancer, Hodgkin’s lymphoma, non-Hodgkin’s lymphoma, leukemia, neuroblastoma, and osteosarcoma. The age at micro TESE and chemotherapy was 34.2 ± 5.1 and 16.2 ± 9.1 years, respectively, and the wives age at ICSI was 34.1 ± 4.8 years.

RESULTS: SRR of micro TESE in post chemotherapy NOA (15/ 32=46.9%) was higher than unexplained NOA (73/254=28.7%) patients (P < 0.05). In sperm retrieved post chemotherapy NOA, age at chemotherapy end was older (21.9 ± 8.0 years) than failure group (11.2 ± 7.0 years) (P < 0.01). With respect of type of cancer, there was no predictor for SRR and no significant differences in the pregnancy and live birth rates. Two of 6 post BMT patients were retrieved spermatozooa. 2PN oocytes, blastocysts development, and good-quality blastocysts rates were 66.5%, 30.0%, and 48.4% in unexplained NOA, 61.0%, 46.5%, and 41.6% in unexplained NOA, and 67.1%, 40.8%, and 42.5% in OA. Post chemotherapy NOA showed higher clinical pregnancy rates per ET (50.0% : 11/22) than unexplained NOA (26.2% : 37/141) (P < 0.01). 5 children have been born and 5 patients are on going pregnancy for post chemotherapy NOA couples.

CONCLUSIONS: The recent success of micro TESE combined with ICSI for patients with NOA indicates that assisted reproductive technologies offer a potential new treatment option for affected couples and so that this procedure provides hope for men of reproductive age who have not undergone sperm cryopreservation before chemotherapy.

P-54 Tuesday, October 18, 2016

CANCER DIAGNOSIS IS ASSOCIATED WITH EQUIVALENT OVARIAN RESERVE, RESPONSE TO OVARIAN STIMULATION AND FERTILITY PRESERVATION OUTCOME WHEN COMPARED TO ELECTIVE OOCYTE CRYOPRESERVATION. M. Quinn, H. Cakmak, J. Letourneau, M. Cedaris, M. Rosen. Department of Obstetrics, Gynecology and Reproductive Sciences, University of California, San Francisco, San Francisco, CA.

OBJECTIVE: Prior studies have reported poorer outcomes for cancer patients undergoing ovarian stimulation for fertility preservation; however, these studies have been limited by small sample size and a dissimilar control population of patients drawn from an infertility practice. We aim to determine whether cancer patients undergoing fertility preservation have
decreased ovarian reserve, response to stimulation or fertility preservation outcome when compared to patients undergoing elective oocyte cryopreservation.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Between January 2009-February 2016, 244 patients with recent cancer diagnosis and no history of infertility and 362 women desiring elective fertility preservation underwent controlled ovarian stimulation with an antagonist protocol for oocyte or embryo cryopreservation. Only first ovarian stimulation cycles were included. These groups were compared with respect to baseline ovarian reserve, ovarian stimulation parameters and outcomes. Statistical comparison between groups was performed by Wilcoxon rank-sum testing of differences in outcomes stratified by age group. Statistical significance was defined as p<0.05.

RESULTS: Cancer patients were younger than patients undergoing elective fertility preservation (34.0±5.4 vs 36.4±3.0 p<0.001). Duration of stimulation and average gonadotropin dose were increased in cancer compared to elective fertility preservation patients (10.1±1.9 vs 9.7±1.6 days p=0.002 and 234.8±75.9 vs 210.4±76.7 IU p<0.001). Maximum serum estradiol (E2) was decreased in cancer patients (1367±1228 vs 2853±1897 p<0.001). In an age-stratified comparison of patients with cancer and those undergoing elective oocyte cryopreservation, there was no systematic difference in baseline ovarian reserve (antral follicle count, AFC), response to stimulation (follicles ≥13mm/AFC) or oocyte yield (total number of oocytes retrieved/AFC). Among cancer patients who underwent embryo cryopreservation (n=297), mean fertilization rate (2PN/MII) was 0.80±0.19.

CONCLUSIONS: In this large cohort of patients, cancer diagnosis is not associated with a decrease in ovarian reserve, response to stimulation or oocyte yield when compared to an appropriate control population.

P-55 Tuesday, October 18, 2016

TITRATION OF LETROZOLE TO MAINTAIN LOW ESTRADIOL (E2) LEVELS DURING FERTILITY PRESERVATION CYCLES FOR ESTROGEN RECEPTOR POSITIVE (ER+) BREAST CANCER PATIENTS DOES NOT IMPACT OVARIAN RESPONSE OR MATURE OOCYTE YIELD. M. Quinn, H. Cakmak, J. Letourneau, M. Cedars, M. Rosen. Department of Obstetrics, Gynecology and Reproductive Sciences, University of California, San Francisco, San Francisco, CA.

OBJECTIVE: Supraphysiologic E2 levels as a result of ovarian stimulation may promote the growth of estrogen-sensitive tumors. Therefore, use of aromatase inhibitors is recommended to keep E2 levels low in patients with estrogen-sensitive cancers undergoing fertility preservation. In this study, we aimed to determine whether letrozole titration in ER+ breast cancer patients affected cycle outcome by comparison with ER- breast cancer patients undergoing fertility preservation without letrozole.

DESIGN: Retrospective cohort analysis.

<table>
<thead>
<tr>
<th>Maximum dose letrozole</th>
<th>None (n=33)</th>
<th>5mg (n=50)</th>
<th>7.5mg (n=34)</th>
<th>10mg (n=40)</th>
<th>12.5mg (n=10)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>34.8±4.8</td>
<td>35.5±4.2</td>
<td>34.6±4.8</td>
<td>34.9±5.3</td>
<td>33.3±4.4</td>
<td>0.70</td>
</tr>
<tr>
<td>AFC</td>
<td>13.4±8.8</td>
<td>12.8±7.5</td>
<td>18.4±9.9</td>
<td>17.6±13.2</td>
<td>20.0±10.1</td>
<td>0.02</td>
</tr>
<tr>
<td>Days of stimulation</td>
<td>10±1.7</td>
<td>10.1±1.9</td>
<td>10.2±1.7</td>
<td>10.4±1.7</td>
<td>10.5±1.5</td>
<td>0.93</td>
</tr>
<tr>
<td>Total dose gonadotropin (IU)</td>
<td>2639±731</td>
<td>2662±833</td>
<td>2411±1012</td>
<td>2387±888</td>
<td>2104±1041</td>
<td>0.31</td>
</tr>
<tr>
<td>Maximum serum E2 (ng/mL)</td>
<td>2023±1554</td>
<td>491±436</td>
<td>738±511</td>
<td>976±793</td>
<td>1088±292</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Oocytes retrieved/AFC</td>
<td>1.4±1.03</td>
<td>1.1±0.71</td>
<td>1.3±0.70</td>
<td>1.6±0.87</td>
<td>1.7±0.83</td>
<td>0.05</td>
</tr>
<tr>
<td>MII/total oocytes</td>
<td>0.7±0.2</td>
<td>0.7±0.2</td>
<td>0.7±0.2</td>
<td>0.7±0.1</td>
<td>0.7±0.1</td>
<td>0.83</td>
</tr>
<tr>
<td>MII/fover≥13mm</td>
<td>0.95±0.3</td>
<td>0.95±0.3</td>
<td>0.93±0.4</td>
<td>0.99±0.4</td>
<td>0.99±0.5</td>
<td>0.97</td>
</tr>
<tr>
<td>Fertil rate after ICSI (2PN/MII)</td>
<td>0.8±0.2</td>
<td>0.7±0.3</td>
<td>0.8±0.2</td>
<td>0.8±0.2</td>
<td>0.8±0.2</td>
<td>0.24</td>
</tr>
</tbody>
</table>

Mean±SD, *p<0.05

MATERIALS AND METHODS: Between January 2009-February 2016, 134 ER+ and 33 ER- breast cancer patients underwent controlled ovarian stimulation with antagonist protocol for oocyte/embryo cryopreservation. All ER+ breast cancer patients received letrozole during ovarian stimulation at a starting dose of 5mg/day, which was titrated by 2.5mg up to 12.5mg to keep E2 levels <500 pg/mL. In contrast, ER- breast cancer patients did not receive letrozole. These groups were compared with respect to ovarian stimulation parameters and outcomes. Statistical comparison between groups was performed with ANOVA and p<0.05 was accepted as significant.

RESULTS: Patients with a higher maximum dose of letrozole had a higher antral follicle count (AFC) and maximum serum E2, in addition to a trend towards higher oocyte yield (total oocytes retrieved/AFC). On comparison of patients who reached maximum daily dose of 5, 7.5, 10 or 12.5 mg letrozole with ER- breast cancer patients, there was no significant difference in days of ovarian stimulation, total dose gonadotropins, maturity rate (MII/total oocytes), mature oocyte yield (MII/fover≥13mm), or fertilization rate.

Peak E2 reached >250 pg/mL in 75% of subjects with AFC<10 and 93% of subjects with AFC≥10.

CONCLUSIONS: Uptitration of letrozole does not have a negative impact on cycle outcome or oocyte maturity.

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REPRODUCTIVE OUTCOME OF 128 PGD CYCLES FOR BREAST CANCER. S. Rechitsky,1 L. P. Shulman,1 T. Pakhalchuk,2 M. Prokhorovich,3 G. San Ramon,1 A. Kuliev.4 1Preimplantation Molecular Genetics, Reproductive Genetic Innovations, Northbrook, IL; 2Division of Obstetrics and Gynecology-Clinical Genetics, Northwestern University: Feinberg School of Medicine, Chicago, IL; 3Reproductive Genetic Innovations, Northbrook, IL.

OBJECTIVE: Thousands of PGD cycles have now been performed for single gene disorders (SGD), with PGD presently offered for some indications that have never been practiced in prenatal diagnosis, such as late onset diseases with genetic predisposition, and preimplantation HLA typing. We present here our PGD experience for breast cancer, determined by BRCA1 and BRCA2 mutations, as part of our overall PGD series of 4501 cycles for PGD, which is the world’s largest PGD experience. Similar to other common conditions with genetic predisposition, breast cancer is important candidate for PGD, as couples with BRCA1 and BRCA2 mutations have a high risk of producing an offspring with predisposition to breast and/or ovarian cancer, so the objective of this work was to investigate the acceptance of the procedure and reproductive outcome of PGD for BRCA1 and BRCA2.

DESIGN: Retrospective Study.

MATERIALS AND METHODS: Our experience of PGD for breast cancer includes 128 PGD cycles performed for 66 couples at risk for producing offspring with predisposition to breast cancer. PGD was performed either
by blastomere or blastocyst sampling, followed by nested PCR, involving mutation and linked marker analysis. This included the analysis for 42 BRCAl (29 of maternal and 14 of paternal origin), and 22 BRC2 mutations (18 of maternal and 4 of paternal origin). The most prevalent mutations involved were: BRCAl - 187 del AG (25 of 42 BRC1 mutations tested), and BRC2 - 6174 del 1T (12 of 22 BRC2 mutations tested). Concomitant aneuploidy testing was performed in 77 of 128 PGD cycles for couples of advance reproductive age, of which 43 cycle were tested by PCR and 34 by array- CGH or next generation sequencing (NGS).

RESULTS: Of a total of 993 embryos tested at the cleavage or blastocyst stage (562 and 431 respectively), 441 free of BRC1 and BRC2 mutations were detected, of which 117 were pre-selected for transfer in 70 cycles (1.6 embryos per transfer on the average), resulting in 39 (56%) clinical pregnancies and birth of 47 children without mutations predisposing to breast cancer. Despite the fact that only 34% of embryos tested by concomitant 24-aneuploidy mutation analysis were available for transfer, as high as 80% pregnancy rate was observed, with corresponding overall reduction of spontaneous abortions rated (SA) to as low as 7.6%, with no SA observed in cycles with 24- chromosome aneuploidy testing.

CONCLUSIONS: The results support a practical value of PGD for breast cancer, which allows these couples to avoid inheritance of the predisposing genes mutations predisposing to breast cancer. Concomitant 24-chromosome aneuploidy testing resulted in significant improvement of reproductive outcome of these cycles, with extremely high pregnancy and reduction of spontaneous abortion rates.

P-57 Tuesday, October 18, 2016

UMBILICAL CORD BLOOD MESENCHYMAL STEM CELLS AS AN INFERTILITY TREATMENT FOR CHEMOTHERAPY INDUCED PREMATURE OVARIAN FAILURE. S. A. Mohamed, a,b S. M. Shalaby, c,b S. Brakta, c L. Stone, c M. Ellakany, c A. Al-Hendy, d Obgyn, Mansoura Medical School, Mansoura, Egypt; dObgyn, Augusta Medical Center, Augusta, GA; cPharma, Tanta Medical School, Tanta, Egypt; Obgyn, Augusta Medical School, Augusta, GA.

OBJECTIVE: To assess the efficacy of Umbilical cord blood mesenchymal stem cells (UCMSCs) ability to to restore fertility in an animal model for chemotherapy-induced premature ovarian failure (POF)

DESIGN: Preclinical murine case versus vehicle control randomized study MATERIALS AND METHODS: Acclimatized 4-6 weeks old female C57BL/6 mice (N=6/group) were randomly assigned to a vehicle treated control group (group 1), a sham chemotherapy group (group 2), or a cell therapy group (group 3). Group 2 & 3 received a single intraperitoneal injection of 70 mg/kg Cyclophosamide and 12 mg/kg Busulfan to induce ovarian failure. Seven days post injection, mice in groups 1 and 2 were subjected to bilateral ovariectomy. Female mice received 10 ul of UCMSCs suspension directly into the oviduct. After seven days, mice were allowed to mate with males at a ratio of 2 females: 1 male. Fruitful mating was determined by the presence of sperm plugs in the vaginal os of females. All pups were gathered, counted and examined closely for weight as well as any evident congenital anomalies or dysmorphism.

RESULTS: All mice in groups 1 and 3 became pregnant at least once, demonstrating a mating rate of 100%, while the mating rate in group 2 was 25% during the three-month breeding test period. Mice in group 2 had only one pregnancy resulting in the live birth of 2 pups within the 3 months test period, while mice in group 3 had a total of 10 pregnancies during the same period resulting in live birth of 26 pups. Mice within group 1, 2 and 3 exhibited no significant difference regarding the days to get pregnant (latency period). Importantly , UCMSCs treatment (group3) mating levels were markedly higher than those in group 2 but lower than those of group 1 (healthy controls). All pups in group 3 appeared physically normal with no visible malformations in comparison to group 1 pups, however; the 2 pups observed in group 2 suffered decreased total body weight

CONCLUSIONS: UCMSCs might present a viable therapeutic option to restore fertility in cancer survivor women affected by chemotherapy-induced POF and provide them hope to have their own biological children

Supported by: This work was supported in part by Dr Allhendy Augusta University Startup package and the core lab, which is supported by the Emagine Kennedy Shriver NICHD/NIH (SCCPIR) Grant U54-HD28934.

P-58 Tuesday, October 18, 2016

IMPACT OF CHEMOTHERAPY ON ANDROGEN AND FOLLICULAR MEASURES OF OVARIAN RESERVE IN FEMALE CANCER SURVIVORS. K. Cameron, a M. D. Sammel, a M. M. Prewitt, a M. E. Lynch, c Gracia. a University of Pennsylvania, Philadelphia, PA; bBiostatistics and Epidemiology, Univ. of Pennsylvania, Perelman School of Medicine, Philadelphia, PA; cObstetrics and Gynecology, University of Pennsylvania School of Medicine, Philadelphia, PA; dUniversity of Pennsylvania School of Medicine, Ardmore, PA.

OBJECTIVE: Future fertility is an important concern for many cancer survivors. Androgen production is necessary for the development of competent follicles and for long term sexual health and well-being. However, the effects of chemotherapy on androgen production have not been examined. This study sought to identify factors associated with circulating androgen levels during and immediately after cancer therapy in young reproductive-aged women.

DESIGN: Prospective cohort.

MATERIALS AND METHODS: Adolescent and young adult females with a new diagnosis of cancer requiring chemotherapy were followed to assess markers of androgen production (free testosterone and dehydroepiandrosterone sulfate (DHEAS)) and ovarian reserve (follicle-stimulating hormone (FSH), anti-mullerian hormone (AMH), antral follicle count (AFC)) at 3 month intervals. Changes in these were quantified for the acute impact of treatment and for the recovery after therapy using mixed effects linear regression models adjusted for baseline ovarian reserve and use of alkylating agent.

RESULTS: Thirty women (median age 30, range 16-39) not using exogenous hormones, with at least 1 pretreatment and 2 post-treatment study visits were included (median number of posttreatment study visits 2.8, median follow-up after treatment 14 months). Testosterone, but not DHEAS, demonstrated significant impairment during cancer therapy. Unlike follicular measures of ovarian reserve, alkylating agent exposure was not associated with the magnitude of impairment in testosterone levels. In addition, testosterone levels demonstrated no appreciable recovery within the 14-month post treatment window, compared to follicular measures which each began to recover significantly within the follow-up period (p<0.01).

CONCLUSIONS: Young women undergoing cancer therapy experience acute changes in testosterone production which do not appear to recover post therapy. This indicates a degree of stromal cell impairment secondary to chemotherapy that is independent of alkylator agent use and may not recover over time. Such findings may have significant implications in the long term sexual health and well-being of young survivors.

Supported by: 1R01HD062797.
PERIRETHRAL TRANSVESICAL ROUTE FOR OOCYTE RETRIEVAL: AN OLD TECHNIQUE FOR A NEW INDICATION. M. Khrouf, M. Bouyahia, K. Berjeb, M. Braham, H. Elloumi, G. Merdassi, A. Zhioua, F. Zhioua. Obstetrics and Gynecology, ART center Aziza Othmana Hospital, Tunis, Tunisia.

OBJECTIVE: We observed that almost all non-married female patients (adolescent or young women), referred for fertility preservation, refused transvesical procedure for cultural reasons. In this particular population, we offered the possibility to use an old technique: the per-urethral transvesical route (PUTV) to retrieve oocytes. We aimed in this study to evaluate the safety and efficiency of this procedure.

DESIGN: A Retrospective study comparing outcomes of PUTV and transvesical route for oocytes retrieval.

MATERIALS AND METHODS: The study group consisted of 18 pubertal adolescents or young women affected by hematologic malignancies, referred for fertility preservation, and who refused transvesical procedure. All these patients had oocytes retrieval using PUTV procedure. The control group consisted of 18 infertile patients, aged less than 25 years, who underwent IVF in our center, with transvaginal oocyte pick up. In all cases, ovarian stimulation was performed using gonadotrophins and agonist or antagonist Gn-RH. Outcomes of ovarian stimulation and oocyte retrieval were compared between the two groups using t-Student test for mean comparison. A p< 0.05 was considered significant.

RESULTS: Fertility preservation was indicated for Hodgkin Lymphoma in 15 cases, non-Hodgkin lymphoma in 2 cases and in one case for leukemia. Ovarian stimulation was started during early follicular phase in 10 patients, late follicular phase in 3 patients and in luteal phase in 5 patients. There was no difference between study and control groups regarding age (21.5 ± 3.8 vs 23.6 ± 2.5 years), E2 level on triggering day (1637.8 ± 1219 vs 2043.8 ± 1299 pg/ml) and mean number of follicles > 15 mm on ultrasound on triggering day (7.3 ± 3.4 vs 7.8 ± 6.9). The Ovarian stimulation was significantly longer on study group (11.8 ± 1.8 vs 9.8 ± 2.8 days). There was no difference between 2 groups regarding mean number of cumulus oocytes complex (9.1 ± 6.6 vs 11.4 ± 6.6) and Metaphase II oocytes (6.6 ± 5 vs 7.7 ± 4.9). The mean number of vitrified oocytes in FP group was 8 ± 5.6. Two patients of study group and one of control group had no oocytes at ovum pickup. There was no complication in both groups.

CONCLUSIONS: The PUTV procedure for oocytes retrieval is an alternative for young patients undergoing oocytes vitrification for fertility preservation, when the transvaginal route is refused.

NEOVAGINAL CONDYLOMATOSIS AND CARCINOMA FOLLOWING MCDONDOEVAGINPLASTY. D. A. Schirmer, A. N. Gordon, C. P. Roberts. Department of Gynecology and Obstetrics, Emory University School of Medicine, Atlanta, GA; Reproductive Surgical Specialists, Northside Hospital, Atlanta, GA.

OBJECTIVE: To present a case in which a patient who had previously undergone McIndoe vaginoplasty developed severe neovaginal condylomatisos and carcinoma, and to review the literature regarding human papilloma virus (HPV) infection and cancer screening in patients who have undergone McIndoe vaginoplasty.

DESIGN: This is a case report describing the diagnosis and management of neovaginal carcinoma arising from condylomatisos, as well as a review of the literature pertinent to HPV infection, carcinoma, and cancer screening in patients who have undergone McIndoe vaginoplasty.

MATERIALS AND METHODS: A comprehensive review of the patient’s chart and the relevant literature was performed.

RESULTS: A 45 year old female with vaginal agenesis resulting from Mayer-Rokitansky-Kuster-Hauser (MRKH) syndrome previously treated at the age of 18 with McIndoe vaginoplasty presented with extensive condylomatisos occluding the neovagina. She had heavy bleeding originating from the vagi/vaginoplasty, and over time developed symptomatic anemia requiring transfusion. Biopsies were obtained and revealed invasive carcinoma and severe dysplasia. MRI and PET-CT revealed a large pelvic mass and evidence of lymphatic metastasis. The patient was treated with pelvic radiation therapy and six cycles of cisplatin, with resolution of her bleeding. Her vaginal condylomatisos disease and pelvic mass initially decreased in size, however her disease subsequently progressed and did not respond to further treatment. A review of the literature revealed that patients who have undergone McIndoe vaginoplasty are susceptible to complications related to HPV infection, however there are no reported cases of primary neovaginal carcinoma associated with extensive neovaginal condylomatisos.

CONCLUSIONS: There are few reported cases of neovaginal carcinoma of any origin, and we believe that this is the first time that neovaginal carcinoma in a patient with extensive neovaginal condylomatisos has been reported. There are no guidelines for screening patients who have undergone McIndoe vaginoplasty for HPV, neovaginal dysplasia or neovaginal carcinoma. Because patients with MRKH syndrome lack a cervix, they may not receive HPV and neovaginal cytology screening during routine gynecologic examinations. The present case highlights the risks of HPV infection in patients who have undergone McIndoe vaginoplasty, and raises the question of whether routine screening with cytology and HPV testing would be beneficial in this population.

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OBJECTIVE: To assess the challenges faced by oncology providers when discussing fertility preservation (FP) with young women with cancer and to explore their views about the usefulness of a FP decision aid (DA).

DESIGN: We conducted a grounded theory study with oncology providers at a large comprehensive cancer center.

MATERIALS AND METHODS: Eighteen semi-structured interviews with oncology providers were conducted; 13 were physicians, 4 were nurses and 1 was a physician assistant. There were 13 female and 5 male participants with a median of 9 years (range 3–18 years) of practice. Participants were purposefully selected based on theoretical sampling and availability. The interviews were transcribed and analyzed using NVivo software. Strauss and Corbin’s (1990) open coding method was used for data analysis.

RESULTS: Three major themes were identified: 1. Provider Background: Provider attributes may influence his/her approach to FP discussions. These include provider knowledge, ethnic/minority background and their professional role. 2. Provider Challenges when Discussing FP: Patient, provider and system factors present challenges in approaching FP discussions. These include lack of knowledge about FP services, concerns about delay in treatment and obstacles to referral. 3. Provider Perspective on the Use of a FP decision aids: Providers felt that a DA could be a viable tool for patients if it is user-friendly, meaningful, and customized to the individual needs of a patient. Particular considerations included usefulness, challenges in development, ideal attributes and dissemination.

CONCLUSIONS: Multiple factors affect how oncology providers approach FP discussions with their patients. Generally, providers viewed a decision aid as a potentially useful tool to help facilitate and standardize these discussions and help patients make informed decisions. Most providers have specific suggestions on how a DA should be designed and disseminated. This feedback should be considered during the development of a FP DA.

Supported by: This work is supported by a Duncan Family Institute Seed Funding Research Grant.

OBJECTIVE: One of the strongest risk factors for breast cancer is high mammographic density (MD), a measure of fibroglandular tissue of the breast. Women with high MD (≥75%) have a 4- to 6-fold greater risk of breast cancer compared to women with low MD. While previous studies have investigated MD among women who have been infertile or ever used fertility treatment with mixed results, no study has investigated the relationship between infertility diagnosis or fertility treatment type.

DESIGN: We conducted a cross-sectional analysis among 1,281 premenopausal women not previously diagnosed with breast cancer in the Nurses’ Health Study II cohort for whom we had collected screening mammograms.

MATERIALS AND METHODS: We measured average percent MD using a validated computer-assisted method. Multivariable linear regression – a priori adjusted for age, current body mass index (BMI), BMI at age 18, alcohol consumption, family history of breast cancer, smoking history, history of benign breast disease, parity, age at first birth, age at menarche, oral contraceptive history, and breastfeeding – was used to estimate the association of infertility diagnoses (ovulatory, tubal, cervical, and male-factor) and fertility treatment (clomiphene and gonadotropin usage), with percent MD.

RESULTS: The percent MD (41.5%) among women who had ever experienced infertility (tried to conceive for ≥12 months without success) did not differ significantly from women who never experienced infertility (MD=40.4%) (p=0.48). Women who reported ovulatory infertility had significantly lower average percent MD (38.5%) compared to women whose infertility was attributed to male factor (MD=43.2%) (p=0.02). No difference in MD was found for women with tubal (MD=36.1%, p=0.21) or cervical (MD=44.1%, p=0.54) infertility compared to women with male factor infertility. Percent MD was similar for women who reported only clomiphene usage (MD=42.0%, p=0.77) and gonadotropin usage (MD=44.1%, p=0.98) and women who did not utilize fertility treatment.

CONCLUSIONS: In the first study to investigate infertility diagnoses, fertility treatment type, and their association with MD, we found that women with ovulatory infertility had significantly lower percent MD compared to women whose partners had male factor infertility. However, there was no association for infertility overall or for cervical or tubal infertility specifically. These results highlight the importance of understanding infertility mechanisms and their impact on hormonal and other milieu when investigating associations with breast health, breast cancer, and other chronic diseases.

Impact of Tamoxifen on Ovarian Reserve, Fertility, and Breast Cancer Outcomes

OBJECTIVE: To determine if tamoxifen use is associated with a decreased ovarian reserve and/or with a decreased probability of having a child following breast cancer diagnosis.

DESIGN: The Furthering Understanding of Cancer, Health, and Survivorship in Adult (FUCHSIA) Women’s Study is a population-based study of reproductive-aged female cancer survivors in Georgia.

MATERIALS AND METHODS: This analysis includes women aged 22-45 years who were diagnosed with breast cancer between the ages of 20-35 years and who were at least 2 years post-diagnosis at recruitment. After excluding those with a hysterectomy or bilateral oophorectomy before diagnosis, 397 breast cancer survivors were included in this analysis. All participants were interviewed about their reproductive history. Cancer treatment outcomes were abstracted from medical records. Tamoxifen use was defined as at least 6 months of tamoxifen use. Transvaginal ultrasounds and serum anti-Müllerian hormone (AMH) levels were measured on 108 breast cancer survivors.

RESULTS: Women who took tamoxifen were substantially less likely to have a child after breast cancer diagnosis than those who did not take tamoxifen (hazard ratio [HR] 0.30 [95% confidence interval [CI]: 0.16, 0.55]). After adjusting for age at diagnosis, alkylation agent exposure, and race, the HR was 0.18 (95% CI: 0.09, 0.38). The association between tamoxifen use and being less likely to have a child after cancer diagnosis remained strong among women who were childless at diagnosis (HR 0.36, 95% CI: 0.17, 0.77) and among women who had not met their reproductive goals at diagnosis (HR 0.33, 95% CI: 0.18, 0.60). To assess the association of tamoxifen on ovarian reserve, AMH and antifolic acid count (AFC) of those who did and did not take tamoxifen were compared. After adjusting for age at clinic visit, chemotherapy exposure, cancer stage, race, and gonadotropin-releasing hormone agonist use, women who took tamoxifen had estimated geometric mean AMH levels 2.47 (95% CI: 1.08, 5.65) times higher than women who did not take tamoxifen. AFC was also higher in tamoxifen users (adjusted risk ratio 1.21, 95% CI: 0.84, 1.73).

CONCLUSIONS: Breast cancer survivors who used tamoxifen were less likely to have a child following cancer diagnosis compared to survivors who did not use tamoxifen. Tamoxifen users were not found to have additional damage to the ovaries beyond that which may be done by traditional breast cancer treatment. The decreased likelihood of having a child following breast cancer diagnosis for those who used tamoxifen compared with those who did not may be due to time spent taking tamoxifen or concerns about pregnancy after tamoxifen use. Counseling tamoxifen users about pregnancy may help improve tamoxifen compliance and allow women to make more informed decisions regarding their reproductive goals.

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HIGH DOSE RADIOIODINE THERAPY AFFECTS OVARIAN RESERVE. F. Azem G. Shefer. Sorously Medical Center, Tel-Aviv, Israel.

OBJECTIVE: Women undergoing radioactive (RAI) therapy are advised to refrain from conceiving for 6-12 months following treatment as ovaries are exposed to radiation. It is unclear if this exposure carries a risk for reduced fertility, however earlier menopause has been reported in women undergoing RAI treatment. Given the finite number of primordial follicles women are endowed with at birth, radiation injury to germinal cells is not expected to be reversible. We sought to assess the effect of RAI on ovarian reserve of women undergoing treatment for differentiated thyroid cancer (DTC) by prospectively examining blood levels of anti-Müllerian hormone (AMH), and accepted index of the size of this reserve.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: Thirty premenopausal women (aged 33.3±1.4, 20-45 y), scheduled to undergo RAI treatment for the first time after surgery for DTC, were enrolled in the study. Subjects with prior pelvic surgery or irradiation were excluded. Blood levels of AMH were assessed by immunoassay at baseline, and every 3 months for up to 1 year following RAI.

RESULTS: All 30 women reported regular menses prior to treatment. Nineteen had borne children. Baseline AMH levels were, as expected, inversely correlated with age (r = -0.49, P = 0.006). To this date, 23 women all AJCC Stage 1, have received treatment at a mean dose of 110.7±9.9 mCi (30-150). Of those, 18 have been reevaluated after treatment. Baseline AMH levels of these 18 women were 3.4±0.65 ng/ml. A 45% decrease in AMH levels was observed 3 months after treatment (1.9±0.4 ng/ml, P = 0.001). The level improved somewhat afterwards, but it remained significantly lower than at baseline (2.6±0.4 ng/ml, 2.6±0.6, 2.8±0.6, respectively). As most of these subjects had received high doses RAI of 100 and 150 mCi, we could not determine if there was a dose effect. In order to examine this issue, we grouped the 4 subjects who had received an ablative dose of 30 mCi for DTC with 5 women who had been treated with RAI for Graves’ disease in doses ranging from 10-22 mCi. In these 9 subjects (aged 34.9±2.3, 22-43 y), baseline AMH levels were 2.5±0.7 ng/ml and did not change after treatment. They were 2.4±0.8, 2.5±0.8, 3.0±1.0, and 2.6±0.8 ng/ml at 3, 6, 9, and 12 months respectively.

CONCLUSIONS: Large doses of RAI given as adjunct therapy to women with DTC appear to impair ovarian reserve as assessed by AMH levels. A nadir for this effect is seen 3 months after treatment, but there is no complete recovery even after a year. In contrast, lower doses up to 30 mCi, such as those given for ablation of thyroid remnant of for hyperthyroidism, appear to be innocuous. The question whether this effect translates in decreased recovery even after a year. In contrast, lower doses up to 30 mCi, such as those given for ablation of thyroid remnant of for hyperthyroidism, appear to be innocuous. The question whether this effect translates in decreased

Table 1

<table>
<thead>
<tr>
<th>Did not report infertility</th>
<th>Before cancer diagnosis</th>
<th>Only after cancer diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percent who met their reproductive goals</td>
<td>(n=761)</td>
<td>(n=336)</td>
</tr>
<tr>
<td>Percent ever using fertility treatment</td>
<td>48</td>
<td>40</td>
</tr>
<tr>
<td>Among those who met their reproductive goals</td>
<td>2</td>
<td>14</td>
</tr>
<tr>
<td>Among those who did not meet their reproductive goals</td>
<td>6</td>
<td>19</td>
</tr>
<tr>
<td>Mean time to pregnancy (months)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1st pregnancy before cancer diagnosis</td>
<td>5</td>
<td>20</td>
</tr>
<tr>
<td>1st pregnancy after cancer diagnosis</td>
<td>5</td>
<td>22</td>
</tr>
</tbody>
</table>

CONCLUSIONS: Cancer survivors first experiencing infertility after cancer diagnosis differed from those who reported infertility before cancer. Although the majority of cancer survivors did not report fertility issues, most survivors had fewer children than they desired, regardless of whether they reported infertility.

Supported by: NICHD 5R01HD066059, TL1TR000456, UL1TR000454.

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OBJECTIVE: Ovarian cryopreservation is still considered an experimental fertility preservation strategy and the success rates with the transplantation (OT) of previously banked ovarian tissue are unknown. Here we sought to meta-analyze published and unpublished data, including our own to determine success rates of OT.

DESIGN: Meta-analysis combined with original data.

MATERIALS AND METHODS: Medical literature was reviewed from the year 2000, when the first case of OT with autologous cryopreserved tissue was reported. Additional cases were retrieved from review articles, meeting abstracts and personal communications. These included 7 OT cases performed by us. When there was lack of clarity, authors were contacted for additional information.

RESULTS: 201 OTs were performed with cryopreserved tissue between 1999 and 2016. Of those where the surgical technique was described, 163 (3 with robot assistance) were performed laparoscopically and 14 via laparotomy. Twenty women underwent repetitive OT with their banked tissue. There were 68 babies born and 6 pregnancies were ongoing; six women had 2 or more children after OT. Two children were born after heterotopic (abdominal wall) OTs. Of the live births, 50% were from ART and 50% from spontaneous conception. The cohort characteristics and success rates are shown in Table 1.

The mean age at ovarian cryopreservation was 26.2 with women undergoing OT at the mean age of 32.9. In only five and seven studies the numerators and denominators could be determined for clinical pregnancy (CPR) and livebirth rates + ongoing pregnancy (LBR+OG), respectively. The CPR and LBR+OG were 56.3% and 35.4% respectively among women desiring pregnancy. The overwhelming majority of livebirths occurred after 2010, compared to the prior period (58 vs. 8, respectively) indicating accelerated pregnancy. Of note, 14% of patients underwent OT for...
endocrine restoration and regardless of the intent, 95.4% of all OTs resulted in the restoration of ovarian endocrine function.

CONCLUSIONS: Success rates of OT with previously cryopreserved banked ovarian tissue have reached acceptable levels, with ovarian endocrine function restored in nearly all patients. Given this recent convincing data and the ability of OTs to restore fertility without a need for ART, there should be a discussion for its removal from the experimental category.

Supported by: NIH R21HD061259 and R01HD053112.

P-68 Tuesday, October 18, 2016
COMPARISON OF GNRH AGONIST AND HCG FOR PRIMING IN VITRO MATURATION (IVM) CYCLES IN CANCER PATIENTS UNDERGOING URGENT FERTILITY PRESERVATION (FP).

OBJECTIVE: To compare the number of metaphase 2 (M2) oocytes vitrified following GnRH agonist (GnRHa) or hCG priming, 36h before oocyte retrieval, in cancer patients undergoing IVM for urgent FP.

MATERIALS AND METHODS: From January 2009 to April 2015, we prospectively studied 373 patients, aged 18-41 years and candidates for FP with IVM of oocytes followed by oocyte or embryo cryopreservation. All patients met the following inclusion criteria: two ovaries visible and easily accessible to ultrasound-guided puncture and antral follicle count (AFC) > 8. Exclusion criteria were previous history of chemotherapy and poly cyclic ovarian syndrome (PCOS). Priming was achieved with either GnRHa (trip-torelin 0.2 mg, SC, n=235) or hCG (recombinant hCG, 250 µg, SC, n=138).

RESULTS: Patients in the hCG and the GnRHa groups were comparable in terms of age (32.2 ± 4.9 vs 31.7 ± 4.4 years, respectively, NS), body mass index (22.8 ± 3.9 vs 23.2 ± 4.3 kg/m², respectively, NS) and ovarian reserve tests (AFC: 18.6 ± 8.0 vs 18.8 ± 7.6 follicles, respectively, NS; serum Anti-Mullerian Hormone (AMH) levels: 3.6 ± 2.7 vs 3.6 ± 2.4 ng/mL, respectively, NS). The number of immature oocytes retrieved was significantly higher in the GnRHa group compared to hCG group (9.1 ± 6.8 vs 7.7 ± 5.5 oocytes, respectively, p = 0.04) but the maturation rate after 48h was statistically similar (59.2 ± 31 vs 64.2 ± 26 %, respectively, p = 0.07). Finally, the total number of vitrified M2 oocytes was comparable between the two groups (5.2 ± 2.2 vs 4.9 ± 4.0, respectively, p = 0.6).

CONCLUSIONS: Priming with administration of hCG has been shown to improve outcomes of IVM cycles in PCOS infertile women. In addition, it has been suggested that a mild stimulation with FSH before hCG priming could further increase the oocyte yield. However, this double priming is not always feasible in cancer patients undergoing urgent FP with IVM. GnRHa offer the advantage of stimulating a combined endogenous FSH and LH surge in a single injection. Our study showed that GnRHa priming leads to similar outcomes than hCG in IVM cycles for urgent FP. Randomized control trials are needed to objectively assess the need for priming in normo-ovulatory cancer patients, and the best way to provide it if required.

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EVALUATION OF TESTIS SPERM EXTRACTION (TESE) AND TESTIS HISTOLOGY IN THE GENDER CONFIRMING SURGERY PATIENT.

OBJECTIVE: Patients undergoing gender confirming surgery (GCS) from male to female may consider initiating future fertility. WPATH guidelines recommend discussion of fertility early in protocol prior to transition. Little is known regarding spermatogenesis potential in male transsexuals treated with estrogen supplementation therapy (EST). Since sperm production is highly androgen dependent, use of EST preoperatively may affect spermatogenesis and maturation. Furthermore, there is scant literature regarding the testicular changes associated with EST, and there is no published literature assessing the role of sperm retrieval at the time of GCS. The objective of this study is to review TESE and histology results in GCS patients and propose an algorithm for male fertility preservation.

MATERIALS AND METHODS: Seven male to female transgender patients underwent either complete GCS (4) or bilateral orchietomies (3). One patient consented to testicular sperm extraction (TESE) after the patient was unable to produce an ejaculate. Testis histology was reviewed on all 7 patients. Patient age ranged from 24-54 years old. Two patients were not

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WOMEN WITH OVARIAN FUNCTION AFTER BREAST CANCER RECOVERY HALF OF THEIR ANTRAL FOLLICLE COUNT 1 YEAR AFTER EXPOSURE TO CYTOXAN-BASED CHEMOTHERAPY.

OBJECTIVE: Previous data have shown that breast cancer patients treated with chemotherapy are at increased risk of reproductive compromise. The majority of women will either have persistent menses or return of menses within 1 year, but may suffer from early menopause and infertility. In this study, we sought to characterize the loss of ovarian reserve and the time to maximum ovarian recovery in women who have menstrual function after exposure to chemotherapy.

DESIGN: Prospective Cohort study
MATERIALS AND METHODS: 199 breast cancer patients were seen prior to chemotherapy for a fertility preservation consult and consented for follow-up ovarian function assessment (every 3-6 months) with Antral Follicle Count (AFC). Each patient received Cytoxan-based chemotherapy. Follow-up AFC was compared to initial, pre-treatment AFC to create a ratio of the person’s follow-up AFC versus their original AFC. T-tests and general linear models (GLM) were used as appropriate to assess differences in AFC.

RESULTS: The average age of the 199 women in our cohort was 35 ± 5 at their intake fertility preservation consult visit. Average intake (pre-chemo) AFC was 14.7 ±/− 11.6. 47 of the 199 women took Lupron during their chemotherapy, for ovarian protection. To date, 66 of the 199 breast cancer patients have returned for repeat AFC assessment. Of those who returned, the average number of AFC assessments was 3.5 ±/− 1.9. AFC rebound appeared to plateau at 1 year, at an average of 50% of original AFC. After adjustment for age and initial AFC, there was a trend toward increased AFC at 1 year for those women who underwent Lupron therapy (versus not) for ovarian protection during chemotherapy (p = 0.04, GLM coef = 0.32 for Lupron versus not at 13 or more months; p = 0.07, GLM coef = 0.37 for Lupron versus not at 18 or more months).

CONCLUSIONS: Women with ovarian function appear to recover about half of their observable ovarian reserve 1 year after chemotherapy for breast cancer. Treatment with Lupron during chemotherapy may be associated with an increase in ovarian recovery. These findings provide important references for counseling patients pre-chemotherapy about their expectations for ovarian recovery.
on EST due to history of stroke and personal preference respectively, and 5 patients were on EST up to 2 weeks prior to GCS or through surgery. 

RESULTS: Patient 1 (No EST) had Sertoli Cell only (SCO) histology upon review of the orchitectomy specimens. Patient 2 (No EST) had normal spermatogenesis bilaterally. Three patients underwent GCS while undergoing EST. Patient 3 (EST) was found to have SCO histology, with early maturational arrest bilaterally. Patient 4 (EST) underwent a testicular sperm retrieval during GCS. Sperm was successfully cryopreserved, with normal spermatogenesis on histology. Patient 5 (EST) had mostly hypospermatogenesis, but full sperm present in biopsy. Patients 6 and 7 (EST) both showed early maturation arrest and no full sperm seen. Forty three percent of patients (3/7) had sperm seen on histology. Histology was independently reviewed by the author.

CONCLUSIONS: The effect of estrogen on spermatogenesis is incompletely studied and poorly understood. The surprisingly wide range of histology findings prompts additional questions about the interaction between estrogen and testosterone in spermatogenesis. This is the first documented case report of successful testicular sperm retrieval at the time of GCS, and this provides evidence that TESE is a viable option if ejaculation is not possible or pre-operative semen analysis reveals azospermia.

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FERTILITY PRESERVATION WITH THE USE OF GNRH ANALOGUE IN WOMEN UNDERGOING CHEMOTHERAPY FOR LYMPHOMA: A SYSTEMATIC REVIEW AND META-ANALYSIS. R. L. Tavares,a J. C. Senra,a M. C. Talim,a F. M. Reis.b

OBJECTIVE: To evaluate the effectiveness of GnRH analogue before and during chemotherapy in premenopausal women with lymphoma for the protection of ovarian reserve.

DESIGN: Systematic Review and Meta-analysis.

MATERIALS AND METHODS: Electronic search was conducted until August 2014 in CENTRAL databases, LILACS, MEDLINE and Clinical-Trials.gov. Only randomized controlled trials (RCTs) comparing concurrent use of GnRH analogue plus chemotherapy with chemotherapy alone were eligible. Two reviewers analyzed, independently, the inclusion criteria, bias risk and extracted data from included studies. Any disagreements were addressed and resolved between both reviewers.

RESULTS: The search identified 171 articles and only 3 of these were included. They evaluated the rate of premature ovarian failure (POF) and pregnancy rate after treatment. Only two studies had serum Anti-Mullerian hormone (AMH) levels as a marker of ovarian reserve. There was no statistically significant difference in POF rate between the control and intervention groups (RR 0.83, 95% CI 0.24 to 2.88), as well as pregnancy rate at follow-up (RR 0.83, 95% CI 0.24 to 2.88), as well as pregnancy rate at follow-up (RR 0.83, 95% CI 0.24 to 2.88). There was no statistically significant difference in POF rate between the control and intervention groups (RR 0.83, 95% CI 0.24 to 2.88). There was no statistically significant difference in POF rate between the control and intervention groups (RR 0.83, 95% CI 0.24 to 2.88).

CONCLUSIONS: High levels of satisfaction with care were expressed by ovarian reserve.


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SUBJECTIVE AND OBJECTIVE EVALUATION OF A TEACHING HOSPITAL ONCOFERTILITY SERVICE. M. McEvoy, S. Molakatalla, M. Cheah. Flinders Fertility, Flinders Medical Centre, South Australia, Australia.

OBJECTIVE: This study is designed to assess subjective and objective valuation of an Australian teaching hospital oncofertility service.

DESIGN: In an Australian Teaching Hospital Fertility Unit 29 consecutive oncofertility female patients (oncology group) having oocyte collection prior to chemotherapy were compared to a group of 20 consecutive control patients without malignancy (control group) having their first oocyte pickup as part of their IVF treatment.

MATERIALS AND METHODS: In each group we measured demographic and endocrine data. In a questionnaire sent by post after verbal consent we surveyed patient satisfaction with the number of oocytes retrieved, consent processes, nursing care, procedures, post procedural pain, financial satisfaction and future plans to utilize gametes collected in the two groups. Results were expressed as percentages plus standard deviation using Excel statistical analysis. Statistical advice suggested adequacy of numbers in each group.

RESULTS: The oncofertility and the control group were similar with respect to age, anti-mullerian hormone level, maximal estradiol achieved, number of oocytes retrieved, and discomfort from the procedure. Adequacy of consent processes, nursing care, post procedural pain, and financial satisfaction were similar in the two groups. Oncology patients were significantly (p=0.05) more likely (68%) to have an agonist (Lucrin) trigger than controls (10%). Intention for future usage was noted at 62% in the oncology group Differences occurred in the perception of success with the oncofertility group showing higher levels of satisfaction with lower numbers of oocytes retrieved compared to controls> With low retrieval rates of less than 10 oocytes the satisfaction rate was 50% in the oncofertility group and 35% in the control group (P=0.08) With higher than 10 oocytes similar levels of expectations were achieved.

CONCLUSIONS: High levels of satisfaction with care were expressed by both oncology and control groups. Both groups can be safely offered egg retrieval with similar outcomes. Oncofertility patients were more likely to be satisfied with the oocyte yield when this was less than 10 compared to controls. Offering oncofertility services prior to chemotherapy may therefore have economic, qualitative value unrelated to the quantitative results of retrieval. The oncofertility service was highly valued by patients. This project was self funded and prospectively approved by the Southern Adelaide Human Research and Ethics Committee.


FERTILITY & STERILITY®
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A NOVEL PREDICTIVE MODEL OF THE PROBABILITY OF LIVE BIRTH WHEN USING VITRIFIED HUMAN OCYTES AS A MEANS OF FERTILITY PRESERVATION. A. L. Mauner,a E. Surrey,b R. L. Gustofson,a L. A. Kondapalli,a W. B. Schoolcraft,b Embryology, Fertility Laboratories of Colorado, Lone Tree, CO; Department of Obstetrics and Gynecology, Colorado Center for Reproductive Medicine, Lone Tree, CO.

OBJECTIVE: Develop a predictive model to aid physicians in providing patients a realistic probability of live birth in consideration of their post oocyte retrieval data.

RESULTS: The study population consisted of patients aged 19-44 (mean ± std. error: 27.27 ± 0.40) with average Anti-Müllerian hormone (AMH) levels of 4.00 ± 0.20, day 3 Follicle Stimulating hormone (FSH) levels of 6.83 ± 0.47, Body Mass Index (BMI) of 24.21 ± 0.32, warming 15.98 ± 0.44 oocytes, and transferring 1.74 ± 0.04 embryos. The final model contained number of oocytes warmed, AMH level of oocyte source, percentage of post retrieval oocytes that were mature, age of oocyte source, total gonadotropin dose, number of days of oocyte source, number of days oocytes were cryopreserved, number of days on stimulation medication and BMI of oocyte source. This model had a C index of 0.779 (bootstrapped 95% CI 0.676, 0.821), a Brier score of 0.190 (bootstrapped 95% CI 0.176, 0.221), and a Hosmer-Lemeshow test statistic of 0.646.

CONCLUSIONS: Overall calibration of the model was good, except for upper bound probabilities (60-100%) where the model slightly over-estimated probabilities. While acknowledging its limitations, this model will be translated into an application for physician use. This will serve as an invaluable tool for physicians as they consult with patients on their future probability of success and the potential for requiring multiple oocyte vitrification cycles to achieve a live birth.

CRYOPRESERVATION AND FROZEN EMBRYO TRANSFER

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THE OPTIMAL TIMING OF BLASTOCYST VITRIFICATION AFTER TROPHODECTOMY BIOPSY OF PREIMPLANTATION GENETIC SCREENING. C. Lee,a T. Lee,a M. Lee,a aDepartment of Obstetrics and Gynecology, Chung Shan Medical University Hospital, Taichung, Taiwan; bDepartment of Obstetrics and Gynecology, National Taiwan University Hospital, Taipei, Taiwan; cInstitute of Medicine, Chung Shan Medical University, Taichung, Taiwan.

OBJECTIVE: Vitrification was recommended for cryopreservation of biopsied blastocysts. We investigated whether the timing of vitrification after trophectoderm (TE) biopsy for preimplantation genetic screening (PGS) program associated with the success of implantation and pregnancy after frozen blastocyst transfer.

DESIGN: A retrospective cohort study.

MATERIALS AND METHODS: There were 1,329 blastocysts from 223 patients underwent the TE biopsy and array CGH. The PGS and frozen blastocyst transfer cycles were performed from Dec. 2012 to May, 2015. Only the good blastocyst (Gardner grading system: grade 4, 5 and 6) on day 5 or day 6 were selected for biopsy. All blastocyst were underwent vitrification immediately (0.5 hour) or 1 to 6 hours after biopsy. At the time of vitrification, the interval between TE biopsy and vitrification and the morphology of blastocyst re-expansion relative to original expansion cavity was recorded. The re-expansion grades were including (1) without significantly re-expansion (NE) (2) 3/4 re-expansion (3/4E) (3) full re-expansion or hatching. The euploidy blastocyst(s) (1~2 embryos) was/were selected first for transfer on the next cycle. According to the transferred blastocyst which showed different re-expansion grade at time of vitrification, all patients were divided into four groups: (Group I: non-expansion (n=40), Group II: 3/4 re-expansion (n=29) and Group III: all re-expansion or hatching (n=154)).

RESULTS: At 0.5 hour after biopsy, 100% of biopsied blastocyst was without significantly re-expansion; at 1 hour after biopsy, only 5.7% of biopsied blastocyst reached 3/4E or E grade; at 3 hours after biopsy, more than 86% blastocyst reached 3/4E or E. The survival rate of biopsied blastocyst was 100% (337/357) after biopsy. The implantation rate in Group III (63.1%, 159/252) was significantly higher than that in Group I (45.2%, 28/62; p=0.010). The clinical pregnancy rates in Group III (73.4%, 113/154) and Group II (75.9%, 22/29) were significantly higher than that in Group I (52.5%, 21/40; p=0.011 and p=0.048, respectively). Combining two factors which included the re-expansion grades and timing of vitrification, the implantation and clinical pregnancy rates in the Group of biopsied blastocyst with ≥3/4E and interval≥3 hours (63.7%, 179/281; 74.0, 128/173, respectively) were significantly higher than that in the Group of biopsied blastocyst with NE and interval<3 hours (45.3%, 24/53; 50.0, 17/34; p=0.012 and p=0.005, respectively). The optimal timing of vitrification is biopsied blastocyst keeping culturing to reach ≥3/4 re-expansion and ≥3 hour after TE biopsy.

CONCLUSIONS: The optimal timing of vitrification after TE biopsy provides high implantation and pregnancy rates after frozen blastocyst transfer.

References:
- The most effective route of administration of G-CSF is the subcutaneous one.
- Further study is required.

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OBJECTIVE: Commercial vitrification solutions (VS) possessing 30-32% cryoprotective agents (EG-DMSO or EG-FPG; 4.4 to 4.7M) are relatively unstable solutions, susceptible to ice-induced cryo-injury under insufficient cooling/warming conditions. Alternatively, a more concentrated EG-Glycerol VS (I.C.E. ; > 7.9M, Schiewe et al., 2015) is metastable at lower cooling/warming rates. We have recently shown that the latter VS mixture is equally non-toxic to blastocysts (BL) for up to a 10 min exposure. The aim of this study was to evaluate the physical stability of an unstable versus metastable VS when challenged to repeated re-vitrification (rVTF). DESIGN: Research consented, discard BL were randomly assigned to a 3x2 factorial design. Three rVTF treatments (1x, 3x, 5x) were conducted in a closed VTF model, without intermittent VS elution and dilution equilibration, using either a non-DMSO VS (I.C.E. BL-VS) or a standard 30% EG-DMSO solution (n=50 BL/VS). The latter solutions were contrast to a control apriori treatment where standard elution and dilution equilibration of I.C.E. BL-VS treated human BLs (n=50) was allowed between each rVTF (3 steps, 3min each), equilibrated and cultured. Embryo survival assessments were performed at 0 and 24hr post-final warming.

RESULTS: A total 6 min exposure to Glycerol/EG following up to 5x-rVTF by the microSecure VTF method had no effect on post-warming survival / development (98%), being similar to the control, equilibrated rVTF group (100%). Meanwhile, the DMSO/EG treatment experienced seemingly unhindered survival (98%), but reduced (p<0.05) development (1x vs 5x rVTF; 35% and 20%, respectively) compared to 1x rVTF (90%).

CONCLUSIONS: VS induced cryo-sensitivity of DMSO/EG exposed re-vitrified human BL to cryo-injury, brings into question the true safety of unstable solutions attempting to reduce cytotoxicity. Our rVTF model exerted a repeated physical stress to an unstable VS incapable of inhibiting recrystallization events under the slower cooling and warming of a closed system. Similarly, the intra- and inter-facility variation seen with open VTF systems in clinical use may well be due to unstable VS sensitivity to suboptimal handling events. As aseptic closed VTF systems (e.g., mS-VTF, HSV , VitriSafe) continue to prove their excellence in clinical practice, perhaps it is time we produce and use more metastable solutions capable of maintaining their vitrified “glassy” state without the need for ultra-rapid cooling and even higher warming rates to optimize sustained embryo viability.

References:

Supported by: Conducted, in part, in our Summer Student Science Training Program using internal funding.

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EFFECTS OF CYCLIC ADENOSINE MONOPHOSPHATE MODULATORS ON INTEGRITY AND MATURATION OF VITRIFIED-WARMED MOUSE GERMINAL VESICLE OOCYTES. J. Youn, H. Lee, S. Kim, J. Lee, B. Jee, J. Suh, S. Kim, S. Kim; "Department of Obstetrics and Gynecology, Seoul National University Bundang Hospital, Seongnam-si, Korea, Republic of; "Department of Obstetrics and Gynecology, Seoul National University College of Medicine, Seoul, Korea, Republic of; "Center for Fertility and Repro-uction, American-Sino Women’s and Children’s Hospital, Kansas City, KS.

OBJECTIVE: To achieve a successful cryopreservation and in-vitro maturation (IVM) of Germinial vesicle (GV) stage oocytes, synchronization of nuclear and cytoplasmic maturation is critical. The aim of this study is to evaluate whether cyclic adenosine monophosphate (cAMP) modulator treatment can improve the outcomes of vitrification and IVM of GV oocytes. DESIGN: Experimental animal study.

MATERIALS AND METHODS: GV oocytes were obtained from 4-week-old BDF1 mice and treated with two different cAMP modulators, dibutyl cAMP salt (dbcAMP) or 3-isobutyl-1-methylxantine (IBMX), for 30 min. These reversible GV arresting agents were used to synchronize nuclear and cytoplasmic maturation of the oocytes by postponing meiosis. All GV oocytes in the control and treated groups were vitrified with our new vitrification solution. After warming the chromatin integrity of the nucleus was assessed and meiotic resumption of vitrified-warmed GV was analyzed by MMP-2 and cyclin B1 labeling. In addition, F-actin expression for cytoskeletal integrity was assessed. After IVM the rate and quality of matured oocytes including chromosome and spindle organization were evaluated.

RESULTS: The ratio of GV with a normal chromatin pattern was significantly higher with dbcAMP and IBMX treatment (84.9 and 96.0%) compared to that with the control (36.7%). MMP-2 and cyclin B1 expression within the nucleus was not significantly different, but suppressed in the cytoplasm with cAMP modulator treatment. F-actin expression was significantly higher in the dbcAMP group (29.6%) compared to the control (16.3%). The maturation rate was increased in both treatment groups, although the difference was not statistically significant (57.9, 67.8, and 65.6% in control, dbcAMP, and IBMX groups, respectively). The survival rates and chromosome-spindle organization patterns after IVM did not show any statistical difference among groups.

CONCLUSIONS: Treatment with cAMP modulators may assist synchronization of meiosis and the integrity of chromatin and cytoskeleton of the GV oocytes when vitrifying GV oocytes, which can lead to better IVM outcomes with vitrified-warmed GV stage oocytes.
efficiency and wider variation in performance into account when selecting among the many options for utilizing DOs. These data also demonstrate that development beyond 2PN is not influenced by whether an oocyte was previously vitrified.

Comparison of developmental milestones between fresh and vitrified donor oocytes

<table>
<thead>
<tr>
<th></th>
<th>Fresh</th>
<th>Vitrified</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>% M2s progressing to UB</td>
<td>46.6% (3745/8045)</td>
<td>37.7% (403/1070)</td>
<td>&lt;0.0001</td>
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<tr>
<td>Fertilization Rate</td>
<td>87.0% (7001/8045)</td>
<td>76.2% (771/1070)</td>
<td>&lt;0.0001</td>
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<tr>
<td>% 2PNs progressing to UB</td>
<td>53.5% (3745/7001)</td>
<td>52.1% (403/771)</td>
<td>0.42</td>
</tr>
</tbody>
</table>

References:

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FRESH VS FROZEN EMBRYO TRANSFER IN FROZEN DONOR EGG IVF AND PREIMPLANTATION GENETIC SCREENING CYCLES. J. Shah, a C. Huang, a A. Vigil, a C. Barr, b S. K. Nurudeen, c W. Wei-Hua, c M. Abdallah, c UT-Houston/Memorial Hermann, Houston, TX; University of Houston, Houston, TX; Houston Fertility Institute, Houston, TX.

OBJECTIVE: To evaluate whether freezing embryos, for a subsequent frozen embryo transfer (FET), would compromise the outcome in frozen donor egg IVF cycles when preimplantation genetic screening (PGS) was performed.

DESIGN: A retrospective study of frozen donor egg IVF with PGS cycles done at the same IVF lab where blastocyst stage embryos were either biopsied on day 5 for PGS and transferred fresh on day 6 of culture or blastocyst stage embryos were biopsied for PGS on day 5, 6 or 7 of culture then frozen. The frozen embryos were subsequently transferred in a frozen embryo transfer cycle.

MATERIALS AND METHODS: Charts were reviewed for patient’s and partner’s age, number of frozen donor eggs thawed, number of eggs surviving the thaw, number of fertilized eggs, number of embryos biopsied on day 5, 6 and 7 of culture, PGS results, whether the transfer was a fresh or frozen embryo, transferred embryos number and grade, implantation, pregnancy and viable pregnancy rates. Chi square and student’s t-tests were performed to compare categorical and continuous variables, respectively.

RESULTS: From January 2014 until January 2016, 19 frozen donor egg IVF with PGS cycles were identified. In 6 cycles, embryo biopsy was performed on culture day 5 with 24 hour turnaround PGS and embryo transfer on day 6; 4 cycles (66.7%) resulted in biochemical pregnancy and delivery and one cycle resulted in an ectopic pregnancy. The implantation rate was 70% (14/20). There was no significant difference in the biochemical pregnancy, clinical pregnancy/delivery and implantation rates between the 2 groups. There was no significant difference in the age of the recipients, fertilization rate, number of biopsied embryos or number and grade of transferred embryos. 6 of the 13 FET cycles had only embryos biopsied on culture day 6 or 7 available for transfer, where a fresh embryo transfer after 24 hour turnaround PGS would not have been feasible.

CONCLUSIONS: Freezing embryos after blastocyst stage biopsy for PGS in a frozen donor egg IVF cycle does not seem to result in lower success rate when compared to a fresh embryo transfer. Frozen donor egg IVF with PGS and subsequent FET would allow for the biopsy of culture day 6 and 7 blastocysts.

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LASER COLLAPSE OF BLASTOCYSTS PRIOR TO VITRIFICATION LEADS TO LOWER SPONTANEOUS ABORTION RATES. N. J. George, R. Halverson, C. R. McCann, C. Hibray, G. Letterie, G. Ball. Seattle Reproductive Medicine, Seattle, WA.

OBJECTIVE: This retrospective study aimed to evaluate whether or not laser collapsing of blastocysts prior to vitrification affected treatment outcomes.

DESIGN: The study included 200 frozen embryo transfer cycles, 100 with embryos that were collapsed prior to vitrification and 100 with embryos that were not collapsed prior to vitrification. No embryos underwent pre-implantation genetic screening. All embryos were frozen using the same vitrification method (Global Fast Freeze method in 0.25cc straws).

MATERIALS AND METHODS: For the collapsed group, a Hamilton Thorne LYKOS laser with settings of 100% power and 450µs pulse was aligned between trophectoderm cell junctions (away from the inner cell mass) and one pulse was administered. Within approximately five minutes the blastocysts were vitrified per protocol. For the non-collapsed group, blastocysts were vitrified per protocol.

RESULTS: The average age for each group was not different, the collapsed group was 33.4 and the non-collapsed group was 34.9 (p>0.05). The average number of embryos transferred was not different (p>0.05), a total of 134 embryos transferred in the collapsed group and 127 embryos transferred in the non-collapsed group. The survival rate between groups was not different (p>0.05), 93% for the collapsed group and 96% for the non-collapsed group. The implantation rate was not different (p>0.05), 50% for the collapsed group and 41% for the non-collapsed group. The clinical pregnancy rate approached significance (p=0.06), 50% for the collapsed group and 37% for the non-collapsed group. While the biochemical rate was not different (p>0.05), 12% for the collapsed group and 13% for the non-collapsed group, the spontaneous abortion rate was significantly different (p<0.05), 5% for the collapsed group and 13% for the non-collapsed group. Of note, there were 13 sets of twins in the collapsed group (one monozygotic) and one set of twins in the non-collapsed group. As a result, when 2 collapsed embryos were transferred, there was a 35% twin rate.

CONCLUSIONS: Laser collapse of blastocysts prior to vitrification leads to a decrease in spontaneous abortion rates and a trend toward higher overall clinical pregnancy rates. Due to the increased trend in clinical pregnancy rates and higher implantation rate, providers and patients should consider transferring just one embryo per FET cycle in order to avoid multiple pregnancies.

<table>
<thead>
<tr>
<th></th>
<th>Survival Rate</th>
<th># Transferred</th>
<th>+ HCG</th>
<th>Biochemical Rate</th>
<th>Implantation Rate</th>
<th>Spontaneous Abortion Rate</th>
<th>Clinical Pregnancy Rate</th>
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<tr>
<td>Collapsed</td>
<td>93% (134/144)</td>
<td>134</td>
<td>67% (67/100)</td>
<td>12% (12/100)</td>
<td>50% (67/134)</td>
<td>5% (5/100)</td>
<td>50% (50/100)</td>
</tr>
<tr>
<td>Not Collapsed</td>
<td>96% (130/136)</td>
<td>127</td>
<td>64% (64/100)</td>
<td>13% (13/100)</td>
<td>41% (52/127)</td>
<td>13% (13/100)</td>
<td>37% (37/100)</td>
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</tbody>
</table>
GNRH AGONIST VERSUS HUMAN CHORIONIC GONADOTROPIN FOR TRIGGERING OVULATION IN ANTICOLLIST LANES: A RANDOMIZED CONTROLLED TRIAL. M. I. Mostafa,1 E. A. Elgindy,1 H. Sibai,1 E. Darwish1; H. Maghraby2; 1Ob/Gyn, Cairo University, Cairo, Egypt; 2Ob/Gyn, Zagazig University, Zagazig, Egypt; 3Ob/Gyn, Alexandria University, Alexandria, Egypt.

OBJECTIVE: To compare the outcomes of antagonist cycles triggered by agonist with specialized luteal support regimen to that triggered by hCG in patients with a high risk of ovarian hyperstimulation syndrome (OHSS).

DESIGN: Prospective randomized controlled trial.

MATERIALS AND METHODS: One hundred ninety women were randomized on the day of final oocyte maturation into two groups, in group A (V) triggering was done using GnRH agonist followed by specialized regime (1500 IU hCG at time of oocyte retrieval as well as oral estradiol and intramuscular progesterone during luteal phase), while in group B, 5000 IU of hCG was given with luteal support (oral estradiol and vaginal progesterone). Ongoing pregnancy rate was the primary outcome and occurrence of ovarian hyperstimulation syndrome (OHSS) was the secondary outcome.

RESULTS: The two groups were comparable in basal characters. Ongoing pregnancy rate per randomized patient was comparable in the 2 groups (49/95 (51.6%) in group A and 50/95 (52.6%) in group B (RR=0.98, 95% CI=1.29 to 0.751). Freeze all policy was performed in 5 cases in group A and in 7 cases in group B. Three cases developed severe OHSS in group B. Moderate OHSS developed in 5 cases in group A and in 10 cases in group B (P=0.18).

CONCLUSIONS: Antagonist cycles triggered by agonist with the aforementioned specialized luteal support have comparable ongoing pregnancy rate to that triggered by hCG. Although OHSS is less liable to occur in the first protocol, its occurrence still remains a possibility.

RE-EXPANSION OF WARMED VITRIFIED BLASTOCYSTS BEFORE EMBRYO TRANSFER: ARE WE TOO CONCERNED? N. Esfandiari,1 D. B. Della Cruz,1 K. Rao,1 R. Casper,1 2OB/Gyn and Pathology, Dartmouth Hitchcock Medical Center, Lebanon, NH; 3Human Embryology and Andrology Laboratory, Embryologist, Hanover, NH; 1TVF, Embryologist, Toronto, ON, Canada; 2Professor, University of Toronto, Toronto, ON, Canada.

OBJECTIVE: Improvement in blastocyst culture and vitrification has resulted in routine cryopreservation of blastocysts with remarkable survival and implantation rates in frozen embryo transfer cycles (FET). Vitrified blastocysts are collapsed upon warming and it is sometimes difficult to assess whether they have survived intact. Generally, blastocysts are cultured for a few hours after warming, and sometimes overnight, to assess re-expansion as an indicator for survival and reproductive potential. We sought to determine if incubation between thawing and transfer to allow blastocyst re-expansion or immediate transfer without incubation influences clinical outcomes of FET with vitrified blastocysts.

DESIGN: Retrospective study in a University of Toronto affiliated infertility program.

MATERIALS AND METHODS: Six hundred and twenty FET cycles were started between Jan 2013 and December 2014. The blastocysts were vitrified with the Kitazato kit and Cryotop vitrification devices on day-5 or day-6 of development. The blastocysts were thawed in the morning and transferred after 1-3 hours of incubation in GII-plus culture medium, or immediately after warming in the warming solution. Seven cycles were cancelled because no blastocyst survived. Five hundred and sixteen embryo transfers were performed by 5 staff and 4 REI fellows (group I). One REI provider, with a very busy morning OR schedule, had to complete embryo transfers as soon as the blastocysts were thawed (group II, n=97).

RESULTS: A total of 1036 vitrified blastocysts was warmed and 1003 survived (96.8%). The overall PRs in groups I and II were 39.5% and 56.7%, respectively (p=0.053). Patient age, number of embryos transferred, and pregnancy outcome between the two groups are shown in table 1. Transferring blastocysts that were vitrified on day-5 resulted in a higher pregnancy rate compared to day-6 in both groups.

CONCLUSIONS: Re-expansion of vitrified-warmed blastocysts to assess viability does not appear to be necessary and immediate embryo transfer after warming seems to have no negative impact on blastocyst implantation potential.

Table: 1

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<tbody>
<tr>
<td>Group I</td>
<td>516</td>
<td>395</td>
<td>35.6 ± 5.04</td>
<td>1.67 ± 0.8</td>
<td>43.3</td>
<td>121</td>
<td>37.3 ± 3.98</td>
<td>1.6 ± 0.68</td>
<td>28.1</td>
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<tr>
<td>Group II</td>
<td>97</td>
<td>71</td>
<td>35.2 ± 5.26</td>
<td>1.5 ± 0.55</td>
<td>62</td>
<td>26</td>
<td>35.27 ± 5.3</td>
<td>1.6 ± 0.68</td>
<td>42.3</td>
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FROZEN EMBRYO TRANSFER (FET) OUTCOMES FROM DAY 4 EUPLOID BLASTOCYSTS. M. E. Thompson,1 M. P. Portmann,1 B. Scott,1 M. Kelly,1 M. J. Tucker,1 I. Sasson,1 M. Avella,1 Shady Grove Fertility of PA, Wayne, PA; 2Society Hill Reproductive Medicine, Philadelphia, PA; 1TVF, Shady Grove Fertility, Rockville, MD.

OBJECTIVE: To assess the impact of biopsied and vitrified day-4 blastocysts on frozen embryo transfer (FET) outcomes.
The study compared IVF outcomes from blastocysts that underwent trophoderm biopsy for preimplantation genetic screening (PGS) and were vitrified on day 4, day 5, or day 6. We compared IVF outcomes from blastocysts that underwent trophoderm biopsy for preimplantation genetic screening (PGS) and were vitrified on day 4, day 5, or day 6. MATERIALS AND METHODS: A total of 2897 letters were sent to patients with frozen embryos obtained from cycles performed between April 2008 and December 2013. Factors such as nationality, maternal age, origin of the oocytes (donated or not), marital status and previous cycle outcome were correlated both, to the frequency of replying and with the patients’ decision. Chi square and ANOVA tests were used for statistical analysis.

RESULTS: Answers were obtained from 1171 patients (40.42%), and this percentage was independent of their nationality, maternal age, origin of the oocytes and marital status. However, couples who delivered at least one child after the treatment were more predisposed to answer than the ones with a negative outcome (38.30% vs 30.00%; p<0.05). Overall, percentage of choices were similar: to keep their embryos for further cycles (26.39%); to discard them or to donate them either to other couples or for research purposes. The aim of this study was to assess patients’ decision about disposition of their embryos and evaluate which variables could affect that choice.

DESIGN: Retrospective observational study.

MATERIALS AND METHODS: A total of 2897 letters were sent to patients with frozen embryos obtained from cycles performed between April 2008 and December 2013. Factors such as nationality, maternal age, origin of the oocytes (donated or not), marital status and previous cycle outcome were correlated both, to the frequency of replying and with the patients’ decision. Chi square and ANOVA tests were used for statistical analysis.

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RESULTS:

CONCLUSIONS: Our results show promise in performing PGS and transferring day-4 blastocysts on implantation rates and pregnancy. Moreover, we propose late day-4 embryo observations as a valid alternative to the conventional day-3 embryo check. There are reports of transferring “day 4” morula, but only few studies show blastocyst formation, cryopreservation and subsequent embryo transfer at day 4. We are currently recording data from more but only few studies show blastocyst formation, cryopreservation and subsequent day-3 embryo check. There are reports of transferring ‘‘day 4’’ morula, but they were more reluctant to give their embryos for research purposes (19.56% vs 14.04; p<0.05). When we compared oocyte recipients vs. regular patients ones preferences, we observed that the percentage of embryo maturation 3 hours after removal of each cumulus cell complex, with subsequent vitrification of those eggs that extruded their polar bodies (MI-II oocytes). B. Sibling oocytes from both groups were warmed at the same time. Warmed oocytes were fertilized by ICSI after 3 hours of in vitro culture and osmotic equilibrum. On day 5, blastocyst formation was assessed and embryo transfer was performed. Results were analyzed by the Chi-square (P<0.05) statistical test.

RESULTS:

CONCLUSIONS: To our knowledge, these are the first reported pregnancies resulting from vitrified MI-II donor oocytes. The two clinical pregnancies recorded in this study both delivered at or near term without complication to either mother or either fetus. These deliveries offer ‘proof of concept’ for this management of immature eggs at the time of egg collection. The ability to bring immature oocytes from MI to MII in culture and then vitrify them for later use provides a novel strategy to increase the number of usable eggs in each IVF procedure and have the potential to increase the total reproductive potential of each egg retrieval.

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SURPLUS FROZEN EMBRYOS. WHAT PATIENTS DECIDE ABOUT THEM? J. Molina, M. Riqueros, M. Florensa, A. Ballesteros Boluda, M. Esbert. IVF Laboratory, IVI Barcelona, Barcelona, Spain; IVF laboratory, IVF Director, Barcelona, Spain; IVI Barcelona, Barcelona, Spain.

OBJECTIVE: IVF treatments can produce a high number of surplus frozen embryos. Two years after the treatment, according to the Spanish law, patients may decide to keep their frozen embryos for further cycles, to discard them or to donate them either to other couples or for research purposes. The aim of this study was to assess patients’ decision about disposition of their embryos and evaluate which variables could affect that choice.

DESIGN: Retrospective observational study.

MATERIALS AND METHODS: A total of 2897 letters were sent to patients with frozen embryos obtained from cycles performed between April 2008 and December 2013. Factors such as nationality, maternal age, origin of the oocytes (donated or not), marital status and previous cycle outcome were correlated both, to the frequency of replying and with the patients’ decision. Chi square and ANOVA tests were used for statistical analysis.

RESULTS: Answers were obtained from 1171 patients (40.42%), and this percentage was independent of their nationality, maternal age, origin of the oocytes and marital status. However, couples who delivered at least one child after the treatment were more predisposed to answer than the ones with a negative outcome (38.30% vs 30.00%; p<0.05). Overall, percentage of choices were similar: to keep their embryos for further use (26.39%); to discard them (24.93%); to donate them to other couples (17.68%) and to give them to research (31.00%). Maternal age was higher in couples who decided to donate their embryos to other patients (41.38±4.55) respect the ones that preferred the donation for research purposes (39.56±4.89), the maintenance for their future use (37.38±4.72) or the disposal (40.87±5.21) p<0.05. We found that foreign patients preferred to dispose (26.81% vs 21.30%; p<0.05) or to donate their embryos to other couples (19.56% vs 14.04; p<0.05) in a higher proportion than national patients do, but they were more reluctant to give their embryos for research purposes (28.50% vs 35.84%; p<0.05). When we compared oocyte recipients vs. regular patients ones preferences, we observed that the percentage of embryo maturation 3 hours after removal of each cumulus cell complex, with subsequent vitrification of those eggs that extruded their polar bodies (MI-II oocytes). B. Sibling oocytes from both groups were warmed at the same time. Warmed oocytes were fertilized by ICSI after 3 hours of in vitro culture and osmotic equilibrum. On day 5, blastocyst formation was assessed and embryo transfer was performed. Results were analyzed by the Chi-square (P<0.05) statistical test.

RESULTS:
 donation to other couples was higher (21.67% vs 5.26%; p<0.05) while less of them wanted to maintain their embryos for further cycles (21.44% vs 41.75%; p<0.05).

CONCLUSIONS: Patients who have delivered a child after an IVF treatment are more predisposed to reply how to act with their frozen embryos, although the global percentage of answers is low and a major effort should be done to increase it. The four options available are elected in similar frequencies. According to our study maternal age, nationality and the origin of the oocytes used in the treatment can interfere in patients’ decision. A more sociological survey should be performed in order to understand patients’ decision.

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A NOVEL HIERARCHICAL CLASSIFICATION METHOD BASED ON MORPHOLOGY DYNAMICS OF VITRIFIED-WARMED BLASTOCYSTS TO FORECAST IMPLANTATION POTENTIAL. A. Coello, A. Cobo, A. Galan, L. Alegre, M. Nohales, M. Meseguer. IVI, Valencia, Spain.

OBJECTIVE: The analysis of warmed blastocysts by time lapse-imaging is providing new markers for implantation, establishing quantitative values linked with clinical outcome. The objective of this study is to identify predictive morphological variables for implantation and develop a hierarchical model subdividing warmed blastocysts into categories with different implantation potential.

DESIGN: Retrospective study.

MATERIALS AND METHODS: The study included 435 thawed blastocysts with known implantation data which were evaluated using time lapse imaging. Blastocysts were routinely placed in Embryoscope® (Unisense-FertiliTech, Denmark) from immediately after warming until transfer (>3.5h). Embryos were vitrified and warmed with Cryotop method (Kita zatoBiopharma). Variables studied included initial and minimum thickness of zona pellucida (ZP) (μm), initial and maximum area of blastocyst (μm²), area of inner cell mass (μm²), expansion (whether the embryo expands or not after warming) and presence of collapse or contraction after warming procedure. After defining optimal ranges according to consecutive quartiles, a logistic regression analysis was performed combining the variables described before and blastocyst morphological classification criteria defined by the Spanish Association of Embryologists (ASEBIR) into A, B, C or D.

RESULTS: We observed that expansion of warmed blastocysts is strongly correlated with implantation (32.8% in blastocysts that expand (132/403) vs 9.4% in blastocysts that do not expand (3/32); P=0.006). Throughout logistic regression analysis the model identified the maximum area of the blastocyst OR=0.41 (95%CI 0.22 - 0.77) followed by the initial area OR=0.62 (95%CI 0.35 - 1.08) as the most predictive variables characterizing implanting embryos (blastocyst morphology was not considered relevant in our model). We made a hierarchical model representing a classification tree, which subdivision embryos into four categories from A to D with decreasing expected implantation potential.

CONCLUSIONS: We propose a hierarchical model to classify warmed blastocysts according to their probability of implantation. This model is not considering relevant standard blastocyst morphology classification when compared with morphology dynamics. To our knowledge, this is the first attempt of making a model for implantation using time lapse imaging in warmed blastocysts. This novel classification may be useful to consider implantation potential.

Distribution of warmed blastocysts according to the model category.

<table>
<thead>
<tr>
<th>Categories</th>
<th>N</th>
<th>IR (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>268</td>
<td>40.0</td>
</tr>
<tr>
<td>B</td>
<td>65</td>
<td>32.3</td>
</tr>
<tr>
<td>C</td>
<td>47</td>
<td>23.1</td>
</tr>
<tr>
<td>D</td>
<td>23</td>
<td>5.4</td>
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SUCCESSFUL VITRIFICATION OF HUMAN EMBRYOS USING EQUILIBRATION SOLUTION. O. Bern, Y. Nathan, R. Ron-El, A. Arav; IVF, Assaf Harofeh, Beer Yaacov, Israel; FertileSafe Ltd., Ness Ziona, Israel.

OBJECTIVE: Vitrification is an alternative method to slow freezing, which reduces chilling sensitivity and crystallization damages. However, vitrification requires high concentrations of cryoprotectants (CPs) which exposes cells to osmotic and toxicity damages. We modified the minimal drop size (MDS) technique by exposing the embryos only to equilibration solution (ES), after that partial drying and finally plunged into liquid nitrogen (LN).

DESIGN: To compare survival and blastulation rates of day 2 embryos resulting from one and three pronuclei (1PN and 3PN) undergoing conventional vitrification or vitrification using only equilibration solution (ES).

MATERIALS AND METHODS: Day 2 embryos resulting from land 3PN oocytes were randomized into two groups: Group A - embryos that were vitrified utilizing the vitrification cooling kit according to the manufacturer instructions (Origo-Sage); Group B - one or two embryos were transferred with minimal volume of culture medium to the top of the drop of ES with a free-fall for 10 minutes. The drop containing the embryo/s with a volume of < 0.15μL was transferred to a Kita zato CryoTop Vitrification Device and hold for 30 seconds before plunging into LN. Warming was performed with the vitrification warming kit (Origo-Mediculit). The embryos were cultured to the blastocyst stage in GTM medium (Vitrolife Sweden). The outcome of the warmed groups A and B embryos was compared in terms of survival and blastulation rates.

RESULTS: There were 71 warmed embryos in group A and 62 in group B. Mean patients’ age was 32.6±5.9 and 32.9±5.6 years respectively, and the mean number of blastomeres was 4.6±1.8 and 4.6±1.6. Mean number of abnormal fertilizations (1PN and 3PN) per patient was 2±2.1 in both groups. The rates of intact embryos were 56% (40/71) in group A and 66% (41/62) in group B. The overall survival rate (intact embryos and embryos with ≥50% viable blastomeres) was 91% (65/71) and 89% (55/62) respectively. The blastulation rate was 21% (14/65) and 20% (11/55) which is comparable with the rate in our center (19%) for embryos emerging from 1 and 3PN. All the above figures are with no statistical significance.

CONCLUSIONS: In the present study we have demonstrated that using a minimal volume of ES (MDS technique, Arav 1989) enables vitrification of embryos if partially dried before cooling in liquid nitrogen. The 30 sec dehydration of the drops permits the vitrification of the drops probably due to an increase in the viscosity when the water in the sample dehydrates and the concentration in the solution increases. Also, the fact that the volume of the drop decreases along with the dehydration, contributes to the success of this method. The simplicity of the technique may reduce toxicity of cryoprotectants and improve the safety of the vitrification process.

P-89 Tuesday, October 18, 2016

TIME FROM EGG RETRIEVAL TO FIRST EMBRYO TRANSFER DOES NOT AFFECT LIVE BIRTH RATES IN A FREEZE-ALL STRATEGY. K. Lattes, R. Vassena, D. Garcia, M. Brassecos, V. Vernaeve; "Centro de Infertilidad y Reproducción Humana, Barcelona, Spain; Clinica EUGIN, Barcelona, Spain; Fundacio Privada EUGIN, Barcelona, Spain; Eugin, Barcelona, Spain.

OBJECTIVE: Controlled ovarian stimulation (COH) leads to decreased reproductive outcomes by affecting the embryo-endometrium synchrony. So far, there is no agreement on the best moment to perform a FET after freeze-all in order to maximize outcomes for the patient. The aim of this study is to determine whether time from ovum pick-up (OPU) to the first frozen embryo transfer (FET) affects live birth rates in a freeze-all strategy.

DESIGN: Retrospective analysis of the first FET in IVF-ICSI cycles in which all embryos were vitrified electively.

MATERIALS AND METHODS: We analyzed 680 freeze-all cycles, performed between January 2012 and December 2014. Reproductive outcomes between the first FET who took place within the first menstrual cycle following OPU (n=324) or afterwards (n=356) were compared. Student’s t-test for independent samples and Chi-square analysis were used as needed. A multivariate logistic regression analysis was performed adjusting for

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maternal age, ovulation trigger drug (hCG vs. GnRH agonist), number of retrieved oocytes, day of embryonic development at transfer, number of transferred embryos and reason for freezing. Differences were considered significant if \( p < 0.05 \).

RESULTS: There was no difference in live birth rate between FET performed during the first menstrual cycle following OPU vs. subsequent menstrual cycles (36.4% vs 32.3%, respectively; \( p=0.258 \)). Moreover, we found no difference in implantation rate (32.5% vs 29.5%; \( p=0.289 \)), as well as biochemical pregnancy (49.7% vs 48.3%; \( p=0.719 \)), clinical pregnancy (43.5% vs 41.3%; \( p=0.555 \)), and pregnancy loss (13.3% vs 15.7%; \( p=0.363 \)) between groups. The multivariate analysis found no impact of time from retrieval to effective FET on live birth rates (OR 0.90; 95% CI 0.65-1.25).

The factors that significantly affected live birth rates were, as expected, maternal age (OR 0.93, 95% CI 0.89-0.97), number of retrieved oocytes (OR 1.03, 95% CI 1.001-1.06), day of embryonic development at transfer (day 4+ vs 4; OR 1.53; 95% CI 1.02-2.29) and number of transferred embryos (OR 1.72, 95% CI 1.23-2.41).

CONCLUSIONS: According to our results, clinicians do not need to wait more than one menstrual cycle before performing the first FET in freeze-all cycles. This allows for the reduction of the psychological impact that delaying embryo transfer can have on patients, without compromising reproductive outcomes.

P-91 Tuesday, October 18, 2016

IMPACT OF DIFFERENT VITRIFICATION DEVICES ON OOCYTE DNA INTEGRITY IN OOCYTES. H. L. Feng T. Tsai Ob/Gyn, New York -Presbyterian Health System Queens, Cornell University, New York, NY.

OBJECTIVE: In our previous study, we showed a clinical improvement in Human IVF outcomes with iVitri \(^a\) versus cryotop. The devices ability to protect DNA integrity may be the reason for this difference. This study evaluated the DNA integrity between 3 different devices.

DESIGN: In vitro experimental animal model.

MATERIALS AND METHODS: Total of 6200 bovine cumulus-oocyte complexes (COCs) were commercially purchased and matured in vitro for 24 hours at 38.5°C in an atmosphere of 5% CO2 in air. 3200 matured bovine oocytes were selected for vitrification by using commercial cryoloops; cryoleaf, cryotop and iVitri. The survival rate, DNA apoptosis and DNA methylation were assessed after vitrified bovine oocytes were thawed.

RESULTS: The study results demonstrated that there were no significant differences in the survival rates (9.1%, 89.4% and 92.2%) of bovine oocyte with loading vitrification fluid under 0.5μl by using Cryoleaf, Cryotop and iVitri. However, the survival rates (98.5% and 98.8%) were higher in iVitri in the 1.0 μl and 1.5 μl fluid as compared with Cryoleaf (90.1% and 93.2%) and Cryotop (90.1% and 88.1%). Furthermore, there was a lower DNA apoptosis (8.1%) and DNA methylation (2.1%) in iVitri comparing with Cryoleaf (45.8% and 11.5%), Cryoleaf (35.2% and 8.5%), and Cryotop (29.9% and 5.5).

CONCLUSIONS: Our results demonstrate that the type of vitrification device and loading volumes may play an important role in reducing DNA apoptosis and methylation. This may be one reason why iVitri \(^b\) was superior to the cryotop in our human IVF study.

Supported by: The study was partially supported by NSFC abroad young scientist fund (31128013C120205) (H.L.F) and the Academic Research Project (IIS no. 39252) from Merck and Co. Inc. (T.T/ H.L.F).

P-92 Tuesday, October 18, 2016

ABSTRACT WITHDRAWN
THE EFFECT OF ASSISTED HATCHING ON FROZEN EMBRYO TRANSFER LIVE BIRTH RATE AND CLINIC TRENDS. J. Knudtson, C. Failer, J. Gelfond, T. A. Chang, R. S. Schenken, R. D. Robinson, Obstetrics and Gynecology, University of Texas Health Science Center San Antonio, San Antonio, TX; Epidemiology and Biostatistics, University of Texas Health Science Center San Antonio, San Antonio, TX.

OBJECTIVE: To identify the effect of assisted hatching on live birth rate in a large cohort of first cycle frozen embryo transfers (FETs) and define practice trends for the use of Assisted Hatching (AH) via the Society for Assisted Reproductive Technology Clinical Outcomes Reporting System (SART CORS).

DESIGN: Retrospective cohort using cycles reported in the SART CORS between 2004 and 2013.

MATERIALS AND METHODS: 166,318 first, frozen, autologous IVF cycles in women undergoing frozen embryo transfer from 2004-2013 SART registries were analyzed. Main outcome was live birth rate in cycles in which all embryos received assisted hatching (allAH) and those in which none received assisted hatching (noAH). Patients with and without AH were matched by propensity scores, and logistic regression was used to adjust for potential confounders. Multiple imputation was used for missing covariates. Secondary outcomes included fetal anomalies and monozygotic twinning. Differences in the AH groups in regards to etiology of infertility, and previous gravidity were analyzed. Clinics use of AH were analyzed yearly and by clinic location.

RESULTS: The study population included 55,891 live births. Of the 76,220 cycles with allAH, there was a 33.7% live birth rate compared to 33.6% from noAH. After propensity matching and multiple imputation, logistic regression showed that AH had no significant effect on the probability of live birth (OR 1.02, 95% CI 1.00 to 1.04, p=0.08). The allAH cohort had significantly different etiologies of infertility, and previous gravidity (p<0.001) compared to noAH. There was no difference in monozygotic twinning in live births with allAH vs. noAH (1.1% vs 1.1%, p=0.45). There was no difference in the number of reported fetal anomalies with allAH vs. noAH (0.6% vs 0.5%, p=0.53). From 2004-2013, the rate of clinics performing at least 50% of their cycles with AH has been stable ranging from 25.5% to 28.0%. Cycles from clinics in the Midwest (37.9%) and Northeast (33.0%) receiving at least 50% of their cycles with AH has been stable ranging from 25.5% to 28.0%.

CONCLUSIONS: In all first cycle FETs analyzed, there was no difference in live birth rate with AH. However, the groups were different in relation to etiology of infertility and previous gravidity. Further characterization of the specific differences in the groups may identify individual patients that benefit from AH. There was no increase in fetal anomalies or monozygotic twinning with AH.

Supported by: Departmental.

FREEZE-ALL POLICY IN POOR RESPONDERS. M. Roque, M. Valera, F. Guimaraes, A. Kostolias, M. Sampaio, S. Geber. Reproductive Medicine, ORIGEN - Center for Reproductive Medicine, Rio de Janeiro, Brazil; ORIGEN - Center for Reproductive Medicine, Rio de Janeiro, Brazil; Reproductive Medicine, ORIGEN - Center for Reproductive Medicine, Belo Horizonte, Brazil.

OBJECTIVE: Elective frozen-thawed embryo transfer (FET) - freeze-all policy - has emerged as an alternative to fresh embryo transfer (ET) during in vitro fertilization (IVF) cycles. Although fresh ET is the norm during assisted reproductive therapies (ART), there are many concerns about the possible adverse effects of controlled ovarian stimulation (COS) over the endometrium. The supra-physiologic hormonal levels that occur during a conventional COS are associated with modifications in the peri-implantation endometrium that may be related to decrease in implantation and pregnancy rates when comparing fresh to frozen-thawed embryo transfers. To date, there are no studies evaluating this strategy in poor responder patients. The main objective of this study was to compare IVF outcomes between fresh ET and elective FET (freeze-all) in poor responders.

DESIGN: Prospective observational cohort study.

MATERIALS AND METHODS: The study was conducted between July 2012 and December 2015. A total of 378 poor responder patients (following Bologna criteria) submitted to COS with gonadotropin-releasing hormone ( GnRH ) antagonist protocol and cleavage stage embryo transfer were included. In the fresh group (n=247), embryo transfers were performed only if progesterone levels were <1.5 mg/mL on the trigger day. The freeze-all group (n=131) comprised patients that had all embryos cryopreserved in the fresh cycle and had the first embryo transfer after endometrial priming and embryo thawing. Data were described as the mean +/- standard deviation or percentages. The statistical analysis was performed using Student’s t test, the chi-square test, and linear regression models. A p value of
<0.05 was considered statistically significant. Statistical analysis was done with the Statistical Package for Social Sciences (SPSS version 24.0). The main outcome measure was ongoing pregnancy rate. The secondary outcomes were implantation, pregnancy, and clinical pregnancy rates.

RESULTS: IVF outcomes in fresh and freeze-all groups are expressed in Table 1.

CONCLUSIONS: This is the first study evaluating the freeze-all strategy in poor responder patients. There were no differences in IVF outcomes when comparing fresh to elective frozen-thawed embryo transfer. These results suggest that in poor responders the IVF outcomes may not be improved by performing the freeze-all strategy.

P-96 Tuesday, October 18, 2016

LIVE BIRTH RATE AFTER FRESH OR FROZEN-TAHWED EMBRYO TRANSFERS IN RELATION TO MATERNAL AGE: A RETROSPECTIVE COHORT STUDY OF 13426 CYCLES. X. Li, R. Huang, C. Fang, Y. Wang, X. Liang. Sixth Affiliated Hospital of Sun Yat-sen University, Guangzhou, China.

OBJECTIVE: This study aimed to assess live birth rate after fresh or frozen thawed embryo transfers in relation to maternal age for an individualized strategy for overall reproductive outcome.

DESIGN: A retrospective cohort study.

MATERIALS AND METHODS: All patients undergoing fresh or frozen embryo transfers from 2010 to 2015 in our unit were enrolled. Individualized controlled ovarian hyper-stimulation protocols included long GnRH agonist, GnRH antagonist and minimal stimulation protocols. 5000-10,000 IU HCG (Ovidrel, Merck Serono) was utilized for follicular maturation and oocyte retrieval performed when appropriate. Intracytoplasmic sperm injection was adopted if the concentration of motile sperm was <1×10^6/mL otherwise in vitro fertilization was used. Vitrification was performed for embryo freezing. The primary outcome was Live birth rate (LBR), defined as rate of deliveries that resulted in at least one live born baby per transfer. Chi-square and binary regression analysis were used for data analysis. A P<0.05 indicated significant result.

RESULTS: A total of 13426 cycles were assessed. We stratified patients into different age groups: i.e. 18-30 years, 30-34 years, 35-39 years and >39 years. Firstly, we found frozen cycles had higher LBR than that of fresh cycles (42.62% vs.38.81%, P<0.01). As expected, in blastocyst embryo transfer, LBR was significantly higher in frozen cycles in patients older than 30 years (56.02% vs.53.71%, P<0.106; 52.46%vs.42.93%, P<0.01; 38.11% vs. 29.27%, P<0.01; 19.38%vs.11.21%, P=0.01 for group1-4 respectively). However, for cleavage-stage embryo, frozen cycles had lower LBR than fresh cycles (39.43% vs.42.62%, P<0.05; 35.70% vs.44.58%, P <0.01; 23.75%vs.29.09%, P= 0.01; 8.70% vs.10.38%, P=0.17 for age group1-4 respectively), despite difference didn’t reached statistical significance in those over 40 years. Further multivariate analysis confirmed the above results after adjusting covariates (such as age, number of embryo transferred, embryo quality, infertility etiologies etc.). Specifically, frozen blastocyst embryo transfers in cases over 40 years had more than twice chance getting live born baby than that of fresh cycles (adjusted OR 2.18,P=0.04). In term of miscarriage rate, no significant difference was observed between fresh and frozen cycles regardless of maternal age.

CONCLUSIONS: In every age-group, frozen cleavage-stage embryo transfers had lower LBR than that of fresh cleavage-stage embryo transfers, while frozen blastocyst transfers resulted in higher LBR than that of fresh cycles, showing blastocyst was the suitable stage for cryopreservation. Frozen blastocyst transfers obtained a comparatively stable high LBR, especially in cases over 40 years.

P-97 Tuesday, October 18, 2016

ZYGOTE BANKING OFFERS POOR PROGNOSIS PATIENTS HIGH IMPLANTATION AND CLINICAL PREGNANCY RATES. A. E. Batcheller, W. B. Schoolcraft, M. Katz-Jaffe. tCRM Minneapolis, Edina, MN; 3Medical Director, Colorado Center for Reproductive Medicine, Lone Tree, CO; 4Colorado Center for Reproductive Medicine, Lone Tree, CO.

OBJECTIVE: Poor prognosis in vitro fertilization (IVF) patients of advanced maternal age (AMA) and diminished ovarian (DOR) reserve of struggle with fertility treatment burn out. Additionally, while many desire more than one child, pregnancy near the end of the reproductive lifespan may negate the possibility of future conception following successful delivery of an ART conceived child. Banking euploid embryos during this critical time period may offer these patients the opportunity to expand their genetically linked family.

DESIGN: Observational Study.

MATERIALS AND METHODS: 532 patients identified as poor prognosis by AMH <1.1 ng/mL or antral follicle count <7 underwent 1-2 zygote banking cycles, followed by warming of these vitrified zygotes and culture alongside fresh zygotes resulting from the patients final retrieval, culminating in trophectoderm biopsy of all resulting blastocysts. Euploid blastocysts were transferred in a subsequent frozen embryo transfer (PET).

RESULTS: Characteristics of zygote banking cycles by age listed in Table 1. 389 patients (73.1%) had euploid embryos for transfer. No blastocyst development was noted in 4.7% of patients (mean age 43.1 years). The mean age of patients with all aneuploid cycles was 41.8 years, while the mean age of patients with euploid embryos was 37.9 years. We experienced 98.7% survival of blastocysts after thaw. On average, 1.4 embryos were transferred, with an implantation rate of 67.8%, a missed abortion rate of 4.7%, and an ongoing pregnancy rate of 71.2% noted.

CONCLUSIONS: Zygote banking offers poor prognosis IVF patients the opportunity to achieve high blastocyst conversion, implantation, and clinical pregnancy rates. Given that many of these patients are nearing the end of the reproductive potential, a banking strategy may allow them to increase the number of euploid blastocysts cryopreserved for multiple transfer attempts while reducing patient frustration and burn out. Notably, blastocyst conversion decreases and all aneuploid results increase dramatically after age 43.

P-98 Tuesday, October 18, 2016

CLINICAL OUTCOME OF TWO POPULAR VITRIFICATION DEVICES FOR HUMAN IVF. T. Tsai H. L. Feng. Obst/Gyn, New York Presbyterian Health System Queens, Cornell University, New York, NY.

OBJECTIVE: Currently, highly efficient vitrification devices for cryopreservation of human oocytes and embryos play an important role in protecting DNA integrity and consequently impacting IVF pregnancies. Two popular vitrification devices were selected for this study; the results may provide useful guidance for IVF laboratories to select the best device.

DESIGN: Prospective.

MATERIALS AND METHODS: 375 consecutive IVF/Donor cycles were included in the study. 1083 mature donor oocytes, 929 cleavage embryos and 695 blastocysts were vitrified 50/50 between cryotop and iVitri® devices. The outcomes of survival, fertilization, pregnancy, and miscarriage rates were compared.

RESULTS: There were no significant differences in the survival rates of oocytes (98% vs 99%), cleavage stage (97% vs. 98%) and blastocyst stage (93% vs. 99%) between cryotop and iVitri® devices; However, the increased implantation rate ( donor eggs, 85% vs. 70%; cleavage 56% vs. 50%;
blastoscyt 55% vs. 48%) and decreased miscarriage rate (donor eggs, 4% vs. 7%; cleavage 5% vs. 9%; blastocyst 2% vs. 6%) were found in the iVitri® group as compared to cryotop group.

CONCLUSIONS: Our results demonstrate there is significant difference between vitrification devices. In our study the iVitri® groups had better outcomes and significantly reduced miscarriage rate in donor and IVF cycles. This may be due to iVitri® device better ability to protect DNA integrity according to previous study.

Supported by: The study was partially supported by the Academic Research Project (IIS no. 39252) from Merck and Co. Inc. (H.L./F/T).

**P-99** Tuesday, October 18, 2016

**MOTHER DOESN’T ALWAYS KNOW BEST: EMBRYOS DERIVED FROM CYROPRESERVED OOCYTES EXHIBIT DEVELOPMENTAL DELAY PRIOR TO ZYGOTIC TRANSITION.** A. K. Masbou, S. Druckenmiller, D. H. McCulloch, C. McCaffrey, K. N. Goldman, N. Noyes, NYU Fertility Center, New York, NY; NYU School of Medicine, New York, NY; Department of Obstetrics and Gynecology, New York University Fertility Center, New York, NY; Obstetrics and Gynecology, New York University Fertility Center, New York, NY; Obstetrics and Gynecology, New York University, New York, NY.

OBJECTIVE: To compare early embryo development rates in fresh IVF (FRESH) vs previously cryopreserved oocyte thaw (OOT) cycles.

DESIGN: Retrospective cohort study including all FRESH and OOT from 2005-2015 at a single, high-volume university-based fertility center.

MATERIALS AND METHODS: Embryos derived from FRESH (n=95,260) were compared to those from OOT (n=1,730) on a per-embryo basis. Primary outcome measures included number of cells present on embryonic day (D) 2 and D3, overall blast formation rate (BFR) and BFR achieved on D5. Chi-square was used for analysis.

RESULTS: The table shows early embryo development of FRESH vs. OOT embryos. 2PN fertilization rates were clinically comparable. On D2 and D3, the mean no. of cells and % of embryos reaching 4 and 8 cells were significantly lower for OOT compared to FRESH. Additionally, overall BFR was lower in OOT (48.3%) vs. FRESH (60.8%), although both groups had a near 50% BFR by D5 (46.7% and 48.4%, respectively).

CONCLUSIONS: Previous research at our facility has shown no difference in live birth rate per mature oocyte retrieved or per embryo transferred when comparing OOT and FRESH; however, a lower BFR was demonstrated [1]. Here, we confirm the latter and pinpoint the developmental perturbation to an earlier embryonic stage, signifying a maternal genome signaling insult. Although little research has been performed in the OOT population, mouse studies on standard frozen embryos suggest human genes may be linked to embryonic growth control [2]. Other animal studies show that cryoprotectants may impact chromosomal function or cause osmotic damage to oocytes [3-5]. Reassuringly, D5 BFR was not different when comparing FRESH and OOT; this signifies developmental competence even after freezing and vitrification as a valuable means of fertility preservation. We are supporting the latter and pinpoint the developmental perturbation when comparing OOT and FRESH; however, a lower BFR was demonstrated [1].

**References:**

**P-100** Tuesday, October 18, 2016


OBJECTIVE: To delineate the optimal hormonal criteria for luteinizing hormone (LH) and estradiol in efforts to optimally identify the LH surge in natural cycle frozen-thawed embryo transfer (NC-FET).

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Patients who underwent blastocyst NC-FET between January 2013 and August 2015 and who either had preimplantation genetic screening (PGS) or were ≤ 35 years old but did not undergo PGS (non-PGS) were included. Patients who were recipients of donated oocytes or had a history of Asherman syndrome were excluded. Group A includes patients whose LH surge was defined as the first LH ≥ 15 IU/L during the follicular phase. Group B encompasses those whose LH level continued to rise and the surge was defined as the highest LH level occurring a day after LH ≥ 15 IU/L. χ² and Fisher’s exact tests were used for categorical variables. Odds ratio (OR) with 95% confidence intervals (CI) were calculated and adjusted for patient’s age, number of transferred embryos, blastocyst grading, peak endometrial thickness, and body mass index.

RESULTS: A total of 403 non-PGS and 333 PGS NC-FET were included. In non-PGS patients, group B (n=186) had a significantly higher live birth rate (LBR) (52% vs. 39.2%; p=0.01) than group A (n=217). The increased odds ratio remained significant after adjusting for patient’s age, number of transferred embryo, peak endometrial thickness, blastocyst grading, and BMI (aOR=2.1; 95% CI=1.2-3.6). In contrast, group A had a comparable LBR with group B in PGS patients (59% vs. 56.1% respectively; p=0.59). The odds ratio remained unchanged after adjusting for all identified confounders (aOR=0.9; 95% CI=0.5-1.4). Patients who had a drop in estradiol level on the day of the defined LH surge had a comparable LBR with those who did not, in both PGS (p=0.4) and non-PGS patients (p=0.6).

CONCLUSIONS: In patients who are not undergoing PGS, measuring LH level day after LH ≥ 15 ng/mL and defining the LH surge as the highest LH level attained are associated with better NC-FET outcomes than defining it at the first LH ≥ 15 ng/mL. However, both LH surge definitions are associated with comparable outcomes for patients undergoing PGS, which is possibly due to the effect of assisted hatching that occurs during embryo biopsy. Estradiol trend does not appear to be a good indicator to define the LH surge associated with optimal NC-FET outcomes.

**References:**
THE SIGNIFICANT EFFECT OF CRYOPRESERVATION IN FRESH IN VITRO FERTILIZATION (FRESH) AND PREVIOUSLY-CRYOPRESERVED OOCYTE THAW CYCLES (OOT) IS APPARENT EARLY AND UNRELATED TO PLOIDY. A. K. Masbou,a D. H. McCulloch,2 M. Black,2 N. Noyes,3 J. Grifo.4 NYU Fertility Center, New York, NY;2Obstetrics and Gynecology, New York University Fertility Center, New York, NY;4NYU Langone School of Medicine, New York, NY;5NYU School of Medicine, New York, NY; NYU Langone Medical Center, New York, NY.

OBJECTIVE: To compare the rates of euploid embryos in FRESH vs. OOT cycles.

DESIGN: Retrospective cohort study of all FRESH vs. OOT cycles, including donors, undergoing preimplantation genetic screening (PGS) with microarray-based comparative genomic hybridization (aCGH) or next-generation sequencing (NGS) from 2011-2015 at a single, high-volume university-based fertility center.

MATERIALS AND METHODS: Embryos biopsied for PGS derived from FRESH were compared to those from OOT on a per-cycle basis (n=1643 and 111, respectively). PGS was performed by aCGH or NGS for both FRESH (n=1149 and 504, respectively) and OOT (n=64 and 47, respectively). Age was controlled for by linear regression analysis of euploidy rate vs. age. Euploid embryos were divided into no. euploid per egg and no. euploid per embryo biopsied and by method of PGS performed; comparison was made by examining residuals from the regression line for FRESH. SEM and t test were used.

RESULTS: The average no. of euploid blasts per FRESH cycle was 1.77±2.26 and 1.19±1.61 for aCGH and NGS respectively; the average no. of eggs was 13.8±8.0 and 13.8±8.4. The average no. of euploid blasts per OOT cycle was 1.24±1.65 and 0.85±1.01 for aCGH and NGS respectively; the average no. of eggs per thaw was 14.72±8.8 and 13.69±5.71. Euploidy rate per egg was significantly lower in the OOT than in the FRESH for both aCGH and NGS when analyzing the mean residuals from the regression line. However, there was no difference in euploidy rate per biopsied blast in either group, irrespective of PGS method.

CONCLUSIONS: Previous research at our facility has shown that the blast formation rate is significantly lower in OOT vs FRESH [1]. After controlling for the age-effect on aneuploidy, we observed that the euploidy rate per egg was lower in the OOT vs the FRESH for both aCGH and NGS; this difference disappears once the embryos make it to blastocyst stage, as there was no difference in no. of euploid per embryos biopsied. The difference in average no. eggs in FRESH vs OOT is insignificant and a misleading comparison as all oocytes retrieved were not thawed in totality for each OOT. The data suggest that attrition in the OOT group may be secondary to the cryopreservation technique, although attrition occurs regardless of ploidy. Further improvements in cryopreservation technique are necessary to optimize patient outcomes.

References:

Table 1

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<th>OOT euploid/egg (residual)</th>
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HIGH VARIABILITY IN CHROMOSOME ABNORMALITY RATES IN EMBRYOS FROM YOUNG INFERTILE WOMEN. S. S. Sawarkar,a J. Zhang,a D. L. Hill,a J. S. Hesla,a A. Coates,a L. Ribustello,a S. Ghadir,a S. Munne.9 Research, Reprogenetics, Livingston, NJ; 9New Hope Fertility Center, New York, NY; 9ART Reproductive Center, Beverly Hills, CA; 9Oregon Reproductive Medicine, Portland, OR; 9Reprogenetics, Livingston, NJ; 9Southern California Reproductive Center, Beverly Hills, CA.

OBJECTIVE: To analyze whether Preimplantation Genetic Diagnosis (PGD) for chromosome abnormalities should be offered to all infertile patients irrespective of maternal age.

DESIGN: Patients under the age of 35 years, undergoing IVF and PGD for chromosomal abnormalities using either array CGH or high resolution next generation sequencing (hr-NGS) and blastocyst biopsy were included in this retrospective study. 22,052 Embryos from 3,028 patient cycles that produced 4 or more embryos per cycle were included in this study. Patients who used egg donors and women 35 and older were excluded.

MATERIALS AND METHODS: The IVF cycle was performed in 127 different IVF clinics, and the PGD analysis performed by the same PGD laboratory. The analysis was performed using Microsoft Excel and R statistical package.

RESULTS:

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<tr>
<th>MATERNAL AGE</th>
<th>RANGE OF % ABNORMAL EMBRYOS</th>
<th>% OF PATIENTS WHO HAVE &gt;50% ABNORMAL EMBRYOS</th>
<th>NUMBER OF CYCLES EMBRYOS ANALYZED</th>
<th>AVERAGE ABNORMALITY RATE</th>
</tr>
</thead>
<tbody>
<tr>
<td>17-25</td>
<td>0%-43.33%</td>
<td>35.28%</td>
<td>68</td>
<td>511</td>
</tr>
<tr>
<td>26-29</td>
<td>0%-45.71%</td>
<td>34.79%</td>
<td>58</td>
<td>430</td>
</tr>
<tr>
<td>&gt;30</td>
<td>0%-100%</td>
<td>50.00%</td>
<td>85</td>
<td>623</td>
</tr>
<tr>
<td>28-30</td>
<td>0%-46.77%</td>
<td>36.36%</td>
<td>152</td>
<td>1203</td>
</tr>
<tr>
<td>31-33</td>
<td>0%-49.00%</td>
<td>37.04%</td>
<td>194</td>
<td>1462</td>
</tr>
<tr>
<td>34-35</td>
<td>0%-49.50%</td>
<td>37.79%</td>
<td>258</td>
<td>1983</td>
</tr>
<tr>
<td>&gt;35</td>
<td>0%-50.00%</td>
<td>38.89%</td>
<td>338</td>
<td>2511</td>
</tr>
</tbody>
</table>

CONCLUSIONS: Age is only a gross indicator of chromosomal abnormalities and there seems to be great variation within all ages. Specifically in young patients, who historically were not recommended PGD for chromosome abnormalities, variation is as high as 0-100% rate of abnormalities almost at any age. In contrast to current standard of offering PGD to AMA patients, the high rate and extreme variation of chromosomal abnormalities in human embryos may warrant PGD for all IVF cycles irrespective of the age of the patient. Better indicators other than maternal age are needed to determine which patients are at higher risk of producing high levels of aneuploid embryos.

ELEVATED MITOCHONDRIAL DNA IN EMBRYOS REFLECTS ANEUPOLOYDI AND CORRELATES WITH DEVELOPMENTAL ARREST. J. R. Ho,a N. Arrach,b W. Salem,a S. Ingles,a K. Bendikson,c K. Chung,c R. Paulson,c A. Ahmady.6 University of Southern California, Los Angeles, CA; 6Progenesis Inc, La Jolla, CA.

OBJECTIVE: Mitochondrial DNA content (MC) is thought to reflect metabolism in developing embryos. MC has been studied as a potential biomarker for embryo quality. Limited data suggests that increased MC is associated with older age, aneuploidy and decreased implantation rates in euploid embryos. We sought to investigate MC in conjunction with time-lapse morphokinetics (TLM) to see if TLM could provide insight on how...
MC is distributed over time in embryos. In this study, we describe the change in MC between day 3 and day 6, and its relationship with chromosomal status.

**DESIGN:** Prospective study of previously cryopreserved human embryos.

**MATERIALS AND METHODS:** 25 embryos cryopreserved at the zygote stage were thawed and cultured in the ESCO Mini-Time Lapse incubator. On day 3, each embryo underwent blastomere biopsy, and on day 6, all embryos regardless of progression were sent for comprehensive chromosomal screening (CCS). At both time points, cells were assessed for MC by NC for next generation sequencing (NGS), defined as mitochondrial to genomic DNA ratio. CCS analysis was performed by NGS. Kruskall Wallis was used to analyze the relationship among TLM parameters, MC, blastulation, and euploid status.

**RESULTS:** 22 out of 25 embryos survived the thaw process. On average, the MC on day 3 was higher than MC on day 6 (median 0.011 vs 0.001). Of those embryos that progressed to the blastocyst stage (n=11), MC was higher on day 3 (p=0.048) and lower on day 6 (p=0.001), compared to embryos that arrested. CCS results revealed that 10 out of 11 embryos were euploid. Aneuploid embryos had slower division from the 5-cell to 8-cell stage, with a trend towards significance (19.6 hr vs 27.5 hr, p=0.06). Lower MC at day 6 correlated significantly with euploid status (p=0.005), while day 3 MC showed no correlation.

**CONCLUSIONS:** This is the first study where TLM was used to investigate mitochondrial distribution in embryos. We show that abnormal embryos have a slower division rate between the 5 and 8-cell stage compared to normal euploid embryos. These abnormal embryos arrested prior to compaction, and show a slower decline in MC, with some having an increase in MC by day 6. This suggests that elevated MC in abnormal embryos may not be related to DNA repair mechanisms associated with aneuploidy, but rather slower cell division leading to an accumulation of mitochondria over time.

**References:**
2. Fragouli F, Spath K, Alfarawati S. Altered levels of mitochondrial DNA are associated with female age, aneuploidy and provide an independent measure of embryonic implantation potential. PLOS Genet 2015 11:e1005241.

**Supported by:** Progenics, Inc. (La Jolla, CA).

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**P-105** Tuesday, October 18, 2016

**IS THERE AN INCREASE IN ANEUPLOIDY RATE WITH DELAYED BLASTULATION, MULTINUCLEATION OR CLEAVAGE ANOMALIES?** N. Desai a, P. Rambha b, OB-GYN/Women’s Health Institute, Cleveland Clinic, Beachwood, OH; aCase Western Reserve School of Medicine, Case University, Cleveland, OH.

**OBJECTIVE:** Time lapse imaging and morphokinetics provide invaluable information on embryonic implantation potential. In this study we combine morphokinetics with chromosome data from preimplantation genetic screening (PGS) to evaluate the effect of cleavage anomalies, multinucleation, cell kinetics and delayed blastulation on genetic status of embryos.

**DESIGN:** Retrospective analysis of morphokinetic and PGS data from patients undergoing IVF.

**MATERIALS AND METHODS:** Normally fertilized zygotes were cultured in the Embryoscope time-lapse incubation chamber. Embryo growth kinetics were evaluated by viewing time lapse video footage. Time to specific cell stages was assessed as well as the presence of multinucleation (M), direct uneven cleavage (DUC) and reverse cleavage (RC). Trophoectoderm biopsy was performed on expanded blastocysts, either day 5 or 6 of culture. The relationship between the various parameters and chromosomal status was assessed. Statistical differences between treatment groups were analyzed using the Chi square and students t-test; p values <0.05 were considered significant.

**RESULTS:** A total of 853 zygotes were cultured in the Embryoscope from 51 patients. The mean patient age was 37.6 ± 4.3. The overall incidence of multinucleation, reverse cleavage and direct uneven cleavage was 31%, 15% and 7%, respectively. PGS results were obtained for 292 biopsied blastocysts and 40% (n=118) were diagnosed as euploid. Amongst biopsied blastocysts, 109 were from multinucleated embryos. The euploidy rate was not significantly different between MU, and non-MU blastocysts (37%, 40/109...
vs 43%, 78/183, respectively). With reverse cleavage only 27% of blastocysts were euploid (7/26) as compared to 42% of non RC blastocysts (111/265) but differences did not reach significance. Cell cycle timings and time to synchrony were also examined. Table 1 shows the euploidy rate for blastocysts with kinetics in desired range or out of range (shown bolded).

**TABLE 1. Kinetics and Chromosomal Status**

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Range</th>
<th>Embryos</th>
<th>Euploidy Rate</th>
<th>Aneuploidy Rate</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>t3-t2</td>
<td>&gt; 5</td>
<td>248</td>
<td>102 (41%)</td>
<td>146 (59%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>≤ 5</td>
<td>23</td>
<td>6 (26%)</td>
<td>17 (74%)</td>
<td>NS</td>
</tr>
<tr>
<td>t4-t3</td>
<td>&lt; 3</td>
<td>260</td>
<td>108 (42%)</td>
<td>152 (58%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>≥3</td>
<td>32</td>
<td>10 (31%)</td>
<td>22 (69%)</td>
<td>NS</td>
</tr>
<tr>
<td>tSB</td>
<td>&lt;100</td>
<td>128</td>
<td>58 (45%)</td>
<td>70 (55%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>≥100</td>
<td>140</td>
<td>52 (37%)</td>
<td>88 (63%)</td>
<td>NS</td>
</tr>
<tr>
<td>tEBL</td>
<td>&lt;116</td>
<td>153</td>
<td>71 (46%)</td>
<td>82 (54%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>≥116</td>
<td>102</td>
<td>31 (30%)</td>
<td>71 (70%)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

CONCLUSIONS: Delay in formation of an expanded blastocyst was associated with a lower euploidy rate. Multicellulation, reverse cleavage and direct uneven cleavage did not appear to increase the rate of aneuploidy. A larger data set is still needed to understand if these factors have any bearing on the blastocyst’s chromosomal status.

**P-106** Tuesday, October 18, 2016

**DAY 7 BLASTOCYST EUPLOIDY AND IMPLANTATION RATES WARRANT IMPLANTATION FOR ALL PROGRAMS USING PRE-IMPLANTATION GENETIC SCREENING (PGS).** J. B. Whitney, R. E. Anderson, M. C. Schieve, Research Division, Ovation Fertility, Newport Beach, CA; SCCRM, Southern California Center for Reproductive Medicine, Newport Beach, CA.

OBJECTIVE: To determine if embryos that blastulate 168 hours post-ICSI merit transfer by comparing aneuploidy and implantation rates for day 5, 6 and 7 blastocysts (BL).

DESIGN: Prospective observational cohort study analyzed 375 autologous oocyte cycles (average age: 37.5 ± 4.3) and 27 donor oocyte cycles yielding 1,925 fair-to-excellent quality BL. All transfers involved vitrified-warmed oocyte cycles (average age: 37.3 years) and 7 blastocysts (BL).

MATERIALS AND METHODS: All embryos were laser hatched on day 3, cultured to day 5/6/7 for trophectoderm (TE) biopsy and vitrified. All TE biopsy samples were analyzed using NextGen sequencing. Embryos were biopsied when TE herniation was >10%, embryos cultured to day 7 failed to meet expansion criteria for biopsy by day 6. 254 single embryo transfers were performed: 145 day 5 BL, 92 day 6 BL and 16 day 7 BL. Blastocyst quality assessments using a modified Gardner scale were performed at biopsy with AA, AB, and BA termed top quality or BB, BC, CA, AC and CC termed fair quality. Chi-square analysis was used to assess differences.

RESULTS: There were no differences observed for implantation, fetal sac loss or ongoing pregnancies between day 5 and day 6 BL. There was an increased loss rate of 22.2% with the day 7 BL resulting in fewer ongoing pregnancies (Table 1). Although day 7 BL formation was poor and only accounted for 6.6% of all BL development, the resulting transfer of euploid BL achieved a 56.3% implantation, which was not statistically different than day 5 or day 6. Utilizing standard morphology grading, day 5 blastocysts had an overall higher euploidy rate, while day 6 and day 7 showed no difference. Poor quality embryos had an increased aneuploidy potential, being less euploid on day 6 and 7.

CONCLUSIONS: An extra day of embryo growth allows additional possibilities for in vitro development. Culturing embryos to day 7 has proven beneficial to achieving viable euploid blastocysts. Day 7 growth is poor but euploidy is similar to day 6 and implantation remains high. The success obtained questions the universal dogma that late forming human BL, after day 6, are not worth keeping. Although the option to continue development past day 6 holds promise to attaining more viable embryos, it is unknown if these BL are at higher risk for any epigenetic, developmental or congenital risks. Fundamentally, 10 patients in this study achieved their only transferrable embryo from day 7, questioning if routine embryo culture discards potential viable embryos due to conventional ideology on BL development.

**P-107** Tuesday, October 18, 2016


OBJECTIVE: One ASRM 2015 prize abstract [1] suggested that STEET in young GPP was equivalent to FSET. We extended this analysis to assess if embryo selection using chromosome screening was superior, or equivalent to FSET and/or ZSET.

DESIGN: Retrospective cohort study of STEET, FSET and ZSET procedures performed in women age < 41y who had at least 3 Gardner’s Stage 2BC or 2CB blastocysts or better at a single, large university-based center from January 1, 2010 to July 31, 2015.

MATERIALS AND METHODS: We compared 131 STEET (median age: 35 y, IQR: 32-37 y) vs. 207 FSET (median age: 33, IQR: 31-36 y) vs. 95 ZSET (median age 33 y, IQR: 30-35 y) in GPP. Data was mined for: implantation rate (IR), live birth / ongoing pregnancy rate (LBR), and spontaneous abortion rate (SABR). Exclusion criteria included: age >40 y; ≥2 prior ART procedures; ≥2 prior spontaneous abortions; endometrial thickness < 6 mm at progesterone start, or uterine pathology (fibroids or synchiae). Fisher’s exact test (two-tailed) was used for statistical analysis.

RESULTS: When grouping all cycles of women age < 41y, IRs for STEET, FSET, and ZSET were 82/131 (63%), 126/207 (61%), and 50/95 (53%) respectively; p=NS. LBRs were 73/131 (56%), 99/207 (48%), and 39/95 (41%), respectively (LBR was significantly higher with STEET vs. ZSET; p=0.03 but vs. not FSET). SABRs were 8/82 (10%), 24/126 (19%), and 11/50 (22%), respectively; p=NS. The Table divides the data by age. For women age <35 y, no differences in IR or LBR were noted. Between age 35-37 y, IR and LBR were significantly higher with STEET vs. FSET and ZSET vs. ZSET. For women age 38-40 y, IR was not different, but LBR was significantly higher with STEET vs. FSET. SABRs were not statistically different within any of the age groups.

CONCLUSIONS: In younger (age < 35 y) GPP, FSET vs. ZSET appear equally beneficial to STEET, but as female age advances (38-40 y), STEET may have the advantage of producing a higher chance for live birth. While the SABR is not statistically lower with STEET in this data set, it is in others [2], and the lack of statistical significance here may be due to small sample size, especially in the older age groups. The financial costs, emotional burden, and time of storage and transfer of abnormal embryos, miscarriage, and pregnancy termination of chromosomally abnormal fetuses need to be considered when choosing not to perform STEET, especially in older patients, and GPP should be counseled accordingly. We will continue to collect data.

References:
The SPARC score was used to evaluate intermediate spatiotemporal resolution and to predict future development of mosaic blastocysts. The SPARC score was calculated by dividing the percentage of aneuploid cells by the percentage of euploid cells in the trophectoderm. A high SPARC score indicated a greater degree of mosaicism, while a low SPARC score indicated a lower degree of mosaicism.

RESULTS: A total of 438 embryo transfers were completed where 205 only had day 5 embryos transferred and 233 cycles only day 6 embryos transferred. There was a significant (P < 0.02) difference in positive pregnancy rates between the two subgroups. Day 5 resulted in 157 (76%) pregnant outcomes and day 6 had 154 (66%). There was no significant difference for the miscarriage rates for day 5 as compared to day 6. Day 5 embryo transfers resulted in 35 losses (22%) in comparison to 45 (29%) for the day 6 embryo transfers. There was a significantly higher (P < 0.01) ongoing pregnancy for day 5 as compared to day 6 embryo transfers. Day 5 and 6 showed 59% and 47% ongoing pregnancy rates respectively. There was not significant difference in the number of embryos transferred in the two subgroups. Day 5 had 157 (76%) pregnant outcomes and day 6 had 154 (66%).

CONCLUSIONS: This study evaluates the efficacy of day 5 and day 6 embryo transfers. Day 5 transfers does have a significant impact on the overall outcome of the cycle. More studies may be beneficial for evaluating embryo viability, stimulation and luteal support.

P-109 Tuesday, October 18, 2016


OBJECTIVE: To determine the efficacy pre-implantation genetic screening (PGS) of day 5 as compared to day 6 blastocyst embryo transfers.

DESIGN: Retrospective cohort study evaluating PGS success with day 5 and 6 embryos.

MATERIALS AND METHODS: A total of 1327 embryos were available for analysis for PGS from 3642 fertilized oocytes derived from intracytoplasmic sperm injection. Embryos were evaluated on day 3 and assisted hatched embryos on day 5 and 6 with a distinct inner cell mass and multiple cells herniating form the zona pellucida were biopsied for PGS aneuploidy testing. Embryo biopsy consisted of laser removal of 5 to 7 cells from the trophectoderm juxtaposed to the inner cell mass. The biopsied cells were treated according to the reference laboratory protocol for off site aneuploidy screening. Embryos available for testing were vitrified and stored under liquid nitrogen until results were obtained from the reference laboratory.

RESULTS: A total of 438 embryo transfers were completed where 205 only had day 5 embryos transferred and 233 cycles only day 6 embryos transferred. There was a significant (P < 0.02) difference in positive pregnancy rates between the two subgroups. Day 5 resulted in 157 (76%) pregnant outcomes and day 6 had 154 (66%). There was no significant difference for the miscarriage rates for day 5 as compared to day 6. Day 5 embryo transfers resulted in 35 losses (22%) in comparison to 45 (29%) for the day 6 embryo transfers. There was a significantly higher (P < 0.01) ongoing pregnancy for day 5 as compared to day 6 embryo transfers. Day 5 and 6 showed 59% and 47% ongoing pregnancy rates respectively. There was not significant difference in the number of embryos transferred in the two subgroups. Day 5 had 1.09 embryos transferred and day 6 had an average of 1.12 embryos transferred.

CONCLUSIONS: This study evaluates the efficacy of day 5 and day 6 embryo transfers. Day 5 transfers does have a significant impact on the overall outcome of the cycle. More studies may be beneficial for evaluating embryo viability, stimulation and luteal support.

P-108 Tuesday, October 18, 2016

THE TIMING OF ONSET OF MOSAICISM IN HUMAN BLASTOCYSTS IMPACTS THE UTILITY OF NEXT GENERATION SEQUENCING (NGS). C. Dela Cerna, P. Colls, S. Munne. aInstitute for Reproductive Medicine and Science at Saint Barnabas, Livingston, NJ; bIRMS at Saint Barnabas, Livingston, NJ; cReprogenetics, Highland Park, IL; dReprogenetics, Livingston, NJ.

OBJECTIVE: Mitotic errors occur throughout preimplantation development, resulting in mosaicism. Errors that occur after the determination of the inner cell mass (ICM) will result in discordance between the trophectoderm and ICM. Whole blastocysts or isolated ICMs and trophectoderm samples were reanalyzed to determine the degree to which a trophectoderm biopsy reflects the overall status of the blastocyst.

DESIGN: Intra-embryo comparison of NGS results of ICM and trophectoderm specimens.

MATERIALS AND METHODS: Embryos determined to be fully (>90%) aneuploid or mosaic (10-90% abnormal cells, including aneuploid/aneuploid mosaics) during routine NGS cycles were reanalyzed. Whole blastocysts were retested, as were 5-10 cell biopsies of ICMs and multiple 10-15 cell samples of trophectoderm of each embryo. Mosaicism was determined to have been initiated after ICM determination when an ICM sample displayed an abnormality not present in any trophectoderm sample or when a trophectoderm sample displayed an abnormality not present in the ICM.

RESULTS: Among whole mosaic blastocysts, 17/23 (74%) retested ‘normal’, indicating that fewer than 10% of the cells shared any single defect. Mosaicism was initiated after ICM determination in 10 of 61(16%) ICMs, and in 57/271 (21%) individual trophectoderm specimens (some embryos had two distinct aneuploid cell lines). Unique chromosome defects were determined to have occurred after ICM determination in either the ICM or trophectoderm in 39/61 embryos. Total concordance among all samples determined to have occurred after ICM differentiation in either the ICM or trophectoderm and ICM.

CONCLUSIONS: Reanalysis of whole mosaic blastocysts demonstrated that mosaicism occurs in the ICM after it has differentiated from the trophectoderm, and that mitotic errors continue to accumulate in the trophectoderm. The impact of this dynamic of mitotic errors is that a ~5-cell trophectoderm biopsy may not reflect the genetic state of the ICM, and cannot show the full extent of trophectodermal mosaicism. Some degree of trophectodermal mosaicism is compatible with normal development, but it is unknown whether embryos with mosaic ICMs can develop normally.

OBJECTIVE: To develop a mathematical formula resulting in an accurate determination of mitochondrial DNA (mtDNA) levels in human blastocysts stratified by ploidy, age, and implantation potential.

DESIGN: Retrospective analysis of mtDNA content in human blastocysts used in preimplantation genetic diagnosis for IVF selection.

MATERIALS AND METHODS: 833 embryos derived from 181 patients were tested for mtDNA content by next generation sequencing (NGS), and 150 embryos derived from 96 patients were tested by quantitative polymerase chain reaction (qPCR). For each embryo, the level of mtDNA was determined from a trophoderm biopsy by whole genome amplification followed by NGS and/or qPCR. The value was subjected to mathematical analysis tailored to the genomic DNA composition of said embryo. Grouped values were compared by Welch’s two-tailed paired t-test.

RESULTS: On average our quantitation method changed the conventionally determined mtDNA level of a given embryo via NGS by 1.35% +/-1.58%, with changes ranging up to 17.42%, and via qPCR by 1.33% +/-8.08%, with changes ranging up to 50.00%. Levels of mtDNA in euploid and aneuploid embryos showed a statistically insignificant difference of P = 0.102 by NGS (euploid N = 494, aneuploid N = 339) and P = 0.642 by qPCR (euploid N = 100, aneuploid N = 50). Blastocysts derived from younger or older patients had comparable mtDNA values, with P = 0.293 by NGS (20-37 age group N = 559, 38-46 age group N = 274) and P = 0.101 by qPCR (20-37 age group N = 92, 38-46 age group N = 58). Blastocysts that upon transfer resulted in implantation did not contain significantly different mtDNA levels compared to blastocysts that failed to implant, with P = 0.813 by NGS (implanted N = 51, non-implanted N = 69) and P = 0.103 by qPCR (implanted N = 49, non-implanted N = 51).

CONCLUSIONS: We recommend the implementation of our correction factor to all laboratories evaluating mtDNA levels in their embryos by NGS or qPCR. Applied to our in-house data, our quantitation method reveals that overall levels of mtDNA are largely equal between human blastocysts regardless of embryo ploidy, age, or implantation potential.

P-110 Tuesday, October 18, 2016


OBJECTIVE: While preimplantation genetic screening (PGS) has been shown to improve embryo implantation and reduce pregnancy loss, the age-weighted benefits have yet to be established. This study compared the number of egg retrievals, embryo transfers and length of time required to achieve pregnancy after undergoing IVF with and without PGS.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Patients who underwent IVF +/- PGS (trophectoderm bx) from 2010-2015 were included. Cox proportional hazards models with restricted time to event estimates evaluated average number of fresh IVF cycles required to obtain a euploid embryo and average number of embryo transfers (ETs) until first clinical pregnancy. Time to clinical pregnancy was approximated from modeled time estimates and outcomes of fresh IVF and subsequent fresh and frozen ET cycles in non-PGS patients (following ASRM ET guidelines) and PGS patients (frozen SET (FET) used exclusively). Time estimates (days) used were: fresh IVF (21), freeze-all w/FET (45), subsequent FET (21), biochemical (31), clinical loss (91), negative pregnancy test (16), and ongoing pregnancy (42).

RESULTS: A total of 10,642 IVF cycles (2,758 with PGS, 7,884 unscreened) were analyzed. Controlling for age, ovarian reserve, and embryos transferred, PGS improved clinical pregnancy rate (HR 1.4 [1.01-2.0] p = 0.045) with a progressive increase with age (age 38-20: HR 2.0 [1.4-2.9], 41-42: HR 3.4 [2.0-5.8], >42: HR 7.5 [4.4-12.8], p < 0.001). Cycle outcomes are shown (Table 1). In the PGS cohort, there was an age-related increase in retrieval cycles needed to obtaining a euploid embryo. With PGS, there was a reduction in ETs required for clinical pregnancy in patients aged >39, a reduction in time to clinical pregnancy in patients aged >41, 86.6% decrease in multiples and 15.4% reduction in clinical pregnancy loss.

CONCLUSIONS: The use of PGS increases the efficacy and safety of IVF in patients of all ages. In women >40, PGS markedly improves the efficiency

<table>
<thead>
<tr>
<th>Age</th>
<th>Embryos transferred (euploid/unscreened)</th>
<th>Average transfers to euploid embryo</th>
<th>Average transfers to clinical pregnancy</th>
<th>Average time to clinical pregnancy (months)</th>
<th>Multiple pregnancy rate (%) (observed)</th>
<th>Clinical loss rate (%) (observed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>28</td>
<td>1 / 1</td>
<td>1.03 / NA</td>
<td>1.76 / 2.27</td>
<td>4.49 / 4.42</td>
<td>2.9 / 4.1</td>
<td>5.6 / 9.0</td>
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<tr>
<td>32</td>
<td>1 / 1</td>
<td>1.11 / NA</td>
<td>2.12 / 2.91</td>
<td>5.46 / 5.32</td>
<td>4.3 / 2.3</td>
<td>9.9 / 10.0</td>
</tr>
<tr>
<td>36</td>
<td>1 / 2</td>
<td>1.23 / NA</td>
<td>2.18 / 2.14</td>
<td>5.87 / 4.14</td>
<td>0.8 / 30.1</td>
<td>8.2 / 10.0</td>
</tr>
<tr>
<td>39</td>
<td>1 / 2</td>
<td>1.44 / NA</td>
<td>2.2 / 3.39</td>
<td>6.76 / 6.25</td>
<td>2.8 / 19.6</td>
<td>11.3 / 12.1</td>
</tr>
<tr>
<td>41</td>
<td>1 / 3</td>
<td>1.63 / NA</td>
<td>1.96 / 4.29</td>
<td>6.79 / 8.15</td>
<td>3.2 / 29.6</td>
<td>6.5 / 16.5</td>
</tr>
<tr>
<td>43</td>
<td>1 / 3</td>
<td>1.82 / NA</td>
<td>2.01 / 6.88</td>
<td>7.42 / 11.35</td>
<td>0.0 / 8.0</td>
<td>6.2 / 11.0</td>
</tr>
</tbody>
</table>
of treatment, decreasing time to pregnancy by 4 months with a 45.5% relative reduction in loss. The reduction in treatment burden for younger PGS patients is less dramatic. This data is useful to counsel patients regarding the incremental effect to be anticipated by adding PGS to their treatment plan.

P-113 Tuesday, October 18, 2016

IMPACT OF OVARIAN RESERVE ON PGD. M. Cetinkaya, C. Pirkevi Cetinkaya, S. Kahraman. Assisted Reproductive Technologies and Reproductive Genetics Center, Istanbul Memorial Hospital, Istanbul, Turkey.

OBJECTIVE: The number of embryos available for transfer is significantly lower in preimplantation genetic diagnosis (PGD) than in regular IVF because of genetic selection. Thus, the clinical evaluation of a patient applying for PGS is important in order to maximize the possibility of transferring an euploid embryo. The objective of the study was to determine the impact of ovarian reserve on PGD.

DESIGN: This retrospective cohort study was conducted in a private IVF clinic between September 2011 and December 2015. A total of 665 PGD cycles were analyzed and 2558 trophoderm samples were diagnosed by array Comparative Genomic Hybridization (aCGH).

MATERIALS AND METHODS: The probability of finding at least one euploid embryo (POFALOEE) per cycle and the rate of euploid embryos per diagnosed embryos (euploidy rate) were evaluated according to maternal age and ovarian reserve i.e. the number of cumulus-oocyte complexes (COC), metaphase II (MII) oocytes and biopsied embryos.

RESULTS: According to our findings regarding maternal age and POFALOEE, the decline in the POFALOEE per cycle was around 6% for each two-year age group from the age of 35 (<35, 35-37, 38-39). However, from the age of 40, for each two years the patient age increased (40-41, 42-43), the POFALOEE per cycle decreased by 20% approximately. The dataset was also evaluated in five groups according to the number of COCs retrieved (1-5, 6-10, 11-15, 16-20, ≥20). After adjustment for age, POFALOEE was evaluated with logistic regression analysis. When compared to 1-5 COCs, 6-15 COCs increases POFALOEE 2 folds, whereas 16-20 COCs increases POFALOEE 4.6 folds. POFALOEE increases 7 folds. On the other hand, the euploidy rate decreases from 49% to 14% from <35 to 42-43 age groups. When looking at the effect of the number of blastocysts biopsied, we noted that it had a relatively low effect on the euploidy rate (27% and 41%, for 1 and ≥8 embryos, respectively), when compared to the POFALOEE, which increased from 27% to 100% for the same groups.

CONCLUSIONS: Maternal age is the most significant predictor of euploidy rate, which is not directly correlated with the number of retrieved oocytes. However, although POFALOEE decreases significantly with maternal age moreover the number of COCs, MII oocytes and biopsied embryos do affect POFALOEE. Finally, the best approach when counselling PGD patients for aneuploidy testing, should be first to evaluate the ovarian reserve and advise couples by giving an estimation of the possibility of finding at least one euploid embryo specific to maternal age and ovarian reserve.

P-114 Tuesday, October 18, 2016

HIGHLY SUCCESSFUL PREIMPLANTATION GENETIC DIAGNOSIS FOR INDIVIDUALS WITH DE NOVO MUTATIONS. K. McWilliams, T. K. McWilliams, J. Kitchen, M. Hughes, Genetics Genetics, Plymouth, MI.

OBJECTIVE: Current methodologies for preimplantation genetic diagnosis (PGD) require identification of family members who also carry the mutation(s) of concern. This poses significant barriers for families in which the disease originated de novo in either patient or partner, or for those lacking family members able or willing to participate in testing. A solution is to use information gleaned from testing the family’s embryos to set genetic phase for the familial mutation. Herein we set out to measure the performance of this approach, and to identify any disease-specific limitations.

DESIGN: Retrospective, multi-faceted analysis of blastomere and blastocyst cycles submitted for single-gene PGD.

MATERIALS AND METHODS: PGD results from 100 families having undergone testing by de novo approach were studied. Embryonic de novo testing required a combination of direct Sanger sequencing for the parental mutation combined with linkage analysis, which was achieved by either the short tandem repeat method or Karyomapping technology. Successful setting of genetic phase required, on average, 2 embryos exhibiting both the parental mutation and identical inherited parental haplotypes.

RESULTS: Successful genetic diagnosis was achieved for 94% of 100 families requiring PGD testing by de novo approach (39/42, 93% STR approach; 55/58, 95% Karyomapping). Genetic phase was accomplished in the first round of embryo testing in 92 of these 94 cases. Two families required an additional round of PGD to set genetic phase. Families submitted an average of 6.26 embryos (SD +/- 4.01) for analysis. De novo PGD was attempted for 50 various genetic diseases, including: neurofibromatosis (17), hereditary breast cancer (10), Marfan disease (6), poly cystic kidney disease (4), familial adenomatous polyposis (4). 91 of 92 families (98.9%) had an unaffected embryo that was suitable for transfer. 50 of 53 families (94.3%) pursuing PGD combined with chromosome screening (PGS) achieved an embryo suitable for transfer by both technologies. Embryo diagnosis failed for 6 families due to inability to set genetic phase. An average of 6.17 embryos (SD +/- 3.31) were submitted for these families. Three of six (50%) de novo failures were for parental NF1 mutations, for a NF1-specific de novo success rate of 82.4% (14/17). In each instance, the parental NF1 mutation was not detected in embryo biopsies despite embryos having inherited opposite hapl provinces from the affected parent.

CONCLUSIONS: PGD for diseases de novo in prospective parents can be confidently performed by a combination of direct sequencing and linkage analysis by either STR or Karyomapping technologies. De novo PGD resulted in highly successful diagnosis and identification of at least one embryo that was suitable for transfer, even in combination with PGS testing. Failure of diagnosis for de novo PGD is most common in NF1 testing, possibly due to high levels of mosaicism known to occur in sporadic NF1 cases.

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OUTCOMES FROM 9822 ARRAY COMPARATIVE GENOMIC HYBRIDIZATION (ACGH) CYCLES FOR PREIMPLANTATION GENETIC SCREENING (PGS). A. Jordan, H. Nisson, P. Colls, H. Danzer, J. Barratt, E. Mounts, I. I. Zhang, A. Becker, C. Wagner Coughlin, L. B. Welrin, S. Munne. Reprogenetics, Livingston, NJ; Southern California Reproductive Center, Beverly Hills, CA; ART Reproductive Center, Beverly Hills, CA; Oregon Reproductive Medicine, Portland, OR; New Hope Fertility Center, New York, NY; Embryology, New Hope Fertility Center, New York, NY; Aparent IVF Laboratory, Highland Park, IL; Medical Director, Coastal Fertility Medical Center, Irvine, CA.

OBJECTIVE: aCGH is an established chromosome screening technique in use since 2010. All chromosomes are studied, with resolution as low as 6 MB. Over 91679 embryos and 44801 cycles have been screened using this method. In this study we present follow-up of these cycles.

DESIGN: Follow-up data was requested from 202 centers for embryos tested via aCGH from 2011-2016. Day 3 and day 5 were reported separately.

MATERIALS AND METHODS: From 11/2010-4/2016, aCGH was performed on 2141 blastomere cycles (16862 embryos) and 42660 blastocyst cycles (74817 embryos) for a total of 91679 embryos. Each sample was amplified and tested via aCGH (24 sure, Illumina). Follow-up was requested from IVF centers on 18,046 cases for patients with at least one euploid embryo. For this study, a pregnancy includes biochemical, ectopic, and pregnancies that continued in spontaneous abortion or were lost before ongoing gestation.

RESULTS: aCGH data was obtained on 1353 blastomere cycles (1434 embryos) and 6010 blastocyst cycles (6944 embryos). Overall implantation rate for blastomere and blastocyst was 41.7% and 63.9% respectively. Pregnancy rate per cycle was 43.2% and 49.6% respectively, with pregnancy rate per transfer at 59.1% for blastomere and 60.5% for blastocyst. Miscarriage rate was 9.7% and 10.7% respectively, and ongoing pregnancy rate was 41.7% and 55.9% for blastomere and blastocyst samples. For blastocyst biopsy we further stratify the data by age in the following table:

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Implantation</th>
<th>Pregnancy Rate/Transfer</th>
<th>Miscarriage Rate</th>
<th>Ongoing Pregnancy Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>35-36</td>
<td>38%</td>
<td>43%</td>
<td>36%</td>
<td>41%</td>
</tr>
<tr>
<td>37-39</td>
<td>38%</td>
<td>43%</td>
<td>36%</td>
<td>41%</td>
</tr>
<tr>
<td>40-42</td>
<td>37%</td>
<td>43%</td>
<td>34%</td>
<td>39%</td>
</tr>
<tr>
<td>43-45</td>
<td>36%</td>
<td>41%</td>
<td>38%</td>
<td>39%</td>
</tr>
</tbody>
</table>

CONCLUSIONS: For blastocyst biopsy cases, implantation rate across entire maternal age (MA) range was constant. This indicates that once an euploid embryo is replaced it implants well at any MA and further solidifies that loss of implantation with advancing MA is due to chromosome abnormalities. There are patients with euploid embryos that have not yet had a transfer, diluting the pregnancy rate per cycle, however, the pregnancy rate per transfer was calculated based on patients who have had transfers and is a better representation of overall success. For ongoing pregnancy rate, there is a significant difference (p<.001) between blastomere and blastocyst samples reflecting the expected improved outcome of a blastocyst biopsy.
EVOLUTION OF CHROMOSOMAL ABNORMALITIES FROM CONCEPTION TO PREGNANCY LOSS: A COMPARATIVE STUDY OF PGS AND MISCARRIAGE SAMPLES. M. N. Streeker, T. Sahoo, N. Dzidic, S. Commander, T. H. Taylor, K. Hovanes, CombiMatrix, Irvine, CA; Genetic Counseling Services, CombiMatrix, Irvine, CA.

OBJECTIVE: To evaluate the nature and frequency of cytogenomic abnormalities identified in day 3 and day 5/6 embryos vs. those identified in miscarriages of naturally occurring conceptions.

DESIGN: Retrospective comparative analysis of cytogenomic results obtained by array comparative genomic hybridization (aCGH) during preimplantation genetic screening (PGS) of day 3 and day 5/6 embryos vs. results obtained by oligonucleotide or single nucleotide polymorphism (SNP) array of products of conception (POC) tissue.

MATERIALS AND METHODS: Results from 2259 embryo biopsies (day 3 and day 5/6) evaluated by aCGH over a 14 month period were compared to results from 8118 POC samples (fresh and archived FFPE tissue) evaluated by oligonucleotide or SNP microarray over a 44 month period.

RESULTS: PGS by aCGH was successful in 95% (2137/2259) of embryo biopsies. POC by microarray was successful in 91% (7396/8118) of samples. Whole chromosome aneuploidies or unbalanced structural abnormalities (>30 Mb) were identified in 48% (1025/2137) of PGS samples. Complex numeric abnormalities were the most common (32%) followed by single monosomies (25%) and trisomies (19%). For POC samples, whole chromosome aneuploidies or unbalanced structural abnormalities were identified in 54% (3975/7396). Single trisomies were most common (63%) followed by trisomy X (11%). Single monosomies were rare (0.6%). Of chromosomally abnormal embryos (N=1025), the most common single chromosome abnormalities were: trisomy 16 (4%; N=38), monosomy 22 (3%), trisomy 22 (3%), monosomy 16 (2%). Of chromosomally abnormal POCs (N=3975), the most common single chromosome abnormalities were: trisomy 16 (16%), trisomy 22 (10%), trisomy 21 (8%), and trisomy 15 (7%).

CONCLUSIONS: This large retrospective analysis identified significant differences in the types of chromosomal abnormalities seen in day 3 and day 5/6 embryos versus those seen in miscarriages of naturally conceived pregnancies. Although the overall frequency of cytogenetic abnormalities in both sample types was similar (48% vs. 54%), complex numeric abnormalities were nearly 3 times more common in PGS samples compared to POCs (32% vs. 12%), while single trisomies were >3 times more common in POCs than in PGS samples (63% vs. 19%). Single monosomies accounted for a significant proportion (25%) of abnormalities in PGS samples, but were exceedingly rare in POCs (0.7%). These observations provide important clues toward our understanding of implantation failure in the IVF setting compared to the frequent causes of early miscarriages by natural conception.

Common Chromosomal Abnormalities

<table>
<thead>
<tr>
<th>Abnormality</th>
<th>PGS Samples</th>
<th>POC Samples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single chromosome monosomy</td>
<td>252 (25%)</td>
<td>26 (0.7%)</td>
</tr>
<tr>
<td>Single chromosome trisomy</td>
<td>190 (19%)</td>
<td>2516 (63%)</td>
</tr>
<tr>
<td>Numeric abnormality involving more than 2 chromosomes</td>
<td>330 (32%)</td>
<td>162 (12%)</td>
</tr>
<tr>
<td>Trisomy 16</td>
<td>38 (4%)</td>
<td>623 (16%)</td>
</tr>
<tr>
<td>Trisomy 22</td>
<td>28 (3%)</td>
<td>379 (10%)</td>
</tr>
<tr>
<td>Monosomy X</td>
<td>14 (1%)</td>
<td>446 (11%)</td>
</tr>
</tbody>
</table>

References:

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OBJECTIVE: To assess if SART donor oocyte pregnancy rates are consistent with high percentage of aneuploidy and mosaicism in donor oocyte cycles using Preimplantation Genetic Screening (PGS) with Next Generation Sequencing (NGS).

DESIGN: Retrospective study and mathematical analysis.

MATERIALS AND METHODS: All trophectoderm biopsy specimens from donor oocyte cycles received at a genetics laboratory were queried for NGS results. The rate of euploidy, aneuploidy, and mosaicism was calculated for separate analysis seeking to find the overall pregnancy rate (OPR) from patients’ first donor single thawed euploid embryo transfers (STEET) from NGS at a single university fertility center from 2/2015 to 3/2016. Lastly, the 2014 SART National Summary data on non-tested donor embryo transfers and their live birth rates was used to calculate the expected live births from tested donor embryo transfers based on euploidy and mosaicism rates from NGS donor data, applying the OPR from donor STEET data. The calculated expected live birth rate was then compared to the actual live birth rate of untreated donor embryo transfer cycles.

RESULTS: 268 donor cycles from 38 IVF centers showed a euploid rate of 48.7±2.38, aneuploid rate of 22.9±20.4 and mosaicism rate of 28.4±21.9 (Table 1). Thirty two patients were included in the donor NGS STEET cycle analysis. The average age at transfer was 42.7±3.9 years with an average donor age of 26.5±2.0 years, for an OPR of 62.2% (n=20/32). The 2014 SART National Summary shows 6070 non-PGS donor egg transfers, averaging 1.7 embryos per transfer, for an estimate of 10319 embryos transferred in total. The reported live birth rate of 53.3% (36.9% singletons, 16.2% twins and 0.2% triplets) gives a cumulative 4242 babies delivered (41.1% per embryo). When the euploid rate of 48.7% is applied, 5025 embryos transferred are estimated to have been euploid. The 62.2% OPR of donor STEETs applied to this gives an expected 3126 singleton deliveries (95% CI 3027-3246). The mosaicism rate of 28.4% plus data showing an overall approximate 20% OPR of mosaic embryos adds 586 (95% CI 421-524) singleton births. The total expected babies born is 3712 (95% CI 3505-3877) with a live birth rate of 35.9% (95% CI 34.0-37.6) from donor egg transfers.
CONCLUSIONS: High rates of aneuploidy and mosaicism in donor oocyte cycles are consistent with the pregnancy rates of untested donor embryos transfers. The use of PGS with NGS can prevent transfer of aneuploid embryos in donor cycles.

Donor Oocyte NGS Results from Reference Genetics Laboratory

| Total cycles | 208 |
| Total Trophoderm Biopsy Specimens for NGS | 2062 |
| Avg age of Donors (years) | 25.8±2.3 |
| Avg age of Recipient (years) | 43.1±6.3 |
| Avg Number Cycles per Center | 7.1±10.5 |
| Avg Number Blastocysts Biopsied per Patient | 7.7±4.1 |
| Euploid (%) | 48.7±23.8 |
| Aneuploid (%) | 22.9±20.4 |
| Mosaic (%) | 28.4±21.9 |
| No Amplification (%) | 2.5±7.3 |
| Rate of Degraded DNA (%) | 0.8±4.1 |

References:

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IMPACT OF 24-CHROMOSOME ANEUPLOIDY TESTING ON THE OUTCOME OF PGS FOR SINGLE GENE DISORDERS. S. Rechitsky, a T. Pakhalchuk, a M. Prokhorovich, G. San Ramon, a Z. Zlatopolsky, b A. Kuliev. aPreimplantation Molecular Genetics, Reproductive Innovations, Northbrook, IL; bCytogenticists, Reproductive Genetic Innovations, Northbrook, IL; cResearch, Reproductive Genetic Innovations, Northbrook, IL.

OBJECTIVE: Although preimplantation 24-cromosomes aneuploidy testing (24-AT) is becoming an attractive option for ART patients of advanced reproductive age, it may be also useful as an additional test in the practice of PGS for single gene disorders (SGD). So the objective of this work is to investigate the impact of 24-AT on the reproductive outcome of PGS for SGD in couples of advanced reproductive age, based on our experience, representing the world’s largest PGS series for SGD.

DESIGN: Retrospective Study
MATERIALS AND METHODS: PGS for SGD was performed using the whole genome amplification (WGA) product, obtained in 24-AT procedure, allowing both PGS for SGD and concomitant 24-AT in the same biopsy sample. A combined testing was performed in 762 (21.7%) cycles of a total of 4501 PGS cycles performed for SGD and HLA typing by the present time. This involved PGD for SGD combined with 24-AT for SGD and HLA typing, and should be given the appropriate replacement priority if no euploid or instead to be mosaic (10-90% abnormal cells) during routine procedures were reanalyzed with Next Generation Sequencing (NGS). An ICM sample, usually consisting of 5-10 cells, was initially isolated. Subsequently, 2-4 trophodermal samples ranging in size from 10 to ~50 cells were taken from each embryo. The NGS result from each specimen was compared to the original biopsy. Mosaics were sub-classified as complex mosaics (3 or more chromosome abnormalities), aneuploid mosaics (1-2 chromosomes being mosaic) or partial aneuploid mosaic (normal/partial aneuploidy).

RESULTS: The results are shown in the table. Five embryos were normal in all retested samples (5/43, 11.6%). All partial mosaic embryos with normal ICMs had normal or mostly normal retested trophoderm samples (8/8), compared to 2/8 with full aneuploid mosaicism.

Distribution of Normal Biopsy Samples in Mosaic Embryos

<table>
<thead>
<tr>
<th>Initial NGS Diagnosis</th>
<th>Total Embryos</th>
<th>Normal ICM</th>
<th>Normal Trophoderm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full Aneuploidy</td>
<td>19</td>
<td>0/19 (0%)</td>
<td>4/70 (6%)</td>
</tr>
<tr>
<td>Full Partial</td>
<td>3</td>
<td>0/3 (0%)</td>
<td>2/10 (20%)</td>
</tr>
<tr>
<td>Aneuploidy</td>
<td>12</td>
<td>2/12 (17%)</td>
<td>14/44 (32%)</td>
</tr>
<tr>
<td>Complex Mosaic</td>
<td>15</td>
<td>8/15 (53%)</td>
<td>30/59 (51%)</td>
</tr>
<tr>
<td>Partial Aneuploid Mosaic</td>
<td>16</td>
<td>8/16 (50%)</td>
<td>10/55 (18%)</td>
</tr>
<tr>
<td>Mosaic Full Aneuploidy</td>
<td>43</td>
<td>10/43 (23%)</td>
<td>54/158 (34%)</td>
</tr>
</tbody>
</table>

CONCLUSIONS: A diagnostic biopsy of ~5 trophoderm cells may detect mosaicism that does not exist in the ICM and may be highly localized in the trophoderm. In this group of 43 mosaic embryos, there were 12 (28%) with normal ICMs that also tested normal for all or several trophoderm specimens. The presence of aneuploid cell lines only in limited areas of the trophoderm suggests that the initial chromosomal malsegregation event occurred relatively close to the time of biopsy. The implantation potential of a blastocyst with a normal ICM and a mildly or highly mosaic trophoderm remains unknown. Embryos with an initial diagnosis of complex mosaic are less likely to have a normal ICM. Embryos diagnosed as partial aneuploid mosaic may be more likely to possess both a normal ICM and substantially normal trophoderm, compared to full aneuploid mosaics. These findings may aid the determination of mosaic embryos that are suitable for transfer. Depending on patient age, a mosaic embryo may have the same or lower chance of being compromised by aneuploidy as an undiagnosed embryo, and should be given the appropriate replacement priority if no euploid embryos are available.

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DISCORDANCE AMONG SERIAL BIOPSIES OF MOSAIC EMBRYOS. G. Garrisi, a R. H. Walmesly, b K. Bauckman, b R. J. Mendola, a P. Colls, a S. Munne. a Institute for Reproductive Medicine and Science at Saint Barnabas, Livingston, NJ; bReprogenetics, Highland Park, IL; cReprogenetics, Livingston, NJ.

OBJECTIVE: Some embryos determined to be mosaic have been shown to be capable of normal implantation and development, albeit with reduced implantation and increased miscarriage rates. This study correlates the original biopsy findings with details of the localization of aneuploid cells in mosaic blastocysts.

DESIGN: Comparison of PGS results to inner cell mass (ICM) and several trophoderm samples of the same embryo.

MATERIALS AND METHODS: Embryos determined to be fully (90-100%) aneuploid or instead to be mosaic (10-90% abnormal cells) during routine PGS cycles were reanalyzed with Next Generation Sequencing (NGS). An ICM sample, usually consisting of 5-10 cells, was initially isolated. Subsequently, 2-4 trophodermal samples ranging in size from 10 to ~50 cells were taken from each embryo. The NGS result from each specimen was compared to the original biopsy. Mosaics were sub-classified as complex mosaics (3 or more chromosome abnormalities), aneuploid mosaics (1-2 chromosomes being mosaic) or partial aneuploid mosaic (normal/partial aneuploidy).

RESULTS: The results are shown in the table. Five embryos were normal in all retested samples (5/43, 11.6%). All partial mosaic embryos with normal ICMs had normal or mostly normal retested trophoderm samples (8/8), compared to 2/8 with full aneuploid mosaicism.

Distribution of Normal Biopsy Samples in Mosaic Embryos

<table>
<thead>
<tr>
<th>Initial NGS Diagnosis</th>
<th>Total Embryos</th>
<th>Normal ICM</th>
<th>Normal Trophoderm (Total of all samples)</th>
</tr>
</thead>
<tbody>
<tr>
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<td>19</td>
<td>0/19 (0%)</td>
<td>4/70 (6%)</td>
</tr>
<tr>
<td>Full Partial</td>
<td>3</td>
<td>0/3 (0%)</td>
<td>2/10 (20%)</td>
</tr>
<tr>
<td>Aneuploidy</td>
<td>12</td>
<td>2/12 (17%)</td>
<td>14/44 (32%)</td>
</tr>
<tr>
<td>Complex Mosaic</td>
<td>15</td>
<td>8/15 (53%)</td>
<td>30/59 (51%)</td>
</tr>
<tr>
<td>Partial Aneuploid Mosaic</td>
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<td>8/16 (50%)</td>
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</tr>
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<td>54/158 (34%)</td>
</tr>
</tbody>
</table>

CONCLUSIONS: A diagnostic biopsy of ~5 trophoderm cells may detect mosaicism that does not exist in the ICM and may be highly localized in the trophoderm. In this group of 43 mosaic embryos, there were 12 (28%) with normal ICMs that also tested normal for all or several trophoderm specimens. The presence of aneuploid cell lines only in limited areas of the trophoderm suggests that the initial chromosomal malsegregation event occurred relatively close to the time of biopsy. The implantation potential of a blastocyst with a normal ICM and a mildly or highly mosaic trophoderm remains unknown. Embryos with an initial diagnosis of complex mosaic are less likely to have a normal ICM. Embryos diagnosed as partial aneuploid mosaic may be more likely to possess both a normal ICM and substantially normal trophoderm, compared to full aneuploid mosaics. These findings may aid the determination of mosaic embryos that are suitable for transfer. Depending on patient age, a mosaic embryo may have the same or lower chance of being compromised by aneuploidy as an undiagnosed embryo, and should be given the appropriate replacement priority if no euploid embryos are available.

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TIME-LAPSE IMAGING OF MULTINUCLEATED EMBRYOS AND THE ASSOCIATION WITH ANEUPLOIDY DETERMINED BY PREIMPLANTATION GENETIC SCREENING. L. R. Goodman, J. M. Goldberg, T. Falcone, N. Desai. Women’s Health Institute, Cleveland Clinic, Cleveland, OH.
OBJECTIVE: To determine if embryo multinucleation visualized by continuous time-lapse imaging is associated with an increased risk of aneuploidy.

DESIGN: Prospective cohort study

MATERIALS AND METHODS: A series of patients under the age of 38 years undergoing in-vitro fertilization for unexplained infertility were recruited to participate when at least 20% of their embryos exhibited evidence of multinucleation (MU) on day two of continuous time-lapse culture in the EmbryoScopeTM. All expanded blastocystst underwent trophectoderm (TE) biopsy on day 5 or 6 for genetic screening. Un-biopsied early blastocysts, as well as embryos arrested at cleavage/chorial stage, were also sent for analysis. Continuous variables were compared with the student’s-t-test, categorical with chi-squared and logistic regression was performed to account for confounding variables.

RESULTS: A total of 133 embryos from nine couples were evaluated for genetic analysis. The average age of patients was 31.9 +/- 3.2 years, who had 15.3 +/- 7.3 embryos with an average of 56.3 +/- 18.9% exhibiting MU. Of the 133 embryos, 72 (54.1%) developed to the expanded blastocyst stage and were able to undergo TE biopsy. There was no difference in embryo development to the expanded blastocyst stage between MU embryos and those without evidence of MU (56.9 vs. 43.1%; p = 0.37). When all embryos were evaluated, 57 (42.9%) were euploid, 49 (36.8%) exhibited aneuploidy, 22 (16.5%) were experienced as nonconcurrent and the remaining 5 (3.8%) had no amplification. There was no difference aneuploidy rate between MU and non-MU embryos (45.5 vs. 44.4%; p = 0.83). When accounting for confounding factors, MU embryos were equally as likely to be genetically normal (OR 1.08 95% CI 0.48 - 2.46; p = 0.85) and to make it to the blastocyst stage (OR 0.69 95% CI 0.31 - 1.48; p = 0.34) as those without evidence of MU. Of the TE biopsied embryos with diagnosis (n = 53), the rate of aneuploidy was also found to be similar between MU and non-MU embryos (45.5 vs. 35.0%; p = 0.57). When evaluating genetic parameters available though continuous time-lapse imaging, none of the timing of developmental milestone differed by MU. Stage of arrest was also similar between the two groups.

CONCLUSIONS: In this study, there was no increase in risk of aneuploidy in multinucleated embryos. Additional data is needed to corroborate these findings.

Supported by: The Foundation for Embryonic Competence.

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ACURATE DETECTION OF SEGMENTAL ANEUPLOIDY IN PREIMPLANTATION GENETIC SCREENING USING TARGETED NEXT-GENERATION DNA SEQUENCING. M. A. Umbarger, K. Germain, A. Gore, B. Breton, L. C. Walters-Sen, T. Mullen, N. Faulkner. Good Start Genetics, Cambridge, MA.

OBJECTIVE: To evaluate the sensitivity and specificity of segmental aneuploidy detection as a function of segmental copy number variant (CNV) size using EmbryVu, a targeted next-generation DNA sequencing (NGS) assay.

DESIGN: We have previously described a targeted NGS-based method for preimplantation genetic screening (PGS) that has been validated for accurate detection of full chromosome aneuploidy (Gole et al., 2016). The EmbryVu test leverages the FAST-SeqS NGS technology to target tens of thousands of gene regions for segmental aneuploidies, unlike whole chromosome aneuploidy that has detection sensitivity is reduced, these regions often coincide with heterochromatic and/or highly repetitive regions that are likely problematic with most PGS technologies. The EmbryVu PGS test, using the FAST-SeqS targeted NGS technology, is capable of accurately detecting sub-chromosomal changes of 10 Mb and larger with an analytic sensitivity of >97% and a specificity of >99% in a patient population.

RESULTS: Over 5,000 embryo biopsies from over 1,000 patient cycles were retrospectively studied. Segmental changes were observed in each age group and clinical indication for testing, and re-analyzed using a modified algorithm to identify sub-chromosomal abnormalities.

CONCLUSIONS: Over 5,000 embryo biopsies from over 1,000 patient cycles were retrospectively studied. Segmental changes were observed in each age group and clinical indication for testing, and re-analyzed using a modified algorithm to identify sub-chromosomal abnormalities.

Supported by: This study was funded by Good Start Genetics, Inc.

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SEGMENTAL ANEUPLOIDY IN PREIMPLANTATION GENETIC SCREENING STRATIFIED BY AGE AND CLINICAL INDICATION USING TARGETED NEXT-GENERATION DNA SEQUENCING. N. Faulkner, L. C. Walters-Sen, B. Breton, A. Gore, M. Zhu, K. Robinson, S. E. Hallam. Good Start Genetics, Cambridge, MA.

OBJECTIVE: To present the clinical experience of evaluating >5,000 patient embryos for segmental aneuploidy using a targeted next-generation DNA sequencing (NGS) assay.

DESIGN: The EmbryVu assay is a targeted NGS-based method for preimplantation genetic screening (PGS; initially validated for accurate detection of full chromosome aneuploidy). The method targets tens of thousands of gene regions across the genome and therefore has the potential to detect segmental aneuploidy. We recently validated the sensitivity and specificity of this test with a modified analysis algorithm. Here we share data from a retrospective analysis of clinical patient data reprocessed through the modified algorithm.

MATERIALS AND METHODS: Trophoderm biopsies containing 5-10 cells from blastocyst-stage embryos scheduled for FET were submitted for clinical PGS analysis. All samples were analyzed using the EmbryVu assay and associated bioinformatics pipeline. Data was then de-identified, except for egg age and clinical indication for testing, and re-analyzed using the modified algorithm to identify sub-chromosomal abnormalities.

RESULTS: Over 5,000 embryo biopsies from over 1,000 patient cycles were retrospectively studied. Segmental changes were observed in each age group and clinical indication for testing, and re-analyzed using a modified algorithm to identify sub-chromosomal abnormalities.

CONCLUSIONS: Og, 2016. The EmbryVu test leverages the FAST-SeqS NGS technology to target tens of thousands of gene regions for segmental aneuploidies, unlike whole chromosome aneuploidy that has detection sensitivity is reduced, these regions often coincide with heterochromatic and/or highly repetitive regions that are likely problematic with most PGS technologies. The EmbryVu PGS test, using the FAST-SeqS targeted NGS technology, is capable of accurately detecting sub-chromosomal changes of 10 Mb and larger with an analytic sensitivity of >97% and a specificity of >99% in a patient population.

Supported by: This study was funded by Good Start Genetics, Inc.

Supported by: This study was funded by Good Start Genetics, Inc.

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MISCARRIAGE AND ANEUPLOIDY RATES ARE HIGHER IN VERY YOUNG DONORS. J. LLACER, J. Guerrero, B. Lledo, J. Ortiz, J. Ten, R. Bernabeu. Reproductive Medicine, Instituto Bernabeu, Alicante, Spain.
OBJECTIVE: To study ongoing pregnancy rates and miscarriage rates in egg recipients receiving oocytes coming form very young donors (< 20 y) compared with treatments using older donors. Furthermore, to analyze comparatively the results of Comprehensive Chromosomal Screening (CCS) in embryos originated from very young donors.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Retrospective study including 514 oocyte donation treatments performed in a private fertility clinic from January to December 2015. Two groups were established according on the age of the donor. Group 1, donors 18-19 years old (45) group 2, donors 20-32 years old (469). We studied positive pregnancy test, clinical pregnancy, implantation, miscarriage and ongoing pregnancy rates. On the other hand, we recover CCS data from 237 blastocyst coming from egg donation analyzing aneuploidy rates between the two mentioned groups. Statistical analysis was performed by t-student for continuous variables and chi-square test for categorical parameters. Logistic regression was performed to rule out confounding factors.

RESULTS: The main results are shown in the table below.

<table>
<thead>
<tr>
<th>Study Group</th>
<th>Control Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Donors&lt; 20 y.)</td>
<td>(Donors 20-32 y.)</td>
</tr>
<tr>
<td>Positive Pregnancy Test</td>
<td>60.0 %</td>
</tr>
<tr>
<td>Clinical Pregnancy Rate</td>
<td>51.1 %</td>
</tr>
<tr>
<td>Implantation Rate</td>
<td>45.3 %</td>
</tr>
<tr>
<td>Miscarriage Rate</td>
<td>43.5 %</td>
</tr>
<tr>
<td>Ongoing Pregnancy Rate</td>
<td>28.9 %</td>
</tr>
<tr>
<td>Aneuploidy Rate</td>
<td>40%</td>
</tr>
</tbody>
</table>

CONCLUSIONS: Egg donation treatments using eggs from donors of less than 20 years of age have higher risk of miscarriage when compared with older donors. Higher rates of chromosomal alterations can explain this situation since aneuploidy rate was higher after CCS in embryos coming from very young donors. Further studies are needed to consider the exclusion of women younger than 20 years of age for donation. This data could help to understand the generation mechanisms of aneuploidies.

P-125 Tuesday, October 18, 2016

THE INTERCHROMOSOMAL EFFECT IN EMBRYOS DERIVED FROM BALANCED CHROMOSOMAL REARRANGEMENT CARRIERS. J. Kim, a Y. Hur, a H. Lee, a J. Kim, a W. Lee, a S. Shim. aObstetrics and Gynecology, Fertility Center, CHA Gangnam Medical Center, CHA University, Seoul, Korea, Republic of; aGenetics Laboratory, Fertility Center, CHA Gangnam Medical Center, CHA University, Seoul, Korea, Republic of.

OBJECTIVE: The balanced chromosomal rearrangements in the general population are detected in 1/500 to 1/1000 of newborns. The presence of a rearrangement increased the risk of unusual chromosome segregation during meiosis and the production of gamates with losses and/or gains of chromosomal material. It leads to repeated spontaneous abortions and reduced fertility. Besides the direct effect on the chromosomes involved in the rearrangement, there may also be an impact on the segregation of other structurally normal chromosomes during meiosis. This phenomenon is known as an inter-chromosomal effect (ICE). Recently, comprehensive chromosomal screening (CCS) in a carrier such as microarray, comparative genomic hybridization (aCGH) have begun to apply to PGD, and it facilitate to detect not only abnormalities affecting the specific chromosomes involved in the rearrangement, but also aneuploidies affecting any other chromosomes. In this study, we aimed to analyze the occurrence of ICE in human preimplantation embryos derived from carriers with balanced chromosomal rearrangements and the associated with specific types of chromosomal rearrangement.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: All patients had their chromosomal rearrangements accurately defined by clinical cytogeneticists using standard chromosome banding techniques. Overall, 49 couples underwent 71 cycles of PGD for balanced translocations from January, 2014 to September, 2015 at the Fertility Center of CHA Gangnam Medical Center. 302 PGD cycles of 220 chromosomally normal control patients were performed embryo testing as part of a routine IVF cycle with the aim of reducing the risk of miscarriage or aneuploidy. A single blastomere of cleavage stage embryo was used for analysis.

RESULTS: The main results are shown in the table below.

<table>
<thead>
<tr>
<th>Group</th>
<th>Euploidy Rates of Embryos within Groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>22.1%</td>
</tr>
<tr>
<td>Group 2</td>
<td>32.6%</td>
</tr>
<tr>
<td>Group 3</td>
<td>23.8%</td>
</tr>
<tr>
<td>Group 4</td>
<td>47.4%</td>
</tr>
</tbody>
</table>

CONCLUSIONS: A small percentage of blastocysts may possess mosaicism of chromosomal constitution, representing a possible limitation to the predictive value of CCS for clinical outcomes. However, contemporary methods of CCS may be capable of diagnosing aneuploidy in trophoderm biopsies which possess a mixture of aneuploid and euploid cells. This study evaluates the sensitivity and specificity of 2 CCS platforms to detect aneuploidy in a cell line mixture model of a mosaic trophoderm biopsy.

DESIGN: Prospective blinded.

MATERIALS AND METHODS: In order to establish positive controls for specific levels of mosaicism, 4 cell lines were obtained with known chromosomal status and mixed together at known ratios of 6 total cells (0:6, 1:5, 2:4, or approximately five cells from the trophoecloderm layer of blastocyst were analyzed with aCGH.

RESULTS: A total of 482 samples derived from balanced chromosome rearrangement carriers and 1655 samples derived from control group were analyzed. Cumulative aneuploidy rate in embryo derived from balanced chromosome rearrangement carriers was found to be similar with control group (70.1% vs. 70.4%, p = 0.9). But higher aneuploidy rate was observed in the embryos obtained from chromosome rearrangement carriers with maternal age of <36 compared with the control group (72.2% vs. 61.1%, p < 0.01). Interestingly, aneuploidy of chromosome 3 was significantly more in the embryo obtained from chromosome rearrangement carriers compared with the control group (9.6% vs. 3.5%, p < 0.01).

CONCLUSIONS: An ICE affects carriers of balanced translocation and may contribute to higher rates of abnormal embryos.

P-126 Tuesday, October 18, 2016

IMPROVING EUPLOIDY RATES IN PATIENTS UNDERGOING PREIMPLANTATION GENETIC SCREENING (PGS). S. Dogan, a E. Slutsky, b M. Urich, c J. W. Ayers, d L. Khan, d A. Hammoud, d F. Li, a F. N. Shamma, a IVF Michigan Fertility Center, Bloomfield Hills, MI; aDep't of Obstetrics Gynecology, Toledo, OH; bIVF Michigan, Ypsilanti, MI.

OBJECTIVE: To investigate the differences in euploidy rates between PGS techniques in patients undergoing blastomere vs trophoderm biopsy.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Data used in this study were collected from our routine PGS patients who used either autologous and or donor oocytes from 2014 to 2016 for incubation following insemination (n=365). Translocation and PGD cycles were excluded. The resulting embryos were divided into four groups based on biopsy day (blastomeres versus trophoderm) and PGS technique used (comparative genomic hybridization microarray [aCGH] vs Next Generation Sequencing (NGS)) (n=2010): Group 1 (aCGH blastomere, n=873), Group 2 (aCGH trophoderm, n=239), Group 3 (NGS blastomere, n=21) and Group 4 (NGS trophoderm, n=877). The use of oocyte donor was similar between groups. Patients’ ages were ranged as following; Group 1 (20-48), Group 2 (25-46), Group 3 (27-36) and Group 4 (23-47). Euploidy rates were analysed using chi square test among the groups.

RESULTS: According to our findings, euploidy rates (n) were found to be 22.1% (193) and 32.6% (78) (p<0.001) within Group 1 vs Group 2, respectively. Likewise, the euploidy rates were different in Group 3 as 23.8% (5) and Group 4 as 47% (12), respectively (p<0.035). The euploidy rate in Group 4 was higher than that in Group 2 (p<0.0001). The results were shown as a table below. There was no difference between Group 1 vs Group 3 (p>0.05).

CONCLUSIONS: In this study, we showed a higher rate of euploidy when using trophoderm compared to blastomere biopsies, and higher rate of euploidy in trophoderm biopsy when NGS was used in comparison to aCGH. According to our findings, euploidy rates in PGS cycles may be increased by performing trophoderm biopsy and NGS technology.
3: 3, 4: 2, 5: 1, and 6: 0). A euploid and a trisomy 18 cell line were used for one set, and a trisomy 13 and trisomy 15 cell line were used for another set. Replicates of each mixture were made and randomized to 1 of 2 CCS platforms, qPCR (FEC), and VeriSeq Next Generation Sequencing (NGS)(Illumina). Blinded prediction of aneuploidy was made with each platform and both sensitivity and specificity were determined.

RESULTS: Table 1 presents the results of comparing platforms for their sensitivity to detect aneuploidy at different mixture levels. The sensitivity of qPCR and VeriSeq were not statistically different (p > 0.05). Specificity was 100% for all mixtures and platforms.

CONCLUSIONS: Reasonable success was achieved at 50% aneuploidy within mosaic fetal-cell samples using 2 different methods of CCS. Although many other aspects of mosaicism may factor into the predictive value of a trophoderm biopsy for the actual clinical outcome, including distribution of aneuploidy in the remaining embryo, the level of aneuploidy present, and the type of chromosome involved, these results demonstrate the ability to detect aneuploidy within a mosaic sample. These results also demonstrate that the ability to detect mosaicism is not unique to NGS based testing.

Mosaicism detection rates by qPCR and VeriSeq CCS

<table>
<thead>
<tr>
<th>Spike-In</th>
<th>qPCR Sensitivity</th>
<th>VeriSeq Sensitivity</th>
<th>Fisher Exact Test</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0%-17%</td>
<td>0% 17% 33% 50% 67% 83% 100%</td>
<td>0% 6% 22% 44% 56% 83% 100%</td>
<td>1 1 0.33 0.29 1 0.23 1</td>
<td></td>
</tr>
</tbody>
</table>

P-128 Tuesday, October 18, 2016

PROSPECTIVE RANDOMIZED AND BLINDED COMPARISON OF NGS CCS PLATFORMS. R. S. Zimmerman,a N. Treff,b Y. Zhan,a X. Tao,a R. T. Scott,III,a K. Scott,a R. T. Scott;ii Foundation for Embryonic Competence, Basking Ridge, NJ; iiiReproductive Medicine Associates of New Jersey, Basking Ridge, NJ.

OBJECTIVE: To compare reproducibility of two contemporary methods of next generation sequencing (NGS) based comprehensive chromosome screening (CCS).

DESIGN: Prospective randomized blinded.

MATERIALS AND METHODS: 98 blastocysts which had been donated for research were subjected to 4 biopsies. These were randomly assigned to 1 of 2 NGS CCS methods, a targeted amplification NGS (tNGS) and a commercially available method (VeriSeq). All results were analyzed using the available automated software. After unblinding, two fundamental comparisons were completed. First, the number of samples where all four evaluations were in agreement was calculated. Subsequently, concurrence was calculated for each of the two platforms by assessing how often the two specimens analyzed were in agreement. A chi square test was used to evaluate statistical significance among comparisons. Frequency of segmental and mosaic aneuploidy from tNGS computational predictions (autocalls) were obtained. Similar data were unavailable from default BlueFuse based analyses of VeriSeq data.

RESULTS: All specimens were analyzed as planned with two biopsies analyzed by VeriSeq and two by tNGS. Seventy of the 98 embryos (71.4%) had identical results from all four biopsies. Amongst the embryos with discordant results, VeriSeq was discordant in 19 (19.4%) while tNGS was discordant in 9 (9.2%). The probability of obtaining discordant results was significantly lower with tNGS than those attained with VeriSeq (P = 0.04). Autocalls for mosaicism or segmental abnormalities were only available on tNGS platform. Mosaicism was identified in 38 of 198 tNGS (19.2%) specimens. Segmental abnormalities were found in 30 of 198 tNGS (15.2%).

CONCLUSIONS: This study demonstrates a higher level of concurrence for specimens evaluated using tNGS. The lack of defined criteria for diagnosing segmental aneuploidy and mosaicism also may have contributed to reduced reproducibility observed with VeriSeq technology. Further study will be required to determine the clinical impact of these findings.

P-129 Tuesday, October 18, 2016

ASSOCIATION BETWEEN HIGH GONADOTROPIN DOSAGE, EUPLOIDY AND PREGNANCY RATES IN PGT CYCLES. O. Barash, K. Ivani, L. Weckstein, S. Willman, E. Rosenbluth, D. Wachs, M. Hinckley, Reproductive Science Center of the San Francisco Bay Area, San Ramon, CA.

OBJECTIVE: Preimplantation genetic testing (PGT) has been proven to be the most effective and reliable method for embryo selection in IVF cycles [1, 2]. Euploidy and blastulation rates decrease significantly with advancing maternal age [3, 4]. At the same time, in order to recruit an adequate number of embryos, the average dosage of gonadotropins administered during controlled ovarian stimulation in IVF cycles increases significantly with advancing maternal age. The objective of this study was to evaluate the association between the euploidy rates and pregnancy rates, and total dosage of gonadotropins administered in matched age groups in IVF PGT cycles.

DESIGN: A retrospective study of SNP PGT outcome data from blastocysts biopsied on day 5 or day 6 was conducted to identify differences in euploidy and clinical pregnancy rates.

MATERIALS AND METHODS: 479 cycles of IVF treatment with PGT between January 2013 and February 2016 followed by 497 frozen embryo transfers were included in the study (351 patients, maternal age - 37.6 ± 4.1). A total of 2610 embryos were analyzed by SNP PGT (5.45±2.6 per cycle) for euploidy rates. All embryos were vitrified after biopsy; and selected embryos were subsequently thawed for a hormone replacement frozen embryo transfer cycle. All cycles were divided in three groups by total gonadotropin dosage (<3000 IU, 3000–5000 IU, and > 5000 IU), in four groups by number of eggs retrieved (1-5, 5-10, 10-15, and >15 eggs) and in four age groups (<35, 35-37, 38-40, and ≥ 41 y.o.). Clinical pregnancy rate was defined by the presence of a fetal heartbeat at 6-7 weeks of pregnancy.

RESULTS: Euploidy rates within the same age group were not statistically different regardless of the total dosage of gonadotropins used or the number of eggs retrieved in IVF PGT cycles. In a group of young patients (<35 y.o. - 101 patients) euploidy rates ranged from 61.03% to 66.67%, when analyzed by total dosage of gonadotropins used in the IVF cycle and from 59.82% to 67.12%, when assessed by the total number of eggs retrieved, χ² = 0.3059, p = 0.5802. Similar data were obtained in a group of older patients (≥41 y.o. - 137 patients): euploidy rates ranged from 25.78% to 32.86% when analyzed by total dosage of gonadotropins used in the IVF cycle and from 29.47% to 46.15% when assessed by the total number of eggs retrieved, χ² = 1.117, p = 0.2906. Ongoing pregnancy rates were similar, not only within particular age groups, but also between different age groups regardless of the total dosage of gonadotropins used or the number of eggs retrieved: ranging from 56.57% to 68.18% (p = 0.3642, χ² = 0.6357).

CONCLUSIONS: High gonadotropin dosage does not affect euploidy and pregnancy rates in IVF PGT cycles. Euploidy rates are defined primarily by patient age regardless of the number of eggs retrieved.

References:

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THE INCIDENCE OF DELETIONS AND DUPLICATIONS IN PRE-IMPLANTATION EMBRYOS AS DETERMINED BY ENHANCED NEXT GENERATION SEQUENCING. P. R. Brezina,a K. Tobler,b R. A. Kaufmann,” R. Ross,a A. K. Dubey,” W. G. Kearns.1 Reproductive Endocrinology and Infertility, Vanderbilt University School of Medicine, Memphis, TN; 2Reproductive Endocrinology and Infertility, Womack Army Med Ctr Obstetrics and Gynecology, Fort Bragg, NC; 3Reproductive Endocrinology and Infertility, Fort Worth Fertility, Fort Worth, TX; 4Fort Worth Fertility, Fort Worth, TX; 5Advagenix and North Carolina IVF Labs, Fayetteville, NC; 6Advagenix and Johns Hopkins Medical Institutions, Rockville, MD.

OBJECTIVE: To determine the incidence of deletions and duplications in euploid embryos as identified by enhanced next generation sequencing (NGS) technology as part of preimplantation genetic screening (PGS).

DESIGN: Retrospective Review.

MATERIALS AND METHODS: A retrospective review was conducted of embryos that underwent PGS by enhanced NGS. Trophodermct (TE) cells were lysed and the DNA was amplified using a modified whole genome amplification protocol. DNA libraries were prepared, followed by emulsion PCR and DNA sequencing was done by a personal genome machine (PGM).
The data was then transferred to an Ion Reporter Server for comprehensive data analysis and interpretation. The PGM sequencing provided over 3.6 million reads with a median sequencing fragment length of 176 bp. 

RESULTS: PGS results from 10,801 embryos were reviewed. 3.9% (421 / 10,801) of embryos were euploid but included a clinically significant del or dup. These dels or duped ranged in size from approximately 800kb to 139Mb. The range for deletions was 800kb to 90.7Mb and the range for duplications was between 1.2Mb and 139Mb. Upon detailed molecular analysis of genes located within these deleted or duplicated regions, a potentially significant phenotype was observed in 2.9% (313 / 10,801) of samples analyzed.

CONCLUSIONS: Our results indicate that using an enhanced NGS technology, approximately 2.9% of euploid embryos contain clinically significant dels or dupes and should not optimally be considered for transfer.

P-131 Tuesday, October 18, 2016

THE ASSOCIATION BETWEEN MITOCHONDRIAL DNA CONTENT AND IMPLANTATION POTENTIAL DURING IVF AND PRE-IMPLANTATION GENETIC SCREENING CYCLES. A. K. Dubey,1 K. J. Tobler,2 N. Massahi,1 J. Crochet,3 W. G. Kearns,2 V. Schnell,3 1NorthCarolina IVF labs, Fayetteville, NC; 2Obstetrics and Gynecology, Womack Army Medical Center, Fayetteville, NC; 3Advenix, Rockville, MD.

OBJECTIVE: Mitochondria (Mt) play an important role in embryo development. However, little is known in regards to embryo development and implantation. We determined whether Mt content play a role in implantation.

DESIGN: Retrospective.

MATERIALS AND METHODS: 409 euploid blastocyst from 125 patients of all ages were included in this study from a single IVF clinic. Trophoderm cells from Day 5 and day 6 were lysed and underwent whole genome DNA amplification. Next, DNA libraries were prepared and an emulsion PCR step was completed. Next generation sequencing was completed by a personal genome machine (PGM). The data was then transferred to an Ion Reporter Server for comprehensive data analysis and interpretation. The PGM sequencing provided over 3.6 million reads with a median sequencing fragment length of 176 bp. The mt DNA content was determined as the ratio of Mt DNA to nuclear DNA within the same cell. The euploid embryos(s) were transferred fresh on day 6 or as a frozen-thaw follow up cycle. The differences in the mean value of the ratios were compared using the Wilcoxon rank sum test for each age category. A p-value < 0.05 was considered statistically significant.

RESULTS: The mean values of the Mt DNA to nuclear DNA ratio in euploid embryos were compared between patients achieving successful clinical pregnancy and no pregnancy. Age categories and number of patients included <35 (37 patients), 35-37 (23 patients), 38-40 (27 patients), 41-42 (14 patients), >43 (24 patients). Statistical significance was identified in only the 38-40 year category. The differences in the ratio was not significant in all other categories.

CONCLUSIONS: Our data shows that the ratio of Mt DNA to nuclear DNA is only correlated to implantation potential in the 38-40 year old age group. In our opinion, the relationship between Mt DNA content and implantation is unclear at this time.

Mean ratio values of mitochondrial to nuclear DNA

<table>
<thead>
<tr>
<th>Age Group</th>
<th># patients</th>
<th>Pregnancy</th>
<th>No pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;35</td>
<td>37</td>
<td>0.015</td>
<td>0.057</td>
</tr>
<tr>
<td>35-37</td>
<td>23</td>
<td>0.0109</td>
<td>0.0007</td>
</tr>
<tr>
<td>38-40</td>
<td>27</td>
<td>0.0237</td>
<td>0.0004</td>
</tr>
<tr>
<td>41-42</td>
<td>14</td>
<td>0.0069</td>
<td>0.035</td>
</tr>
<tr>
<td>&gt;42</td>
<td>24</td>
<td></td>
<td>0.019</td>
</tr>
</tbody>
</table>

P-132 Tuesday, October 18, 2016

PREGNANCY AND SPONTANEOUS ABORTION RATES FOLLOWING PGD FOR TRANSLocations COMBINED WITH 24-CHROMOSOME ANEUPLOIDY TESTING. A. Kuliev, Z. Zlatopolksy, G. San Ramon, S. Rechitsky. Reproductive Genetic Innovations, Northbrook, IL.

OBJECTIVE: PGD is the only hope for carries of balanced translocations, as their reproductive outcome is extremely poor, despite remote chance of having a normal offspring after numerous natural attempts. However, the present technologies still have limitations for accurate diagnosis depending on the type, size and position of translocated segments. The recent application of NGS for PGD of translocations allows a concomitant 24-chromosome aneuploidy testing, expected to improve the reproductive outcome of PGD for translocations in patients of advanced reproductive age. So the objective of this work was to investigate the reproductive outcome of cycles performed with chromosome-CGH and NGS for array translocations combined with 24-chromosome aneuploidy testing compared to translocation cycles performed by FISH, without aneuploidy testing.

DESIGN: Retrospective Study.

MATERIALS AND METHODS: A total of 893 PGC cycles for translocations were performed, using all available technologies. Biopsy procedures varied from polar bodies (PB) removal to blastomere (BL) or blastocyst biopsy, by mechanical or laser methods. Nuclear transfer or chemical conversion techniques were used to visualize second PB (PB2) and BL chromosomes. Biopsied materials were tested by FISH, microarray (aCGH), or next generation (NGS) technologies.

RESULTS: A total of 666 PGC cycles was performed by FISH for 433 patients with translocations, which resulted in 486 transfers, yielding 193 (39.7%) pregnancies, 156 deliveries of 187 unaffected children, with 32 (16.5%) spontaneous abortions. In contrast, array-CGH or NGD testing of 217 cycles for 93 patients with translocations, which involved also a concomitant 24-chromosome aneuploidy testing, resulted in 117 embryo transfers, 76 (64.7%) pregnancies, and birth of 77 unaffected children in 73 deliveries, with only 3 (3.9%) spontaneous abortions. So introduction of the next generation technologies with a concomitant aneuploidy testing leads to an almost two-fold increase of pregnancy rate and four fold reduction of spontaneous abortion rate.

CONCLUSIONS: Introduction of next generation technologies for PGD of chromosomal rearrangements resulted in significant improvement of reproductive outcome, involving almost two-fold improved pregnancy rate and four-fold reduction of spontaneous abortion rate. This may be due to the concomitant 24-chromosome aneuploidy testing, which allows avoiding the transfer of balanced or normal embryos with aneuploidies, incompatible with implantation and early embryonic development.

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OBJECTIVE: To investigate the differences of the timing of cytokinesis with embryos of paternally derived and maternally derived chromosomal aberration in euploid blastocysts, euploid blastocysts and non-biopsy embryos.

DESIGN: A retrospective cohort study from July 2013 to October 2015. This study were analysed embryos of 60 ICSI-PGS patients diagnosed with chromosomal aberration. 168 embryos were cultured in time-lapse system (Primo Vision) and images were recorded. A total of 70 embryos underwent trophectoderm (TE) biopsy on 5 day and 6 day were analysed using array comparative genomic hybridization (aCGH).

MATERIALS AND METHODS: We were classified into 2 categories, paternally derived vs maternally derived; 1) developing time of euploid blastocysts (n=14), euploid blastocysts (n=56) and non-biopsy embryos (n=98); 2) phenotype of cytokinesis of euploid, euploid blastocysts and non-biopsy embryos. The timing of cytokinesis were evaluated; cell divisions (tIS, tSC, t2-t5, t8, tSB, tIB) and interval (c2c, cc3, s1, s2, s3).

RESULTS: No significant differences were found time of division and intervals between euploid and aneuploid blastocysts with paternally derived or maternally derived chromosomal aberration. A significant differences were showed between euploid blastocysts and non-biopsy embryos; tSC (38.0±2.8 and 26.7±3.6; p=0.0276) in maternally derived chromosomal aberration. A significant differences were showed between euploid blastocysts and non-biopsy embryos; tIS (92.1±4.0 and 99.5±8.8; p=0.0322) and tSB (99.3±5.7 and 113.6±11.0; p=0.0021) in paternally derived chromosomal aberration. Also, there was a statistically significant difference in euploid blastocysts and aneuploid blastocysts respectively between paternally derived and maternally derived chromosomal aberration; tIS (21.7±1.4 and 25.1±2.0; p=0.0209) and tSB (22.6±2.2 and 24.8±3.1; p=0.0056), tSC (23.6±1.6 and 27.0±2.6; p=0.0116), t2 (23.6±1.6 and 27.3±2.6; p=0.0102), t4 (35.8±2.2 and 39.3±2.9; p=0.0388), and t4 (36.6±4.7 and 39.4±3.6; p=0.0240). Although there was no significant differences, they showed abnormal phenotype of cytokinesis in aneuploid blastocysts and non-biopsy embryos of paternally derived and maternally derived chromosomal aberration.

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aberration respectively; direct cytokinesis (3.1% and 32.7%, 8.3% and 25.6%), reverse cytokinesis (6.5% and 22.0%, 8.3% and 4.7%) and chaotic cytokinesis (0.0% and 14.5%, 4.2% and 14.0%).

CONCLUSIONS: These findings may indicate that time-lapse system provides cytokinetic differences of embryos diagnosed with paternally or maternally derived chromosomal aberration. Significant differences were found cytokinetic parameters between maternally derived and paternally derived chromosomal aberration with euploid or aneuploid blastocysts. Also, there wasn’t showed abnormal phenotype of cytokinesis in euploid.

P-134 Tuesday, October 18, 2016
NON-INVASIVE CHROMOSOME SCREENING OF HUMAN EMBRYOS BY GENOME SEQUENCING FROM BLASTOCYST CULTURE MEDIUM: VALIDATION & A PILOT STUDY. S. Lu, L. Cai, B. Yao, X. Xie. *Yikon Genomics Co., Ltd., Shanghai, China; †The Reproductive Medical Center of Nanjing Jinling Hospital, Nanjing, China; ‡Harvard University, Cambridge, MA.

OBJECTIVE: Pre-implantation genetic screening (PGS) enables the selection of in-vitro-fertilized embryos to avoid chromosomal imbalance, and is currently widely used to improve the clinical outcome of in-vitro fertilization (IVF). However, PGS requires embryo biopsy before implantation, which limits the clinical applicability of PGS due to the invasiveness and complexity in the embryo biopsy process. Here we present and validate a non-invasive chromosome screening (NICS™) method using blastocyst culture medium.

DESIGN: By performing whole genome amplification and sequencing on the blastocyst culture medium, we obtained the ploidy information on all 24 chromosomes. We then validated the ploidy information obtained from the culture medium by comparing with the corresponding donated blastocyst embryos.

MATERIALS AND METHODS: All embryos were fertilized by ICSI. After warming, embryos were placed in 30 μl droplets of blastocyst medium (SAGE, US) under washed and pre-gassed mineral oil (SAGE) and then further cultured to the blastocysts under 5.5% CO2, 5% O2, and balance N2 at 37°C in Labotect C16 incubators (Labotect, Germany). To prevent media contamination, individual Pasteur pipettes were used for each embryo. The blastocysts for final confirmation were transferred into RNase-DNase-free polymerase chain reaction (PCR) tubes that contained 5 μl of cell lysis buffer (Yikon Genomics, China). The same quantity of blastocyst culture medium without embryo culture was collected as a negative control. All collected samples were frozen immediately by liquid nitrogen and stored under -80°C until NICS™ assay. The MALBAC™ single-cell WGA method was used to amplify the culture medium as well as the embryos, following the protocol provided by the manufacturer (Cat. No. YK001B; Yikon Genomics, China). The amplifications products were then used for constructing sequencing libraries for sequencing on an Illumina HiSeq 2500 platform, yielding ~2 million sequencing reads on each sample. The read number per single blastocyst were counted along the whole genome with a bin size of 1 Mb. A copy number gain from 2 to 3 copies results in a 50% increase in read counts, while a copy number loss from 2 copies to 1 copy results in a 50% decrease in read counts.

RESULTS: With the NICS™ method, we perform chromosome screening on the IVF embryos from a patient carrying balanced chromosome translocation, and obtained a successful pregnancy and live birth with balanced chromosomes, which was confirmed by amniocentesis. We then applied the NICS™ assay on 15 patients and here we report the clinical outcome of our first 15 patients. We obtained a sensitivity of 0.882 and a specificity of 0.840 for identifying chromosomal abnormalities.

CONCLUSIONS: The NICS™ method avoids invasive and sophisticated embryo biopsy procedure and can potentially enables the wide applicability of chromosome screening in the clinical practice of IVF.

P-135 Tuesday, October 18, 2016
SELECTION OF SINGLE BLASTOCYSTS FOR TRANSFER VIA TIME-LAPSE MONITORING ALONE AND WITH NEXT-GENERATION SEQUENCING TO REDUCE MULTIPLE PREGNANCIES: A RANDOMIZED PILOT STUDY. Z. Yang, J. Lin, S. Zhang, Y. Kuang, J. Liu. *Clinical Research, ZytoGen, Timonium, MD; †ART, Reproductive Fertility Center, Irvine, CA; ‡ART, Sir Run Run Shaw Hospital, Zhe Jiang University School of Medicine, Hangzhou, China; †ART, Ninth People’s Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China; ‡ART, Jiaen Deyun Hospital, Beijing, China.

OBJECTIVE: Recent advances in time-lapse monitoring and next-generation sequencing (NGS) have provided new methods for selecting competent embryos for transfer in IVF treatments. The present study aim to investigate the effects of time-lapse monitoring and NGS testing on clinical and ongoing pregnancy outcomes of single embryo transfer for good prognosis patients to reduce multiple pregnancies.

DESIGN: IVF patients with a good prognosis (under 35 years old and no prior miscarriage) and normal karyotype were prospectively randomized into two groups: 1) Group A: patients (n=105) had embryos cultured in a time-lapse system and tested with NGS and 2) Group B: patients (n=104) had embryos cultured in a time-lapse system only. The two study groups were mutually exclusive and no study patient had embryos assigned to both groups. All patients signed the consents for single embryo transfer to reduce multiple pregnancy rate.

MATERIALS AND METHODS: For both groups, embryos were cultured in a time-lapse system to blastocyst stage. For Group A, trophoderm biopsy was performed on Day 5 (up to 11:00 pm) and blastocysts were vitrified individually after biopsy. One euploid blastocyst with the most predictive morphokinetic parameters available was thawed and transferred to individual patients. For Group B, blastocysts were vitrified individually on Day 5 (up to 11:00 pm). One blastocyst with the best predictive morphokinetic parameters available was warmed and transferred. Clinical and ongoing pregnancy rates were compared between the two groups. The categorical variables were analyzed by Chi-square analysis or Fisher’s exact test as appropriate. A two-tailed value of p<0.05 was considered statistically significant.

RESULTS: There were no significant differences in female patient’s mean age, Day 3 FSH, AMH, E2, antral follicle number between the two groups (p>0.05). However, there was significant difference in clinical pregnancy rates between Group A and Group B (72.5% vs. 49.5%, respectively, p<0.05). The observed ongoing pregnancy rate was also significantly higher in Group A compared to Group B (71.6% vs. 47.6%, respectively, p<0.05).

CONCLUSIONS: This is the first prospective investigation to evaluate the efficiency of selecting single competent blastocysts for transfer by combining time-lapse monitoring and NGS testing for IVF patients. Our data clearly demonstrate that the combined use of these two advanced technologies to select single blastocysts for transfer results in improved clinical and ongoing pregnancy rates and reduced multiple pregnancy rates for IVF patients with a good prognosis.

References:

Supported by: This study was supported by internal funds.

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OBJECTIVE: To identify if the rate of mosaicism and aneuploidy differ among different IVF centers performing trophoderm biopsy on blastocysts for Preimplantation Genetic Screening (PGS) with Next Generation Sequencing (NGS).

DESIGN: Retrospective analysis.

MATERIALS AND METHODS: All donor oocyte cycles undergoing PGS with NGS from trophoderm biopsy specimens, received by a large United States Genetics Laboratory, were queried. Only centers with biopsy specimens from ten or more patients were included in the study. Analysis was limited to cycles from donors between the ages of 18 and 30 years old. Blastocyst biopsy results were classified as being euploid, aneuploid or mosaic. Embryos defined as mosaic showed a 20 percent or greater mosaicism rate within the biopsy specimens. Biopsy results showing mosaicism or mosaicism with a single aneuploidy were classified the same (only 0.97% of all NGS samples run show mosaic with single aneuploidy). Any result with two or more aneuploidies plus mosaicism was classified to be complex abnormal and defined as aneuploid. Statistical analysis was done using ANOVA and linear regression.

References:

Supported by: This study was supported by internal funds.
NGS Results for Donor Cycles aged 18 to 30 years old from IVF Centers with Ten or More Cycles

<table>
<thead>
<tr>
<th>No. Cycles per Center (a-i)</th>
<th>Avg Donor Age</th>
<th>Avg No. Biopsy per Patient</th>
<th>No Amplification (%)a</th>
<th>Degraded DNA (%)a</th>
<th>Euploid (%)b</th>
<th>Aneuploid(%)b</th>
<th>Mosaic (%)b</th>
</tr>
</thead>
<tbody>
<tr>
<td>a-16</td>
<td>24.00±2.31</td>
<td>7.06±2.86</td>
<td>0.88±4.17</td>
<td>2.65±5.46</td>
<td>44.95±28.11</td>
<td>32.11±26.90</td>
<td>22.94±13.58</td>
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<tr>
<td>b-23</td>
<td>25.27±2.35</td>
<td>6.55±3.53</td>
<td>0.63±1.78</td>
<td>0.69±4.26</td>
<td>52.08±27.70</td>
<td>18.06±18.98</td>
<td>29.86±26.63</td>
</tr>
<tr>
<td>c-12</td>
<td>22.92±1.44</td>
<td>7.75±3.14</td>
<td>4.10±10.76</td>
<td>2.15±3.73</td>
<td>43.68±20.17</td>
<td>39.08±19.17</td>
<td>17.24±12.20</td>
</tr>
<tr>
<td>d-41</td>
<td>25.50±2.44</td>
<td>7.30±3.83</td>
<td>1.03±5.45</td>
<td>2.40±4.86</td>
<td>56.29±25.07</td>
<td>26.22±22.86</td>
<td>17.48±18.73</td>
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<tr>
<td>e-14</td>
<td>24.00±2.04</td>
<td>10.43±4.11</td>
<td>0.68±4.45</td>
<td>1.37±10.69</td>
<td>50.35±21.62</td>
<td>17.48±10.69</td>
<td>32.17±19.79</td>
</tr>
<tr>
<td>f-19</td>
<td>24.52±3.02</td>
<td>9.21±5.48</td>
<td>1.14±3.33</td>
<td>4.00±10.44</td>
<td>38.82±20.88</td>
<td>27.65±19.82</td>
<td>33.53±15.07</td>
</tr>
<tr>
<td>g-18</td>
<td>25.41±3.10</td>
<td>8.53±4.52</td>
<td>0.00±0.00</td>
<td>2.76±11.04</td>
<td>47.92±24.64</td>
<td>18.06±21.02</td>
<td>34.03±21.67</td>
</tr>
<tr>
<td>h-36</td>
<td>26.14±2.58</td>
<td>8.03±4.74</td>
<td></td>
<td>1.38±7.84</td>
<td>45.49±23.29</td>
<td>26.74±17.13</td>
<td>27.78±26.31</td>
</tr>
<tr>
<td>i-13</td>
<td>25.31±2.36</td>
<td>5.31±2.56</td>
<td>0.00±0.00</td>
<td>2.90±11.09</td>
<td>37.31±22.20</td>
<td>14.93±12.18</td>
<td>47.76±21.26</td>
</tr>
<tr>
<td>p</td>
<td>0.005</td>
<td>0.055</td>
<td>0.35</td>
<td>0.987</td>
<td>0.169</td>
<td>0.018</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

a. Percent expressed as total over total number biopsied. b. Percent expressed as total over total embryos with diagnosis given.

RESULTS: A total of 268 cycles from 38 different IVF centers resulted from the query. A total of 192 cycles from 9 different IVF centers were included in the analysis. The average age of patients was 25.15±2.60 years old (range 19-30), with a cumulative total of 1492 blastocysts biopsied. The overall euploid rate was 48.94%±24.61, with an aneuploid rate of 24.65%±20.76 and mosaic rate of 26.41%±25.0. When the 9 centers were compared as a group, there was a significant difference in mosaic rate (p<0.001) and aneuploid rate (p=0.018), but not in the euploid rate (p=0.166). Linear regression on all 268 cycles showed no association between age and rate of euploidy (R=0.025), aneuploidy (R=0.056) or mosaicism (R=0.054); indicating differences in donor ages amongst centers has no affect. There was no significant correlation between the number of blastocysts for biopsy and the percent euploid (R=0.123), aneuploid (R=0.035) or mosaic (R=0.099).

CONCLUSIONS: The difference in mosaic and aneuploid rates with NGS amongst donor cycles within different IVF institutions shows that there may be a significant practice or laboratory component affecting outcomes. The lack of association of mosaicism and aneuploidy in this population further indicates environmental factors may play an important role.

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DISCORDANCE RATES BETWEEN DAY 3 AND DAY 6 CHROMOSOME RESULTS AND THE PREDICTIVE VALUE OF TIME-LAPSE MORPHOKINETICS. J. R. Ho,a N. Arrach,a W. Salem,a S. A. Ingles,a K. Bendikson,a K. Chung,a R. Paulson,a A. Ahmady,a University of Southern California, Los Angeles, CA;

OBJECTIVE: Time-lapse morphokinetics (TLM) may provide a noninvasive method for selecting higher quality embryos for transfer. Some studies suggest early kinetic parameters may give insight to embryos with better developmental competence. However, there are mixed results regarding the ability of TLM to predict blastulation and chromosomal status. In this study, we investigate the relationship of TLM with blastulation and ploidy status. Comprehensive chromosomal screening (CCS) was performed on day 3 and day 6 on the same embryo, allowing us to also evaluate discordance rates between results.

DESIGN: Prospective study of previously cryopreserved human embryos.

MATERIALS AND METHODS: 25 cryopreserved zygote embryos were thawed and cultured in the ESCO Mri-Time Lapse incubator. On day 3, each embryo underwent blastomere biopsy, and on day 6, all embryos regardless of progression were sent for CCS. CCS analysis was performed by next generation sequencing (NGS). Kruskal Wallis was used to analyze the relationship between TLM parameters, blastulation, and ploidy status. For TLM, we included time at which embryos reached each developmental stage. We included second and third cell cycle duration (CC2 and CC3), as well as time between 3-cell to 4-cell (S2), and 5-cell to 8-cell (S3) stages in the analysis.

RESULTS: 22 out of the 25 embryos survived the thaw process. 11 embryos (50%) grew to full blastocyst stage. Contrary to previous studies, timing of the second and third cycle (CC2 and CC3), were not predictive of blastulation or euploidy status. There were no significant differences in TLM medians between those that formed full blastocysts vs those that arrested early. Other TLM parameters did not predict ploidy status. 14 out of 22 (63%) of NGS results on day 6 were euploid. Of 12 euploid embryos, corresponding day 3 results were discordant in 7 (58%) and showed aneuploidy. Table 1 displays discordant results.

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OBJECTIVE: Preimplantation Genetic Diagnosis (PGD) has helped couples avoid inherited genetic diseases for over 25 years. Karyomapping can streamline this process with a high resolution and rapid result test design. This study is an evaluation of the Single Nucleotide Polymorphism (SNP)-based karyomapping platform as the best standard for preimplantation genetic diagnosis of single gene disorders, using an analysis of over 9,000 trophectoderm biopsies and 304 diverse genetic conditions. DESIGN: Retrospective, multi-faceted analysis of embryo biopsies submitted for single-gene diagnosis on the new karyomapping test platform.

MATERIALS AND METHODS: Familial DNA from either buccal swabs or blood samples was analyzed along with amplified embryo DNA using the Illumina Karyomapping assay. The data was analyzed with BlueFuse Multi software to detect affected familial haplotypes and determine disease status of embryos. When requested, aneuploidy screening was performed in parallel using either Comparative Genomic Hybridization microarray (aCGH) or Next Generation Sequencing.

CONCLUSIONS: In our study, early TLM parameters did not predict blastulation or euploid status on day 3 or day 6 using CC2 and CC3 data. Discordant results were as high as 58% between day 3 and 6. This supports the theory that abnormal blastomeres likely undergo selective apoptosis and repair mechanisms during embryo growth, making day 3 CCS inaccurate. It is also possible that limited DNA material present in single cells is prone to chromosome dropout during the whole genome amplification process, leading to false positives (aneuploids).
RESULTS: 1,417 families were analyzed using the karyomapping technology, with an average PGD probe design length of 4 weeks. In total, 9,426 blastocyst biopsies were assessed, averaging 6.8 samples per couple. Of the samples tested, 4.8% were given a “no result” diagnosis because quality control metrics were not met, or the sample had poor amplification. 1.4% were given a “no diagnosis” or “inconclusive” result due to sample contamination or partial/incomplete results. The remaining 8,848 biopsies (93.9%) were successfully diagnosed for 304 different genetic conditions. Karyomapping alone was performed on 294 cases (2,013 samples), resulting in a transfer rate (proportion of assessed embryos available for transfer) of 46.7%. Aneuploidy screening was included in the remaining 1,123 cases, resulting in a transfer rate of 29.9%.

CONCLUSIONS: Karyomapping has proven to be a reliable and reproducible test, as evidenced by the robust diagnosis of 93.9% of the 9,426 biopsies analyzed over the course of 2 years. With karyomapping, the vast number of data points available across the entire genome allows for diagnosis of common, uncommon, and novel genetic disorders with a single standard test platform. This is in stark contrast to the time-consuming customization required by the previous methodology using short tandem repeats. The families undergoing PGD are benefiting from this technology, particularly those in need of a rapid test design. Great success with this technology demonstrates that karyomapping has become the new gold standard for PGD.

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PREIMPLANTATION GENETIC DIAGNOSIS OF RECIPROCAL TRANSLOCATIONS USING POLAR BODIES - FIRST VALIDATION USING A NEXT-GENERATION SEQUENCING PLATFORM. S. M. Taylor, a S. Knebel, b S. Alfarawati, c E. Fragioulis, c D. Wells, c K. R. Held. a Reprogenetics UK, Oxford, United Kingdom; b Reprogenetics Germany GmbH, Hamburg, Germany; c Reprogenetics, Oxford, United Kingdom.

OBJECTIVE: There has been great interest in using next-generation sequencing (NGS) for the cytogenetic assessment of preimplantation embryos. Several studies have examined the potential of NGS in the context of comprehensive chromosome screening, but there have been few studies assessing its use for preimplantation genetic diagnosis (PGD) of chromosome rearrangements and none evaluating NGS applied to polar bodies (PBs) biopsied from oocytes. We sought to validate NGS for the PGD of translocations in PBs.

DESIGN: Blinded technical validation using clinical material.

MATERIALS AND METHODS: First and 2nd PBs were biopsied from 54 oocytes, from 24 female translocation carriers. The PBs were subjected to whole genome amplification and tested using a well-validated aCGH protocol, revealing any losses/duplications of specific chromosomal regions. Subsequently, the amplified DNAs were blindly analyzed by NGS (VeriSeq, Illumina).

RESULTS: NGS succeeded in yielding results for all 108 PBs and correctly identified 100% of unbalanced reciprocal translocations. The smallest unbalanced fragment assessed was ~2.5MB, indicating that the resolution of NGS is at least as good as aCGH. NGS was seen to have a greater dynamic range than aCGH, allowing single chromatid losses/gains to be readily distinguished from errors involving entire chromosomes in 1st PBs. NGS detected 48 MI aneuploidies unrelated to the translocations readily distinguished from errors involving entire chromosomes in 1st PBs. NGS was seen to have a greater resolution of NGS is at least as good as aCGH, allowing single chromatid losses/gains to be

CONCLUSIONS: The results confirm that NGS accurately detects unbalanced products of reciprocal translocations in PBs. The few discrepancies between aneuploidy detection using NGS and aCGH may be related to limitations in the ability of aCGH to distinguish chromatin abnormalities from those involving whole chromosomes. The highly sensitive NGS analysis revealed that translocations imbalances most frequently arise due to malsegregation of chromatids rather than chromosomes. Given that PB analysis is preferred by some patients for ethical/religious reasons and that testing of embryonic stages is forbidden in some countries, the verification of the accuracy of NGS, reported here is of some importance.

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TRANSLOCATIONS AND SEX DOES SIZE MATTER?. T. Escudero, c E. M. Armenti, a A. S. Berkeley, j J. M. Norian, c D. Shapiro, b S. J. Chantilis, c C. Racowsky, l L. Ribustello, c E. Liu. b Reprogenetics, Livingston, NJ; c NYU Fertility Center, NYU School of Medicine, New York, NY; c HRC Fertility, Pasadena, CA; l RBA, Atlanta, GA; c Dallas-Fort Worth Fertility Associates, Dallas, TX; l Brigham and Women's Hospital ART Center, Boston, MA.

OBJECTIVE: Determine if the gender of the translocation carrier and the size of chromosome fragments involved in a translocation impact the segregation pattern during meiosis.

DESIGN: Retrospective analysis of PGS results for embryos analyzed for reciprocal translocations (RT).

MATERIALS AND METHODS: Results obtained from PGS lab internal data. Fragment sizes (FS) calculated using the UCSC Genome Browser and calculating the distance from the breakpoint of the translocation to the telomere and centromere. FS over 6 megabases (Mb) in size were considered "large"; those under 6Mb were considered “small.” Segregation patterns were classified as: alternate, adjacent I, adjacent II, 3:1, 4:0 and atypical configurations (AC). An AC is characterized as one that cannot be explained by the standard segregation patterns and involves the breakage of the chromosomes involved in the RT.

RESULTS: We review segregation patterns for 1,159 embryos (640 from female carriers, 519 from male carriers) for RT via array comparative genome hybridization (aCGH). Of the embryos, 58.2% involved RT where all FS were classified as large and 41.8% involved RT where one or more FS were classified as small. Embryos with one or more small FS were significantly more likely (p<0.001) to segregate in ACs than those with all large FS. When sorted by the gender of the parent with the RT, a significant increase in occurrence of 3:1 segregation was seen in female carriers (p<0.001); when divided by FS, female carriers of translocations with at least one small FS were more likely to have 3:1 configurations (p<0.001) (table 1).

CONCLUSIONS: Patients with RT presenting for PGD testing are anxious to know the likelihood of identifying an embryo suitable for transfer and often inquire about numbers specific to their RT. As the almost endless permutations of RT make such numbers difficult to generate, this data suggests trends that may provided additional information for these patients. Those with small FS are more likely to produce embryos with ACs. Further, female carriers of RT, particularly those with small FS, are more likely to produce embryos with 3:1 segregations, and thus, may be more likely to produce unbalanced embryos than male carriers. This data will help manage expectations of RT patients presenting for PGD.

Table 1

<table>
<thead>
<tr>
<th>Segregation Patterns</th>
<th>Small Fragments</th>
<th>Large Fragments</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Female Carrier</td>
<td>Male Carrier</td>
</tr>
<tr>
<td></td>
<td>(# of embryos)</td>
<td>(# of embryos)</td>
</tr>
<tr>
<td>Alternate</td>
<td>111</td>
<td>98</td>
</tr>
<tr>
<td>Adjacent I</td>
<td>76</td>
<td>57</td>
</tr>
<tr>
<td>Adjacent II</td>
<td>33</td>
<td>19</td>
</tr>
<tr>
<td>3:1</td>
<td>39</td>
<td>13</td>
</tr>
<tr>
<td>4:0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Atypical Configuration (AC)</td>
<td>23</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>283</td>
<td>202</td>
</tr>
<tr>
<td></td>
<td>317</td>
<td></td>
</tr>
</tbody>
</table>

Statistics
OBJECTIVE: To determine the incidence of triploidy found during preimplantation genetic screening (PGS) using single nucleotide polymorphism (SNP) microarrays with bioinformatics.

METHODS: This was a retrospective chart review. MATERIALS AND METHODS: All patients who submitted documents to NIH and were reviewed for compliance. RESULTS: Of the six C9orf72-Exp affected embryos, three were used for PGD and aneuploidy screening, elective single embryo transfer (eSET) with unaffected euploid embryos and donation of C9orf72-Exp embryos for ds-hESC derivation. PGD was designed with ALS/FTD at-risk couple informative short tandem repeat (STR) markers linked to the pathogenic C9orf72 allele. Blood samples from the couple and an affected grandparent were used to design primers for identification of the expansion haplotype in embryos. Following IVF, blastocyst biopsies were used for whole genome amplification (WGA) and PGD, perform IVF with C9orf72-Exp PGD to obtain offspring from unaffected embryos, derive C9orf72-Exp ds-hESCs and place ds-hESC line(s) on the National Institutes of Health (NIH) hESC registry making them available for Federally-funded research.

CONCLUSION: This study aimed to determine the frequency that patients tested for C9orf72-Exp had at least one euploid embryo available for a true choice of offspring sex. This data likely overestimates the true incidence, as patients without blastocysts available for biopsy were not included in the dataset. Patients, particularly those with increasing maternal age, should be counseled about the significant possibility of not having both male and female euploid embryos available for transfer (Table I).

OBJECTIVE: The hexanucleotide expansion at C9orf72 is the most common genetic alteration in Familial Amyotrophic Lateral Sclerosis (ALS)/Frontotemporal Dementia (FTD). Objectives were to design C9orf72-Exp PGD, perform IVF with C9orf72-Exp PGD to obtain offspring from unaffected embryos, derive C9orf72-Exp ds-hESCs and place ds-hESC line(s) on the National Institutes of Health (NIH) hESC registry making them available for Federally-funded research.

METHODS: A couple without infertility, with a family history of FTD caused by C9orf72-Exp, proactively requested IVF with PGD/aneuploidy screening, elective single embryo transfer (eSET) with unaffected euploid embryos and donation of C9orf72-Exp embryos for ds-hESC derivation. PGD was designed with ALS/FTD at-risk couple informative short tandem repeat (STR) markers linked to the pathogenic C9orf72 allele. Blood samples from the couple and an affected grandparent were used to design primers for identification of the expansion haplotype in embryos. Following IVF, blastocyst biopsies were used for whole genome amplification, PGD, 24-chromosome microarray and blastocysts vitrified. A warmed euploid unaffected blastocyst was used for eSET. Inner cell masses of affected blastocysts were cultured on human foreskin fibroblast in xeno-free DMEM + glutamine, alpha-MEM, and DMEM/F12 media. Embryonic tissues were cultured on Matrigel-coated plates in DMEM/F12 supplemented with 30% fetal bovine serum. After 48 hours, embryos were transferred to 3D culture conditions for drug screening. Results: The two unaffected and one affected euploid embryos successfully used to establish a ds-hESC line with normal karyotype and retention of endoderm, mesoderm, and ectoderm. Embryo donation and ds-hESC derivation documents were submitted to NIH and reviewed for compliance.

RESULTS: Among patients undergoing IVF with PGS for sex selection, there is a high incidence of not having both male and female euploid embryos available for a true choice of offspring sex. This data likely overestimates the true incidence, as patients without blastocysts available for biopsy were not included in the dataset. Patients, particularly those with increasing maternal age, should be counseled about the significant possibility of not having both male and female euploid embryos available for transfer (Table I).

RESULTS: The included population consisted of 321 IVF-PGS cycles for which sex selection was an indication. By age 40, less than a third of couples undergoing IVF with PGS for sex selection had at least one euploid embryo of each sex available for transfer (Table I).

<table>
<thead>
<tr>
<th>Age</th>
<th>Patients with ≥1 euploid embryo of each sex</th>
<th>Patients with ≥1 euploid embryo</th>
<th>Mean no. of blastocysts</th>
</tr>
</thead>
<tbody>
<tr>
<td>26-27</td>
<td>58%</td>
<td>100%</td>
<td>6.3</td>
</tr>
<tr>
<td>28-29</td>
<td>95%</td>
<td>100%</td>
<td>7.8</td>
</tr>
<tr>
<td>30-31</td>
<td>65%</td>
<td>94%</td>
<td>6.6</td>
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<tr>
<td>32-33</td>
<td>64%</td>
<td>94%</td>
<td>6.3</td>
</tr>
<tr>
<td>34-35</td>
<td>54%</td>
<td>81%</td>
<td>5.5</td>
</tr>
<tr>
<td>36-37</td>
<td>54%</td>
<td>89%</td>
<td>5.3</td>
</tr>
<tr>
<td>38-39</td>
<td>42%</td>
<td>83%</td>
<td>4.7</td>
</tr>
<tr>
<td>40-41</td>
<td>25%</td>
<td>91%</td>
<td>4.1</td>
</tr>
<tr>
<td>41-42</td>
<td>11%</td>
<td>61%</td>
<td>4.4</td>
</tr>
</tbody>
</table>
CONCLUSIONS: This report details a collaborative pathway providing couples an opportunity to: i) build a family without continuation of a monogenic familial disease; ii) donate otherwise discarded embryos for derivation of ds-hESCs; and thus iii) establish a universally-shared resource to study molecular causes and consequences of familial monogenic diseases and discover future treatments and/or cures of diseases that affect them.

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OBJECTIVE: Full autosomal monosomy embryos are lethal, so they don’t implant or result in early pregnancy loss. In cases where no euploid embryos are available, the transfer of monosomic embryos might be considered. The objective of this study was to report the results in which only monosomic embryos were transferred.

DESIGN: Retrospective analysis of 13 frozen embryo transfers (FET) between January 2013 to April 2016 in which only full monosomic embryos were transferred.

MATERIALS AND METHODS: Multiple trophectoderm cells were biopsied on day 5/6 blastocysts and sent for preimplantation genetic screening (PGS) by array-comparative genomic hybridization (aCGH). Embryos were vitrified and used for subsequent FET. If no, or inadequate number of euploid embryos were present, the patient was offered the transfer of selected monosomic embryo(s) for FET. Patients were counseled of risk and signed an informed consent.

RESULTS: From January 2013 to April 2016, 1076 FET-PGS cycles were performed. The transfer of monosomic embryos was made available for 13 women whom IVF had resulted in no euploid embryos. The clinical outcomes are reported in the table I.

<table>
<thead>
<tr>
<th>Patient n°</th>
<th>Karyotype of transferred embryos</th>
<th>Clinical outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>45, XX, -4</td>
<td>Baby healthy at birth</td>
</tr>
<tr>
<td>2</td>
<td>45, XX, -22</td>
<td>No pregnancy</td>
</tr>
<tr>
<td>3</td>
<td>45, XX, -1</td>
<td>No pregnancy</td>
</tr>
<tr>
<td>4</td>
<td>45, XX, -45, XX, -21</td>
<td>No pregnancy</td>
</tr>
<tr>
<td>5</td>
<td>45, XX, -5</td>
<td>No pregnancy</td>
</tr>
<tr>
<td>6</td>
<td>45, XX, -5</td>
<td>No pregnancy</td>
</tr>
<tr>
<td>7</td>
<td>45, XX, -21; 45, XY, -22</td>
<td>No pregnancy</td>
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<tr>
<td>8</td>
<td>45, XX, -5</td>
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<tr>
<td>9</td>
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<tr>
<td>12</td>
<td>45, XX, -15</td>
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<tr>
<td>13</td>
<td>45, XX, -19</td>
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</tbody>
</table>

CONCLUSIONS: A concern of PGS is ‘false positive’ embryos being discarded or ‘false negative’ embryos transferred. In our study an embryo that was diagnosed as full monosomy 4 was transferred resulting in a healthy live birth. A possible explanation for the misdiagnosis may be mosaicism, where different genetic cell lines are segregated in the trophectoderm of the embryo, while the inner cell mass contained only euploid cells. Sampling errors during biopsy and the lack of sensitivity necessary to detect minor cell populations makes mosaicism difficult to detect for aCGH, resulting in misdiagnosis. aCGH in PGS is still not fully definitive in the diagnosis of aneuploidy. The patient must be appropriately counseled of risk, requirement of prenatal screening and possibility of termination of pregnancy before the transfer of full autosomal monosomic embryos.

References:

P-146 Tuesday, October 18, 2016

DIAGNOSTIC AND CLINICAL OUTCOMES OF 694 CYCLES USING KARYOMAPPING FOR PREIMPLANTATION GENETIC DIAGNOSIS (PGD) OF SINGLE GENE DISORDERS. D. Goldberg-Strassler,a R. Cabey,a A. Jordan,a R. Prates,b E. Mounts,c e. barbieri,c A. Hershlag,c M. Guarnaccia,c S. Murre,d S. Munne,e Reprogenetics, Livingston, NJ; bMolecular, Reprogenetics, Livingston, FL; cOREP Reproductive Medicine, Portland, OR; dHofstra Northwell School of Medicine, Manhasset, NY; eREI, Columbia University, NY, NY; fSouthern California Reproductive Center, Beverly Hills, CA.

OBJECTIVE: Karyomapping (Kmap) is a linkage-based single nucleotide polymorphism technology proven to be highly efficient in PGD diagnosis and applicable to most single gene disorders (SGD). Here, outcomes of such testing are reviewed.

DESIGN: Kmap with and without comprehensive chromosome screening (CCS) via array comparative genomic hybridization (aCGH) (24sure, Illumina) or next generation sequencing (NGS) (VeriSeq, Illumina) was used to screen embryos (blastocysts) undergoing PGD for SGDs.

MATERIALS AND METHODS: Between 1/2014-4/2016, PGD was performed on 694 cycles (4284 blastocyst biopsies) with subsequent cryopreservation. Each sample was whole genome amplified and analyzed using Kmap (Illumina, USA). Additionally, 96.1% (609/694) of cases had CCS. Follow-up data was obtained for 478 cycles with embryos suitable for transfer (free from SGD and euploid if CCS performed). At the time of data collection, 223 cycles had undergone embryo transfer.

RESULTS: The 694 Kmap cycles comprised 105 SGDs, human leukocyte antigen (HLA) matching, and microdeletions/duplications. Diagnostic results were available from 97% (4154/4284) of samples. Implantation rate was 75.9% (151/199) for PGD+CCS (average maternal age (MA): 32.9 years) and 64% (16/25) for PGD only (average MA: 34.3 years). The pregnancy rate per transfer was 74.7% (124/166) for PGD+CCS and 78.9% (15/19) for PGD only. Single embryo transfer was performed for most; 20 had double embryo transfer. The average number of embryos suitable for transfer per cycle was 1.95 (PGD+CCS) and 2.56 (PGD only). A total of 30 live births and 96 ongoing pregnancies were reported. Confirmatory testing via chorionic villus sampling (CVS) or amniocentesis was performed for 6 pregnancies. Follow-up testing via newborn screening panel for 9 live births was in concordance with Kmap diagnosis. Results were in complete concordance with Kmap diagnosis; no misdiagnoses have been reported to date from the 121 cycles with successful pregnancy outcomes.

CONCLUSIONS: With the increase in patient awareness regarding availability of PGD and the rise of preconception carrier screening, there is a growing demand for PGD. Higher implantation rates were observed for patients who underwent CCS in combination with Kmap. Pregnancy rates were similar as sample size for “PGD only” was smaller and 62.5% of “PGD only” patients had a double embryo transfer. Due to the high diagnostic accuracy, comprehensive analysis and short preparation time, Kmap is a successful treatment strategy for patients requesting PGD for inherited disorders.

P-147 Tuesday, October 18, 2016

VALIDATION OF DETECTING MONOGENIC DISEASES & ANEUPLOIDY SIMULTANEOUSLY BY NEXT GENERATION SEQUENCING WITH LINKAGE ANALYSIS. S. Lu,a J. Qiao,a X. Xie,c aYikon Genomics Co., Ltd., Shanghai, China; bDepartment of Obstetrics and Gynecology, Third Hospital, Peking University, Beijing, China; cHarvard University, Cambridge, MA.

OBJECTIVE: Here we report three supportive cases by screening embryos with our well-established and published method, named “mutated allele revealed by sequencing with aneuploidy and linkage analyses” (MARSALA), which combines multiple annealing and loop based amplification cycles (MALBACTM) and Next Generation Sequencing with linkage analysis. The MARSALA strategy is able to detect aneuploidy and targeted gene mutations simultaneously in preimplantation genetic diagnosis (PGD) process during an in vitro fertilization (IVF) cycle.

DESIGN: We sequence the genome of the parents and relatives carrying the monogenic disease allele with the depth of 2x genome coverage. Then, from the sequencing results of each embryo, the SNP readouts (heterozygous or homozygous) adjacent to the disease-cause mutation sites allowed the identification of the disease-carrying allele in the embryos.

MATERIALS AND METHODS: Blastocyst Biopsy We collected a few TE cells from each hatching blastocyst on day 5 or day 6. All embryos
were obtained from patients who chose to be subjected to an IVF procedure and voluntarily gave their consent for providing the samples for this study. Single cell whole genome amplification (WGA) with MALBAC. The WGA process was performed with the standard protocol provided by the commercial kit, MALBAC<sup>SM</sup> Single Cell WGA Kit (Cat. #: YK001A/B, Yikon Genomics). For blood samples, we extracted the gDNA by using the QIAamp DNA Blood Mini Kit (QIAGEN) and amplified 1 ng gDNA using the MALBAC<sup>SM</sup> Single Cell WGA Kit (Cat. #: YK001A/B, Yikon Genomics). MARSALA method: Eight nano-grans of MALBAC products were used as the template for PCR reactions targeting disease-cause mutation sites. The PCR products were then added into the corresponding MALBAC products at 1-5%. The mixture was used to construct a sequencing library using the NEBNext Ultra DNA library Prep kit (New England Biolabs). The sequencing was done on the Illumina HiSeq 2500 platform with a low depth of 0.1x genome coverage. Following this procedure, targeted point mutations and aneuploidy can be detected simultaneously.

RESULTS: 1. MARSALA analyses of blastocyst sequencing for case 1 in which both the husband and wife were carrying SLC26A4 mutations that cause autosomal recessive deaf. 2. MARSALA analyses of blastocyst sequencing for case 2 in wife was affected by a PKD1 mutation that causes autosomal dominant polycystic kidney. 3. MARSALA analyses of blastocyst sequencing for case 3 in wife was affected by the X chromosomal gene F8 that cause hemophilia A.

CONCLUSIONS: We demonstrated that our streamlined MASALA method can simultaneously screen aneuploidy and monogenic diseases, accurately and cost-efficiently, combining the MALBAC<sup>SM</sup> technology and NGS platform.

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**P-148 Tuesday, October 18, 2016**

CLINICAL EXPERIENCE WITH A TARGETED NGS-BASED PRE-IMPLANTATION GENETIC SCREENING ASSAY. N. Faulkner, L. Walters-Sen, D. Neitzel, B. Breton, S. Hallam. Good Start Genetics, Cambridge, MA.

OBJECTIVE: To report our clinical experience karyotyping trophectoderm biopsies using a targeted next-generation DNA sequencing (NGS) assay.

DESIGN: Chromosome aneuploidy, often associated with increased maternal age, represents one of the most common reasons for the failure of assisted reproductive technologies (ART) such as in vitro fertilization (IVF) as the majority of aneuploid embryos either fail to implant or miscarry. Preimplantation genetic screening (PGS) offers a means to identify euploid embryos prior to implantation with the goal of increasing pregnancy and live birth rates. We have modified the FAST-Seq<sup>s</sup> method, which amplifies >10,000 repetitive LINE1 elements across the genome, in order to determine the molecular karyotype of trophectoderm biopsies from blastocyst-stage embryos.

MATERIALS AND METHODS: Good Start Genetics, Inc. (GSG) launched an NGS-based PGS assay, EmbryVu, in September 2015. Trophectoderm biopsies containing 5-10 cells from blastocyst-stage embryos from infertility patients scheduled for frozen embryo transfer were submitted for analysis. All samples, including biopsy wash-buffer negative controls, were analyzed using the EmbryVu assay and associated bioinformatics pipeline. We analyzed our EmbryVu data to date, including patient age, clinical indication, and NGS results.

RESULTS: To date we have analyzed a total of 4625 embryos from 1007 patients. The age of female patients seeking PGS testing (including egg donors if used) ranged from 21 to 46. The largest age group, which made up approximately 21% of our dataset, was women ages 31-34. In the total population of biopsies, slightly less than half were aneuploid. As expected, the rate of aneuploidy varied between age groups, with a low of 31% in women ages 21-25 and a high of 89% in women ages 43-46. These results are highly concordant with published aneuploidy rates (Franasiak JM, et al. 2014). The majority of aneuploid embryos had a single abnormality; however, a small number of embryos had five or more abnormalities or were chaotic in nature. The most common abnormalities were trisomy 16, monosomy 22, monosomy 16 and monosomy 21.

CONCLUSIONS: EmbryVu is a rapid, accurate, and cost-effective method for determining the euploid status of embryos scheduled for frozen transfer. The ability to determine embryos with the greatest chance of implantation and subsequent live birth is vital to improve IVF success rates. PGS has traditionally been reserved for patients with specific clinical indications (i.e. advanced maternal age) and has been cost-prohibitive to many. We believe advances in our accurate, lower cost NGS technology, coupled with mounting evidence that PGS increases positive outcomes, are making it possible for PGS to be offered to all IVF patients.

References:

Supported by: This study was funded by Good Start Genetics, Inc.

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**P-149 Tuesday, October 18, 2016**

**SUB-OPTIMAL OVARIAN RESPONDERS HAVE AN INCREASED EMBRYO ANEUPLOIDY RATE.** B. LLEDÓ, J. A. ORTIZ, R. MORALES, E. GARCIA-HERNANDEZ, T. Jen, R. LLACER, R. Bernabeu. *Instituto Bernabeu BIOTECH, ALICANTE, Spain; Instituto Bernabeu, Alicante, Spain.

OBJECTIVE: To investigate if women with sub-optimal ovarian response have an increased rate of embryo chromosomal alterations when compared to women who present normal response.

DESIGN: We performed a retrospective observational study (from January 2013 to December 2015). We analysed 624 blastocyst from 197 comprehensive chromosome screening (CCS) cycles. Couples undergoing CCS cycles were subdivided into two groups: Sub-optimal Responder group (n=32), patients who obtained less than 8 MII and Normoresponder group (n=165), patients who produced =>8 MII. The groups were compared regarding the cycle outcome and the embryo aneuploidy rate.

MATERIALS AND METHODS: PGS was performed to couples who attended with a clinical history of repetitive miscarriage, recurrent implantation failure, severe male factor or advanced maternal age. For PGSv2.0, trophoectoderm genome was amplified and aCGH performed using Agilent® SurePrintG3 8x60K. The association between variables was evaluated by logistic regression for aneuploidy rate, by t-student for maternal age and chi-square for cycle outcome (SPSSv20.0).

RESULTS: Results from CCS were obtained in 97.3% of the biopsied embryos (607/624). Overall, the embryo aneuploidy rate was 40.6%. A total of 71 embryos were biopsied in the sub-optimal group and 553 in the normal responders group. The initial analysis was to determine the prevalence of aneuploidy embryos according to sub-optimal or normal ovarian response. A significant difference between groups was reported for maternal age (36.6y vs 30.4y, p<0.01). The logistic regression analysis including maternal age as a confounding factor showed an influence of ovarian response on the incidence of embryo aneuploidy rate (60.6% vs 37.8%, p<0.05). Suboptimal response was determinant of the likelihood of higher embryo rate (OR: 1.77, CI: 1.03-3.02). According to the cycle outcome no significant differences were reported for pregnancy rate (47.1% vs 58.6%, p=0.362) and implantation rate (33.3% vs 43.4%, p=0.450).

CONCLUSIONS: Recently, a new ovarian response group was defined: the sub-optimal ovarian responders. To the best of our knowledge nothing is known about the embryo aneuploidy rate of these patients and their cycle’s outcomes using CCS. Our data suggest that patients with sub-optimal ovarian response are at two-fold higher risk of producing chromosomally abnormal embryos as compared with normal responders. Once we selected the euploid embryo the pregnancy rate was similar between both groups, showing the beneficial effect of CCS. Sub-optimal responders have been suggested to produce poor quality oocytes because they are close to the last oocytes available from the ovarian pool and are at increased risk for chromosomal abnormalities. Application of CCS to increase the IVF results mainly in patients at risk for chromosomally abnormal embryos is a promising tool.

Supported by: Conflicts of interest and source of funding none declared.

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**P-150 Tuesday, October 18, 2016**


OBJECTIVE: The ratio of male to female babies conceived from IVF has been reported to be biased towards males, particularly following extended culture and blastocyst transfer. This study investigates if such differences in gender ratio exist in euploid blastocysts obtained and b) if there is a gender difference in live births achieved following frozen embryo transfer (FET) of blastocysts of known gender.

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OBJECTIVE: hr-NGS detects mosaicism in about 20% of trophectoderm biopsies while aCGH in about 4%. Mosaic embryos are at a higher risk of miscarriage, have lower implantation potential; however some may result in a live birth. The objective of this study is to determine if the rate of miscarriage is reduced in PGS cycles by transferring non-mosaic embryos selected by NGS compared to cycles performed by aCGH.

DESIGN: Analysis of PGS procedures involving blastocyst biopsy and aCGH or hr-NGS in 4 different fertility clinics.

MATERIALS AND METHODS: All PGS procedures were performed by the same reference laboratory but biopsies were performed by 4 different fertility centers. Pregnancy follow up was obtained from 96 and 444 clinical pregnancies (+ sac) after transfer of euploid embryos by NGS and aCGH, respectively. Average maternal ages were comparable at 36 and 38, respectively. Pregnancy loss was scored as complete loss of pregnancy, while twin pregnancies with one fetus ongoing were counted as ongoing.

RESULTS: Overall miscarriage rates were 6% (5/81) for NGS and 13% (54/429) for aCGH. The PGM sequencing provided over 3.6 million reads with a median sequencing fragment length of 176 bp. Proportions were compared using Chi-square and Fisher’s exact tests. A p-value < 0.05 was considered statistically significant.

RESULTS: Day 5 versus day 6 embryo biopsy demonstrated no significant difference in the prevalence of aneuploidy (55% and 60% respectively). This trend was also present when analyzed by separate age categories.

CONCLUSIONS: The incidence of aneuploidy is no different between day 5 and day 6 blastocysts. This suggests that the biopsy of day 6 embryos could increase the number of potentially transferable embryos for patients undergoing IVF and PGS.

Day 5 and 6 Biopsy and PGS

<table>
<thead>
<tr>
<th>Day 5</th>
<th>35-37</th>
<th>38-40</th>
<th>41-42</th>
<th>43-44</th>
</tr>
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<tbody>
<tr>
<td>Euploid</td>
<td>53.1%</td>
<td>46.8%</td>
<td>35.6%</td>
<td>38%</td>
</tr>
<tr>
<td>Aneuploid</td>
<td>46.9%</td>
<td>53.2%</td>
<td>64.4%</td>
<td>62%</td>
</tr>
<tr>
<td>Day 6</td>
<td>35-37</td>
<td>38-40</td>
<td>41-42</td>
<td>43-44</td>
</tr>
<tr>
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<td>43.4%</td>
<td>38%</td>
<td>41.9%</td>
<td>38.9%</td>
</tr>
<tr>
<td>Aneuploid</td>
<td>56.6%</td>
<td>62%</td>
<td>58.1%</td>
<td>61.1%</td>
</tr>
</tbody>
</table>

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PLOIDY OUTCOMES FOR DAYS 5 AND 6 BLASTOCYSTS ANALYZED BY NEXT GENERATION SEQUENCING FOR PREIMPLANTATION GENETIC SCREENING. K. J. Tobler, N. Massahi, R. Kaufman, P. R. Brezina, A. K. Dubey, W. G. Kearns. Obstetrics and Gynecology, Womack Army Medical Center, Fayetteville, NC; Adavagenix, Rockville, MD; Fort Worth Fertility, Fort Worth, TX; Reproductive Endocrinology and Infertility, Vanderbilt University School of Medicine, Memphis, TN; North Carolina IVF Labs, Fayetteville, NC.

OBJECTIVE: To compare the ploidy status of embryos that undergo biopsy on day 5 versus day 6 and to determine whether a day six blastocyst biopsy is worth incorporating in an IVF program.

DESIGN: Retrospective.

MATERIALS AND METHODS: This study included 2,943 embryos that underwent trophectoderm (TE) biopsy either on day 5 (2627) or day 6 (286). TE cells were lysed and the DNA was amplified by a modified whole genome amplification protocol. DNA libraries were prepared, followed by emulsion PCR. DNA sequencing was completed by the Personal Genome Machine (PGM) and data was analyzed and interpreted using an Ion Reporter Server. The PGM sequencing provided over 3.6 million reads with a median sequencing fragment length of 176 bp. Proportions were compared using Chi-square and Fisher’s exact tests. A p-value < 0.05 was considered statistically significant.

RESULTS: Day 5 versus day 6 embryo biopsy demonstrated no significant difference in the prevalence of aneuploidy (55% and 60% respectively). This trend was also present when analyzed by separate age categories.

CONCLUSIONS: The incidence of aneuploidy is no different between day 5 and day 6 blastocysts. This suggests that the biopsy of day 6 embryos could increase the number of potentially transferable embryos for patients undergoing IVF and PGS.

<table>
<thead>
<tr>
<th>Center</th>
<th>NGS total Preg loss cases</th>
<th>NGS-%</th>
<th>aCGH total Preg loss cases</th>
<th>aCGH-%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>8</td>
<td>1%</td>
<td>36</td>
<td>11%</td>
</tr>
<tr>
<td>2</td>
<td>21</td>
<td>2%</td>
<td>108</td>
<td>12%</td>
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<td>3</td>
<td>14</td>
<td>1%</td>
<td>125</td>
<td>15%</td>
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<td>4</td>
<td>38</td>
<td>1%</td>
<td>70</td>
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</tr>
<tr>
<td>total</td>
<td>81</td>
<td>5%</td>
<td>429</td>
<td>13%</td>
</tr>
</tbody>
</table>

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CHROMOSOMAL CONSTITUTION AND MORPHOKINETICS OF ARRESTED AND NON-VIABLE EMBRYOS. K. Sorby, E. Dimitriadis, T. Osianlis, Hudson Institute of Medical Research, Clayton, Australia; Monash University, Clayton, Australia; Ritchie Centre, Monash University, Melbourne, Australia.

OBJECTIVE: To determine the chromosomal constitution of embryos failing to develop to a clinically viable blastocyst following extended culture in vitro and whether the morphokinetic behaviour of such embryos relates to their chromosomal content.

DESIGN: Prospective analysis of morphokinetic and chromosomal data for non-viable embryos following independent determination of their unsuitability for clinical use.

MATERIALS AND METHODS: Embryos were cultured in an Embryoscope time lapse incubator. After six days in culture embryos not suitable for transfer or freezing, due to cleavage arrest, multinucleation, failure to cavitate, cellular degeneration or failure to form a blastocyst of sufficient quality for clinical use, were subjected to whole genome amplification and Next Generation Sequencing.
RESULTS: Interpretable results were obtained from 136 embryos. Embryos deemed unsuitable for clinical use displayed an aneuploidy rate of 95.6%, with only 6 embryos demonstrating an apparently euploid chromosomal complement. Of these 6 embryos, 3 were excluded from use due to abnormal inner cell mass and 3 due to inadequate trophectoderm formation and/or cellular degeneration. Of note, every embryo returning a euploid result underwent cavitation, leaving a 100% aneuploidy rate for embryos that failed to reach the blastocyst stage. When comparing embryos that did or did not attempt to cavitate (excluding triploid embryos), embryos failing to reach this stage contained on average twice the number of chromosomal errors (4.52 vs 2.25; p<0.0001). Unlike previously reported data utilising clinically viable blastocysts, these embryos exhibited a majority of monosomies over trisomies (65.8% vs 34.2%), likely reflecting the poorer developmental potential of monosomic embryos. Of interest, although triploid embryos are seen at the blastocyst stage, of the 7 triplloid embryos identified in this cohort, 6 arrested at either one cell (3 embryos) or following their first cleavage division. The remaining triploid embryo reached cavitation but was of extremely poor quality. This suggests the rate of triploidy in early embryos may be significantly higher than that seen in clinical blastocyst samples. In addition to their standard aneuploidies, 15 embryos contained a segmental aneuploidy, however, in only one embryo was a segmental aneuploidy its only chromosomal error. Similarly, 29 embryos contained additional mosaic aneuploidies, below 50% increase or reduction but distinctly identifiable as a gain or loss.

CONCLUSIONS: Embryos failing to reach the blastocyst stage in our culture system displayed universal aneuploidy, a significant finding when counselling our patients. The specific chromosomal errors in non-viable embryos do appear to impact their morphokinetic parameters, however, further work is required to elucidate these potential relationships.

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INTRACYTOPLASMIC MORPHOLOGICALLY SELECTED SPERM INJECTION (IMSI) DOES NOT IMPROVE CLINICAL OUTCOMES AND EMBRYO PLOIDY IN ASSISTED REPRODUCTIVE CYCLES. L. Keskiinne,1 Z. Beyhan,2 M. Dayal,3 J. Hart,4 M. Keskiinne,5 1SIRM/Integrated Management, Las Vegas, NV; 2SIRM, Las Vegas, NV; 3SIRM, Creve Coeur, MO.

OBJECTIVE: It has been suggested that injection of morphologically normal spermatozoa could improve implantation and pregnancy outcomes by promoting better embryo viability, quality and euploidy during IVF-ICSI cycles (1). The intracytoplasmic morphologically selected sperm injection (IMSI) procedure utilizes differential interference contrast microscopy at high magnification (x6000) to select sperm cells without major abnormalities before ICSI (2). Clinical efficacy of the IMSI however, has been controversial and questioned vigorously (3). The objective of the current study is to compare the ploidy status of embryos and the clinical outcomes of PGS cycles randomly assigned to either IMSI or conventional ICSI.

DESIGN: Retrospective study in a private in vitro fertilization laboratory.

MATERIALS AND METHODS: A total of 169 patients were included in this retrospective study, and had undergone PGD/PGS performed as blastomere biopsy for array CGH. The mean ages of the ICSI (Group 1) and IMSI (Group 2) groups were 35.2 ± 4.8 years and 35.4 ± 4.3 years, respectively. Indications for PGS were as follows: advanced maternal age (n=29). Male factor (n=12), immunologic infertility (n=27); decreased ovarian reserve (n=32), unexplained (n=37), or multiple factors (n=32).

RESULTS: In group 1, 87 patients had 728 day 3 embryos biopsied, and 33% (240/728) was euploid, 64% (466/728) was aneuploid 3% (19/728) inconclusive. Only 32% of those biopsied embryos on day 3 was developed to blastocyst. In group 2, 82 patients had 723 day 3 embryos biopsied, and 32% (231/723) was euploid, 66% (473/723) was aneuploid 3% (19/723) inconclusive. Only 33% of those biopsied embryos on day 3 was developed to blastocyst. In group 2, 55 patients had at least one normal blastocyst to transfer on day 5 of the fresh cycle. The PR and IR were 49% (27/55) and 39% (30/77). In group 2, 50 patients (61%) had embryo transfer with at least 1 euploid blastocyst embryos. The PR and IR were 50% (25/50) and 43% (32/75).

CONCLUSIONS: Our data suggest that ploidy status of embryos derived by IMSI or ICSI are similar and clinical outcomes of those methods are comparable.

References:

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DAY 5, 6, AND 7 BLASTOCYST PLOIDY STATUS STRATIFIED BY PATIENT AGE. J. Nguyen,1 R. A. Fields,2 A. Picou,2 K. Silverberg,3 M. VerMilyea,4 Ovation Fertility, Austin, TX; 2Fairfax EggBank, Austin, TX; 3Embryology, Ovation Fertility, Austin, TX; 4Texas Fertility Center, Austin, TX.

OBJECTIVE: To determine if a relationship of ploidy status in day 5, 6, and 7 blastocysts exists amongst patient age groups.

DESIGN: Retrospective study within a private in vitro fertilization laboratory.

MATERIALS AND METHODS: Blastocysts underwent trophectoderm biopsy and subsequent comprehensive chromosomal screening over the course of 3 years. PGS results were retrospectively compared to the day of blastocyst morphology and stratified by patient age. Oocytes were fertilized using ICSI and embryos were group cultured to the blastocyst stage for up to 7 days using Continuous Single Culture Medium (Irvine Scientific). On Day 3, all multi-cell embryos were artificially hatched by laser ablation of the zona pellucida. Blastocyst morphology was dependent upon good quality hatching of blastocysts on either Day 5, 6 or 7 that showed a well-defined inner cell mass and trophectoderm. Biopsied blastocysts were subsequently vitrified for potential future use in a warmed embryo transfer cycle, dependent on a euploid result. Biopsied samples were analyzed by array comparative genomic hybridization (aCGH) or next generation sequencing (NGS) technology by a reference laboratory.

RESULTS: 1,915 embryos were biopsied yielding an overall euploid rate of 45% (862). Of the Day 5, 6 and 7 blastocysts, 46% (485), 46% (328) and 35% (49) were determined to be euploid respectively based on the day of biopsy. Chi-square analysis revealed that euploid status is dependent upon day of biopsy (p<0.0001). When stratified by age, a significant difference (p<0.05) in euploid rate exists between D5 & D6 and D5 & D7 blastocysts, with no significance between D6 & D7 blastocysts in patients <34 years old. Blastocysts from patients 35-37 revealed a significant difference (p<0.05) in D5 & D7 and D6 & D7 embryos but no difference between D5 & D6. No significant difference in euploid rate between day of biopsy was shown to exist in the 38-40, 41-42 and 43+ age groups.

CONCLUSIONS: Aneuploidy is a very common abnormality in human embryos, particularly for those women with advanced maternal age (Franasiak, 2014). Up to 61% of all embryos can be aneuploid in women who are 38-47 years old, although younger women (<35) with good prognosis also have a high rate of aneuploidy (Alfarawati, 2011; Munne, 2006). A recent report also indicates that D6 embryos have the highest euploid rate with D5 and D7 embryos contributing equally to overall ploidy status of an embryo cohort (Vaccari, 2014). Our data suggests that patients <34 have a higher rate of euploid embryos on D5 compared to D6 or D7. Day 7 embryos from patients 35-37 have the highest rate of aneuploidy. Interestingly, day of biopsy does not appear to make a significant difference in the ploidy rate of embryos from patients who are older than 38. Further investigation into the implantation and live birth rates amongst different age groups resulting from the transfer of a euploid embryo(s) biopsied on different days is currently ongoing.

References:

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BLASTOCYST MORPHOLOGY IS A POOR INDICATOR OF EUPLID STATUS. A. Picou, A. Hellmers, S. Silverberg, M. VerMilyea, Embryology, Ovation Fertility, Austin, TX; Ovation Fertility, Austin, TX; Texas Fertility Center, Austin, TX.

OBJECTIVE: To evaluate the importance of blastocyst morphology in known euploid blastocysts.

DESIGN: Retrospective study in a private assisted reproductive technology program.

MATERIALS AND METHODS: The euploid status of blastocysts considered to be of marginal morphology was compared to that of good morphology blastocysts following trophectoderm biopsy and preimplantation genetic screening (PGS). Over a period of 9 months, 683 blastocysts of marginal and good quality were selected for trophectoderm biopsy and aneuploidy screening. All embryos were cultured in Continuous Single Culture Media (Irvine Scientific) to the blastocyst stage. On Day 3 of embryo development, multi-cell embryos were artificially hatched by laser ablation of the zona pel lucida. Hatching blastocysts with a differentiated inner cell mass and trophectoderm were biopsied on either Day 5, 6 or 7 of culture. Biopsied embryos were categorized by morphology grade. The embryo grading scheme used in our laboratory is an adaption of the Gardner Grading Scale where AA is best quality and ED is poor quality. Blastocysts that had a grade of CC or better (ie. C or better for both the inner cell mass and trophectoderm) were placed in the good morphology group (Group 1), whereas marginal quality blastocysts (Group 2) were graded as CD, EC, or ED. Biopsied samples were analyzed by comprehensive chromosomal screening (CCS) involving the use of array comparative genomic hybridization (aCGH) or next generation sequencing (NGS) technology by a reference laboratory. Biopsies which resulted in no signal were excluded from the study. All age groups were included.

RESULTS: Of the 683 embryos, 554 were categorized into Group 1, while 129 were categorized into Group 2. Group 1 embryos had a normal ploidy rate of 44% compared to 34% for Group 2 blastocysts. Statistical analysis by Chi-Square demonstrated no statistical difference ($p > .05$) between the euploid rate of Group 1 and Group 2 embryos.

CONCLUSIONS: Recent studies have suggested that all poor morphology and slower growing blastocysts should be biopsied to determine euploid status and therefore implantation potential (Capalbo, 2014). Our results indicate that marginal quality blastocysts are capable of being euploid at a comparable rate to good quality embryos and should therefore be considered for trophectoderm biopsy and PGS. Further evaluation of the implantation potential of euploid marginal and good quality blastocysts is currently ongoing. Determination of implantation rates of marginal quality euploid blastocysts will take time, as typically the best morphological grade blastocysts are prioritized for transfer. Regardless, these findings suggest that the morphologic criteria used by most IVF laboratories in determining biopsy suitability for blastocysts may need to be reassessed in order to afford patients an optimal opportunity for pregnancy per IVF retrieval.

References:

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LIVE BIRTHS AFTER TRANSFER OF REBIOPIST AND REVITRIFI-


OBJECTIVE: Report of successful clinical outcomes and live births following transfer of re-biopsied and re-analyzed blastocysts that had yielded no diagnosis from the initial biopsy and array comparative genomic hybridization (aCGH) procedure.

DESIGN: Retrospective cohort analysis.

MATERIALS AND METHODS: Trophectoderm (TE) biopsy and aCGH for aneuploidy screening was performed on blastocysts generated from 1035 patients between January 2011 to 2014 at an academic based institute. All blastocysts were vitrified immediately following TE biopsy pending aCGH analysis. Forty-six patients lower miscarriage rates than those who had at least one blastocyst that did not result in aCGH diagnosis opted to undergo warming, re-biopsy and re-vitrification of “no diagnosis” blastocyst in an effort to obtain a diagnosis second time around. Blastocysts resulting in a euploid diagnosis following the re-biopsy procedure were transferred in subsequent frozen embryo transfer (FET) cycles. The main outcome measures were euploidy, implantation and live birth rates.

RESULTS: Overall, 5060 blastocysts were analyzed from 1035 preimplantation genetic screening (PGS) cycles, 155 (3%) of all biopsied blastocyst had “no diagnosis”. Of these 155 blastocysts without diagnosis, 88 blastocysts were warmed, 82(93%) survived and underwent re-biopsy for re-analysis. Twenty-one re-biopsied blastocysts from a total 17 individual patients were diagnosed as euploid (26%) and were suitable for subsequent FET. Seven patients have already undergone a subsequent FET of a re-biopsied single euploid blastocyst. The survival rate for blastocysts undergoing second warming was 100% (7/7) resulting in an implantation rate of 57% (4/7) and birth of three normal healthy babies (male) to date.

CONCLUSIONS: A small percentage of TE samples fail to yield a diagnosis following PGS analysis. Our observations show that blastocysts that have undergone PGS with no diagnosis after biopsy can be safely re-biopsied, implanted and result in live birth despite repeated vitrification, biopsy and warming procedures. This particularly relevant in cases where no other euploid blastocyst are available for transfer.

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THE EFFECT OF EMBRYO SELECTION BY PREIMPLANTATION


OBJECTIVE: The aim of this retrospective analysis is to compare the conventional morphology-based embryo selection (MBS) method to the use of PGD-A in case of patients with advanced maternal age.

DESIGN: Retrospective data analysis.

MATERIALS AND METHODS: Data were collected between January of 2013 and February of 2016 at our clinic. All autologous cycles were included with advanced maternal age (AMA; 37-42 years of age) and fresh embryo transfer. Patients with known chromosome rearrangement were excluded. In PGD-A group all transferred embryo(s) were known euploid, while in MBS group transferred embryos had an unidentified chromosome profile. Oocytes were fertilized using ICSI or IVF in the MBS group while in PGD-A group only ICSI was used. In case of PGD-A group blastomere biopsies were carried out and the samples were analyzed with 24sure BAC microarrays (Illumina). All embryo transfers were carried out at day 5. Chemical, clinical, ongoing pregnancy and miscarriage rates were recorded. Ongoing pregnancy was noted if pregnancy had completed at least 12 weeks of gestation. Miscarriage was noted in case of pregnancy loss after detected fetal sac.

RESULTS: In the PGD-A group 78 euploid embryos were transferred in 63 cycles with an average number of 1.24 embryos per cycle. The chemical, clinical and ongoing pregnancy rates were 50.79%, 44.44% and 36.51%, respectively. In the MBS group the average number of transferred embryos was significantly higher (1.49 vs. 1.24; $p<0.01$) compared to PGD-A group. No difference was found in chemical (47.06%) and clinical (37.65%) pregnancy rates. However the ongoing pregnancy rate was significantly lower in the MBS group (22.35% vs 36.51%, $p<0.05$) compared to PGD-A group. A significantly lower miscarriage rate (14.29 vs. 40.63, $p<0.05$) and a higher sustained implantation rates (34.62% vs. 16.54%, $p<0.01$) were observed in the PGD-A than in the MBS group.

CONCLUSIONS: Here we show that PGD-A is a more efficient for AMA patients to select viable embryos for transfer than conventional morphology-based selection. PGD-A not only supported higher ongoing and sustained implantation rates but also lower miscarriage rate. With the advent of PGD-A not only the number of embryos transferred can be decreased but the risk for miscarriage can be lowered which is a major benefit compare to conventional IVF/ICSI treatments.
P-159 Tuesday, October 18, 2016

PERINATAL OUTCOMES FOLLOWING INTRACYTOPLASMIC SPERM INJECTION (ICSI) VERSUS CONVENTIONAL IN VITRO FERTILIZATION (IVF). S. Keyhan, *Y. Li, *T. Truong, *T. Jackson-Bey, *J. L. Eaton. *Division of Reproductive Endocrinology and Infertility, Duke University Medical Center, Durham, NC; †Dept of Biostatistics and Bioinformatics, Duke University, Durham, NC.

OBJECTIVE: Previous studies have demonstrated that assisted reproductive technology is associated with preterm delivery (PTD) and low birth weight (LBW).1-3 The existing literature suggests that these risks may be reduced with ICSI compared to conventional IVF. We hypothesized that differences in obstetric outcomes are driven by baseline patient characteristics rather than the fertilization method itself.4 The objective of our study was to determine whether ICSI is associated with singleton perinatal outcomes after stratification by male factor infertility, sperm source, and female prognostic factors.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: We utilized the Society for Assisted Reproductive Technologies- Clinical Outcomes Reporting System (SART-CORS) database to identify first, fresh, autologous IVF/ICSI cycles between 2004 and 2013 in women less than 43 years of age. Only singleton live births were included in the analysis. Cycles were excluded for the use of preimplantation diagnosis, split ICSI or second-day ICSI, mixed or unknown sperm source, missing birth weight data, or the presence of more than one fetal heartbeat on ultrasound. Primary outcomes were PTD (<37 weeks), LBW (<2500 g), term LBW (LBW; LBW at ≥37 weeks), and preterm LBW (pLBW; LBW at <37 weeks). Student’s t-test and the χ² test were used to analyze continuous and categorical variables, respectively. A propensity matched dataset was assembled to control for confounding baseline characteristics. Multiple logistic regression models were then used to test the effect of IVF vs. ICSI while controlling for other covariates. P<0.05 was considered statistically significant. Subgroup analyses were performed after stratification by male factor infertility, donor/autologous sperm source, and female prognostic factors (age <35 with >3 oocytes retrieved; tubal factor or unexplained infertility).

RESULTS: Of the 90,401 cycles included in the analysis, ICSI was utilized in 60,719 (67.2%) and conventional IVF was used in 29,682 (32.8%). The incidence of PTD in the pre-matched dataset was lower with ICSI than IVF (11.7% vs. 12.4%, P=0.0001) while the incidences of other outcomes were similar between the two groups. After propensity score matching, 13,277 ICSI and 11,373 IVF cycles were included in the analysis. The odds of pLBW were lower with ICSI than IVF after propensity matching and adjusting for covariates (OR=0.81, 95% CI=0.68-0.97, P=0.02) while the incidence of PTD was no longer different between the groups. After stratification by male factor infertility, donor/autologous sperm source, and female prognosis, there was no significant association between fertilization method and any perinatal outcome.

CONCLUSIONS: Differences in adverse perinatal outcomes between ICSI and IVF may be secondary to parental characteristics and infertility diagnoses rather than the fertilization method itself.

References:

Outcomes after Day 3 ET (2014) vs. Pushing to Day 5 (2015). Data listed as mean (95%CI) or %.

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>2014</th>
<th>2015</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 3 Embryo Cell Count</td>
<td>6.9 (6.9-7.0)</td>
<td>6.6 (6.5-6.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Day 3 Embryo Fragmentation</td>
<td>4.1% (3.7-4.6)</td>
<td>5.2% (4.7-5.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Embryos Transferred/Transfer</td>
<td>1.8 (1.7-1.9)</td>
<td>1.6 (1.5-1.6)</td>
<td>0.24</td>
</tr>
<tr>
<td>No ET due to Embryo Arrest or Poor Quality</td>
<td>4% (39/976)</td>
<td>18.2% (189/1038)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Clinical Pregnancy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All 1-3 2PN Cycles</td>
<td>28.1% (298/1061)</td>
<td>21.1% (253/1199)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Excluding PGS</td>
<td>29.9% (298/997)</td>
<td>23.8% (253/1063)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Excluding All Planned Freeze-all Cycles (any cause)</td>
<td>30.5% (298/976)</td>
<td>24.4% (253/1038)</td>
<td>0.01</td>
</tr>
<tr>
<td>Clinical Pregnancy/ET</td>
<td>31.8% (298/937)</td>
<td>29.8% (253/849)</td>
<td>0.26</td>
</tr>
</tbody>
</table>
TOTAL NUMBER OF OOCYTES AND 2PN EMBRYOS ARE PREDICTIVE OF LIVEBIRTH PREGNANCY IN FRESH DONOR OOCYTE CYCLES. E. Hariton, a K. Kim, b S. L. Mumford, b M. Palmor, a P. Bortoletto, a E. R. Cardozo, a A. Karmon, a A. K. Stryer, a Massachusetts General Hospital/Harvard Medical School, Boston, MA; Eunice Kennedy Shriver National Institute of Child Health and Human Development, Bethesda, MD.

OBJECTIVE: The association of donor-recipient characteristics and perifertilization factors with live birth (LB) remains controversial and warrants further study. The objective of this study is to identify factors predictive of LB following fresh donor oocyte IVF cycles.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Two hundred seventeen consecutive fresh IVF donor oocyte embryo transfer (ET) cycles from 2007-2013 at Massachusetts General Hospital were analyzed. Multivariable Poisson regression with a sandwich estimator of the variance was used to identify predictors of LB. Models were adjusted for donor and recipient demographic, reproductive, and clinical factors.

RESULTS: The mean age of oocyte donors and recipients was 26.9 (±3.7) and 41.4 (±4.6) years, respectively. Oocyte donor demographic/reproductive characteristics, ovarian reserve testing, and peak serum estradiol during ovarian stimulation (OS) were similar among LB and non-LB groups. Overall implantation, clinical pregnancy, and LB rates per ET were 40.3%, 64.1%, and 56.7%, respectively. In multivariable analysis (Table), <10 oocytes retrieved during a cycle was associated with a lower likelihood of LB compared to cycles with >10 oocytes retrieved (RR=1.56, 95% CI 1.08-2.26). Compared to cycles with >10 two pronuclear embryos (2PN) on day 1, LB was less likely in cycles with <10 2PN embryos. The total amount of gonadotropins during OS, number of mature oocytes, number of cleaved embryos, and number and quality of embryos transferred were not associated with LB.

CONCLUSIONS: Number of oocytes retrieved and number of 2PN embryos on day 1 are associated with LB following donor oocyte IVF cycles. These findings support the potential significance of perifertilization factors which may predict treatment success and provide guidance for clinicians during donor cycles.

Supported by: The Deborah Kelly Center for Outcomes Research.

Multivariable analysis of factors associated with live birth in fresh donor oocyte IVF cycles

<table>
<thead>
<tr>
<th>Predictors</th>
<th>Number of Categories of Cycles</th>
<th>RR</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of retrieved oocytes</td>
<td>≤10</td>
<td>52</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt;10</td>
<td>135</td>
<td>1.56</td>
<td>1.08, 2.26</td>
</tr>
<tr>
<td>Number of mature oocytes</td>
<td>≤10</td>
<td>74</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt;10</td>
<td>113</td>
<td>1.24</td>
<td>0.92, 1.67</td>
</tr>
<tr>
<td>Number of 2PN oocytes</td>
<td>≤10</td>
<td>112</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt;10</td>
<td>75</td>
<td>1.30</td>
<td>1.01, 1.68</td>
</tr>
<tr>
<td>Number of cleaved embryos</td>
<td>≤10</td>
<td>116</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt;10</td>
<td>71</td>
<td>1.26</td>
<td>0.97, 1.63</td>
</tr>
</tbody>
</table>

Models were adjusted for donor’s age (year), BMI (kg/m²), gravidity, day 3 FSH, AFC, peak E2, amount of gonadotropin used, and day of hCG trigger, and recipient’s age (year), BMI (kg/m²), gravidity, and endometrial thickness.

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INFLUENCE OF PATERNAL AGE ON PERINATAL OUTCOMES IN PREGNANCIES ACHIEVED WITH ASSISTED REPRODUCTIVE TECHNOLOGIES. E. G. Hurley E. DeFranco. OBGYN, University of Cincinnati Medical Center, Cincinnati, OH.

OBJECTIVE: To determine the influence of paternal age on perinatal outcomes of pregnancies achieved with assisted reproductive technology (ART).
OBJECTIVE: To determine the relationship between ovarian aging and perinatal outcomes by comparing the outcomes from Assisted Reproductive Technologies (ART) cycles in patients with advance reproductive age using autologous oocytes versus those in the same age group using donor oocytes.

DESIGN: Population-based retrospective cohort study of cycles from the SART CORS database.

MATERIALS AND METHODS: ART cycles in women 40–43 years old between 2009 and 2013 were assessed. Only cycles with fresh embryo transfers were included. Cycles missing birth weight or gestational age at delivery were excluded. Live birth was defined as birth ≥ 24 weeks gestational age and ≥500g at birth. Preterm birth was defined as live birth < 37 weeks. The primary outcome was preterm singleton live birth rate. Mann-Whitney U test, Chi-square test, and logistic regression were used for statistical analysis. Age, BMI, prior preterm birth, smoking, uterine factor infertility and ethnicity were controlled for.

RESULTS: Among 135, 252 ART cycles, 10263 autologous live births and 8248 donor live births were included. As expected, autologous cycles had a higher miscarriage rate than donor cycles. Surprisingly, autologous cycles resulted in a lower singleton preterm live birth rate when compared to donor oocyte cycles. No significant difference was observed in low birth weight (LBW) at term (<2500g) or intrauterine fetal demise (IUDF) rates between both groups (Table 1).

CONCLUSIONS: In women with advanced reproductive age, autologous oocyte cycles resulted in higher miscarriage rate and yet lower preterm birth rate, compared to donor oocyte cycles. This suggests that the negative impact of oocyte aging on fetal survival or perinatal outcomes is minimal beyond early gestational age.

Table 1

<table>
<thead>
<tr>
<th>Autologous Cycles</th>
<th>Donor Cycles</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preterm birth</td>
<td>1235/10125 (12.2%)</td>
<td>1424/8185 (17.4%)</td>
</tr>
<tr>
<td>Miscarriage</td>
<td>6912/19389 (35.7%)</td>
<td>2275/14493 (15.7%)</td>
</tr>
<tr>
<td>IUDF</td>
<td>74/17315 (0.4%)</td>
<td>60/10627 (0.6%)</td>
</tr>
<tr>
<td>LBW</td>
<td>303/8910 (3.4%)</td>
<td>198/6743 (2.9%)</td>
</tr>
</tbody>
</table>

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OBJECTIVE: To characterize mechanical properties of human embryos after IVF and correlate them with developmental outcomes.

DESIGN: We are conducting an ongoing prospective, observational clinical study on patients undergoing infertility treatment at Lucille Packard Children’s Hospital (LPCH), have at least 5 oocytes retrieved, and will undergo single embryo transfer. We measure the mechanical parameters of all fertilized embryos at the 2PN stage and record outcomes such as day 3 morphology, day 5/6 morphology, preimplantation genetic screening (PGS) results (if available), hCG levels after transfer and pregnancy ultrasound results.

MATERIALS AND METHODS: In our previous research, we developed a quantitative and noninvasive method to measure an embryo’s mechanical parameters by observing its response to a negative pressure applied through a micropipette. We have applied machine learning methods to construct a classifier which can assign a viability score to an embryo based on its mechanical parameters at the 2PN stage. The effectiveness of our classifier in predicting a given outcome (such as blastocyst formation or pregnancy) is quantified based on the area under the ROC curve which is calculated using 10-fold cross-validation on our data.

RESULTS: So far we have recruited 22 patients, and measured 150 embryos which have resulted in 6 single embryo transfers. The measurement itself did not affect blastocyst formation rates so we believe it to be safe. We found that the fertilization method can affect embryo mechanical parameters, so that intra-cytoplasmic sperm injection (ICSI) results in stiffer, less viscous embryos compared to conventional IVF. We found that 2PN embryo mechanics can predict blastocyst formation with an area under the ROC curve of 0.86 and 0.85 in embryos fertilized IVF or ICSI respectively. We also found that 2PN embryo mechanics can predict blastocyst formation better than day 3 morphology, and are not correlated with PGS results at the blastocyst stage. Although our pregnancy data set is small and we are continuing cross-validation on our data.

CONCLUSIONS: Measuring embryo mechanical parameters could be a valuable addition to existing embryo viability assessments.

References:
1. L. Z. Yanez, J Han, B R Behr, A Reijo Pera, D B Camarillo. “Human oocyte developmental potential is predicted by mechanical properties within hours after fertilization.” Nature Communications 7, 2016. Supported by: SPECTRUM pilot grant from Stanford University.

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IMPACT OF OVARIAN AGING ON PERINATAL OUTCOMES: ANALYSIS OF 135,252 ART CYCLES REPORTED TO SART. M. G. Vega, S. Zagh, S. K. Jindal, E. Buyuk, B. Yu. "Department of Obstetrics & Gynecology & Women’s Health, Montefiore Medical Center & Albert Einstein College of Medicine, Bronx, NY; †ObGyn and Women’s Health, Montefiore’s Institute for Reproductive Medicine and Health, Hartsdale, NY; ‡Albert Einstein College of Medicine, Bronx, NY; ¦ObGyn and Women’s Health, Montefiore’s Institute for Reproductive Medicine and Health, Hartsdale, NY; ‡Albert Einstein College of Medicine / Montefiore M, Bronx, NY; †ObGYN, University of Washington, Seattle, WA.

OBJECTIVE: To analyze the influence of maternal age on pregnancy outcomes in patients undergoing ART cycles.

MATERIALS AND METHODS: Our study included 135,252 ART cycles reported to SART. Objective was to see if the preterm birth and low birth weight were increased in patients in older age groups. Age-adjusted logistic regression was performed to test for the relationship between maternal age and adverse outcomes: preterm birth, low birth weight and neonatal death.

RESULTS: The study population included 451,975 pregnancies: 447,510 singleton, 8,778 twin, and 13,687 triplet. The results of this study are shown in the following table. The risk for all adverse outcomes were significantly increased in the subfertile and ART groups.

CONCLUSIONS: The risks for adverse pregnancy and birth outcomes are significantly increased for both subfertile and ART-treated women, even after stratifying by plurality and adjusting for confounding factors.

Supported by: NIH grant R01 HD067270.
OBJECTIVE: GnRH agonist triggering is used instead of hCG in antagonist cycles, in order to diminish ovarian hyperstimulation in high risk patients. GnRH agonist triggering acts by eliciting an endogenous surge of LH and FSH, this effect on early embryonic development is still unknown. Our aim was to compare embryo morphokinetic parameters following GnRH agonist with hCG ovulation triggering, using the EmbryoScope time lapse monitoring system (TMS).

DESIGN: A retrospective cohort study.

MATERIALS AND METHODS: All TMS data of fresh ICSI cycles with antagonist protocol between 4/2013 - 12/2016 was analyzed. Embryo morphokinetic parameters\(^1\) and pregnancy rates were compared between the two groups. Timing of PB-extrusion, PN-fading, and cell cleavage from division to 2 cells (T2) up to the 5-cell stage (T5), second cell cycle duration (CC2=T3-T2) and synchrony in division from 2-cell to 4-cell blastomere embryos (S2=T3-T2) were compared. Optimal CC2 was defined as \( \geq 5\) hours and optimal S2 was defined as \(<1\) hour. A separate analysis for the embryo culture medium: CSC (Irvine, USA), Global (Virollite, USA) and Sage (Cooper-Surgical, USA) was performed.

RESULTS: 1954 embryos derived from cycles triggered with hCG (Group 1) and 606 embryos derived from cycles triggered with GnRHa (Group 2) were analyzed (274 and 60 patients, respectively). Oocyte maturation rates and fertilization rates were similar in both groups [84% and 72% in Group 1; 83% and 76% in Group 2]. Polar body (PB) extrusion occurred earlier in Group 1 than in Group 2 (3.8h \( \pm \) 2.2 vs 4.2h \( \pm \) 3.6, \( p < 0.015 \)) and remained significant also in embryos cultured in CSC medium [Group 1 (n=1358) 3.9h \( \pm \) 23 vs Group 2 (n=379) 4.6h \( \pm \) 4.1, \( p < 0.001 \)]. Embryos cultured in Global medium had a shorter PN fading in Group 1 (n=352) than Group 2 (n=204) (24.8 \( \pm \) 4.1 vs 26.0 \( \pm \) 3.6, \( p < 0.0001 \)). At the 2-cell stage, the percentage of embryos with no multinucleation and the proportion of symmetric-blastomere embryos was significantly higher in Group 1 than in Group 2 (49.9% and 36.2% (p<0.001) and 87.1% and 82.9% (p=0.033), respectively). There were no differences in the number of cells reached an optimal CC2 duration in Groups 1 and 2 was similar (79.1% (1543/1951) and 76.1% (461/606), \( p=0.1 \)). The percentage of embryos with an optimal S2 was higher in Group 1 than in Group 2 (50.5% (985/1950) vs 43.2% (262/6060), \( p<0.002 \)). Pregnancy rates in cycles with fresh embryo transfers were similar in Groups 1 and 2 (40.2% and 35.6%, \( p=0.5 \)).

CONCLUSIONS: Morphokinetic parameters of embryos derived following hCG or GnRHa ovulation triggering were overall similar. It is yet to be determined whether the longer duration of several of the developmental kinetic parameters in embryos following GnRHa agonist triggering is of any clinical significance.

Reference:

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POSSIBLE PATIENTS CONCERNS REGARDING THE BLASTOCYST EUPLOIDY RATES OF DONOR OCYCTES.

J. B. Whitney, a K. Waggoner, b M. C. Schiewe, b aSCCRM, Ovation Fertility, Newport Beach, CA; bART Lab, Ovation Fertility, Newport Beach, CA.

OBJECTIVE: Is there a benefit to aneuploidy screening embryos derived from donor oocytes? What predictive value does knowing embryo ploidy statistics offer donor cycle recipients?

DESIGN: A retrospective observational cohort analysis of 59 donor oocyte cycles, producing 564 PGS tested embryos (BL), was evaluated between 10/2013 to 01/2016. Aneuploidy rate and BL production were assessed and used to correlate predictive outcomes.

MATERIALS AND METHODS: Patient embryos were cultured in Life Global media + LGPS, and biopsied at the BL stage. All biopsy samples were analyzed using NGS or aCGH. These cycles resulted in 667BL and 79 transfers. In an effort to generate predictive values, cycles were analyzed to determine if the: (1) best quality embryo was euploid; (2) euploid embryo was on day 5; or (3) cycle produced \( \geq 2\) top quality day 5 euploid embryos.

RESULTS: Euploidy at the BL stage was 67.7% with a mean of 6.5 euploid BL produced per cycle. 11 cycles failed to produce a euploidy rate above 50% and 6 cycles failed to attain a day 5 euploid BL (10%). With subjective morphology dictating standard transfer selection, we observed 17 cycles having their best quality embryo be aneuploid. At transfer, we achieved a 74.7% implantation rate, with a 4.7% spontaneous miscarriage rate. Using a theoretical model where morphology dictated transfer, the implantation rate would have been 50.8%, lower (\(<0.01\)) than with PGS (74.7%). In contrast, 71.1% of cycles produced their two best quality embryos as euploid. In these cycles, using standard dual embryo transfers, we would have expected a twinning rate of at least 55%. Contrasting our 2010 data, we performed 23 dual, untested ET donor eggs cycles resulting in a 91% live birth rate and 67% twins. Applying morphology alone for single embryo transfer (SET), 29% of the cycles would have had an aneuploid transfer.

CONCLUSIONS: Patient age is the leading factor contributing to aneuploidy. The international demand for routine SET for all cycles has placed increased pressure on improved embryo selection for transfer. While in the USA, SET of donor oocyte cycles is still not widely accepted, as dual embryo transfers offer increased success. Without knowing the ploidy status, many SET cycles would fail to result in a pregnancy, while >50% of the dual embryo transfers would produce twins. Embryo ploidy status is not the only factor contributing to implantation. When choosing to transfer on good prognosis cycles, unknown factors may negatively impact SET success. Thus, a conservative approach allowing multiple attempts for pregnancy is best. When embryo aneuploidy is unknown, risks for twins or failed implantation remain high. Although it is true that the aneuploidy rate of donated oocytes is relatively low, many cycles still produced sub-optimal euploidy and BL yields. Overall, single euploid ET is the best approach to optimize patient success and minimize multiple implantation risks.

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RISKS OF ADVERSE PERINATAL AND INFANT OUTCOMES BY PLURALITY AND MATERNAL FERTILITY STATUS. B. Luke, a D. Gopal, a H. Diop, b J. E. Stern. aObstetrics, Gynecology, and Reproductive Biology, Michigan State University, East Lansing, MI; bCommunity Health Sciences, Boston University School of Public Health, Boston, MA; cMass Department of Public Health, Mass Department of Public Health, Boston, MA; dObstetrics and Gynecology, Dartmouth-Hitchcock, Lebanon, NH.

OBJECTIVE: To evaluate the effect of maternal fertility status on the risk of perinatal and infant outcomes by plurality.

DESIGN: Longitudinal cohort study, linking cycles from the SART CORS, hospital discharge, and vital records from 2004-2010 in Massachusetts.

MATERIALS AND METHODS: The study included three fertility groups: women without ART or other infertility treatment (fertile); women
with indicators of subfertility but no ART treatment (subfertile), and women with ART treatment. The risks of perinatal and infant outcomes were modeled by plurality using logistic regression, adjusted for parental ages, race/ethnicity, education, payor status, and maternal pre-existing conditions (diabetes and chronic hypertension), and infant gender(s). Adjusted odds ratios (AORs) and 95% confidence intervals are reported. Fertile women were the reference group.

RESULTS: The study population included 451,975 pregnancies: 447,510 fertile, 8,778 subfertile, and 13,687 ART; and 459,623 singleton and 10,352 twin pregnancies. The risks of adverse perinatal and infant outcomes by fertility status and plurality are shown below. The risks were significantly increased for singleton and twin infants born to both subfertile and ART-treated women for low birthweight and prematurity, for singletons born to ART women for small-for-gestational age and infant death, and for singletons and twins born to subfertile women for infant death.

CONCLUSIONS: The risks for adverse perinatal and infant outcomes are significantly increased for both subfertile and ART-treated women, even after stratifying by plurality and adjusting for confounding factors.

Supported by: NIH grant R01 HD07270.

P-170 Tuesday, October 18, 2016

FMR1 CGG REPEAT LENGTH AND OVARIAN FUNCTION IN A DONOR POPULATION. N. Banks, G. Patounakis, C. M. Owen, M. W. Healy, B. W. Whitcomb, M. E. Hartman, K. Devine, K. S. Richter, A. DeCherney, E. Levens, M. J. Hill, NICHHD, Bethesda, MD; University of Massachusetts Amherst, Amherst, MA; Shady Grove Fertility Reproductive Science Center, Rockville, MD.

OBJECTIVE: Previous studies have suggested that low FMR1 CGG repeat length (<26) may be a predictor of decreased functional ovarian reserve, but this has not been confirmed. Our objective is to study FMR1 CGG repeat length in a fertile donor population.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: From 2011-2015, a total of 326 egg donors were available for FMR1 testing and underwent 514 stimulation cycles. The primary outcome was mature oocyte (MII) yield. Analysis was performed separately using patient maximum and minimum repeat length alleles. Generalized estimating equations (GEE) modeled the association of repeat length with MII yield while adjusting for female age and multiple cycles. A separate analysis with GEE modeling was performed grouping patients by FMR1 allele combinations using the definitions low repeats <26, normal 26-34 and high 34-55 and allele combinations designated by low-low, low-normal and high-normal. A separate analysis with GEE modeling was performed grouping patients by FMR1 allele combinations using the definitions low repeats <26, normal 26-34 and high 34-55 and allele combinations designated by low-low, low-normal and high-normal.

RESULTS: A total of 16087 cycles were studied. Patient's demographic, stimulation, laboratory parameters and clinical outcomes are shown in Table 1. Normal (n=10797; P4: 4.4±2.0), intermediate rise (n=3535; P4: 2.0±0.3), low rise (n=1321; P4: 1.3±0.2) and absent luteinization (n=434; P4: 0.8±0.2) were identified. Age (r=-0.17), BMI (r=0.09), day 3 FSH (r=-0.19) and total GND dose (r=-0.23) had a negative correlation and AMH (r=0.18) had a positive correlation with the level of P4. Fertilization rate was observed similar between <2.3 or 2.3 to 4.2 mg/mL: 51.7% vs. 53.6% vs. 54.2% vs. 55.8% (p=0.05), P4 level was similar when compared according to fertilization rate (<25, 25-50, 51-75 and >75); 29 vs. 3.4 vs. 3.6 vs. 3.2 mg/mL, respectively. Raw data analysis showed PR (34.4% vs. 41.6% vs. 49.6% vs. 56.5%, respectively; p<0.05), clinical PR (26.4% vs. 32.5% vs. 39.7% vs. 46.5%, respectively; p<0.05), loss rate (16.2% vs. 17.2% vs. 18.1% vs. 18.2%, respectively; NS) and LBR (17.4% vs. 23.8% vs. 30.9% vs. 38.0%, respectively; p<0.05) increased with increasing P4 level. After adjusting for age, FSH, AMH, BMI and total GND dose in a logistic regression model, elevated P4 was still associated with increased odds of pregnancy (OR 1.074 (95% CI 1.056 - 1.092), p<0.05), clinical pregnancy (OR 1.086 (95% CI 1.051 - 1.108), p<0.05) and live birth (OR 1.074 (95% CI 1.057 - 1.093), p<0.05), with no influence on loss rate (OR 1.009 (95% CI 0.998 - 1.030), NS).

Supported by: Work supported in part by the NICHD intramural research program.

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OBJECTIVE: A rise in LH and P4 after an r-hCG trigger, which mimics an endogenous LH flare, indicates oocyte maturation initiation. P4 level post-trigger has been characterized as an independent predictor of number of total and mature oocytes retrieved. This study sought to analyze clinical outcomes in patients with differing levels luteinization.

DESIGN: Retrospective.

MATERIALS AND METHODS: Patients underwent an IVF cycle with a hCG trigger between 2002-2015. Patients post-trigger β-hCG<40 mIU/mL were excluded. P4 (ng/mL) rise post-trigger was considered absent (<1), low (1.0-1.5), intermediate (1.6-2.3) or normal rise (>2.3). Cohorts were segregated by fertilization rate (<25%, 25-50%, 51-75%, >75%) and P4 level was compared. Pearson correlations were used to analyze correlation between age, BMI, FSH, AMH and total GND dosage with post-trigger P4 levels. A binary logistic regression analysis was used to model the influence of P4 level on pregnancy rate (PR), clinical PR, loss rate and live birth rate (LBR).

RESULTS: A total of 16087 cycles were studied. Patient’s demographic, stimulation, laboratory parameters and clinical outcomes are shown in Table 1. Normal (n=10797; P4: 4.4±2.0), intermediate rise (n=3535; P4: 2.0±0.3), low rise (n=1321; P4: 1.3±0.2) and absent luteinization (n=434; P4: 0.8±0.2) were identified. Age (r=-0.17), BMI (r=0.09), day 3 FSH (r=-0.19) and total GND dose (r=-0.23) had a negative correlation and AMH (r=0.18) had a positive correlation with the level of P4. Fertilization rate was observed similar between <2.3 or 2.3 to 4.2 mg/mL: 51.7% vs. 53.6% vs. 54.2% vs. 55.8% (p=0.05), P4 level was similar when compared according to fertilization rate (<25, 25-50, 51-75 and >75); 29 vs. 3.4 vs. 3.6 vs. 3.2 mg/mL, respectively. Raw data analysis showed PR (34.4% vs. 41.6% vs. 49.6% vs. 56.5%, respectively; p<0.05), clinical PR (26.4% vs. 32.5% vs. 39.7% vs. 46.5%, respectively; p<0.05), loss rate (16.2% vs. 17.2% vs. 18.1% vs. 18.2%, respectively; NS) and LBR (17.4% vs. 23.8% vs. 30.9% vs. 38.0%, respectively; p<0.05) increased with increasing P4 level. After adjusting for age, FSH, AMH, BMI and total GND dose in a logistic regression model, elevated P4 was still associated with increased odds of pregnancy (OR 1.074 (95% CI 1.056 - 1.092), p<0.05), clinical pregnancy (OR 1.086 (95% CI 1.051 - 1.108), p<0.05) and live birth (OR 1.074 (95% CI 1.057 - 1.093), p<0.05), with no influence on loss rate (OR 1.009 (95% CI 0.998 - 1.030), NS).
CONCLUSIONS: Even though all study cohorts demonstrated adequate fertilization rates, luteinization was correlated with the likelihood of live birth, with a P4 level >2.3 ng/mL, as reflected by the highest LBR in study. The level of P4 at trigger is an accurate prognostic indicator of cycle outcome and can be used prior to oocyte retrieval to enhance patient counseling and expectations.

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EGG DONATION CYCLE OUTCOMES ACCORDING TO RECIPIENT PROGESTERONE LEVEL ON THE DAY OF FRESH BLASTOCYST TRANSFER. R. Sherbahn M. Catenacci. Advanced Fertility Center of Chicago, Gurnee, IL.

OBJECTIVE: To study the relationship between serum progesterone levels on the day of embryo transfer and cycle outcomes using fresh donor eggs and fresh blastocyst transfers.

DESIGN: Retrospective chart review.

MATERIALS AND METHODS: All 243 fresh day 5 transfers with donor eggs between January 2012 and December 2014 were included. Cases were put in 2 groups based on the serum progesterone level (Immunoassay) on day of transfer. Cycle characteristics and outcomes were compared. Chi-square, Fisher’s exact test and T-tests were used for statistical analysis.

RESULTS: Cycle characteristics and cycle outcomes did not show any significant differences for the parameters that were studied. See Table.

<table>
<thead>
<tr>
<th>Characteristics and Outcomes of Groups</th>
<th>P4 &lt; or = 40 ng/ml</th>
<th>P4 &gt; 40 ng/ml</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of transfer procedures</td>
<td>82</td>
<td>161</td>
<td>-</td>
</tr>
<tr>
<td>Oocytes retrieved (a)</td>
<td>19.6 ± 6.4</td>
<td>18.7 ± 6.1</td>
<td>NS</td>
</tr>
<tr>
<td>Embryos transferred</td>
<td>1.7 ± 0.4</td>
<td>1.7 ± 0.5</td>
<td>NS</td>
</tr>
<tr>
<td>Clinical miscarriage rate (%)</td>
<td>4/73 (5.5%)</td>
<td>11/137 (8.0%)</td>
<td>NS</td>
</tr>
<tr>
<td>Ectopic pregnancy rate (%)</td>
<td>0/73 (0%)</td>
<td>0/137 (0%)</td>
<td>NS</td>
</tr>
<tr>
<td>Implantation rate (%)</td>
<td>111/143 (77.6%)</td>
<td>214/272 (78.7%)</td>
<td>NS</td>
</tr>
<tr>
<td>Clinical pregnancy rate per transfer (%)</td>
<td>73/82 (89.0%)</td>
<td>137/161 (85.1%)</td>
<td>NS</td>
</tr>
<tr>
<td>Live birth rate per transfer (%)</td>
<td>69/82 (84.2%)</td>
<td>126/161 (78.3%)</td>
<td>NS</td>
</tr>
</tbody>
</table>

CONCLUSIONS: Previous published studies looking at progesterone levels on the day of transfer in IVF cycles requiring complete hormone replacement (fresh egg donation transfers and/or frozen embryo transfers) have shown divergent results. Kofinas et al. in 2015 showed lower live birth rates and higher miscarriage rates with higher progesterone levels on day of transfer as compared to lower levels for frozen embryo transfers. However, Brady et al. in 2014 had higher clinical pregnancy and live birth rates for fresh donor egg transfers with higher progesterone levels. Our results differ from both of these other studies by showing high clinical pregnancy rates and live birth rates and low miscarriage rates regardless of the progesterone level for fresh day 5 transfers using donor eggs.

REFERENCES:

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BIRTH WEIGHT IN SINGLETONS AFTER AUTOLOGOUS FRESH TRANSFER ACCORDING TO THE OVARIAN HYPERSTIMULATION PROTOCOL USED. L. C. Londra a S. L. Mumford. a Reproductive Endocrinology and Infertility, Ohio State University, Columbus, OH; bNICHID, NIH, Rockville, MD.

OBJECTIVE: To evaluate whether the type of ovarian hyperstimulation protocol is associated with birth weight (BW) among singleton births from fresh autologous embryo transfer cycles.

DESIGN: Cohort study.

MATERIALS AND METHODS: The Society for Assisted Reproductive Medicine (SART) registry was used, including data collected from fresh autologous cycles that resulted in a singleton birth between years 2008-2013. ANOVA and chi square tests were used as appropriate to compare BW categories and gestational age characteristics by protocol. Modified Poisson regression with robust error variance was used to estimate risk ratios (RR) and 95% confidence intervals for low birth weight (LBW), very low birth weight (VLBW) by ovarian hyperstimulation protocol (luteal agonist, agonist flare, and antagonist). Models were adjusted for age, body mass index, race, previous full term birth, previous preterm birth, infertility diagnosis, oocytes retrieved, embryos transferred, embryo stage, vanishing twin and infant gender. Interactions between protocol and infertility diagnosis were also explored.

RESULTS: There were 54,041 births in the luteal agonist group, 10,943 in the agonist flare group and 47,886 in the antagonist group. There were no significant differences in BW, except in VLBW (BW less than 1,500 g), which was 2% in the antagonist protocol group vs 1.8% in the luteal agonist and 1.6% in the agonist flare (P=0.0095). After adjusting for covariates, this difference remained significant (RR 1.16, 95% CI 1.02 to 1.31). A significant interaction was observed for LBW and VLBW between endometriosis and protocol. We found that among those with endometriosis, the agonist flare protocol was associated with a higher risk of LBW or VLBW compared to the luteal agonist protocol; for those without endometriosis there was no effect of the protocol.

CONCLUSIONS: The association between BW and the type of protocol used does not appear to be clinically relevant, although a modest increase in VLBW among antagonist cycles suggest suboptimal placentation in some patients. Data from hormonal monitoring during the cycle -not available for analysis in the SART database- might be useful in understanding differences in obstetric outcomes of singleton births after fresh autologous cycles.

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EFFECT OF ELEVATED PROGESTERONE ON DAY OF TRIGGER ON LIVE BIRTH WITH A DAY 5 VERSUS DAY 6 BLASTOCYST TRANSFER. M. W. Healy, a K. S. Richter, b M. Yamakami, b N. Banks, b C. M. Owen, a A. DeCherney, a K. Devine, a M. J. Hill, a National Institutes of Health- NICHD, Bethesda, MD; bShady Grove Fertility Reproductive Science Center, Rockville, MD; cDepartment of OB/GYN, Walter Reed National Military Medical Center, Bethesda, MD.

OBJECTIVE: Recent literature demonstrates a negative effect of elevated progesterone (P) on day of oocyte maturation trigger causing endometrial-embryo asynchrony, ultimately leading to decreased live birth rates. In fresh blastocyst transfers, this effect may be more pronounced in day 6 compared to day 5 embryo transfers (ET), as embryo growth would be slower while endometrial development more advanced. Our objective was to evaluate the effect of P on the day of trigger in fresh IVF transfer cycles on day 5 versus day 6.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Autologous IVF cycles with fresh ET on day 5 and day 6 from 2011-2014 were included if P was measured on the day of trigger. The primary outcome was live birth. GEE modeling was performed to control for confounders including embryo quality, stage, age, and number of embryos transferred and account for multiple cycles. GEE modeling was used to determine the effect of P on day versus day 6 ET comparing P as a continuous variable and P as a threshold variable ≥1.5ng/mL. ROC curves were evaluated for P and live birth.

RESULTS: 4,120 day 5 ETs and 230 day 6 ETs were analyzed. Day 6 transfers were less likely to have good quality embryos than day 5 (73% vs 83%) but both cohorts had similar rates of blastocyst stage ET (92% vs 91%). Live birth was less likely in day 6 embryo transfers (34% vs 46%) even when controlling for embryo confounders. In adjusted GEE models, the effect of P was more pronounced on day 6 ET compared to day 5 ET (OR 0.6 vs 0.56 or OR 0.77). Similarly, the effect of P=1.5 ng/mL was more pronounced on day 6 ET than day 5 ET (OR 0.40 vs OR 0.69). Day 6 ET live birth rates were moderately lower when P was in the normal range, but became much lower when P was >1.5ng/mL (Table 1). The AUC for P predicting live birth was higher in day 6 embryos than day 5 embryos (0.58 vs 0.54). Interaction testing of P on day of ET demonstrated P<0.0001, further suggesting that the effect of P was more pronounced on a day 6 ET.
Table 1: The effect of P on live birth among day 5 versus day 6 ET.

<table>
<thead>
<tr>
<th>P</th>
<th>P&lt;1.5</th>
<th>P&gt;=1.5</th>
<th>Difference</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 5</td>
<td>47%</td>
<td>37%</td>
<td>-10%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Day 6</td>
<td>39%</td>
<td>20%</td>
<td>-19%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Difference</td>
<td>-8%</td>
<td>-17%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P value</td>
<td>0.04</td>
<td>&lt;0.01</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CONCLUSIONS: P had a greater effect on day 6 ET compared to day 5. This suggests further endometrial-embryo asynchrony on day 6 and a lower threshold for freezing day 6 blastocysts for frozen ET.

Supported by: This research was supported, in part, by Intramural research program of the Program in Reproductive and Adult Endocrinology, NICHD, NIH.

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OBJECTIVE: To summarize the available literature regarding continuance with in-vitro fertilization (IVF) versus conversion to IUI in poor responders.

DESIGN: Systematic review.

MATERIALS AND METHODS: Following the PRISMA guidelines, a PubMed literature search, for studies published between January 1996 through February 2016, was performed to identify trials comparing pregnancy and live birth rates with conversion to IUI versus continuance of IVF in patients with poor response. All fresh, non-donor ART cycles with ≤ 4 follicles produced after ovarian hyper-stimulation were included. An additional literature search was conducted on references in the identified studies. A planned meta-analysis was not performed secondary to the high degree of heterogeneity of data with respect to outcome measures and definition of poor responders. The prior primary outcome measures were clinical pregnancy and live birth rates. Failure to retrieve oocytes was also evaluated.

RESULTS: Eighteen studies were identified and evaluated for inclusion and exclusion criteria of which seven articles met inclusion criteria. These studies comprised 1327 patients that converted to IUI and 2060 patients whom continued with IVF. When evaluating poor responders as a group, six studies reported higher overall clinical pregnancy rates and five studies demonstrated overall increased live birth rates with continued IVF. When stratified by the number of follicles produced, continuance of IVF demonstrated higher clinical pregnancy and live birth rates with ≥ 2 follicles. When only one follicle was produced there were no significant differences in clinical pregnancy or live birth rates between the two cohorts. In those patients continuing with IVF, failure to retrieve oocytes occurred in 2.4-16% of patients.

CONCLUSIONS: In patients undergoing IVF with ≤ 4 follicles, continuance with IVF leads to higher clinical pregnancy and live birth compared to conversion to IUI except in patients with monofollicular development. The rate of failure to retrieve oocytes are low.

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IVF OUTCOMES IN YOUNG PATIENTS WITH UNEXPLAINED INFERTILITY: AN ANALYSIS OF 273,779 CYCLES FROM THE 2011-2013 SOCIETY FOR ASSISTED REPRODUCTIVE TECHNOLOGY CLINIC OUTCOME REPORTING SYSTEM REGISTRY. G. Collins, S. Thakore, J. M. Goldfarb. Reproductive Endocrinology and Infertility, Case Western Reserve University, Cleveland, OH.

OBJECTIVE: To determine if young patients (age ≤ 25yo) with the diagnosis of unexplained infertility have poorer IVF outcomes than older women with the same diagnosis or than young women with an infertility diagnosis unrelated to age (male or tubal factor infertility).

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: A total of 273,779 IVF cycles from the 2011-2013 Society for Assisted Reproductive Technology (SART) registry were stratified into cohorts based on age and diagnosis (unexplained, male factor, and tubal factor infertility). Live birth rates, cancellation rates, average number of oocytes, transfer rates, and blastulation rates were then assessed between diagnosis and age groups. A two-sample t-test between proportions was performed to determine the difference between percentages and an ANOVA statistical analysis was performed to determine a difference between group means.

RESULTS: In young women ≤ 25 years old with unexplained infertility, there was a trend toward a lower percentage of live births compared with patients 26-30 years old with unexplained infertility, but it was not statistically significant (41.1% vs 44.9%, p < 0.26). There was no difference in the live birth rate or the cancellation rate in the extremely young women with the diagnosis of unexplained infertility compared with women of the same age with the diagnosis of male or tubal factor infertility; however, there was a trend in all diagnoses toward lower pregnancy rates and similar or higher cancellation rates (Table 1). Similarly, there was no difference in the average number of oocytes obtained in women ≤ 25 years old with the diagnosis of unexplained, male or tubal factor infertility (12.1 vs 12.2 vs 12.6 oocytes), and the average number of oocytes declined with an increase in age. There was neither a difference in the number of transfer attempts nor in blastulation rate between the diagnosis and age groups.

CONCLUSIONS: Young women with the diagnosis of unexplained infertility do not have poorer IVF outcomes; however, there is a trend toward lower live born pregnancy rates and higher cancellation rates in this population.

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ANTI-MULLERIAN HORMONE LEVELS DO NOT PREDICT OUTCOMES OF IVF CYCLES UNDERGOING PRE-IMPLANTATION GENETIC SCREENING (PGS). J. Jayakumaran, C. Silva, B. K. Gangrade, S. Patel. Center for Reproductive Medicine, Orlando, FL.

OBJECTIVE: To determine whether anti-mullerian hormone levels (AMH) correlates with number of euploid embryos, pregnancy rates and live birth outcomes in women undergoing IVF/pre-implantation genetic screening (PGS) cycles.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: We reviewed data of 591 women who underwent IVF/PGS cycles between 2010 and 2015 at a single fertility clinic. Trophoderm biopsy was done on day 5 and day 6 blastocysts . They were vitrified pending genetic analysis tests of all 23 chromosomes (SNP Microarray analysis).These women underwent euploid blastocyst transfer in subsequent frozen embryo transfer cycle (FET). They were divided into 2 groups, based on AMH levels. Group 1 had AMH levels more than or equal to 1 ng/ml and Group 2 had AMH levels less than 1 ng/ml . We recorded their baseline and cycle characteristics, clinical pregnancy and live birth rates. Chi-square test and two-tailed Fischer’s exact test were used to calculate statistical significance.

RESULTS: Group 1 had 495 women (84%) and group 2 had 96 women (16%). Mean age of patients in group 2 was higher (37.5) than group 1 (36.6), but there was no statistical significance (p < 0.06). The number of euploid embryos was significantly lower in group 2 (59) than group 1 (478). p < 0.001. There was no statistically significant difference between clinical pregnancy, live birth rates and spontaneous abortion rates between both groups. Results are shown in table 1.

CONCLUSIONS: Women with AMH levels more than or equal to 1 ng/ml had more embryos to biopsy and more euploid embryos available to transfer. But clinical pregnancy rate, live birth rate and spontaneous abortion rates did not differ based on AMH levels. Our study results may help clinicians to counsel patients undergoing PGS.
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OBJECTIVE: Single embryo transfer (SET) reduces IVF multiple gestations. Embryo selection is optimized by morphological grading and preimplantation genetic screening (PGS). While morphology is strongly correlated with implantation potential, it is not known whether poor morphology embryos that do implant result in defective placentation, impaired fetal growth and preterm delivery. This study sought to assess whether reproductively competent embryos with poor morphological grade have delayed perinatal sequelae.

DESIGN: Retrospective cohort, case control study.

MATERIALS AND METHODS: All patients with a singleton live birth after frozen-thawed SET (FET) from 2003-2015 were included. Monzygotic twins were excluded. Cycles were stratified based on the Gardner-Schoorcraft grading for blastocyst expansion (BE), inner cell mass (ICM) and trophectoderm (TE). BE grade ≤ 3 (n=10) were excluded. Age, BMI, endometrial thickness at transfer, gestational age and birthweight at delivery were recorded. Student’s t-test, chi-square, linear and binary logistic regression were used.

RESULTS: A total of 420 live singleton births from frozen SETs were identified. Age, BMI, endometrial thickness at transfer, gestational age at delivery or infant birthweight were similar among morphological grading categories for BE, ICM or TE. A higher proportion of day 5 embryo transfers in expansion 4 vs. 5 and 6 groups were seen. Controlling for embryo age, birthweight was not influenced by expansion (p=0.5), ICM (p=0.4) or TE (p=0.9). However, odds of low birthweight (LBW) (<2500g) was increased for expansion 4 (OR 4.7 [95% CI 1.3-30.0], p=0.04) and 5 (OR 5.2 [95% CI 1.3-34.9], p=0.04) blastocysts compared with 6 (Table). TE (x2=0.8, p=0.7) and ICM (x2=0.9, p=0.6) grade did not influence LBW. Morphological grade of BE, ICM and TE did not significantly influence the odds of macrosomia or preterm delivery.

CONCLUSIONS: In general, transfer of an embryo deemed “poor morphological quality” was not associated with a decrease in gestational age at delivery or infant birthweight. While the overall incidence of LBW was low, we identified a preponderance of LBW singletons after transfer of a less expanded blastocyst. While SET enables maximal embryonic-endometrial synchrony, it is possible that less expanded, slower developing blastocysts are slightly asynchronous with endometrial receptivity, leading to defective placentation and decreased fetal growth in patients with an underlying susceptibility.

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ANTI-MULLERIAN HORMONE (AMH) IN SERUM AND FOLLICULAR FLUID AND APOPTOSIS OF MURAL GRANULOSA AND CUMULUS CELLS IN PATIENTS UNDERGOING IVF/ICSI Y. Fan, L. Wei, J. Chen, Y. Shi, X. Liang. Reproductive Medical Center, The Sixth Affiliated Hospital of Sun Yat-sen University, Guangzhou, China.

OBJECTIVE: To investigate the relationship between anti-Mullerian hormone (AMH) levels in serum and FF and apoptosis of granulosa and cumulus cells in normal ovarian reserve patients undergoing in-vitro fertilization (IVF)/intracytoplasmic sperm injection (ICSI).

DESIGN: Prospective control study.

MATERIALS AND METHODS: A total of 58 women undergoing IVF/ICSI cycle, aged <35 years old, with antral follicle count > 6, implying normal ovarian reserve, were divided into three group according to their serum AMH level before controlled ovarian hyperstimulation (COH). 17 women were in low AMH group (Group A, 1ng/ml<AMH≤2 ng/ml), 18 were in intermediate AMH group (Group B, 2ng/ml<AMH≤4ng/ml) and 23 were in high AMH group (Group C, AMH>4ng/ml). All patients were followed prospectively and their cycle outcomes were recorded. Follicular fluid (FF) samples were obtained from mature follicles during oocyte retrieval for IVF/ICSI. FF AMH and serum AMH concentrations were measured with the same automated AMH assay (Roche; Elecys). Estradiol (E2), progesterone (P), testosterone (T) concentrations in FF were also measured by automated electrochemiluminescence immunoassay(Roche; Elecys). Mural granulosa cells were isolated from follicular fluid and cumulus cell were obtained during oocyte pick-up. Apoptosis of mural granulosa cells and cumulus cells were assessed by flow cytometry using Annexin V-FITC/PI double staining.

RESULTS: There were no significant differences in baseline such as age, duration of infertility, gravity, abortion times and BMI (body mass index). Group C is associated with more antral follicle count (AFC) (p<0.001) and higher FF AMH levels (p<0.001). The number of retrieved oocytes (p<0.05) and top-quality embryos (p<0.05) were significantly higher in group C, but no significant differences were found. And there were no significant differences in total apoptosis of mural granulosa and cumulus cells among three groups. However, the percentage of early apoptotic events (annexin V+, PI-) in cumulus cells were higher in Group A than Group C. Also, T levels in FF were positive related to late apoptotic events (annexin V+, PI-) in cumulus cells were higher in Group A than Group C. And higher FF AMH and serum AMH concentrations were measured with the same automated AMH assay (Roche; Elecys). Estradiol (E2), progesterone (P), testosterone (T) concentrations in FF were also measured by automated electrochemiluminescence immunoassay(Roche; Elecys). Mural granulosa cells were isolated from follicular fluid and cumulus cell were obtained during oocyte pick-up. Apoptosis of mural granulosa cells and cumulus cells were assessed by flow cytometry using Annexin V-FITC/PI double staining.

CONCLUSIONS: In general, transfer of an embryo deemed “poor morphological quality” was not associated with a decrease in gestational age at delivery or infant birthweight. While the overall incidence of LBW was low, we identified a preponderance of LBW singletons after transfer of a less expanded blastocyst. While SET enables maximal embryonic-endometrial synchrony, it is possible that less expanded, slower developing blastocysts are slightly asynchronous with endometrial receptivity, leading to defective placentation and decreased fetal growth in patients with an underlying susceptibility.

Perinatal outcomes stratified by blastocyst expansion

Blastocyst expansion grade | 4 | 5 | 6 | P value
--- | --- | --- | --- | ---
Number of patients | 198 | 96 | 116 | NS
Age | 35.3 ± 4.6 | 35.3 ± 4.1 | 36.4 ± 3.7 | NS
BMI | 22.8 ± 3.8 | 22.7 ± 3.2 | 23.1 ± 4.0 | NS
Endometrial thickness at ET (mm) | 9.5 ± 2.1 | 9.3 ± 2.3 | 9.3 ± 1.8 | NS
Day 5 blastocyst | 52.0% (103/198)* | 30.2% (29/96) | 27.6% (32/116) | <0.05
Day 6 blastocyst | 47.0% (93/198)* | 69.8% (67/96) | 72.4% (84/116) | <0.05
Gestational age at delivery (weeks) | 37.9 ± 2.4 | 38.0 ± 1.9 | 40.7 ± 2.6 | NS
Preterm delivery (<37 weeks) | 19.7% (39/198) | 20.4% (20/98) | 14.7% (17/116) | NS
Birthweight (g) | 3320.5 ± 622.0 | 3312.8 ± 617.3 | 3387.2 ± 497.7 | NS
Low Birthweight (<2500g) | 7.6% (15/198) | 8.3% (8/96) | 1.7% (2/116)* | <0.05
Macrosomia (>4500g) | 0.5% (1/198) | 3.1% (3/96) | 0.9% (1/116) | NS
Comparison of characteristics, clinical outcomes and cell apoptotic rate

<table>
<thead>
<tr>
<th>parameters</th>
<th>group A</th>
<th>group B</th>
<th>group C</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>29.18±3.41</td>
<td>29.72±2.72</td>
<td>29.39±3.34</td>
<td>0.865</td>
</tr>
<tr>
<td>Serum AMH level (ng/mL)</td>
<td>1.65±0.28</td>
<td>1.64±1.23</td>
<td>0.94±3.67</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>AFC</td>
<td>11.76±5.10</td>
<td>15.72±3.57</td>
<td>24.96±5.84</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>FF AMH level (ng/mL)</td>
<td>1.98±1.00</td>
<td>2.88±1.87</td>
<td>6.97±4.17</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>FF T level (ng/mL)</td>
<td>7.27±6.68</td>
<td>5.67±2.39</td>
<td>9.67±11.37</td>
<td>0.327</td>
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<tr>
<td>No. of retrieved oocytes</td>
<td>12.47±6.30</td>
<td>14.78±7.45</td>
<td>17.13±7.63</td>
<td>0.047</td>
</tr>
<tr>
<td>No. of top quality embryos</td>
<td>4.06±3.46</td>
<td>5.82±4.75</td>
<td>7.05±3.93</td>
<td>0.029</td>
</tr>
<tr>
<td>Top quality embryos rate (%)</td>
<td>84.15</td>
<td>69.5</td>
<td>70.4</td>
<td>0.209</td>
</tr>
<tr>
<td>Cumulus cells total apoptotic rate (%)</td>
<td>5.94±9.04</td>
<td>3.60±3.63</td>
<td>5.55±7.70</td>
<td>0.901</td>
</tr>
<tr>
<td>Cumulus cells early apoptotic rate (%)</td>
<td>11.87±10.79</td>
<td>7.48±9.09</td>
<td>4.93±7.68</td>
<td>0.045</td>
</tr>
<tr>
<td>Cumulus cells total apoptotic rate (%)</td>
<td>15.12±15.24</td>
<td>9.7±14.07</td>
<td>7.87±5.93</td>
<td>0.148</td>
</tr>
</tbody>
</table>

References:

Supported by: This study was supported by the National Natural Science Foundation of China (NSFC). (No. 81471507).

P-180 Tuesday, October 18, 2016
BLASTOCYST COLLAPSE: VALIDATION OF PREVIOUS DATA. R. Herrer Saura, J. Marcos, P. Valero, V. Ramirez, J. Serna, E. I. Gil Arribas, M. Meseguer, IVF, IVI Zaragoza, Zaragoza, Spain; IVI, IVI Murcia, Murcia, Spain; IVI Zaragoza, Zaragoza, Spain; Clinical Embryology, Valencia, Spain.

OBJECTIVE: The appearance of time lapse incubators has opened the possibility of studying dynamic embryo behaviors. Blastocyst collapse has been studied in different mammal models. Strong contractions seem to be deleterious for embryo hatching. There is a high consumption of energy in the process of contraction and re-expansion, which could affect the expansion of the blastocyst from de Zona Pellucida (ZP) and, consequently, the possibility of implantation.

DESIGN: Retrospective study to validate the results obtained from IVI Murcia and IVI Valencia (Marcos, J et al, Hum Reprod 2015) analyzing second data set of embryos, in a different laboratory and with different culture conditions. Marcos et al. found that blastocyst collapse affects implantation, but not hatching rate. Time of collapse and duration of contraction were similar in non-implanted collapsed blastocyst (KID- CB) when compared to implanted collapsed ones (KID+ CB).

MATERIALS AND METHODS: 340 cycles from the oocyte donation program of IVI Zaragoza (999 blastocysts (both fresh and cryopreserved) were transferred, from whose 375 had known implantation data (KID). Embryos were incubated in Embryoscope™ (Vitrolife) at 37°C, 5% CO2, 5% O2 and single step media (GLOBAL, Quermed). Only strong contractions were taken into account in the embryo selection for transfer.

RESULTS: From the 499 blastocysts transferred, 25.1% presented at least one contraction. According with the study of Marcos et al, there were no differences in hatching rate between CB (46.8%, [CI95% 38.0-55.6]) and NCB (43.5%, [CI95% 38.4-48.5]), but implantation rate was statistically lower in CB (46.8%, [CI95% 38.0-55.6]) and NCB (38.4%, [CI95% 38.0-48.5]), respectively. There were no differences in hatching rate between CB (46.8%, [CI95% 38.0-55.6]) and NCB (43.5%, [CI95% 38.4-48.5]), but implantation rate was statistically lower in CB (46.8%, [CI95% 38.0-55.6]) and NCB (38.4%, [CI95% 38.0-48.5]), respectively.

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DEVELOPMENT OF PERSONALIZED PREDICTIVE MODELS FOR NON-IVF AND IVF PROCEDURES IN LESBIAN AND SINGLE WOMEN SHEDS LIGHT ON APPLICABILITY OF INFERTILITY BIOMARKERS TO WOMEN OF UNKNOWN FERTILITY STATUS. A. Santisteban, K. Hunter Cohn, J. Schnorr, F. Arredondo, B. Miller, M. P. Leondires, J. Gutmann, L. Weckstein, E. S. Katz, J. Nulsen, P. C. Lin, A. B. Copperman, E. A. Widra, P. Yurttas Beim. Celmatix Inc, New York, NY; Coastal Fertility Specialists, Mount Pleasant, SC; Reproductive Medicine Associates of Texas, San Antonio, TX; RMA of Michigan, Rochester Hills, MI; RMA of CT, Norwalk, CT; RMA of Philadelphia, Philadelphia, PA; Reproductive Science Center of the San Francisco B, San Ramon, CA; REACH, Charlotte, NC; Center for Advanced Reproductive Services, Farmington, CT; Seattle Reproductive Medicine, Seattle, WA; Obstetrics and Gynecology, RMANY-Mount Sinai, New York, NY; Shady Grove Fertility, Washington, DC.

OBJECTIVE: Lesbian and single women routinely seek help conceiving at fertility centers. As with women seeking to conceive naturally, a subset of these women will learn that they are infertile. The evidence base for many infertility biomarkers is mostly comprised of data from women already experiencing difficulty conceiving. Here, we developed multi-variate predictive models for non-IVF (nIVF) and IVF outcomes built with data from lesbian and single women to see if infertility biomarkers have the same applicability to women of unknown fertility status.


MATERIALS AND METHODS: 17,149 nIVF and 3,301 autologous IVF cycles were used to model the cumulative probability of achieving ongoing pregnancy using Cox proportional hazard models with time-dependent covariates. All models controlled for described clinical factors. nIVF cycles included cycles with no medication, oral medication, and injectable gonadotropins. IVF cycles were restricted to single embryo transfer or double embryo transfer, and PGS cycles were excluded.

RESULTS: Controlling for patient age, there were no significant differences in success rates between lesbian and single women with nIVF (P=0.63) or IVF (P=0.46). Our models demonstrated that biomarkers significantly associated with nIVF outcomes included age, AMH levels below 1.5 ng/mL, basal antral follicle count (bAFC), BMI, and Day 3 levels of FSH, LH, and E2. By contrast, we were not able to observe a significant association of BMI, Day 3 FSH, LH, and E2 with IVF outcomes.

CONCLUSIONS: Our modeling shows that age, bAFC, and AMH are the most predictive factors across treatment types and women with known and unknown fertility status.

Supported by: Celmatix Inc.
OBJECTIVE: In the single embryo transfer era many ART cycles results in vitrification of supernumerary embryos to be used in a subsequent vitrified-warmed cycle. The purpose of this study is to determine whether the outcome of the fresh single blastocyst transfer may serve as a prognostic factor for the success of the following vitrified-warmed single blastocyst transfers using sibling embryos from the same cohort.

DESIGN: A retrospective cohort study performed at a single academic reproductive center.

MATERIALS AND METHODS: All vitrified-warmed single blastocyst transfers conducted at our center between 2012 and 2014 were reviewed. Data about the fresh cycle in which the embryos were created as well as data about the current vitrified-warmed cycle was collected. Pregnancy rate after vitrified-warmed single blastocyst transfers were compared between patients who conceived after the fresh embryo transfer and those who did not. Subgroup analysis according to the fresh cycle outcome (non-pregnant, biochemical pregnancy, miscarriage and live birth) was performed as well. Results were then validated using a logistic regression analysis adjusting for patient’s age, embryo quality and endometrial thickness.

RESULTS: During the study period 1429 vitrified-warmed single blastocyst cycles were performed. 302 freeze-all cycles (without fresh patient) and 123 cycles with more than one embryo transferred in the fresh cycle were excluded from our analysis. A total of 1004 cycles were analyzed: 432 of which the fresh cycle resulted in a pregnancy and 572 fresh cycles ending with a negative pregnancy result. Demographic characteristics and cycle parameters were comparable between the two groups. Pregnancy rates in the vitrified-warmed group performed with sibling embryos of a previously successful fresh cycle were comparable to those performed in patients with a failed fresh transfer. (52.5% vs 56.8% p = 0.18). However, in subgroup analysis according to the fresh cycles’ outcome (non-pregnant, chemical pregnancy, miscarriage and live birth) higher pregnancy rate were found in the group which achieve live birth in the fresh cycle (53.4% vs. 43.2% p = 0.13 adjusted OR 1.45 95% CI 1.04-2.02).

CONCLUSIONS: Live birth achieved after a fresh embryo transfer, may serve as a good prognostic factor for pregnancy in a subsequent vitrified-warmed single blastocyst transfer originating from the same cohort of embryos.

P-184 Tuesday, October 18, 2016
INCREASED RATE OF ADVERSE NEONATAL OUTCOMES AMONG TWINS FOLLOWING ASSISTED REPRODUCTIVE TECHNOLOGY. A. Y. Wang. Faculty of Health, University of Technology Sydney, Ultimo NSW, Australia.

OBJECTIVE: The literature is inconsistent regarding the association between assisted reproductive technology (ART) and twin outcomes. This study using a population approach investigates the maternal and neonatal outcomes between ART and non-ART twins.

DESIGN: A retrospective population cohort study using data from the National Perinatal Data Collections. The study included 19,662 twins born in Victoria, Queensland, Western Australia, Tasmania and the Australian Capital Territory between 2007 and 2011 in Australia.

MATERIALS AND METHODS: The analysis included 2290 (23.3%) ART twin sets and 7541 (76.7%) non-ART twin sets. Maternal and pregnancy characteristics were compared between ART and non-ART twin sets. The rates of adverse perinatal outcomes were compared between ART and non-ART twins. Chi-squared test and Student’s t-test were used for categorical and continuous variables respectively. Generalized Estimating Equations was used to assess the likelihood of any neonatal outcomes following ART, with adjusted odds ratio (AOR) and 95% confidence intervals (CI) presented. Weiberg’s differential rule was used to estimate the rate of monzygotic twins.

RESULTS: ART mothers were 3.3 years older than non-ART mothers. Compared to non-ART mothers, higher proportions of ART mothers were primiparous, non-smoking, with normal BMI and with private health insurance. The rates of pregnancy-induced hypertension and gestational diabetes were slightly higher for ART mothers than non-ART mothers (12.2% vs. 8.4% and (9.7% vs. 7.5%) respectively. Compared with non-ART twins, ART twins had higher rates of preterm birth (61.5% vs. 56.9% p < 0.01), low birth weight (55.3% vs. 51.3% p < 0.01), resuscitation (56.1% vs. 46.7%; p < 0.01), admission to neonatal intensive care unit (64.3% vs. 57.2%; p < 0.01) and hospital stay ≥ 5 days (80.5% vs. 66.9%; p < 0.01). In contrast, ART twins had significantly higher live birth rate than non-ART twins (98.6% vs. 97.7%; P < 0.01). Liveborn ART twins had 28% (AOR 1.28, 95% CI 1.09-1.80) increased odds of having any adverse neonatal outcome compared to liveborn non-ART twins. The incidence of monzygotic twins was 1.1% for ART twins and 0.6% for non-ART twins.

CONCLUSIONS: As ART twins had higher rates of adverse outcome, special antenatal care is recommended for them. Couples access ART should be fully informed the risk of adverse outcome following twin pregnancies.

References:
DESIGN: A retrospective cohort study.

MATERIALS AND METHODS: All non-polycystic ovary patients who underwent their first frozen-thawed embryo transfers in our unit and had basal serum AMH evaluated between 2010 and 2015 were evaluated in this study. Body mass index (BMI), age, body surface area (BSA), and total motile sperm count (TMC) were measured using the enzyme-amplified two-site immunoassay (ELISA) provided by Beckman Coulter (AMH Gen II ELISA, Beckman Coulter). Individualized controlled ovarian hyper-stimulation (COH) protocols included long GnRH agonist, GnRH antagonist and minimal stimulation protocols, based on individual patient characteristics. When at least two follicles reached 18 mm in diameter, 5000-10,000 IU hCG (Ovidrel, Merck Serono) was adopted to achieve final follicular maturation and oocyte retrieval performed 32-36 hours later. Intracytoplasmic sperm injection was performed if the concentration of motile sperm was <1x10^6/mL, otherwise a conventional in vitro fertilization was used. Vitrification was performed for embryo freezing with the use of a Cryotop (Kitazato Corp.) device. Embryo transfer was operated under trans-vaginal sonography guidance. The primary outcome is Live birth rate, which was defined as rate of deliveries that resulted in at least one live born baby per transfer cycle. Chi-square and binary regression were used for data analysis. A P<0.05 indicated significant result.

RESULTS: In total, 828 patients were included. We grouped them into three groups based on their baseline AMH concentration: low AMH group (<25), middle AMH (25-75) and high AMH level (>75). The results showed lower AMH level was associated with significantly lower implantation rate (21.9% vs. 43.2% vs. 58.8%, P<0.001), clinical pregnancy rate (32.0% vs. 55.2% vs. 65.7%, P<0.001), live birth rate (21.3% vs. 43.6% vs. 52.7%, P<0.001) but higher miscarriage rate (31.8% vs. 17.5% vs. 15.4% P<0.01). After stratifying the patients into two age groups, being younger or older than 35 years, we still observed significant influence of AMH on outcomes in all patients in both age groups. Furthermore, serum AMH kept significant in multivariate analysis when adjusting covariates (i.e. age, FSH, AFC, endometrium thickness, endometrium preparation protocols, number of embryos transferred, etiology of infertility). The area under the curve (AUC) for serum AMH, age, AFC and FSH were 0.635, 0.634, 0.615 and 0.543 respectively, for predicting live birth.

CONCLUSIONS: Our results demonstrated that baseline AMH was an independent predictive factor of live birth rate of frozen embryo transfers, irrespective of maternal age. It had only moderate predictive value on predicting live birth, superior to that of AFC and FSH.

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ADVERSE PERINATAL OUTCOMES ASSOCIATED WITH FERTILITY TREATMENT IN LATE PRETERM INFANTS. L. W. Sundheimer, E. T. Wang, C. Quant, C. Spades, C. F. Simmons, M. D. Pisarska. OB/GYN, Division of Reproductive Endocrinology and Infertility, Cedars-Sinai Medical Center, Los Angeles, CA; Obstetrics and Gynecology, Cedars Sinai Medical Center, Los Angeles, CA; Family Medicine, Cedars-Sinai Medical Center, Los Angeles, CA; OB/GYN, Cedars-Sinai Medical Center, Los Angeles, CA; Pediatrics, Cedars Sinai Medical Center, Los Angeles, CA; OB/GYN, Division REI, Cedars-Sinai Medical Center, Los Angeles, CA.

OBJECTIVE: To assess whether late preterm infants conceived by in vitro fertilization (IVF) and non-IVF treatment (NIFT) are at risk for adverse perinatal outcomes compared to spontaneously conceived infants.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: We included all singletons delivering between 340/7 to 36 6/7 gestational weeks at our center from January 1, 2013 to December 31, 2014. Mode of conception (spontaneous, IVF or NIFT) was determined from an electronic chart review of delivery, perinatal, neonatal intensive care unit (NICU) reports. Standard descriptive statistics were used to describe the study population and compared across the three groups. The primary outcome was NICU admission; secondary outcomes were Apgar scores and length of infant hospital stay. To determine whether IVF or NIFT infants had a higher risk of NICU admission, we performed multivariate logistic regression adjusting for maternal age, delivery method, and gestational age.

RESULTS: Of 585 singleton deliveries, there were 523 spontaneous, 47 IVF (8.0%) and 15 NIFT conceptions (2.6%). The fertility treatment women were older (32.9±5.4 vs. 33.6±4.6 vs. 39.5±4.3 years, P<0.001) and of a lower parity (0.71±0.94 vs. 0.47±0.83 vs. 0.33±0.53, P<0.001), but otherwise similar across race, BMI, and infant birth weight and gestational age at delivery (p>0.05). Notably, IVF infants were more likely to be delivered by cesarean section (73.9%) compared to spontaneous (40.3%) and NIFT (46.7%) infants (p<0.001). Sixty percent of NIFT infants and 46.8% of IVF infants were admitted to the NICU compared to 28.5% of spontaneous infants (p=0.002). Five minute Apgar scores were lowest among IVF infants (8.2±1.3), while spontaneous and NIFT infant scores were 8.7±0.8 and 8.8±0.4 respectively (p=0.0039). In multivariate logistic regression analyses, NIFT infants (Odds Ratio 4.11, 95% CI 1.33-12.76) and IVF infants (OR 2.28, 95% CI 1.13-4.60) had a higher risk of NICU admission.

CONCLUSIONS: Within the late preterm cohort, the IVF and NIFT infants are admitted to the NICU more often with lower Apgar scores and a longer hospital stay, despite similar gestational age and birth weights as compared to spontaneously conceived infants.

Supported by: NICHD R01 HD074368.

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OBJECTIVE: To elicit the impact of ovulation method and cycle stimulation on pregnancy and live birth rates in intra-uterine insemination (IUI) candidates using donor semen.

DESIGN: A retrospective cohort study of patients undergoing IUI using donor semen who attended a hospital-based fertility clinic between January 2009 and December 2014. A total of 632 cycles were evaluated from 233 patients.

MATERIALS AND METHODS: Cycles were analysed based on ovulation method, natural luteinizing hormone (LH) surge (n=280) versus ovulation trigger with hCG or Ovidrel® (n=320), and 32 cycles were excluded from this evaluation due to hybrid methodology. Cycles were separately analysed based on cycle stimulation, natural unmediated (n=222) versus medicated (n=410) with further subdivision based on medication type (clomiphene citrate, gonadotropin only, aromatase inhibitor, gonadotropin plus GnRH antagonist). Patients were followed for clinical pregnancy rate and live birth rate per insemination overall as well as specifically for multiples. Data was analysed for statistical significance using the statistical package for the social sciences (SPSS).

RESULTS: In the ovulation method analysis there was a trend towards higher clinical pregnancy rates [22.2%(71/320) versus 17.9%(50/280)] and live birth rates [19.1%(61/320) versus 16.4%(46/280)] in the trigger group relative to the natural LH surge. Five minute Apgar scores were lowest among IVF infants [8.8±0.94 versus 8.7±0.47 versus 8.4±0.83, p=0.014]. After stratifying the patients into two age groups, being younger or older than 35 years, we still observed significant influence of AMH on outcomes in all patients in both age groups. Furthermore, serum AMH kept significant in multivariate analysis when adjusting covariates (i.e. age, FSH, AFC, endometrium thickness, endometrium preparation protocols, number of embryos transferred, etiology of infertility). The area under the curve (AUC) for serum AMH, age, AFC and FSH were 0.635, 0.634, 0.615 and 0.543 respectively, for predicting live birth.

CONCLUSIONS: Our results demonstrated that baseline AMH was an independent predictive factor of live birth rate of frozen embryo transfers, irrespective of maternal age. It had only moderate predictive value on predicting live birth, superior to that of AFC and FSH.

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OOCYTE UTILIZATION RATE AS PREGNANCY POTENTIAL INDICATOR (A MULTICENTRIC STUDY). S. Hamamaha P. Barriere a, b CHU Nantes, Nantes, France; b CHU Nantes, Nantes, France.

OBJECTIVE: How many mature (MII) oocytes obtained after ICSI are required to achieve an ongoing pregnancy in different age classes of women undergoing ICSI?

STUDY OF INTRA-UTERINE INSEMINATION WITH DONOR SEMEN: A RETROSPECTIVE COHORT STUDY. S. Hamamaha P. Barriere. a, b CHU Nantes, Nantes, France; b CHU Nantes, Nantes, France.
DESIGN: This was a multicentre retrospective audit on anonymised outcome data captured in an Excel file, then merged and analysed centrally. Overall data came from 7791 females who had 16 279 oocyte retrievals. Data was captured from ICSI only treatment cycles in which ovarian stimulation was with follitropin alfa. Data capture was from 2011 to September 2015. Additional outcome information was obtained from subsequent vitrified embryo transfer cycles carried out in the same female cohort.

MATERIALS AND METHODS: Five French IVF centres having been involved in Fertility treatment for over 10 years participated. Female age was categorized into 5 groups (25-29 years; 30-34; 35-37; 38-39 and ≥40). Main assessment criterion was clinical pregnancy. Nonparametric LOESS method was used to estimate the relationship between pregnancy and the number of MII oocytes (on all attempts). Relationship between pregnancy at 1st attempt and female age and number of MII oocytes was estimated by logistic regression. Each cycle was considered as independent. Furthermore, over 30% of the cryopreserved embryos have not been used yet, representing residual clinical pregnancy and live birth potential not evaluated by the method.

RESULTS: The mean female age was 33 ±5 years and 74.6% of cycles were the first attempt and only a few (2.6%) were in the rank of 5 or more. There were in total 3979 clinical pregnancies and 804 (21.5%) from subsequent vitrified-thawed cycles. The pregnancy rate increased with the number of MII oocytes (up to 20), but in women older than 38 as few high numbers of MII oocytes were retrieved, it is not possible to give an accurate estimate in these age classes. Taking into account all fresh and frozen pregnancies, the number of MII oocytes required to achieve a pregnancy stayed relatively steady below 37 years (25-29, 23.6; 30-34, 24.7; 35-37, 35.0) and then decreased in subsequent age classes: 34.8 at 38-39 years and 37.7 at 40 years or more. These numbers revealed that the pregnancy cumulative OUR remained stable between 4.2% (years 25-29) and 4.0% (years 35-37) and then decreased to 2.7% in women 40 or older. In a multiple logistic regression analysis on the first attempt, female age (p < 0.0001) and number of retrieved MII oocytes were negatively (p < 0.0001) and positively related to pregnancy, respectively.

CONCLUSIONS: Our results should lead to improve couple management. Moreover, these data may provide a tool to estimate the number of metaphase II oocytes needed to achieve a clinical pregnancy and live birth in case of female fertility preservation.

Supported by: An educational grant was provided by Finox AG for centralized data management and statistical analysis.

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HOW DOES ART SINGLETONS DIFFER FROM NATURALLY CONCEIVED (NC) SINGLETONS; COMPARISON OF PERINATAL DATA OF 872 ART TO 19317 (NC) SINGLETON BABIES. A. Khudhari, R. Hemmings, S. Phillips, A. M. Badeghiesh, W. Jamal, M. H. V. Gynecology/Infertility and Reproductive Endocrinology, Montreal, QC, Canada; Oh-Gyn, McGill University, Westmount, QC, Canada; OVO Fertility, Montreal, QC, Canada; McGill University, Montreal, QC, Canada; OBGYN University of Montreal, OVO Clinic, Montreal, QC, Canada.

OBJECTIVE: It has been suggested that the fresh transfer of single embryo following ovarian stimulation is associated with smaller birth weight than naturally conceived singleton for a similar gestational age. Perinatal outcomes from a large Danish database (Henningsen et al. 2011) showed that the birth weight of stimulated IVF singleton babies is significantly smaller than naturally conceived ones. There is limited data on the birth weight and the average gestational age at birth of modified natural in vitro-fertilization (mnIVF) conceived babies. Does (mnIVF) singleton birth weight and gestational age at delivery differ from stimulated IVF (sIVF), frozen embryo transfer (FET) and naturally conceived (NC) singleton babies?

DESIGN: A retrospective cohort study chart review between the outcome of IVF cycles and spontaneous pregnancy from January 2010 to December 2014.

MATERIALS AND METHODS: The gestational age and birth weight of singleton babies conceived from (246) mnIVF, (405) sIVF and (233) FET following the single embryo transfer on day 2.3 or 5 post-fertilisation at OVO fertility clinic were compared to 19,317 naturally conceived singleton babies delivered at a community hospital in Montreal. Secondary outcomes included the type of delivery and gender.

RESULTS: The average gestational ages at delivery were not clinically different although statistically significant: 38.8 weeks mnIVF, 38.8 weeks sIVF, 39.2 weeks FET babies versus 39.1 of gestation for naturally conceived babies (p <0.0001). Average birth weight were comparable for mnIVF, sIVF versus NC singleton babies (3301 grams, 3263 grams versus 3353 grams) yet FET babies had significantly higher birth weights 3453 grams (p = 0.0001).

CONCLUSIONS: We found that the mean birth weight of mnIVF conceived singleton babies did not differ significantly from the NC or sIVF singleton babies. Yet in comparison to previous reports, FET singleton babies had higher birth weights. The average gestational age at delivery was

Clinical pregnancy and live birth per cycle relative to donor age group < 25 years

<table>
<thead>
<tr>
<th></th>
<th>All cycles (n=527)</th>
<th>Donor age &lt;25 years</th>
<th>Donor age 25–30 years</th>
<th>Donor age ≥30 years</th>
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</thead>
<tbody>
<tr>
<td>Fresh</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinical pregnancy</td>
<td>n=414</td>
<td>n=153</td>
<td>n=207</td>
<td>n=54</td>
</tr>
<tr>
<td>208 (50.2%)</td>
<td>67 (43.8%)</td>
<td>114 (55.1%)</td>
<td>1.3 [1.01-1.6]</td>
<td>27 (50.0%)</td>
</tr>
<tr>
<td>Live birth</td>
<td>180 (43.5%)</td>
<td>60 (39.2%)</td>
<td>98 (47.3%)</td>
<td>1.2 [0.95-1.5]</td>
</tr>
<tr>
<td>Frozen-thawed</td>
<td>n=113</td>
<td>n=35</td>
<td>n=57</td>
<td>n=21</td>
</tr>
<tr>
<td>Clinical pregnancy</td>
<td>36 (31.9%)</td>
<td>9 (25.7%)</td>
<td>18 (31.6%)</td>
<td>1.2 [0.62-2.4]</td>
</tr>
<tr>
<td>Live birth</td>
<td>33 (29.2%)</td>
<td>9 (25.7%)</td>
<td>15 (26.3%)</td>
<td>1.1 [0.52-2.2]</td>
</tr>
<tr>
<td></td>
<td>n=25</td>
<td>n=8</td>
<td>n=17</td>
<td>n=1</td>
</tr>
</tbody>
</table>

RESULTS: Median donor age was 26 years (range: 18-34), and median recipient age and partner age were both 42 years. Among fresh cycles, increasing donor age was associated with fewer oocytes retrieved (p<0.001), but not with fertilization rate (p=0.86). For both fresh and frozen-thawed cycles, the donor age groups were similar with regard to recipient age and body mass index, as well as partner age, indication for donation, and number of prior treatment cycles. Recipients who used the youngest donors (<25 years) had lower clinical pregnancy and live birth rates compared with the older age groups for both fresh and frozen-thawed cycles, although not all of these findings reached statistical significance. Recipients who used donors age 25 to <30 years had a significantly higher clinical pregnancy rate (relative risk: 1.3; 95% confidence interval: 1.01-1.6) compared with recipients who used the youngest donors.

CONCLUSIONS: Oocyte donor age <25 years was not associated with better outcomes after IVF. The optimal donor age range may be 25 to <30 years.

Supported by: Harvard Catalyst, The Harvard Clinical and Translational Science Center (National Center for Research Resources and the National Center for Advancing Translational Sciences, National Institutes of Health Award UL1 TR001102) and financial contributions from Harvard University and its affiliated academic healthcare centers.
clinically comparable with no influence on the average birth weight of the four cohorts.

References:

Supported by: ovo fertility.

P-191 Tuesday, October 18, 2016

A HIGH PREVALENCE OF ABNORMAL EMBRYOS AFTER AN IVF/PGS CYCLE SHOULD NOT DETER PATIENTS FROM PURSING A SECOND CYCLE. J. Rodriguez-Purata, a L. Sekhon, a, b J. A. Lee, a M. C. Whitehouse, a E. Cervantes, a M. Luna, a C. Briton-Jones, a T. Mukherjee, a, b A. B. Coppersman, a, b B. Sandler, a, b, 9 Reproductive Medicine Associates of New York, New York, NY; 10 Obstetrics, Gynecology and Reproductive Science, Icahn School of Medicine at Mount Sinai, New York, NY.

OBJECTIVE: Preimplantation genetic screening (PGS) remains the most objective selection criterion used by clinicians prior to ET. Aneuploidy assessment by PGS is suggested, among other causes, to patients of advanced maternal age, repeated implantation failure (RIF), recurrent miscarriage or with unexplained factor infertility. Patients who experience an elevated aneuploidy rate after their first cycle find themselves in a challenging position; unsure if pursuing another IVF cycle might attain similar rates. This study sought to evaluate patients with an elevated rate of aneuploidy at first IVF/PGS cycle that completed a second cycle.

DESIGN: Retrospective.

MATERIALS AND METHODS: All patients who underwent 2 IVF/PGS cycles in which the first cycle yielded an aneuploidy rate of >80% were included. Cycles with ≤4 embryos biopsied in any cycle were excluded. Demographics and cycle characteristics were studied. Aneuploidy rate in the second cycle was described. A secondary analysis was carried out to identify variables that associated to embryos display a >80% aneuploidy rate in second cycle assessment. Student’s t-test was used for continuous variables, and the X2 test was used for categorical variables. Significance was confirmed a p<0.05.

RESULTS: Twenty-six patients (n=52 cycles) met the inclusion criteria. Diagnoses included genetic (n=8), male factor (n=5), ovulatory dysfunction (n=4), DOR (n=3), RPL (n=2), elective freezing (n=2), endometriosis (n=2). All demographic characteristics (age, day 3 FSH, AMH, BMI, oocytes retrieved, fertilized and embryos biopsied) were similar between groups. In the first cycle, embryo aneuploidy rates were 91.2% (187/205). During the 2nd cycle, the proportion of embryos with euploidy number was 67.4% (132/196). Three patients (11.5%) presented 100% of aneuploidy in both cycles (34/34). A secondary analysis was carried out comparing patients (n=9) who had ≥80% of the embryos abnormal in the second cycle (94.7% (54/57)) vs. those (n=17) with <80% abnormal (56.1% (78/139)). The average age was higher (38.9±4.1 vs. 36.2±4.5) and the average number of embryos biopsied were lower (6.3±5.0 vs. 8.2±3.8) in the former group, although this was not statistically significant. The average number of oocytes retrieved were statistically lower (13.2±5.2 vs. 20.6±6.8, p<0.05) in patients with ≥80% of the embryos abnormal in the second cycle. Day 3 FSH (4.3±3.1 vs. 5.9±2.2), AMH (2.1± 2.0 vs. 3.3±3.1) and BMI (22.3±2.2 vs. 24.1±5.4) were similar between groups.

CONCLUSIONS: As a selection tool, PGS continues to improve IVF effectiveness. This study’s results demonstrate that patients can be comforted in knowing that their first cycle aneuploidy outcomes are not definite, and, although there is no guarantee, pursuing subsequent cycles might yield high quality embryo.

P-192 Tuesday, October 18, 2016

THE CONFOUNDER EFFECT OF A LIVE DELIVERED PREGNANCY OR NOT IN THE FIRST FRESH EMBRYO TRANSFER (ET) ON THE OUTCOME OF THE FIRST FROZEN ET. J. H. Check, a R. Cohen, a C. Wilson, a Dept. OB/GYN, Cooper Medical School of Rowan University, Melrose Park, PA; a Cooper Institute for Reproductive and Hormonal Disorders, P.C., Mt. Laurel, NJ.

OBJECTIVE: There are only a limited number of chromosomally normal embryos in a given cohort following oocyte retrieval and embryo develop-

ment. Thus, the possibility exists that the live delivered pregnancy rate in the next ET using frozen-thawed embryos will be lower in women with successful live delivery than women who failed to have a success with the fresh ET because of a potential lower likelihood of having a normal embryo by the process of elimination. The present study was designed to corroborate or refute that hypothesis.

DESIGN: Retrospective cohort comparison study.

MATERIALS AND METHODS: All first controlled ovarian hyperstimulation (COH) in vitro fertilization-ET (IVF-ET) cycles in women age ≤39 during a 10-year time period were reviewed. A subset of those having a subsequent frozen ET from that cohort of embryos were identified. This group was then stratified according to whether these women had a live delivery or not from the fresh ET cycle. The pregnancy and implantation rates in the subsequent frozen ET cycle were then compared in 3 age groups; ≤35, 36-39, and 40-42. All ETs were on day 3.

RESULTS:

Pregnancy rates from frozen ET based on achieving a live birth from the fresh ET

<table>
<thead>
<tr>
<th>Patients with previous pregnancy from fresh IVF cycles</th>
<th>Patients without previous pregnancy from fresh IVF cycle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (&lt;35)</td>
<td>Number of transfers</td>
</tr>
<tr>
<td>320</td>
<td>84</td>
</tr>
<tr>
<td>953</td>
<td>396</td>
</tr>
</tbody>
</table>

Though all age groups showed a trend for lower clinical and live delivered pregnancy rates in those failing to have a live baby in the fresh ET, the only significant comparison showing a statistically significant difference by chi-square analysis was the implantation rates in women aged <35 (p<0.01). The live delivered pregnancy rates in women <35 approached significance with p=0.08.

CONCLUSIONS: One study found that the average number of chromosomally normal blastocysts available for transfer in women who averaged age 35 was 1.8, and another study found that there was an average of 1 live baby per IVF cycle considering the eventual transfer of all embryos created. These data refute the hypothesis that a successful pregnancy from the fresh ET has a negative effect on the chance of a live delivery from the frozen ET. These results could be explained by several theories: 1) some women tend to make more chromosomally normal embryos than others and are thus more fertile. 2) Failure to conceive on the first fresh ET may be related to other factors (endometrial or immunological) that persist in the frozen ET cycle. The fact that implantation and pregnancy rates showed a trend in all age groups to be lower in those who failed in the fresh ET suggests that COH adversely effecting implantation does not play a major role as to why a woman fails to conceive in a COH, IVF-ET cycle.

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OBJECTIVE: To model the probability of a live birth and multiple births after assisted reproductive technology using factors in the Society for Assisted Reproductive Technology Clinic Outcomes Reporting System that are available to the treating physician in addition to the demographic and medical history factors used in the patient predictor model.

DESIGN: Longitudinal cohort.

MATERIALS AND METHODS: We included all fresh autologous cycles for reporting years 2006 to 2013. In the patient predictor model, live birth rates were modeled by reporting year, woman’s age, body mass index (BMI), gravidity, prior full-term births, infertility diagnoses, and number of embryos transferred. We extended that model to include number of oocytes retrieved and number of embryos cryopreserved, as well as to be an explicit function of day of transfer (day 3 or day 5).

FERTILITY & STERILITY®
OBJECTIVE: Increased BMI is associated with negative impact on reproductive outcomes in Assisted Reproductive Technology (ART), implying a role of defective endometrial receptivity. Recently, it has been suggested that the oocyte quality contributes to a reduction in clinical pregnancy rates with increasing donor BMI, since the odds of clinical pregnancy and live birth declined with increasing single units of BMI (1 kg/m²). The aim of the present study is to assess the impact of donor BMI in live birth rates (LBR) in a large cohort of recipients of donated oocytes.

RESULTS: Results of the model fitting for a nulligravid woman with endometriosis are shown below, varying BMI within constant age, and varying number of oocytes retrieved and embryos cryopreserved within constant age and BMI.

CONCLUSIONS: Day of transfer, number of embryos transferred, and woman’s age have the greatest influence on live birth rates and multiple birth rates. Number of oocytes retrieved/embryos cryopreserved, as a surrogate measure of embryo quality, also affects these rates.

Supported by: SART.

P-195 Tuesday, October 18, 2016

RISK FACTORS FOR ABNORMAL UMBILICAL CORD INSERTIONS AMONG TERM SINGLETON ART PREGNANCIES.


OBJECTIVE: The placenta with velamentous umbilical cord insertion (VCI) is a rare pathologic condition that is supposed to increase the risk of perinatal complications. The reported adverse outcomes include fetal growth restriction, non-reassuring fetal status requiring emergency Cesarean section, fetal exsanguination due to the rupture of vasa previa, and cerebral palsy. We reported on a study, emphasizing a higher incidence of the placenta accompanied by VCI in ART pregnancies when compared with non-ART cases, at the 70th ASRM Annual Meeting. In this research, we examined the ART-conceived cases closely for the purpose of identifying the ART-associated risk factors that might affect the incidence of the placenta with VCI.

DESIGN: Retrospective cohort study and comparative analysis.

MATERIALS AND METHODS: We reviewed the records of 427 consecutive singleton, term labor and delivery ART-conceived cases from January 2011 to April 2016. Information about maternal age, obstetric history, details of ART treatment, mode of delivery, and insertion site of the umbilical cord was all collected from their medical records. Our study population was divided into two categories as follows: cases with VCI (Group B: n=404), and cases without VCI (Group B: n=404). Odds ratios for VCI, 95% confidence intervals (CI), and significance of the odds ratio were calculated according to ART-related variables (i.e., fertilization method (conventional-IVF vs. ICSI), type of embryo (fresh vs. frozen-thawed), embryo transfer timing (day 2-3 early-cleavage stage embryo vs. day 5-6 blastocyst), and fetal sex), using multivariate logistic regression.

RESULTS: Maternal basal characteristics and odds ratios were shown in the table below. The incidence of VCI in our study population was 5.4% (23/427). The rate of delivery necessitating emergency C-section or operative vaginal delivery in Group A (14/23, 61%) was much higher than in Group B published study that presented opposite results. We observe that increase BMI in the recipient population is associated with a significant decrease in LBR and CLBR most probably due to a defective endometrial receptivity. Therefore, any deleterious effect of the BMI in the reproductive outcomes could be exerted through a defective endometrial receptivity and probably not due to a negative impact at the oocyte level. Main strength: The big sample size in a single center. Limitations: The retrospective design and characteristics of the population of mainly non-obese donors and recipients.

Baseline characteristics and adjusted odds ratio(aOR) for velamentous umbilical cord insertion

<table>
<thead>
<tr>
<th>Group A (cases with VCI: n=23)</th>
<th>Group B (cases without VCI: n=404)</th>
<th>aOR for VCI (95% CI, P value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal age</td>
<td>35.9±3.8</td>
<td>35.5±3.6</td>
</tr>
<tr>
<td>0.05 was considered statistically significant.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| Parity (primipara / multipara)  | 20 / 3                             | 302 / 102                   |
| 1.00 (0.92 - 1.09, 0.18)        |
| c-IVF / ICSI                   | 5 / 18                             | 143 / 261                   |
| 1.00 / 1.96 (0.76 - 0.65, 0.19) |
| Fresh / Frozen-thawed          | 7 / 16                             | 136 / 268                   |
| 1.00 / 1.25 (0.52 - 3.34, 0.63) |
| Early cleavage / Blastocyst    | 1 / 22                             | 117 / 287                   |
| 1.00 / 10.23 (2.09 - 184.78, 0.02*) |
| Male / Female                  | 5 / 18                             | 200 / 204                   |
| 1.00 / 3.48 (1.35 - 10.71, 0.02*) |

Supported by: SART.

**P-196 Tuesday, October 18, 2016**


OBJECTIVE: To update the models used to predict a live birth and multiple births after assisted reproductive technology that is implemented on the Society for Assisted Reproductive Technology website (Predict My Success) (1, 2).

DESIGN: Longitudinal cohort.

MATERIALS AND METHODS: Live birth rates and probabilities of a multiple birth were modeled by woman’s age, body mass index (BMI), gravidity, prior full-term births, infertility diagnosis, oocyte source (autologous, donor), and number of embryos transferred, as well as year of treatment and day of transfer, using backward-stepping logistic regression. We included all fresh cycles for reporting years 2006 to 2013. The estimates were standardized to 2013; i.e., when year is included in the models, the coefficient for 2013 is used for prediction. When models include day of transfer, the estimates are averaged over day of transfer using the relative rates in 2013. Age is modeled by up to a cubic polynomial.

RESULTS: Including age as a polynomial improved the estimates at older ages. During the period 2006-2013 there has been a shift in day of transfer from 3 to 5 (shown for single embryo transfer, SET, and double embryo transfer, DET, in the table below); including day of transfer in the model reduced the effect of year of treatment.

<table>
<thead>
<tr>
<th>Percent Day 5 Transfers of Day 3 + Day 5 Transfers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autologous</td>
</tr>
<tr>
<td>Year</td>
</tr>
<tr>
<td>2004</td>
</tr>
<tr>
<td>2005</td>
</tr>
<tr>
<td>2006</td>
</tr>
<tr>
<td>2007</td>
</tr>
<tr>
<td>2008</td>
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<tr>
<td>2009</td>
</tr>
<tr>
<td>2010</td>
</tr>
<tr>
<td>2011</td>
</tr>
<tr>
<td>2012</td>
</tr>
<tr>
<td>2013</td>
</tr>
</tbody>
</table>

CONCLUSIONS: The updated models provide estimates that are more closely aligned with current results.

References:

**P-197 Tuesday, October 18, 2016**

ECTOCYTOPLACENTAL PREGNANCY RELIANCE DEPENDS ON THE ASSISTED REPRODUCTION PROTOCOL. S. Daneshmand,a,b C. E. Bedient,a,b F. Garner,a,b B. S. Shapiro,a,b aFertility Center of Las Vegas, Las Vegas, NV; bObstetrics and Gynecology, University of Nevada School of Medicine, Las Vegas, NV.

OBJECTIVE: To compare ectopic pregnancy rates among various IVF protocols, using fresh autologous transfers as a control group.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: All pregnancies resulting from blastocyst transfer in 2004-2015 were included. Blastocyst transfer was the standard of care for all patients throughout the study period, regardless of age or cohort size. Ovarian stimulation was performed with HMG and recombinant FSH in combination, with GnRH antagonist for pituitary suppression. Artificial endometrial preparation with exogenous estradiol and progesterone was used in all oocyte donation recipients and frozen-thawed embryo transfers (FET). Pregnancy was indicated by rising serum hCG titers 10 days post-transfer. Ectopic pregnancies included treated persistent pregnancies of unknown location (TPPUL) treated with methotrexate and ultrasonographically visualized ectopic pregnancies (VEP) on the adnexa. Fisher’s exact test was used for all bivariate comparisons. All ectopic pregnancy rates are per pregnancy, not per transfer.

RESULTS: This study included 1011 pregnancies following fresh autologous blastocyst transfer (control group), 433 pregnancies following fresh oocyte donation cycles, 2142 following autologous FET, and 332 following oocyte donation FET. The rates of TPPUL were 2.47% (control group), 0.00% (P = 0.0002), 0.75% (P = 0.0001), and 0.00% (P = 0.0015), respectively. The rates of VEP were 1.48% (control group), 0.00% (P = 0.0081), 0.14% (P = 0.001), and 0.30% (P = 0.1397). Total ectopic pregnancy rates (including TPPUL and VEP) in these groups were 3.96% (control group), 0.00% (P < 0.0001), 0.89% (P = 0.0001), and 0.30% (P = 0.0002), respectively.

CONCLUSIONS: TPPUL, VEP, and total ectopic pregnancy risks are associated with the ART protocol, with fresh autologous transfer having generally greater ectopic pregnancy risk than fresh oocyte donation, Autologous FET, and donor FET cycles. Protocols without recipient uterine exposure to ovarian stimulation had lower ectopic pregnancy risk than did the control group of fresh autologous transfers, suggesting a potential causal relationship.
on first-trimester ultrasound were excluded. Linear regression models were utilized to assess the association between peak estradiol and birth weight with and without adjustment for potential confounders. A receiver operating characteristic (ROC) curve was generated to estimate the optimal peak estradiol cut-point for prediction of LBW based on the Youden index (1 - sensitivity + specificity -1). The area under the curve (AUC), a predicted probability, was calculated to determine the ability of peak estradiol level to discriminate between patients with and without LBW.

RESULTS: One hundred eighty-three cycles met inclusion criteria. Univariate analysis showed that mean birth weight decreased by 45.28 g (95% CI= -84.14, -6.39; P=0.02, R² = 0.02) for each 500 pg/mL increase in peak estradiol. This association was no longer significant after adjusting for maternal age, BMI, infant sex, gestational age, and reason for IVF (-25.88 g per 500 pg/mL, 95% CI = -55.13, 3.36; P=0.08), but these predictors jointly explained 50% of the variance in birth weight. The optimal peak estradiol cut-point for prediction of LBW based on the Youden index was 3,991 pg/mL, resulting in 90% specificity, 33% sensitivity, 94% negative predictive value (NPV), and 23% positive predictive value (PPV). This dichotomized peak estradiol together with maternal age, BMI, infant sex, gestational age, and parity gave an AUC of 89% for LBW.

CONCLUSIONS: Peak serum estradiol is associated with birth weight but the strength of the association is reduced after controlling for potential confounders. The optimal peak estradiol cut-point based on the Youden index is 3,991 pg/mL. At this cut-point, peak estradiol has high NPV but low PPV for prediction of LBW.

References:

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OBJECTIVE: It is recommended that thyroid-stimulating hormone (TSH) level of early pregnant women is maintained below than 2.5 mIU/L. However, the reference value of the preconception TSH has not been established. The purpose of this study is to determine whether the preconception TSH level is affecting the pregnancy outcome in women undergoing in vitro fertilization (IVF).

DESIGN: Retrospective study.

MATERIALS AND METHODS: Six hundred sixty-three infertile patients who had a history of two IVF failure at least and attended to the Assisted Reproduction Clinics of our tertiary care institution between January 2013 and January 2015 were included in this study. PAI-1 gene polymorphisms were detected using PCR prior to any controlled ovarian hyperstimulation. The patients were merged into three groups as followings: 5G/5G (Normal), 4G/5G (Heterozygote), 4G/4G (Homozygote). Individual characteristics and IVF outcomes were compared among groups.

RESULTS: The ages, FSH levels (Day 3), mean number of oocytes retrieved, fertilisation rate and the number of transferred good quality embryos were comparable among groups. Clinical pregnancy rates were 25%, 34.1%, 34.9%, respectively, and there was no significant difference among them. Also, live birth rates were comparable among groups.

CONCLUSIONS: The present study indicated that different PAI polymorphism states had no effect on IVF outcomes of patients who had recurrent IVF failure. Footnote of the table: CI: Confidence interval, PAI: Plasminogen Activator Inhibitor. Values were given as mean±standard deviation, median (range), or number (percentage).

References:

Table. Comparison of demographics and IVF outcomes among PAI polymorphism states.

<table>
<thead>
<tr>
<th>Variables</th>
<th>5G / 5G (n=48)</th>
<th>4G / 5G (n=88)</th>
<th>4G / 4G (n=43)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>31.58±3.96</td>
<td>30.62±4.24</td>
<td>30.18±4.21</td>
<td>0.251</td>
</tr>
<tr>
<td>Day-3 FSH (mIU/mL)</td>
<td>7.22±2.55</td>
<td>7.52±2.28</td>
<td>6.64±1.70</td>
<td>0.109</td>
</tr>
<tr>
<td>Cause of Infertility</td>
<td>48 (26.82)</td>
<td>88 (49.16)</td>
<td>43 (24.02)</td>
<td>0.943</td>
</tr>
<tr>
<td>Duration of infertility (&lt;)</td>
<td>5 (1-15)</td>
<td>6 (1-21)</td>
<td>5 (1-17)</td>
<td>0.398</td>
</tr>
<tr>
<td>Number of retrieved oocytes</td>
<td>10.90±5.63</td>
<td>9.36±4.85</td>
<td>9.95±6.21</td>
<td>0.291</td>
</tr>
<tr>
<td>Number of embryos</td>
<td>3.5 (1-16)</td>
<td>4 (1-14)</td>
<td>2 (1-16)</td>
<td>0.349</td>
</tr>
<tr>
<td>Number of transferred good quality embryos</td>
<td>23 (47.9)</td>
<td>54 (61.4)</td>
<td>26 (60.5)</td>
<td>0.287</td>
</tr>
<tr>
<td>Fertilization rate</td>
<td>60.86±25.85</td>
<td>67.20±22.51</td>
<td>55.73±25.53</td>
<td>0.341</td>
</tr>
<tr>
<td>Clinical pregnancy rate</td>
<td>12 (25.0)</td>
<td>30 (34.1)</td>
<td>15 (34.9)</td>
<td>0.491</td>
</tr>
<tr>
<td>Live birth rate&gt;24 wks</td>
<td>7 (14.6)</td>
<td>9 (10.2)</td>
<td>9 (20.9)</td>
<td>0.250</td>
</tr>
</tbody>
</table>

RESULTS: Four hundred sixty patients of the study subjects had serum TSH level < 2.5 mIU/L and 203 patients ≥ 2.5 mIU/L. There were no statistically significant differences in age, periods of infertility, BMI, the number of metathesis II (MII) oocytes at ovum pick-up day, the number of transferred embryos and anti-mullerian hormone (AMH) level of patients between the study groups. The clinical pregnancy rate in the group of patients with TSH < 2.5 mIU/L and those with ≥ 2.5 mIU/L were 40.90% and 42.90% respectively (p value = 0.632). The live birth rates in the group of patients with TSH < 2.5 mIU/L and those with ≥ 2.5 mIU/L were 33.5% and 35% respectively (p value = 0.707). The chemical abortion rates in the group of patients with TSH < 2.5 mIU/L and those with ≥ 2.5 mIU/L were 11.1% and 8.4% respectively (p value = 0.289). The miscarriage rates in the group of patients with TSH < 2.5 mIU/L and those with ≥ 2.5 mIU/L were 18.1% and 18.4 % respectively (p value = 0.951).

CONCLUSIONS: There was no significant difference between the IVF outcomes of the normal-TSH-level groups of <2.5 mIU/L and ≥ 2.5 mIU/L.

P-200 Tuesday, October 18, 2016
THE FREQUENCY OF PLASMINOGEN ACTIVATOR INHIBITOR (PAI) POLYMORPHISM AND ITS EFFECTS ON RECURRENT IVF FAILURE. E. Ersoy, N. Yilmaz, A. Ersoy, A. Karatas, Y. Engin-Ustun, Obstetrics and Gynecology, Zekai Tahir Burak Women's Healthcare Training and Research Hospital, Ankara, Turkey; Reproductive Endocrinology Department, ZTB, Ankara, Turkey; Zekai Tahir Burak Women's Healthcare Training and Research Hospital, Ankara, Turkey; Obstetrics and Gynecology, Abant Izzet Baysal University, Bolu, Turkey.

OBJECTIVE: Recurrent IVF failure is still a challenging clinical situation. Plasminogen Activator Inhibitor (PAI) enzyme polymorphisms have been recently cited to be associated with endometrial receptivity which is about the differential effect of PAI-1 enzyme activity on extracellular matrix degradation (1). Here we aimed to investigate the frequency of different PAI polymorphism groups and their effects on IVF outcomes.

DESIGN: Retrospective cross-sectional study.

MATERIALS AND METHODS: One hundred seventy-nine nulliparous patients who had a history of two IVF failure at least and attended to the Assisted Reproduction Clinics of our tertiary care institution between January 2013 and January 2015 were included in this study. PAI-1 gene polymorphisms were detected using PCR prior to any controlled ovarian hyperstimulation protocols. The patients were merged into three groups as followings: 5G/5G (Normal), 4G/5G (Heterozygote), 4G/4G (Homozygote). Individual characteristics and IVF outcomes were compared among groups.

RESULTS: The ages, FSH levels (Day 3), mean number of oocytes retrieved, fertilisation rate and the number of transferred good quality embryos were comparable among groups. Clinical pregnancy rates were 25%, 34.1%, 34.9%, respectively, and there was no significant difference among them. Also, live birth rates were comparable among groups.

CONCLUSIONS: The present study indicated that different PAI polymorphism states had no effect on IVF outcomes of patients who had recurrent IVF failure. Footnote of the table: CI: Confidence interval, PAI: Plasminogen Activator Inhibitor. Values were given as mean±standard deviation, median (range), or number (percentage).

References:
**IS THERE ANY PREDICTIVE CAPABILITY OF THE FIRST ß-HCG LEVEL IN IN VITRO FERTILIZATION CYCLES.**

A. Ozkok, N. Yilmaz, A. Karatas, A. Tokmak, S. Cavdar, Zeke Tahir Burak Women’s Health Education and Research Hospital, Ankara, Turkey; Reproductive Endocrinology Department, ZTB, Ankara, Turkey; Obstetrics and Gynecology, Abant Izzet Baysal University, Bolu, Turkey; Obstetrics and Gynecology, Zeke Tahir Burak Women’s Health Education and Research Hospital, Ankara, Turkey; Umraniye Community Health Center, Provincial Public Health Directorate of Istanbul, Istanbul, Turkey.

OBJECTIVE: Presence of a marker that can predict pregnancy results in vitro fertilization cycles and the course of these pregnancies will be a stress mitigating factor for both doctors and the couples receiving treatment. This study was performed to assess whether serum ß-hCG level on the 13th day after embryo transfer (D13 ß-hCG) has a predictive role for different pregnancy results or not.

DESIGN: Retrospective cohort study in a single tertiary center.

MATERIALS AND METHODS: Two thousand two hundred thirty-six ICSI cycles were investigated. A total of 616 fresh, non-donor ICSI cycles who met the inclusion criteria were classified into two groups according to D13 ß-hCG: those ≥10 mIU/mL (pregnant—251 cases) and those <10 mIU/mL (non pregnant—365 cases). D13 ß-hCG after embryo transfer were compared between the two groups and its predictive value for pregnancy outcomes was investigated. Mann Whitney U test, Kruskal-Wallis test, Pearson chi-square and Fisher exact test were used, Post Hoc test was performed. ROC analysis and Spearman correlation were performed. A p value of <0.05 was considered significant.

RESULTS: Demographic characteristics and the number of embryos transferred were similar among groups with and without pregnancy (p>0.05). Among the 251 cases diagnosed with a pregnancy, 67 had miscarriages (55 early, 12 late). In singleton pregnancies; D13 ß-hCG levels was significantly lower in miscarriage group than ongoing pregnancy group (p<0.05). D13 ß-hCG >127 mIU/mL was found to predict that pregnancy will continue ≥20 weeks with a sensitivity of 83% and a specificity of 66.5% (PPV=63.3% and NPV=60%) (95 CI: 68.5-84%, p<0.001). D13 ß-hCG <126 mIU/mL could predict early miscarriage with 72% sensitivity and 82% specificity (95 CI: 74.8-89%) (p<0.001). D13 ß-hCG levels could not predict preterm delivery either in single or multiple pregnancies (p=0.552 and p=0.426, respectively), and had no correlation with birth weight or gestational week at delivery (p=0.102 and p=0.571, respectively).

CONCLUSIONS: According to this study live births were more frequent in patients with ß-hCG >127.5 whereas early pregnancy loss was more likely below a ß-hCG level of 126.85. Levels above 319.5 could predict multiple pregnancy. No prediction for low birth weight or preterm birth could be made according to the ß-hCG level. This is a retrospective analysis. Further prospective studies with more participants are required to predict early pregnancy outcomes in COH cycles.

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### References


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**SUPERNUMERARY BLASTOCYSTS AVAILABLE FOR CRYOPRESERVATION IN FRESH IVF CYCLES: PROGNOSTIC VALUE FOR IVF OUTCOMES?**

N. Pereira, A. P. Hutchinson, A. P. Melnick, J. P. Lekovich, I. Kligman, Z. Rosenwaks, The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: Supernumerary blastocysts attained during in vitro fertilization (IVF) cycles are often cryopreserved. We investigate whether the number of supernumerary blastocysts available for cryopreservation serves as a positive prognostic factor for IVF outcomes.

DESIGN: Retrospective case-control study.

MATERIALS AND METHODS: All patients <40 years undergoing IVF with fresh blastocyst transfer between 2004 and 2013 were assessed for inclusion. Patients with ≥1 blastocyst available for cryopreservation were considered as “cases” while patients with no supernumerary blastocysts served as “controls.” Demographics, baseline IVF characteristics, and ovarian stimulation parameters of the two groups were compared. Cases were stratified into quartiles based on the number of supernumerary blastocysts available for cryopreservation. Implantation, biochemical, clinical pregnancy, miscarriage and live birth rates were compared between cases and controls, with a further sub-analysis between case quartiles and controls. Odds ratios (OR) for implantation, clinical pregnancy and live births were calculated in both analyses and adjusted for age.

RESULTS: 2329 patients underwent fresh blastocyst transfer, of which 1275 and 1054 patients served as cases and controls, respectively. On average (2–5) blastocysts were cryopreserved in the former group. Cases were younger [33 (31-34) vs. 36 (32-34); P<0.001] compared to controls. They also had higher anti-müllerian levels [1.96 (1.82-2.39) vs. 1.14 (0.56-1.66) ng/mL; P=0.02], required less gonadotropins (1725 vs. 2100 IU; P=0.01), and had more oocytes retrieved (15 vs. 11; P=0.02). The odds of implantation (48.7% vs. 33.9%), clinical pregnancy (58.1 vs. 53.0%), and live birth (54.3% vs. 49.6%) were 1.84, 1.22, and 1.11 times higher, respectively in the cases compared to controls. However, the increased odds were not significant after adjusting for age. Comparison of the 1st, 2nd and 3rd case quartiles with controls revealed 2.09 times higher odds of implantation in the 2nd and 3rd quartiles (P=0.02), with a non-significant trend toward higher clinical pregnancy and live birth rates.

CONCLUSIONS: Our findings suggest that supernumerary blastocysts available for cryopreservation serve as a positive prognostic factor for IVF outcomes after fresh blastocyst transfer. Specifically, patients with ≥3 supernumerary blastocysts have higher odds of implantation compared to controls, suggesting potential benefits of elective single embryo transfer in such patients.

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**P-203 Tuesday, October 18, 2016**

**DOES OUTCOME OF THE FIRST IVF CYCLE ALLOW SELECTION OF CANDIDATES FOR REPEAT IVF PRIOR TO PGS?**

E. B. Johnstone, M. Link, B. Patel, J. Hotaling, A. K. Moore, J. Dorais, D. T. Carrell, C. M. Peterson, K. I. Aston, Obstetrics & Gynecology, University of Utah, Salt Lake City, UT; Obstetrics and Gynecology, University of Utah, Salt Lake City, UT; Obstetrics and Gynecology, ASRM, West Valley City, UT; University of Utah, SLC, UT; Surgery (Urology), University of Utah School of Medicine, Salt Lake City, UT; Division of Reproductive Endocrinology and Infertility, University of Utah, Salt Lake City, UT; Surgery (Urology), University of Utah, Salt Lake City, UT.

OBJECTIVE: To determine if the number of blastocyst generated in the first in vitro fertilization (IVF) cycle can be used to predict which women may benefit from repeated IVF cycles prior to preimplantation genetic screening (PGS).

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Charts of patients who underwent >1 cycle of IVF with PGS at a single institution since January 1, 2014 were abstracted. These patients were divided into 3 groups, those with 0, 1 and ≥2 blastocyst to biopsy in Cycle 1. Clinical factors, chances of a euploid embryo, and chances of live birth in the first or successive cycles were compared among the 3 groups, using the Kruskal-Wallis test or chi square as appropriate. Women who are not yet pregnant but have remaining euploid embryos were excluded from outcome statistics.

RESULTS: 30 women underwent 82 cycles with oocyte retrieval, for a mean of 2.7 oocyte retrievals per woman. A total of 173 blastocysts were biopsied, and 59 were euploid (34%). The sustained implantation rate of euploid embryos was 40%, and the ongoing pregnancy rate per woman was 47%, with 3 additional women with remaining euploid embryos. Mean age of the women was 39.2, and mean AMH 1.85.

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**P-204 Tuesday, October 18, 2016**

**PREGNANCY OUTCOMES BY QUARTILES OF D13 ß-HCG LEVEL IN IN VITRO FERTILIZATION CYCLES.**

<table>
<thead>
<tr>
<th>Implantation Rate</th>
<th>Miscarriage Rate</th>
<th>Clinical Pregnancy Rate</th>
<th>Live Birth Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>33.9%</td>
<td>3.42%</td>
<td>53%</td>
</tr>
<tr>
<td>1st Quartile</td>
<td>39.7%</td>
<td>3.29%</td>
<td>59.2%</td>
</tr>
<tr>
<td>2nd Quartile</td>
<td>49.7%</td>
<td>3.61%</td>
<td>59.7%</td>
</tr>
<tr>
<td>3rd Quartile</td>
<td>51.7%</td>
<td>3.33%</td>
<td>60%</td>
</tr>
</tbody>
</table>
CONCLUSIONS: Number of blastocyst embryos developed in the first IVF cycle is an important predictor of whether a couple will achieve an ongoing pregnancy through multiple cycles of IVF with PGS. For patients who fail to have a blastocyst to biopsy in the first cycle, further cycles may not be warranted. Patients with only 1 blastocyst to biopsy in the first cycle likely benefit from additional cycles. Of those with >1 embryo in the first cycle, 80% who transferred this embryo achieved ongoing pregnancy. These patients may not benefit from further embryo collection cycles. A larger sample size is necessary to confirm these findings.

P-205 Tuesday, October 18, 2016

IMPACT OF THE NUMBER OF LEAD FOLLICLES AT TIME OF TRIGGER ON INTRAUTERINE INSEMINATION (IUI) PREGNANCY OUTCOMES. L. N. Beliveau,a A. Vilos,a F. Tekpetey,b K. Shepherd,a C. Newton,b B. Abu-Rafea,a J. Hollett-Caines,a M. Rebel.a *University of Western Ontario, London, ON, Canada; bThe Fertility Clinic, LHSC, London, ON, Canada.

OBJECTIVE: The aim of our study was to assess the impact of the number of lead follicles at the time of trigger on pregnancy and live birth rates in women undergoing controlled ovarian hyperstimulation (COH) with IUI.

DESIGN: Descriptive study.

MATERIALS AND METHODS: A retrospective study of all patients undergoing IUI at The Fertility Clinic in London, Ontario, Canada from January 2009 to January 2014 was undertaken. 1350 IUI cycles using gonadotropins alone were performed in the 5-year period. Lead follicle size was determined to be 16mm or greater. IUI was performed approximately 36 hours after triggering ovulation. Outcomes examined were clinical pregnancy, live birth, and multiple pregnancy rates. Other factors assessed were female age, body mass index (BMI), cause of infertility, day 3 follicle stimulating hormone (FSH), and total motile sperm count (TMC).

RESULTS: The number of lead follicles ranged from 0 to 5. 1321 cycles (97.9%) achieved 1,2, or 3 lead follicles. Positive beta-human chorionic gonadotropin (βhCG) on luteal day (LD) 18, positive fetal heartbeat on LD40 ultrasound, and live birth rates were 18.8%, 13.5%, and 12.7% for one lead follicle; 26.8%, 21.1%, and 19.5% for two lead follicles; and 27.4%, 22.6%, and 21.7% for three lead follicles respectively. All three rates were significantly higher with two compared to one lead follicle (P<0.002 in all cases). There was no evidence that 3 lead follicles resulted in more pregnancies, positive fetal hearts, or live births than one or two lead follicles. Multiple rates were 0.9%, 2.9%, and 4.7% for one, two and three lead follicles respectively. Mean BMI was slightly higher in the one lead follicle group compared to two lead follicles (27.4 vs. 25.7, P<0.05). There was no significant difference between groups with respect to female age, cause of infertility, day 3 FSH, or TMC.

CONCLUSIONS: Our study demonstrated significantly better pregnancy and live birth outcomes with an acceptable multiple rate in cycles of COH/IUI attaining two lead follicles compared to one. This provides valuable information for counselling patients undergoing IUI.

P-206 Tuesday, October 18, 2016

IN-VITRO FERTILIZATION CYCLES AMONG WOMEN AGES 40 AND OLDER. H. Hipp, S. Crawford, J. F. Kawwass, S. Boulet, D. A. Grainer, D. M. Kissin, D. J. Jamieson, Reproductive Endocrinology and Infertility, Emory University Reproductive Center (& CDC), Atlanta, GA; Division of Reproductive Health, Centers for Disease Control and Prevention, Atlanta, GA; *The Center for reproductive Medicine, Wichita, KS.

OBJECTIVE: To characterize the angiogenic and antiangiogenic profile at two time points (day of hCG trigger and day of first serum hCG test) after in vitro fertilization (IVF) in a case-control study of patients with and without subsequent development of a hypertensive disorder of pregnancy.

DESIGN: Case-control study.

MATERIALS AND METHODS: IRB approval was obtained. Patients who conceived using IVF during the study period (2010-2014) were screened for the outcome of interest (hypertensive disorders of pregnancy) by review of obstetric records. All identified cases who conceived from IVF and developed a hypertensive disorder of pregnancy (gestational hypertension, pre-eclampsia, HELLP syndrome, and eclampsia; n=18) were matched based on demographic and clinical characteristics with controls who had uncomplicated live births from IVF during the same study period (n=26). Angiogenic biomarkers were compared between case and control groups at two time points (day of hCG trigger and day of first serum hCG test). A custom-built Luminex multiplex assay was constructed for analysis of the biomarkers in cases (n=18) and controls (n=26).

RESULTS: Selected demographic, clinical characteristics, and results of angiogenic and antiangiogenic biomarkers at both time points between cases and controls were observed. Results in controls. Otherwise no significant differences in the evaluated angiogenic factors at both time points between cases and controls were observed. Results were similar when only singleton pregnancies were considered for analysis.

CONCLUSIONS: In this pilot case-control study of patients with and without subsequent development of a hypertensive disorder of pregnancy after IVF, the angiogenic profile was similar between cases and controls. Further research into this topic may reveal angiogenic profiles that are predictive of hypertensive complications in IVF-conceived pregnancies. Supported by: Presbyterian Health Foundation.

Table 1: Characteristics and angiogenic factors (ng/ml) for cases (n=18) and controls (n=26)

<table>
<thead>
<tr>
<th>Variable (mean ± SEM)</th>
<th>Cases (n=18)</th>
<th>Controls (n=26)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>31.0 ± 1.0</td>
<td>32.3 ± 0.7</td>
<td>0.29</td>
</tr>
<tr>
<td>BMI</td>
<td>26.6 ± 1.5</td>
<td>28.3 ± 1.5</td>
<td>0.44</td>
</tr>
<tr>
<td>Peak estradiol</td>
<td>3074 ± 313</td>
<td>3069 ± 282</td>
<td>0.99</td>
</tr>
<tr>
<td>Gestational age at delivery</td>
<td>37.1 ± 0.4</td>
<td>38.2 ± 0.3</td>
<td>0.02*</td>
</tr>
<tr>
<td>Birth weight</td>
<td>2748 ± 124</td>
<td>3235 ± 128</td>
<td>0.01*</td>
</tr>
<tr>
<td>Angiopoietin 2</td>
<td>7538 ± 3725</td>
<td>1940 ± 301</td>
<td>0.09</td>
</tr>
<tr>
<td>PDGF</td>
<td>7590 ± 2253</td>
<td>11887 ± 2830</td>
<td>0.25</td>
</tr>
<tr>
<td>sVEGFR1 (sFLT1)</td>
<td>375 ± 151</td>
<td>3702 ± 1970</td>
<td>0.11</td>
</tr>
<tr>
<td>Angiopoietin 2</td>
<td>5615 ± 3331</td>
<td>1260 ± 275</td>
<td>0.21</td>
</tr>
<tr>
<td>Time point 2 PDGF</td>
<td>7881 ± 2300</td>
<td>17314 ± 1802</td>
<td>&lt;0.01*</td>
</tr>
<tr>
<td>Time point 2 sVEGFR1 (sFLT1)</td>
<td>442 ± 171</td>
<td>881 ± 183</td>
<td>0.12</td>
</tr>
</tbody>
</table>

*p<0.05. Of patients with >1 blastocyst in Cycle 1, 4 of 5 who have transferred an embryo from Cycle 1 have an ongoing pregnancy (80%), while 4 more have remaining cryopreserved embryos from Cycle 1.
OBJECTIVE: To describe trends and investigate predictors of live birth in women ages 40 and older starting in vitro fertilization (IVF) cycles with autologous oocytes.

DESIGN: Retrospective cohort study using data from the National Assisted Reproductive Technology Surveillance System.

MATERIALS AND METHODS: Linear regression analysis was used to assess trends in number of fresh and frozen IVF cycles and live births among women ≥40 and proportion of cycles in women ≥40 among cycles in all ages using autologous oocytes during 2007-2013. Lqg binomial regression was performed to determine predictors of live birth in fresh IVF cycles resulting in transfer using autologous oocytes during 2007-2013.

RESULTS: From 2007 to 2013, the number of total cycles (fresh and frozen) among women ≥40 years increased significantly from 24,529 to 28,883 (p=0.0009); the number of frozen cycles more than doubled from 2,968 to 7,632 over the study period. The proportion of cycles in women ≥40 among cycles in all ages did not significantly increase (19.82% to 20.95%; p=0.659). The number of live births among women ≥40 years increased from 2,902 in 2007 to 4,217 in 2013 (p<0.0001). In women ≥40 years starting fresh cycles during 2007-2013, the cancellation rate was 17.1% and the live birth rate following transfer was 16.1%. Among fresh cycles resulting in transfer, the following variables were predictive of higher live birth rates: higher parity, no prior IVF cycles, use of an antagonist stimulation, lower gonadotropin dose, higher number of oocytes retrieved, ovarian hyperstimulation, use of pre-implantation genetic diagnosis screening, transferring a higher number of embryos and blastocyst stage embryos, and cryopreservation of more embryos. The diagnoses of ovulatory dysfunction, tubal factor, and uterine factor were predictive of lower live birth rates.

CONCLUSIONS: The total number of cycles and live births to women ≥40 years using autologous oocytes has increased from 2007 to 2013, though the proportion of cycles amongst women in all ages remained stable. Although there is a high cycle cancellation rate, certain predictors of live birth can be identified to facilitate treatment option counseling.

P-207 Tuesday, October 18, 2016

HCG LEVELS AT DIFFERENT TIME POINTS DURING OVARIAN STIMULATION ARE NOT ASSOCIATED WITH OUTCOME IN ICSI CYCLES. F. Shararaab, M. R. Goodwin.a Virginia Center for Reproductive Medicine, Reston, VA; Ob/gyn, George Washington University, Washington, DC.

OBJECTIVE: HP-hMG (Menopur®) has 75 IU of FSH and 75 IU of hCG- derived LH activity. It contains 9.9 IU/vial of hCG and 0.4 IU/vial of LH, making > 90% of its LH activity hCG-derived. Only one study has addressed the hCG levels during ovarian stimulation (Platteau 2004). In that study, hCG levels were assessed on day 6 in 121 IVF and 237 ICSI cycles using HP-hMG. Day 6 hCG > 2.0 IU/L was associated with the highest live birth rate in ICSI but not in IVF cycles. It is unclear why this would be the case on day 6 and for only ICSI cycles. We therefore decided to compare hCG levels at several time points during ovarian stimulation with success rate in our program.

DESIGN: Retrospective analysis.

MATERIALS AND METHODS: A total of 159 ICSI cycles using HP-hMG and fresh transfer at day 5 or 6 were evaluated: 105 HP-hMG-only cycles (mono-hMG group) and 54 mixed FSH-HP-hMG cycles at 1:1 ratio (mixed group). FSH used was uFSH (Brawelle®) or recFSH (Gonal-F® or Follistim®). All patients received HP-hMG (Menopur®) from day one of stimulation. Levels of hCG were assessed on day 5-6, day 7-9, and day of hCG administration. Ongoing pregnancy was assessed by ultrasound at 6-7 weeks gestation.

RESULTS: Levels of hCG increased steadily during ovarian stimulation in both groups but were significantly higher in the mono-hMG group than the mixed group at all time points: 3.41 ± 1.40 vs 1.59 ± 0.87 IU/L, respectively, (P<0.001) on day 5-6; 3.88 ± 1.61 vs 2.14 ± 2.50 IU/L, (P<0.001) on day 7-9; and 3.69 ± 1.55 vs 1.98 ± 0.92 IU/L, (P<0.001) on day of hCG administration. Ongoing/delivered PR was 63.8% (67/105) in the mono-hMG group and 57.4% (31/54) in the mixed group (P=NS). At all time points studied, hCG levels were not different between pregnant and non-pregnant cycles: 2.90 ± 1.43 vs 2.76 ± 1.55 IU/L, respectively, (P=0.64) on day 5-6; 3.19 ± 1.50 vs 3.19 ± 1.80 IU/L, (P=0.94) on day 7-9; and 3.10 ± 1.48 vs 2.79 ± 1.37 IU/L, (P=0.25) on day of hCG administration. Subgroups of hCG (hCG < 1.0, 1.0-1.9, or ≥ 2.0 IU/L) were also assessed at all 3 time points in both pregnant and non-pregnant cycles. Unlike the Platteau study, no differences in cycle outcome were detected.

CONCLUSIONS: Prior studies have suggested that the progesterone:oocyte (P:O) ratio may be more effective for predicting ART outcomes than P alone on the day of ovulation trigger. This study was designed to critically evaluate how to best incorporate P and O in prediction models of ART outcomes.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: 7,608 fresh autologous ART embryo transfers and hCG levels were analyzed. GEE models and ROC curves were utilized to assess the predictive value of P, number of oocytes (O) retrieved, age of patient, and the P:O ratio on ART outcomes. In addition to the ratio P:O, l/oocytes (I/O) was evaluated to allow statistical prediction models to separately estimate discriminatory ability of P and I/O. Sequential models were evaluated to assess the incremental probability of variables to predict the primary outcome of live birth. Predictive ability of models was assessed using area under the curve (AUC).

RESULTS: In single predictor models, O was a stronger predictor than P; however, age was the strongest predictor of live birth (Table 1). Once age was included in models, the incremental predictive ability of either P or I/O to age is similar and small. When considering models using 3 predictors, the highest predictive ability was observed for a model including age, P, and I/O. P:O again did provide incremental value over the model with just P or just I/O.

Table 1:

<table>
<thead>
<tr>
<th>Predictors</th>
<th>AUC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.617</td>
</tr>
<tr>
<td>O</td>
<td>0.582</td>
</tr>
<tr>
<td>1/O</td>
<td>0.582</td>
</tr>
<tr>
<td>P</td>
<td>0.533</td>
</tr>
<tr>
<td>2 Predictor Model</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>0.628</td>
</tr>
<tr>
<td>I/O</td>
<td>0.623</td>
</tr>
<tr>
<td>Age</td>
<td>0.622</td>
</tr>
<tr>
<td>P:O</td>
<td>0.597</td>
</tr>
<tr>
<td>3 Predictor Model</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>0.637</td>
</tr>
<tr>
<td>P:O</td>
<td>0.636</td>
</tr>
<tr>
<td>Age</td>
<td>0.630</td>
</tr>
</tbody>
</table>

CONCLUSIONS: hCG levels steadily increased during ovarian stimulation, and were higher in mono-HP-hMG cycles compared to mixed FSH-HP-hMG cycles. In contrast to the only published paper associating day 6 hCG level with ICSI cycle outcome, we found no association between preg- nant and non-pregnant cycles and hCG levels on days 5-6, 7-9, or day of hCG administration. Our study is ongoing.

References:
OOCYTE BIOLOGY

P-209 Tuesday, October 18, 2016

TRANSCRIPTOMIC ANALYSIS OF ISOLATED SINGLE PRIMORDIAL AND PRIMARY FOLLICLE USING RNA-SEQ IN HUMAN. E. Chang, S. Yoon, J. Kim, Y. Hur, E. Yu, W. Lee, Y. Choi. 1CHA Fertility Center, Seoul, Korea, Republic of; 2Post Doc, Seoul, Korea, Republic of; 3Fertility Center, CHA Gangnam Medical Center, Seoul, Korea, Republic of; 4CHA Gangnam Medical Center, Seoul, Korea, Republic of; 5Fertility Center, CHA Gangnam Medical Center, CHA University, Seoul, Korea, Republic of; 6Ob/Gyn Dept., Gangnam CHA Hospital, Seoul, Korea, Republic of; 7Biomedical Science, CHA University, Seoungnam-si, Korea, Republic of.

OBJECTIVE: Early stage follicle development is far from fully understood. Technical barriers including difficulties in retaining enough human ovarian sample and heterogeneous nature of ovarian tissue which contains various stages of follicles have limited informational accuracy. However recent progression in RNA-Seq has lead to far more precise measurement of levels of transcripts than other methods with less RNA sample. In order to advance our understanding of early folliculogenesis, we performed transcriptomic analysis for isolated human early stage follicle using RNA-Seq.

DESIGN: Transcriptomic analysis of isolated human ovarian follicles using high though-put RNA-seq.

MATERIALS AND METHODS: We isolated primordial (30~40μm; n=6) and primary (50~70μm; n=5) follicles enzymatically and mechanically from human ovarian tissue using 1mg/ml collagenase IV, 0.2mg/ml DNase I and 0.08mg/ml Liberase. For this study primordial follicles were defined as those contain flat pregranulosa cells; primary follicles were defined as those with one layer of cuboidal granulosa cells. From total follicles isolated, single follicle from each stage which passed QC were analyzed with RNA-seq (Illumina HiSeq).

RESULTS: Transcriptomic analysis revealed 2190 up regulated differentially expressed genes (DEGs) and 1565 down regulated DEGs in primary compared to primordial follicle. Compared to mouse data, 175 upregulated and 218 down regulated common DEGs were found. Gene pathway analysis indicates that these DEGs are involved in signaling pathways such as cell cycle, cancer pathway and phosphorous metabolic process.

CONCLUSIONS: Our current study provides first RNA-seq based transcriptome between primordial and primary follicle in human. Many candidate genes which have not been studied previously may reveal novel insights into primordial follicle activation and provides a fundamental basis for the future functional studies in early folliculogenesis.

Supported by: This study was supported by a grant (2014R1A1A1002702) from the National Research foundation of Korea, Ministry of Science, ICT and Future planning.

P-210 Tuesday, October 18, 2016

LIVE CELL IMAGING AND QUANTIFICATION OF CYTOPLASMIC LIPID DROPLETS AS BIOMARKERS IN OOCYTES OF MICE OF DIFFERENT BODY COMPOSITION. L. J. Green, J. Jasensky, Z. Chen, G. D. Smith. 1OBGYN, University of Michigan, Ann Arbor, MI; 2OB/Gyn, University of Michigan, Ann Arbor, MI.

OBJECTIVE: Oocyte and embryo cytosolic lipids are endogenous energy sources, which are important for development. Increased levels of intracellular lipids, however, are inversely related to cryo-tolerance and cryo-survival. Previously, we have demonstrated use of coherent anti-Stokes Raman scattering (CARS) microscopy to non-invasive image cytosolic lipids in live oocytes. Our objectives were to i) determine the developmental competence of zygotes following CARS microscopy laser exposure, and ii) quantify and compare cytoplasmic lipid droplet content in oocytes, during meiosis, from non-obese and obese mice.

DESIGN: Laboratory study.

MATERIALS AND METHODS: Mature wild-type F1 mice of normal body composition (WT) were sacrificed following UCUCA guidelines to isolate germinal vesicle intact (GVI) oocytes and zygotes. Mature mice with obesity, caused by a leptin gene mutation ( ob/ob ), were sacrificed to isolate GVI oocytes. Zygotes were sham exposed (n=48) or exposed to CARS laser (n=52) for 3 minutes prior to placement into culture for 96 hrs to assess blastocyst development. GVI oocytes, from WT and ob/ob mice, were isolated from antral follicles, used for experiments, or in vitro matured to metaphase II (MII). Some oocytes were fixed/stained with Nile Red for reference non-viable lipid quantification. CARS microscopy was utilized for live-oocyte imaging. CARS is a vibrational microscopy that probes intrinsic chemical signatures such as CH2, a main component of lipids. Non-parametric and parametric statistics were performed with z-test and unpaired t-test, respectively.

RESULTS: CARS laser exposure of zygotes had no detrimental effect on blastocyst development ( sham-83%; CARS-85%; p=0.71 ). Cytoplasmic lipid droplet content, as assessed by both live-cell CARS microscopy and non-viable Nile Red staining/microscopy, significantly decreased as oocytes matured from GVI to MII (p<0.01). GVI oocyte lipid droplet content was significantly elevated (p<0.05) when derived from obese ob/ob mice (wt-45 grams) in comparison to normal body composition WT mice (wt-30 grams). This difference in oocyte lipid quantification, in relation to body composition, was significantly different when assessed with both CARS and Nile Red/fluorescent microscopy.

CONCLUSIONS: CARS microscopy can be used as a live-cell imaging system to quantify cytosolic lipid droplet content. Oocyte cytosolic lipid droplet content decreased as oocytes matured and oocytes from obese mice had significantly more lipid droplets compared to normal body composition counterparts. Assessment of human oocyte lipid content with CARS microscopy as a biomarker, in relation to body composition, requires further investigation.

Supported by: CEGYR Foundation.

P-209 Tuesday, October 18, 2016


OBJECTIVE: Nuclear and cytoplasmic oocyte maturation occurs in vivo during follicular growth and ovulation. Both processes are induced by changes in plasma levels of gonadotropins. During their growth, oocytes acquire the ability to restart meiotic maturation in response to gonadotropins stimulation, mainly LH increased. The nuclear envelope breaks down, the first polar body is released and meiosis progresses until metaphase II (MII). The meiosis stops in MII and ovulation occurs. Maturation promoting factor (MPF) and mitogen activated protein kinas (MAPK) play an important role in oocyte maturation.Our group have previously reported that cdc2 phosphorylated in Y15 could be a good marker during oocyte meiosis. Thus, when the oocyte reach the MII stage cdc2-Y15 is very imperceptible, contrary to oocytes going through to MI to MII, cdc2-Y15 levels are high (1/2).

DESIGN: Prospective comparative study.

MATERIALS AND METHODS: Remanent oocytes were obtained from IVF cycles (2013-2016) under informed consent. From 68 patients, 42 MII and 64 unfertilized oocytes after ICSI were studied.The first polar body was collected for chromosomal analysis by aCGH (comparative genomic hybridization) and NGS (next generation sequencing). The remaining oocytes were processed and analyzed for cytoplasmic immaturity by immunocytochemistry-ICC to determine the degree of cytoplasmic maturation: assessment of inactive MPF (cdc2 - Y15) status and the metaphase plate alignment (Hoechst).Two groups were conformed according to the main feature observed: A: cytoplasmic immaturity and B: mature cytoplasm.

RESULTS: Regarding MII - B (26), 89% (23) had a normal metaphase plate and 87% (20) were chromosomally euploid. Contrary, in A oocytes (16), 38% (6) presented a normal metaphase plate and just 33% (2) were euploid.In unfertilized oocytes after ICSI: 92% (24) of mature oocytes (B) (26) had a normal metaphase plate and 83% (20) were euploid. When oocytes had a cytoplasmic immaturity (38), 37% (14) had a normal metaphase plate and 43% (6) were chromosomally normal.The global rate of aneuploidies and metaphase plate disarrangements in immature oocytes (MI+failed-fertilization) was significantly higher than mature oocytes (p<0.05).

CONCLUSIONS: Our results suggest that cytoplasmic oocyte maturation has a higher relevance compared to nuclear maturity. An inadequate cytoplasmic maturation is associated with altered levels of metaphase plate alignment and aneuploidies.

References:

Supported by: CEGYR Foundation.
REVISITING OOLELLA CHARACTERISTICS DURING ICSI IN RELATION TO FERTILIZATION PATTERNS AND EMBRYO DEVELOPMENT AND IMPLANTATION, N. Pereira, T. Cozzubbo, S. Cheung, Z. Rosenwaks, G. D. Palermo. The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: The oolemma response during ICSI has been linked to membrane and cytoplasmic maturity. The former is evidenced by the depth of the funnel and can manifest in the unconception of the second polar body and oocyte lysis, while the latter in absent fertilization. We investigate the occurrence of normal and abnormal fertilization patterns, as well as oocyte survival in relation to ovarian stimulation and eventual reproductive outcomes.

DESIGN: In couples with an adequate cohort of mature oocytes and varying degrees of fertilization, we measured the occurrence of immature membrane and ooplasm (as evident by oocyte lysis), impaired cytoplasmic maturity (as evident by no fertilization), lower membrane maturity (as evident by 3PN embryos) and complete membrane and cytoplasmic maturity (2PN).

MATERIALS AND METHODS: Only ICSI cycles with ≥5 oocytes at MII stage were included. Unexclusion of the second polar body characterized by digynic 3PN, is associated with sudden breakdown of the membrane, short funnel, and indicates ooplasmic maturity but membrane dysmaturity. Oocyte lysis is characterized by absence of funnel development and therefore severe membrane dysmaturity. Absent fertilization presented with adequate funnel development up to the center of the oocyte therefore allowing oocyte survival, but unfortunately with ooplasmic immaturity. ICSI cycles were stratified by fertilization rates, in increments of 20%. The rates of 3-PN embryos and oocyte lysis were plotted against increasing fertilization rates. Demographics and ovarian stimulation parameters were compared across fertilization groups.

RESULTS: 11911 ICSI cycles were identified. The rate of digynic 3PN embryos decreased with increasing fertilization rate (7.19% (≥20%) to 1.00% (81-100%).) Similar trends in the rate of oocyte lysis were observed as well. There was no difference in the median age of patients (36), number of oocytes (9), or total stimulation days (10) across different fertilization groups. Patients with oocyte lysis had a progressively lower dose of gonadotropins (P=0.007) and peak E2 levels (P<0.001) in comparison to those that had no fertilization, digynic 3PN embryos, and both membrane and cytoplasmic maturity (all 2PN). To assess the impact of oolemma/ooplasmic maturity within the cohort of oocyte injected on the embryo developmental outcome, we compared patients with oocyte lysis to those who had normal fertilization (n=384). Lower implantation (16.7% vs. 32.4%; P<0.001) and clinical pregnancy rates (7.01% vs. 34.6%; P<0.001) were noted in the former group compared to the latter.

CONCLUSIONS: During ICSI, membrane funnel characteristics may provide insight into oolemma maturity. Oocyte survival, absent/abnormal fertilization provides invaluable information about ooplasmic maturity and embryo developmental competence. Our study highlights the potential link between oolemma behavior, absent/abnormal fertilization and ovarian stimulation.

P-212 Tuesday, October 18, 2016


OBJECTIVE: To evaluate the efficacy of multiple ovulation induction by modulating angiotensin II receptor (ATTI-Rc) during in vitro maturation of murine ovarian follicle.

DESIGN: In vitro experiment.

MATERIALS AND METHODS: Ovarian preantral follicles isolated from fourteen-day-old C57BL6 mice were cultured with ATTi-Rc agonist (ATTi-Rc agonist group) or antagonist (ATTi-Rc antagonist group) and their maturation outcomes were compared to control group. In each groups, the isolated follicles were cultured as one of follicle for mono-follicular culture to three of follicle cluster for multi-follicular culture in 25 culture droplets per each culture dishes for 12 days with medium Opti-MEM medium that contained insulin plus FBS with FSH and LH as control. ATTi-Rc agonist or antagonist was diluted in media from culture day 5 in ATTi-Rc agonist and antagonist group. Immunohistochemical, qRT-PCR and electron microscope analysis were conducted with cultured follicular cells. After ovulation induction with adding hCG, ovulation and oocyte maturation rate were evaluated, and fertilization rate was evaluated.

RESULTS: When single follicles were cultured, the ovulation and maturation rates were similar in all three groups. When three-follicle clusters were cultured, up to three follicles were ovulated in the ATTi-Rc agonist group while none or one follicle ovulated in control or ATTi-Rc antagonist groups (P<0.0001). The ATTi-Rc agonist group showed similar oocyte maturation rate (76.2% vs. 76.7% vs. 75.7%; P>0.05) and higher number of mature oocyte (28.2±4.9 vs. 6.6±1.5 vs. 5.6±1.9, P<0.0001) per 1 culture dish compared to control or ATTi-Rc antagonist groups. In comparison between mono-follicular in control group and multi-follicular culture in ATTi-Rc agonist groups, there was significant different in obtained mature oocyte (11.0±3.1 vs. 28.8±3.8, P<.0001). Fertilization rate was similar in all groups. There were no significant difference in expressions of oovulational related genes and electron microscopic morphology in all groups.

CONCLUSIONS: This novel culture system with ATTi-Rc modulation for in vitro culture of ovarian multiple follicle showed higher efficacy to obtain mature oocyte to fertilization attempt than the conventional in vitro culture of ovarian mono-follicle.

References:

P-214 Tuesday, October 18, 2016


OBJECTIVE: Although embryologists agree that semen parameters are crucial when determining the optimal mode of insemination, the effect of conventional insemination versus ICSI on a cycle’s fertilization rates utilizing donor sperm is limited within the literature. This study sought to determine if the mode of donor sperm insemination by IVF patients has any adverse effects to the rate of fertilization.

DESIGN: Retrospective.

MATERIALS AND METHODS: Patients who underwent an IVF cycle utilizing anonymous donor sperm were included. PGS split insemination cases were excluded. Fertilization rate was categorized as Normal: >70%, Low: <20% and Failed: 0%. Cohorts were analyzed according to the insemination method. Data was analyzed using student’s T test, chi square, linear and binary logistic regression.

RESULTS: A total of 794 patients underwent 1070 cycles. Of these, 31.9% (n=34) had normal fertilization rate, 5.6% (n=60) had a low fertilization rate and 2.8% (n=30) had failed fertilization. Female patients with Failed Fertilization were older than those with Low Fertilization or Normal Fertilization (41.3 vs. 39.1 vs. 37.5, P<0.05, respectively) and had less oocytes inseminated (4.2 vs. 11.5 vs. 12.2, P<0.05, respectively). When raw data was analyzed by insemination method, low fertilization rate was higher when compared between conventional (9.1% (2C109) vs. 7.9% (35/ 681)); and failed fertilization was also higher with ICSI than in conventional insemination (3.3% (13/389) vs. 2.5% (17/681)). When only considering patients with ≤5 oocytes retrieved, the proportion of patients with no fertilization was similar with both methods: conventional 11.8% (15/127) vs. ICSI 10.5%(9/85). When conventional insemination cases were analyzed with a binary logistic regression analysis, for each extra oocyte retrieved the odds of fertility increased 0.06%; and for each 1 year increase in age the odds of fertilization >20% decreased 0.08%. For ICSI cases, for each extra oocyte retrieved the odds of fertilization increased 0.14%; and for each 1 year increase in age the odds of fertilization >20% decreased 0.08%. For ICSI cases, for each extra oocyte retrieved the odds of fertilization increased 0.14%; and for each 1 year increase in age the odds of fertilization >20% decreased 0.08%. For ICSI cases, for each extra oocyte retrieved the odds of fertilization increased 0.14%; and for each 1 year increase in age the odds of fertilization >20% decreased 0.08%.

CONCLUSIONS: This study shows that fertilization rates are correlated with patient’s age and with the numbers of the oocytes inseminated, but not with the method of insemination.
P-215 Tuesday, October 18, 2016


**OBJECTIVE:** The origin of the pronucleus (PN) in a single PN zygote (1PN), and whether its genome is normal still remains controversial. We recently established a novel method of discriminating between maternally- and paternally-derived PN using immunofluorescence staining and demonstrated the possibility that both the male and female genome could be packed in 1PN in some cases. However, currently analyzing karyotypes is an invasive technique, limiting its clinical application. Therefore, we tried to distinguish between normally-fertilized zygotes and 1PN zygotes by their morphology or developmental behavior. In this study, we used a microscope with time-lapse system to analyze the developmental time course and morphology of human 1PN zygotes, especially parthenogenetic zygotes induced by artificial oocyte activation.

**DESIGN:** Research study.

**MATERIALS AND METHODS:** This study used 32 MII oocytes donated between October 2014 and August 2015 by patients who gave informed consent for this study. Fresh or freeze-thawed MII oocytes were activated electronically and the oocytes were observed by EmbryoScope®. We compared the developmental time course and morphology between parthenogenetic zygotes and normal 2PN zygotes fertilized by assisted reproductive technology.

**RESULTS:** There was no difference in the diameter of the PN in parthenogenetic zygotes compared to the female PN in normal fertilized zygotes (28.9 ± 2.2 vs 26.4 ± 2.0 μm, respectively). There were significant differences between normal 2PN and parthenogenetic zygotes for the time from intracytoplasmic sperm injection or electronic activation to the 2nd polar body (PB) extrusion (3.0 ± 1.7 vs 2.3 ± 0.5 h, respectively), from 2nd PB extrusion to syngamy (20.8 ± 4.1 vs 18.7 ± 2.9 h, respectively), from syngamy to 1st cleavage (3.0 ± 2.3 vs 3.9 ± 1.1 h, respectively), and from 1st cleavage to 2nd cleavage (9.8 ± 4.8 vs 13.6 ± 5.2 h, respectively). In addition, some parthenogenetic zygotes (6 of 21) developed to blastocysts.

**CONCLUSIONS:** The time required from electronic activation to 2nd PB extrusion and from 2nd PB extrusion to syngamy in parthenogenetic zygotes was significantly shorter than in normal zygotes. This may be because oocyte activation or decondensation of the sperm nucleus is not required in parthenogenetic zygotes. In addition, the time required from syngamy to 1st cleavage, and from 1st cleavage to 2nd cleavage in parthenogenetic zygotes was significantly longer than in normal embryos. Thus, differences in the time course of embryonic development in activated zygotes could be used to identify the characteristics of parthenogenetic zygotes, even though further studies are needed. Furthermore, although some parthenogenetic zygotes develop to blastocysts, the clinical use of zygotes with 1PN should be questioned.

**OBJECTIVE:** To evaluate the efficiency of chemical oocyte activation with calcium ionophore on fertilization and pregnancy outcomes after intracytoplasmic sperm injection (ICSI) in patients with previous fertilization failure.

**DESIGN:** Prospective controlled study.

**MATERIALS AND METHODS:** One hundred and eight patients with history of previous fertilization failure undergoing ICSI treatment with long agonist protocol were randomly divided into two groups: group A (n=54) and group B (n=54).

A total of 756 metaphase II (MII) oocytes were retrieved. In the oocytes of group A (n=350 oocyte), routine ICSI was applied; while oocytes in group B (n=406 oocyte) were entered in culture medium supplemented with 5 μM calcium ionophore (A23187) for 10 minutes and then washed at least five times with MOPS solution immediately after ICSI.

In both groups, the fertilization was evaluated after 16-18 hours.

**RESULTS:** The number of fertilized oocytes and embryos obtained were significantly different between two groups (p<0.001*). Fertilization rate was significantly higher in group B -where calcium ionophore was applied-compared to group A-control group (32.2% vs. 9.1%, respectively, p=0.01*).

Cleavage rate also was significantly higher in group B compared to group A (26.7% vs 6.25% respectively, p=0.028*). Implantation rate was significantly higher in group B than in group A (17.64% vs. 2.41% respectively, p=0.035*). Pregnancy rate also was significantly higher in group B than in group A (21% vs. 3.7% respectively, p=0.042*).

**CONCLUSIONS:** Chemical oocyte activation with calcium ionophore resulted in a significant improvement in fertilization, cleavage, implantation and pregnancy rates after ICSI in infertile patients with previous fertilization failure.

**References:**


P-217 Tuesday, October 18, 2016


OBJECTIVE: Mutations in mitochondrial DNA (mtDNA) cause a number of diseases in offspring. Since mtDNA mutations are transmitted exclusively through the oocyte, any manipulation of the oocyte cytoplasm has been proposed to prevent transmission of mtDNA diseases. A method to estimate mtDNA load at the oocyte level would help balance the risk/benefit of oocyte manipulations. We sought to determine whether polar bodies (PB) accurately represent the mitochondrial mutational load in their corresponding oocytes.

DESIGN: Translational science research.

MATERIALS AND METHODS: IRB approval was obtained for use of human discard material and a total of 10 oocyte-PB pairs were obtained. Immature oocytes received 2 hours post retrieval were placed in an incubator for 48 hours and those that matured were subsequently frozen. Prior to freezing, oocytes were processed with pronase and all excess cumulus cells were removed. The PB was then removed mechanically and frozen separately from the oocyte in PBS solution. A real time PCR assay was developed that changed significantly with BMI were distinct from those that changed was 30% and 61.8% in PBs (p = 0.001). The largest percent difference between the oocyte and PB mtDNA deletion ratio was 76%. Prediction of oocyte deletion ratio based on PB deletion ratio is shown with the equation [Oocyte deletion ratio = 0.606(PB deletion ratio) - 0.0078], however this relationship did not reach statistical significance.

CONCLUSIONS: It has been suggested that the PB can be used to estimate mitochondrial mutational load. Here we show that the PB overestimates the mutational load in the oocyte (as high as 76% in some cases). Higher deletion ratios in PBs tended to correlate with higher deletion ratios in associated oocytes. Larger numbers are needed for confirmation, but even from the sample size studied the PB deletion ratio clearly is not representative of its corresponding oocyte.

P-218 Tuesday, October 18, 2016


OBJECTIVE: Advanced reproductive age and increased adiposity are associated with negative in vitro fertilization (IVF) outcomes, but the underlying mechanisms are unclear. The microenvironment in which an oocyte develops can significantly impact its quality. Therefore, the objectives of this study were to assess the cytokine profiles of human follicular fluid and to determine how they change with age and body mass index (BMI).

DESIGN: Translational.

MATERIALS AND METHODS: Follicular fluid from the first follicle retrieved at the time of IVF from a total of 26 patients age 27-44 years was run in duplicate on Human Cytokine C5 Antibody Arrays (Ray Biotech). Probed arrays were developed, intensities were quantified, and data were normalized and analyzed. Information including age, BMI, Anti-Muller hormone (AMH) levels, and infertility diagnosis was also collected.

RESULTS: The mean age of participants was 35.6 ± 5 years, mean BMI was 23.25 ± 2.9 kg/m², and mean AMH was 2.66 ± 1.8 ng/ml. There was a significant negative linear correlation between age and AMH, but no relationship between age and BMI was observed. 80 cytokines were analyzed, and 61 had intensity values above threshold. 39 cytokines showed a significant increase with age; these same cytokines showed a decrease with AMH, with 12 reaching statistical significance (MIP-1-beta, IL-3, IL-7, IL-12-P40, IL-15, TGFb1, TGFb3, VEGF, BDNF, Eotaxin2, PIGF, and Oncostatin M). 4 cytokines had a significant association with BMI; IL-8, MCP1, and Leptin were increased, whereas HGF was decreased. Interestingly, the cytokines that changed significantly with BMI were distinct from those that changed with age or AMH.

CONCLUSIONS: Specific cytokine profiles may be strong predictors of both chronological and reproductive age. Obtaining this information is non-invasive to the oocyte, and thus may have clinical utility. Studies are ongoing to determine whether such cytokines are correlated with IVF outcomes. Our findings also suggest that advanced reproductive age and increased BMI are associated with unique follicular fluid microenvironments that may negatively influence oocyte quality through different mechanisms.

Supported by: Friends of Prentice, P50HD076188, KU Undergraduate Research Award.

P-219 Tuesday, October 18, 2016


OBJECTIVE: To better understand the components of double-strand break (DSB) machinery, in order to gain insight into the first event in meiotic over-recombination.

DESIGN: Basic research animal study of Caenorhabditis elegans.

MATERIALS AND METHODS: We created double mutants and analyzed a matrix of interactions between partial loss-of-function alleles of genes involved in DSB formation in C. elegans. These include mutations in lin-35, cep-1, dsb-2, rec-1, him-17, him-5, parg-1, and mev-11. We have analyzed diakinesis oocytes by whole mount staining followed by confocal microscopy and 3D visualization allowing quantification of crossover
numbers. We have also analyzed the effects of these mutations on brood size and frequency of males, measures of nondisjunction.

RESULTS: The alleles of partial deletion show nondisjunction phenotypes with increased embryonic lethality and decreased brood counts in the double mutant. There are notable interactions between dsb-2 and him-17, lin-35 and him-5, rec-1 and him-17, rec-1 and dsb-2, lin-35 and him-17, as well as dsb-2 and nre-11. There is also potential interaction between lin-35 and par-1.

CONCLUSIONS: Assessment of achiasmatic chromosomes has allowed us to determine synthetic interactions for crossover formation in these sets of mutants, revealing redundancy in this process that ensures robustness. Preliminary analysis suggests that the DSB genes fall into multiple groups that interact synergistically to impact break formation.

P-220 Tuesday, October 18, 2016


OBJECTIVE: To assess the effect of artificial oocyte activation (AOA) on ICSI cycles using testicular surgically retrieved spermatozoa of patients with non obstructive azoospermia (NOA) or severe oligoasthenoteratozoospermia.

DESIGN: Retrospective cohort.

MATERIALS AND METHODS: ICSI cycles of patients with NOA or severe oligoasthenoteratozoospermia who underwent testicular sperm extraction (TESE) from 2010 to 2015 in procrearte, were divided in two groups: study group (ICSI + calcium ionophore A23187) and control group (ICSI) we included women under 38 years old, with FSH<10 U/Ml. And More Than 4 Oocytes Retrieved. Statistical Analysis Was Performed With SPSS 18.0. Mean values were compared by student T test and proportions by chi square test. P<0.05 was considered statistically significant.

RESULTS: We included a total of 75 ICSI cycles with surgically retrieved spermatozoa, 48 in the control group and 27 in the study group. Male and female age, FSH levels and maturation rate were comparable in both groups, (p>0.05). A total of 343 and 311 mature oocytes were injected in ICSI and ICSI+ calcium ionophore groups respectively with a fertilization rate of 66.95% +/- 24 and 60.8% +/- 24% (p=0.23). No difference on cleavage rate was found between the groups (96.1 vs 92%) (p=0.07). Forty-eight and 25 embryo transfers were performed in each group with no difference on embryo stage (p=0.87) or good embryo quality 85% vs 87.2%, respectively (p=0.8). No difference on clinical outcomes were found when the control and study group were compared: pregnancy rate (41.66 vs 36%) (p=0.82), implantation rate (17.8 vs 18.1%) (p=0.87), clinical pregnancy rate (29 vs 25%) (p=0.7) and ongoing pregnancy rate (27 vs 16%) (p=0.6).

CONCLUSIONS: The addition of calcium ionophore in ICSI cycles using testicular surgically retrieved spermatozoa in patients with NOA or severe oligoasthenoteratozoospermia, does not improve neither fertilization rate nor clinical outcomes. The utilization of artificial oocyte activation, should be restricted to cases in which low or total fertilization failure had been previously observed.

OOCYTE MATURATION

P-221 Tuesday, October 18, 2016


OBJECTIVE: Rad51 mediates the homologous recombination repair of DNA double strand breaks (DSBs) that occur during mitosis and meiosis. In addition, Rad51 promotes mitochondrial DNA synthesis when replication stress increased. Rad51 expression decreases in age-dependent manner in the mouse oocytes and it is closely linked to the increased aneuploidy rates. Rad51 are also required for efficient reprogramming and genomic stability of induced pluripotent stem cells. Thus, we conducted the present study to evaluate the role of Rad51 in mammalian oocyte maturation, including genome stability and mitochondrial function.

DESIGN: This was a laboratory research study. We investigated the direct effect of Rad51 on meiosis and mitochondrial quality and quantity in murine oocytes.

MATERIALS AND METHODS: After Rad51 RNA interference (RNAi), oocyte maturation and many cellular and biochemical changes, such as knockdown of mRNAs and proteins, oocyte maturation rate, spindle and chromosome configuration, genomic stability, mitochondrial number and distribution, mitochondrial membrane potential, ATP synthesis, amount of mitochondrial DNA (mtDNA) and mtDNA and miophagy were measured.

RESULTS: Rad51 dsRNA microinjection into GV oocytes resulted in a markedly decreased Rad51 mRNA and protein expression. Based on morphological changes, Rad51 deficiency caused failure of cytokinesis and emission of the first polar body resulting in meiotic arrest at MI stage. Immunofluorescence staining results showed that MI spindles were aggregated and mingled with amassed chromosomes in Rad51-silenced oocytes. In addition, Rad51-silencing led the significantly increased DNA damage that was resulted in genomic instability. These MI-arrested oocytes exhibited dramatically reduced mitochondrial number with altered mitochondrial distribution. In addition, disruption of Rad51 led to decreased mitochondrial membrane potential and the amount of mtDNA that subsequently impaired mitochondrial ATP production. Interestingly, we found that the number of Map1h-3b-positive puncata, used as the marker of mtDNA, increased in the Rad51-silenced MI oocytes, suggesting that mitochondrial reduction caused by the suppression of Rad51 is associated with increased mtDNA.

CONCLUSIONS: We report for the first time that Rad51 regulates quality and quantity of the mitochondria by regulating mtDNA and concurrently controls meiotic maturation in the oocytes. We propose that the preserving certain level of Rad51 in oocytes, such as Rad51 microinjection may contribute to sustain good quality of the oocytes throughout aging and environmental stress during in vitro maturation. It may candidate intervention of the three parents issue in cyttoplasmic transfer in IVF program.

Supported by: This research was supported by the Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education (2009-0093821).

P-222 Tuesday, October 18, 2016


OBJECTIVE: Poor fertilization in ICSI cycles may occur despite normal sperm characteristics and an adequate number of mature oocytes. Asynchrony between nuclear and cytoplasmic maturation of the oocyte has been proposed as a causative factor in such circumstances. We investigate the utility of a combined GnRH-agonist (GnRH-a) ovulatory trigger with human chorionic gonadotropin (hCG) in improving ICSI cycle outcomes in patients with poor fertilization history after standard hCG trigger alone. Dose responsive Non-randomized prospective observational study.

MATERIALS AND METHODS: Patients <40 years, with a known history of poor fertilization with ICSI, undergoing a subsequent ICSI cycle with fresh embryo transfer (ET) at our center between 2004 and 2013 were assessed for inclusion. Poor fertilization was defined as 2 standard deviations below the mean fertilization rate for our center, in the presence of normal sperm characteristics and >5 mature oocytes (index cycles). Patients meeting criteria for poor fertilization prospectively underwent another ICSI cycle with a similar stimulation protocol and hCG trigger alone, or a similar stimulation protocol with combined GnRH-a and hCG trigger, or a different stimulation protocol. Demographics, baseline IVF characteristics, and ovarian stimulation parameters of the three groups were compared with each other and also with index cycles. Fertilization, clinical pregnancy and live birth rates were also compared with respect odds ratio (OR), with appropriate statistical adjustments.

RESULTS: Out of total of 16721 ICSI cycles, 687 (4.11%) patients met criteria i.e., fertilization rate <20%. Of these, 318 (46.3%) patients underwent a subsequent ICSI cycle with a similar stimulation protocol and hCG trigger alone, 109 (15.9%) patients with combined GnRH-a and hCG trigger, and 260 (37.8%) patients with a different stimulation protocol. The demographics and ovarian stimulation parameters of the 3 groups were similar. Compared to the other 2 treatment modalities, patients receiving the combined GnRH-a and hCG trigger had higher odds of mature oocytes (2.19, 95%CI 1.31-2.46; P=0.02), higher odds of fertilization (2.67, 95%CI 1.42-5.02; P=0.01), and higher odds of ICSI cycles resulting in day-3 embryo transfers (9.33, 95%CI 4.87-16.9; P<0.01). The odds of clinical pregnancy
MATURE OOCYTE AND EMBRYO YIELD IN PATIENTS WITH MATURATION (IVM) MEDIUM PRIOR TO IVF/ICSI IMPROVES. DOES SHORT-TERM EXPOSURE OF OOCYTES TO IN VITRO MATURATION (IVM) MEDIUM PRIOR TO IVF/ICSI IMPROVE MATURATION (IVM) MEDIUM PRIOR TO IVF/ICSI IMPROVE MATURATION (IVM) MEDIUM PRIOR TO IVF/ICSI IMPROVE MATURATION (IVM) MEDIUM PRIOR TO IVF/ICSI IMPROVE MATURATION (IVM) MEDIUM PRIOR TO IVF/ICSI IMPROVE MATURATION (IVM) MEDIUM PRIOR TO IVF/ICSI IMPROVE MATURATION (IVM) MEDIUM PRIOR TO IVF/ICSI IMPROVE

DoES TRIGGER OF FINAL OOCYTE MATURATION WITH PURE GNRH-AGONIST HAVE ADVERSE EFFECTS ON PREGNANCY OUTCOMES OF DONOR/RECIPIENT CYCLES?. M. Irani,a V. Gumala,a b C. Racowsky,a Obstetrics, Gynecology and Reproductive Medicine, Weill Cornell Medical Center, New York, NY; aOB/GYN, REI Fellow, New York, NY; bObstetrics, Gynecology and Reproductive Medicine, Weill Cornell Medical Center, Manhattan, NY. Recipient’s peak endometrial thickness (aOR 1.25, 95%CI:1.0-1.43), a 21.5% increase from Cycle 1 versus a 10.3% increase for the non-IVM group (P=0.11). There was a non-significant trend towards a greater number of usable embryos (for freezing or transfer) in the IVM group in Cycle 2.

CONCLUSIONS: The results of this study support the hypothesis that short-term IVM incubation of COCs from women who produce an unusually high percentage of immature oocytes results in an increased yield of mature oocytes and zygotes, which may increase the number of usable embryos. A randomized control trial is warranted to determine whether these increased yields translate into improved clinical outcomes in this challenging group of patients.

Comparison of outcomes with and without short-term IVM medium exposure in Cycle 2

<table>
<thead>
<tr>
<th></th>
<th>IVM Group</th>
<th>Non-IVM Group</th>
</tr>
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<tbody>
<tr>
<td>Number MII</td>
<td>8.27 +/- 4.70</td>
<td>7.53 +/- 5.25</td>
</tr>
<tr>
<td>(mean +/- SD)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number 2PN</td>
<td>6.10 +/- 3.80</td>
<td>5.30 +/- 4.10</td>
</tr>
<tr>
<td>(mean +/- SD)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number Usable</td>
<td>3.45 +/- 1.89</td>
<td>3.29 +/- 2.56</td>
</tr>
<tr>
<td>Embryos (mean +/- SD)</td>
<td></td>
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DOES SHORT-TERM EXPOSURE OF OOCYTES TO IN VITRO MATURATION (IVM) MEDIUM PRIOR TO IVF/ICSI IMPROVE MATUATION (IVM) MEDIUM PRIOR TO IVF/ICSI IMPROVE MATUATION (IVM) MEDIUM PRIOR TO IVF/ICSI IMPROVE MATUATION (IVM) MEDIUM PRIOR TO IVF/ICSI IMPROVE MATUATION (IVM) MEDIUM PRIOR TO IVF/ICSI IMPROVE MATUATION (IVM) MEDIUM PRIOR TO IVF/ICSI IMPROVE MATUATION (IVM) MEDIUM PRIOR TO IVF/ICSI IMPROVE

Objective: A subset of IVF patients has a high incidence of oocyte immaturity, which can lead to poor clinical outcomes. Increasing the number of mature (metaphase II [MII]) oocytes may benefit this population. In this study we tested the hypothesis that short-term IVM of cumulus-oocyte complexes (COCs) before exposure to sperm increases MII oocyte and embryo yield.

Design: Retrospective cohort study.


Objective: Spontaneous ovulation is preceded by a surge of both follicle-stimulating hormone (FSH) and luteinizing hormone. This surge is thought to be necessary for follicular oocyte nuclear maturation and initiation of follicular rupture. This analysis seeks to determine whether the addition of a follicle-stimulating hormone (FSH) bolus administered at the time of human chorionic gonadotropin (hCG) trigger can improve IVF cycle outcomes.

Design: Retrospective cohort.

Materials and Methods: IVF cycles that utilized an ‘FSH boost’ from 2010-2016 at a single infertility center were included. This 450 IU bolus was administered at physician discretion in cycles where oocyte maturity was of concern given prior published data showing benefit (1). Patient demographics, markers of ovarian reserve, stimulation protocol, maximum estradiol (E2) level, number of oocytes retrieved, number of metaphase II (MII) oocytes retrieved, fertilization rate, and blastulation rate were recorded. Controls from the same center who did not utilize the ‘FSH boost’ were also evaluated and matched by age, body mass index (BMI), anti-mullerian hormone.
FEATURES OF EMBRYOS FROM TWO CASES OF RTFF
OBJECTIVE: IVF is currently efficient method for treatment of infertility, and has been applying in this field for about 38 years. However, there still have some patients who recurrently failed to get oocytes or failed to fertilize. While, recent technical advances in sc-Seq makes it possible to determine the number of oocytes retrieved or oocyte maturity with administration of an FSH bolus but the internal mechanism underlying is still elusive due to the technical limitations. CONCLUSIONS: Despite the endogenous FSH surge that precedes spontaneous ovulation, this analysis demonstrates no improvement in the number of oocytes retrieved or oocyte maturity with administration of an FSH bolus at the time of hCG trigger in IVF.

Table 1: There is no difference in IVF cycle outcome after administration of an ‘FSH boost’.

<table>
<thead>
<tr>
<th></th>
<th>‘FSH boost’ cycle</th>
<th>Matched IVF cycle</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean±SD)</td>
<td>37.9±4.7 years</td>
<td>38.1±4.4 years</td>
<td>0.54</td>
</tr>
<tr>
<td>BMI (mean±SD)</td>
<td>26.1±5.4 kg/m²</td>
<td>26.0±5.2 kg/m²</td>
<td>0.83</td>
</tr>
<tr>
<td>AMH (Md)</td>
<td>0.91 ng/mL</td>
<td>0.90 ng/mL</td>
<td>0.82</td>
</tr>
<tr>
<td>Max E2 (mean±SD)</td>
<td>1531.9±737.6 pg/mL</td>
<td>1538.±737.3 pg/mL</td>
<td>0.90</td>
</tr>
<tr>
<td>M2 oocytes retrieved (mean±SD)</td>
<td>7.6±4.5 oocytes</td>
<td>7.6±4.5 oocytes</td>
<td>0.90</td>
</tr>
<tr>
<td>Maturation rate</td>
<td>70.0%</td>
<td>71.7%</td>
<td>0.28</td>
</tr>
<tr>
<td>Fertilization rate</td>
<td>84.1%</td>
<td>86.0%</td>
<td>0.33</td>
</tr>
<tr>
<td>Blastulation rate</td>
<td>40.8%</td>
<td>41.8%</td>
<td>0.65</td>
</tr>
<tr>
<td>M2 oocytes retrieved (mean±SD)</td>
<td>5.4±3.6 oocytes</td>
<td>5.5±3.6 oocytes</td>
<td>0.79</td>
</tr>
</tbody>
</table>

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SINGLE CELL TRANSCRIPTOME REVEAL CHARACTERISTIC FEATURES OF EMBRYOS FROM TWO CASES OF RTFF PATIENTS. L. Suo, Y. Zhou, Y. Kuang. “Shanghai Ninth People’s Hospital, Shanghai, China; Shanghai Jiaotong University, Shanghai, China.

OBJECTIVE: IVF is currently efficient method for treatment of infertility, and has been applying in this field for about 38 years. However, there still have some patients who recurrently failed to get oocytes or failed to fertilize. While, recent technical advances in sc-Seq makes it possible to determine the number of oocytes retrieved or oocyte maturity with administration of an FSH bolus at the time of hCG trigger in IVF.

Table 1: There is no difference in IVF cycle outcome after administration of an ‘FSH boost’.

<table>
<thead>
<tr>
<th></th>
<th>‘FSH boost’ cycle</th>
<th>Matched IVF cycle</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean±SD)</td>
<td>37.9±4.7 years</td>
<td>38.1±4.4 years</td>
<td>0.54</td>
</tr>
<tr>
<td>BMI (mean±SD)</td>
<td>26.1±5.4 kg/m²</td>
<td>26.0±5.2 kg/m²</td>
<td>0.83</td>
</tr>
<tr>
<td>AMH (Md)</td>
<td>0.91 ng/mL</td>
<td>0.90 ng/mL</td>
<td>0.82</td>
</tr>
<tr>
<td>Max E2 (mean±SD)</td>
<td>1531.9±737.6 pg/mL</td>
<td>1538.±737.3 pg/mL</td>
<td>0.90</td>
</tr>
<tr>
<td>M2 oocytes retrieved (mean±SD)</td>
<td>7.6±4.5 oocytes</td>
<td>7.6±4.5 oocytes</td>
<td>0.90</td>
</tr>
<tr>
<td>Maturation rate</td>
<td>70.0%</td>
<td>71.7%</td>
<td>0.28</td>
</tr>
<tr>
<td>Fertilization rate</td>
<td>84.1%</td>
<td>86.0%</td>
<td>0.33</td>
</tr>
<tr>
<td>Blastulation rate</td>
<td>40.8%</td>
<td>41.8%</td>
<td>0.65</td>
</tr>
</tbody>
</table>

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ADDITION OF ENDOTHELIN-1 TO CULTURE MEDIUM PROMOTES HUMAN OOCYTE MATURATION. Y. Ye. Women’s Hospital, Zhejiang University School of Medicine, Hangzhou, China.

OBJECTIVE: To investigate whether the supplementation of culture medium with endothelin-1 may enhance human oocyte maturation and to explore the underlying mechanisms.

RESULTS: Significantly more oocytes reached metaphase II stage after being cultured in medium supplemented with endothelin-1 (68.2% vs 51.5%, p=0.039). Microarray results revealed 25 significant differentially regulated genes in cumulus treated or untreated with endothelin-1, of which Cx26 gene was the most significantly down-regulated gene. Real-time PCR confirmed microarray analysis results: expression of Cx26 was down-regulated in cumulus cells after endothelin-1 treatment (P=0.032). Immunofluorescence assay showed Cx26 was located in cellular membrane and cytoplasm in both cumulus cells and oocyte. The suppressive effect of endothelin-1 on cumulus Cx26 expression was blocked by cotreatment with antagonist for endothelin receptor type B (ETRB), not for type A (ETRA).

CONCLUSIONS: Supplementation of medium with endothelin-1 promotes human GV stage oocyte maturation via Cx26.

References:

Supported by: The study is funded by Natural Science Foundation of China (Grant No. 81170567).

OVARIAN STIMULATION

P-228 Tuesday, October 18, 2016

THE ESPART RANDOMIZED CONTROLLED TRIAL IN POOR OVARIAN RESPONDERS ALIGNED WITH THE BOLOGNA CRITERIA: A POST HOC SUBGROUP ANALYSIS ACCORDING TO POOR OVARIAN RESPONSE INCLUSION CRITERIA.
J. Hubbard,1 W. Chin,1 P. Humaidan.1 1Global Clinical Development Center, EMD Serono Research and Development Institute, Billerica, MA; 1Global Biostatistics & Epidemiology, EMD Serono Research and Development Institute, Billerica, MA; 1Faculty of Health, Aarhus University, The Fertility Clinic Skive, Skive, Denmark.

OBJECTIVE: The ESPART randomized controlled trial (RCT), the largest trial to date in poor ovarian responders (PORs; n=939) aligned with the Bologna criteria, investigated assisted reproductive technology (ART) outcomes following controlled ovarian stimulation (COS) with either recombinant human follicle-stimulating hormone plus recombinant human luteinizing hormone (r-hFSH+r-hLH) or r-hFSH alone. Following a single ART cycle no difference in NOV, ongoing pregnancy rate (OPR) or live birth rate (LBR) was observed between treatments (mean NOV with r-hFSH+r-hLH and r-hFSH, respectively: 3.3 and 3.6; OPR: 11.0% and 12.4%; LBR: 10.6% and 11.7%). It has been suggested that the Bologna criteria may include subpopulations with different characteristics that could affect outcomes. This analysis investigated whether NOV or OPR differed in subgroups stratified by age, anti-Mullerian hormone (AMH) level and ART history.

DESIGN: Post hoc subgroup analysis of the ESPART RCT. For inclusion, PORs had to meet ≥2 of the following: age ≥40-<41 years; AMH level 0.1-1.1 ng/mL; a previous ART cycle with ≤3 oocytes retrieved with conventional stimulation.

MATERIALS AND METHODS: The modified intention-to-treat population was analyzed. (r-hFSH+r-hLH, n=462; r-hFSH, n=477). NOV and OPR were compared between treatment groups stratified by age (<35, ≥35-<38, ≥38-<40, ≥40), AMH level (ng/mL; ≤0.5, >0.5-≤1.1, >1.1) and ART history (previous ART with ≤3 oocytes; previous ART with >3 oocytes; no previous ART) considered individually and in combination.

RESULTS: Overall, the mean age was 38.3 years, mean AMH level was 0.59 ng/mL and 83.2% of participants had ≥1 previous ART cycle with ≤3 oocytes retrieved. There was no difference observed in NOV or OPR between women receiving r-hFSH+r-hLH or r-hFSH, in any of the subgroups analyzed (Table).

CONCLUSIONS: This analysis confirmed the balance and overall homogeneity of the ESPART population. No beneficial effects on outcomes were observed with the addition of r-hLH to r-hFSH for COS in the subgroups investigated. The results are consistent with the postulate that the patients in ESPART had the most severely compromised potential for ovarian response after COS. Further studies are required to identify suboptimal responders who may respond beneficially to addition of LH for COS.

Supported by: This study was supported by Merck KGaA, Darmstadt, Germany.

OPTIMAL OOYTE YIELD FOR CUMULATIVE LIVE-BIRTH RATE: ANALYSIS OF 257,398 IVF CYCLES AND THEIR LINKED FRESH AND FROZEN EMBRYO TRANSFERS.
S. M. Nelson,1 A. Smith,1 K. Tilling,1 D. A. Lawlor,1 1School of Medicine, University of Glasgow, Glasgow, United Kingdom; 2University of Bristol, Bristol, United Kingdom; 3MRC Integrative Epidemiology Unit, University of Bristol, Glasgow, United Kingdom.

OBJECTIVE: To determine the optimal oocyte yield for cumulative live-birth rates incorporating fresh and all frozen embryos per initiated IVF cycle.

DESIGN: Prospective study of 156,947 UK women who received 257,398 IVF ovarian stimulation cycles between 2003 and 2010 and were followed up until June 2012.

MATERIALS AND METHODS: The Human Fertilisation and Embryology Authority (HFEA) provided us with data on all ART events occurring in the United Kingdom between January 1, 2003, and June 30, 2012, with linkage of cycles to individual women and data on birth outcomes. Once a live birth occurred, women were censored from further analysis. We included all embryo transfers, whether the individual transfer was of one or more embryos. The principal exposure was an in vitro fertilization cycle, with a cycle defined as an episode of ovarian stimulation and all subsequent separate fresh and frozen embryo transfers. We assessed the associations in all women and all cycles, then whether results were similar in subgroup analyses of women <35 years, <40 years and first cycle or second cycle or a combination of these two factors. We plotted cumulative live-birth rates relative to oocyte yield and calculated the linear change in log odds above 15 oocytes to evaluate the contribution of oocyte yield to live-birth rates above 15 oocytes.

RESULTS: There was a monotonic increase in live-birth rates up to 15 oocytes and then a decline in fresh cycle live-birth rates with increasing oocyte yield beyond 15 oocytes. Cumulative live-birth rates from the associated frozen embryo transfers increased with increasing oocyte yield. The cumulative live-birth rate incorporating all fresh and frozen embryo transfers from a single ovarian stimulation cycle for women <40 years old in their first cycle (N=133,379 women) rate was not enhanced beyond 15 oocytes (difference in log odds per additional oocyte from 15 to 51 oocytes -0.002 (95% CI -0.007 to 0.002, p=0.34). Similar results were obtained when restricted to women ≤35 years (N=23,016); difference in log odds per additional oocyte from
15 to 51 oocytes is -0.004 (95% CI -0.010 to 0.000, p=0.07), or the second cycle (N=53,568 difference in log odds per additional cycle from 15 to 51 oocytes is 0.007 (95% CI 0.000 to 0.016, p=0.06).

CONCLUSIONS: The cumulative live-birth rate encompassing all fresh and frozen embryo transfers from a single ovarian stimulation cycle increases up to 15 oocytes but does not increase further if more oocytes are obtained. Supported by: Ferring

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HOW MANY OOCYTES ARE OPTIMAL TO MAXIMIZE THE CUMULATIVE NUMBER OF LIVE BIRTHS WITH ONE STIMULATION? A. D. Vaughan, A. Leung, N. Resektova, A. S. Penzias, R. Ruthazer, D. Sakkas, M. M. Alper. Obstetrics and Gynecology, Tufts Medical Center, Boston, MA; Tufts Medical Center, Boston, MA; Beth Israel Deaconess Medical Center, Boston, MA; Boston IVF/Harvard Medical School, Waltham, MA; Medicine, Tufts CSIT/Tufts medical center, Boston, MA; Boston IVF, Waltham, MA; Boston IVF/ Harvard Medical School, Waltham, MA.

OBJECTIVE: Data are conflicting regarding the optimum number of oocytes needed during an IVF cycle. Agressive stimulation may lead to ovarian hyperstimulation syndrome (OHSS), poorer egg quality and abnormal uterine receptivity. However, each fresh stimulation cycle has its own concerns: surgical/anesthesia risks, cost and, not least, dropout rates and emotional stress. In this study we sought to investigate: factors influencing at least one live birth and the cumulative live birth rate across all cycles based on the number of oocytes retrieved. DESIGN: Retrospective cohort study. MATERIALS AND METHODS: We reviewed all homologous, first cycles with oocyte retrieval from January 1st 2012-December 31st 2014. We separated our cohort based on the number of oocytes retrieved (1-3, 4-9, 10-14, 15-25, >25 oocytes). We then retrieved data regarding subsequent thaw cycles using embryos from the index cycle. Chi-squared and t tests were used where appropriate. A univariate model was developed and all statistically significant variables included in our multivariate analysis. Our primary outcomes were live birth rate (LBR) per oocyte and cumulative LBR. Secondary outcomes included fertilization rate, number of blastocysts and clinical pregnancy rate (CPR).

RESULTS: 2226 patients (2987/8959 cycles) met inclusion criteria. 665/2226 (29.9%) patients had at least 1 live birth in the fresh cycle. An additional 225/761 (29.6%) thaw cycles resulted in at least one further live birth. There was a linear increase in blastocyst development corresponding to the number of oocytes retrieved. The pregnancy rate was significantly higher (p<0.01) when ≥15 oocytes were retrieved (289/699, 41.3%) than <15 oocytes (518/1419, 36.5%). Table 1 demonstrates both adjusted and unadjusted variables for outcome of at least 1 live birth in index cycle. Controlling for age, E2, BMI, ICSI, PGD, fertilization rate, P4 on day of trigger, as the number of oocytes retrieved increased, the chance of at least one live birth in cycle 1 increased (p<0.07), with OR=1.02 per additional oocyte (95% CI 1.00 to 1.04).

CONCLUSIONS: Ultimately, more oocytes retrieved result in more embryos frozen and a higher cumulative LBR. This could mean that one cycle could be used to satisfy a couples desires to complete their family without performing multiple mild stimulation cycles.

Table 1. Adjusted and unadjusted variables for outcome of at least 1 live birth in index cycle

<table>
<thead>
<tr>
<th>Variable</th>
<th>Yes</th>
<th>No</th>
<th>Unadjusted p-value</th>
<th>Adjusted OR (95% CI) and p-value**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt;35</td>
<td>27/124 (22%)</td>
<td>394/983 (40%)</td>
<td>&lt;.001</td>
<td>0.29-0.48, p &lt; .001</td>
</tr>
<tr>
<td>BMI ≥35</td>
<td>25/166 (15%)</td>
<td>567/1827 (31%)</td>
<td>&lt;.001</td>
<td>0.95-0.98, p = .003</td>
</tr>
<tr>
<td>Blastocyst transfer</td>
<td>339/883 (45%)</td>
<td>265/1009 (26%)</td>
<td>&lt;.001</td>
<td>0.98-1.66, p = .076</td>
</tr>
<tr>
<td>PGD/PGS</td>
<td>42/200 (21%)</td>
<td>623/2026 (31%)</td>
<td>0.003</td>
<td>0.59-1.42, p = .690</td>
</tr>
<tr>
<td>P4 on day of trigger ≥1ng/ml</td>
<td>159/607 (26%)</td>
<td>229/693 (33%)</td>
<td>0.026</td>
<td>1.13-1.16, p = .005</td>
</tr>
<tr>
<td>Peak E2 (pg/ml) per 1000pg/ml increase</td>
<td>-</td>
<td>-</td>
<td>0.001</td>
<td>0.92-1.15, p = .611</td>
</tr>
<tr>
<td>ICSI</td>
<td>220/752 (29%)</td>
<td>445/1474 (30%)</td>
<td>0.648</td>
<td>0.67-2.64, p = .408</td>
</tr>
<tr>
<td>Fertilization rate (OR per change of 0.1)</td>
<td>-</td>
<td>-</td>
<td>&lt;.001</td>
<td>1.10-1.35, p &lt; .001</td>
</tr>
<tr>
<td># Oocytes retrieved (&gt;30 counted as 30)</td>
<td>-</td>
<td>-</td>
<td>&lt;.001</td>
<td>1.00-1.04, p = .075</td>
</tr>
</tbody>
</table>

+ Data shown as %/n with unadjusted p-value from chi-square test, or linear data analysis where appropriate
++ Adjusted odds ratios and p-values from multivariable logistic regression.

References:

Supported by: Supported by the Turksoy/Marcus grant, Tufts Medical Center.

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PREGNANCY RATES IN FROZEN-THAWED CYCLES AFTER GnRH-AGONIST OR ANTAGONIST PROTOCOLS. R. Mirisol, P. F. Peregrino, S. P. Goncalves, P. G. Petersen, J. Miorin, M. G. Fujii, A. P. Gomes, T. C. Bonetti, P. A. Monteleone. Centro de Reproducao Humana, Sao Paulo, Brazil; Gynecology, Universidade Federal de Sao Paulo, Sao Paulo, Brazil; Discipline of Gynecology, Hospital das Clinicas, U, Sao Paulo, Brazil.

OBJECTIVE: Studies on the impact of GnRH-agonist with GnRH-antagonist protocols on endometrial receptivity remains controversial. The aim of this study was to compare clinical outcomes of frozen-thawed embryos transfers’ cycles in which the pituitary blockage in the stimulation cycle used GnRH-agonist or GnRH-antagonist in good prognosis patients.

DESIGN: Retrospective observational study between 2011-2015.

MATERIALS AND METHODS: Patients had embryo transfers (ET) in the fresh cycle (agonist, n=114, antagonist, n=276), exceeding embryos were cryopreserved and 245 patients underwent frozen-thawed ET. For the frozen-thawed ET, endometrium preparation was performed with estradiol valerate plus vaginal micronized progesterone. The frozen-thawed cycles were split into 2 groups according with pituitary down regulation: agonist (n=68) or antagonist (n=177).

RESULTS: Outcomes for agonist and antagonist groups on fresh cycles were, respectively: patients age (36.3±3.7 x 35.4±3.5; p=0.022), gonadotrophin dose (2075±613 x 1767±414; p<0.001), MII-oocytes (12.3±4.6 x 11.9±4.0; p=0.353), fertilization rate (84.9% x 82.1%; p=0.070), number of ET (2.0±0.5 x 1.6±0.5; p<0.001). Patients who received antagonist presented lower ongoing pregnancy rate (29.3%) than agonist group (42.1%; p=0.015) in the fresh transfer. Logistic regression demonstrated that when GnRH-agonist was used, the chance of become pregnant is reduced (OR: 0.622, p=0.057), adjusted for confounders. In the frozen-thawed cycles, the outcomes for agonist and antagonist groups, respectively, were: number of thawed embryos (5.2±2.8 x 5.5±1.8; p=0.364), post-thaw survival rate (86.0% x 90.0%; p=0.120) and number of frozen-thawed ET (2.2±0.6 x 1.9±0.6; p<0.001). Also, the clinical pregnancy rate in the frozen-thawed embryo transfer is statistically similar (agonist 32.4% x antagonist 37.9%; p=0.423). CONCLUSIONS: Despite of high ovarian response, GnRH-antagonist group presented lower pregnancy rate in fresh cycle. We hypothesized that the use of GnRH-antagonist may have been impaired the endometrial receptivity. Considering the following frozen-thawed ET, although the pregnancy rates were statistically similar, there was a clinical tendency to better
outcomes in the GnRH-antagonist group, which suggest the effect of impaired endometrial receptivity could be compensated in the frozen embryo transfers.

References:

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OBJECTIVE: Random-start ovarian stimulation has usually been applied in patients with cancer for emergency fertility preservation. In such patients, utilizing their oocytes for fertilization and implantation will be performed some years later after survival of cancer. Therefore, there are few studies to show fertilization, pregnancy, implantation and live birth rates just after oocyte retrieval. There are some patients who required fresh testicular sperm extraction (TESE) intracytoplasmic sperm injection (ICSI) (oocyte retrieval and TESE are performed in a same day), whose viable spermatozoa are predicted as very few and no longer tolerable after freeze and thaw if we can retrieve spermatozoa. Random-start ovarian stimulation might be useful in such patients.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: We compared total amount of gonadotropins, stimulation length, number of retrieved oocytes and metaphase II (MII) oocytes rate, 2PN rate, and clinical pregnancy rates between random-start (75 patients, 79 cycles) and conventional-start (257 patients, 297 cycles) from March 2014 through April 2016. We included only patients without cancer. In random-start ovarian stimulation, the starting day was anytime except for during menstruation. In both groups, controlled ovarian stimulation was performed in the same manner. Less than 42 old patient (Mean age 37.9±3.8) such as patients who required fresh TESE-ICSI. A prospective study, however, is necessary for final conclusion.

P-233 Tuesday, October 18, 2016

NOVEL THERAPY FOR OVARIAN DYSFUNCTION BY REDUCING ADVANCED GLYCAATION END-PRODUCT: HISHI-EXTRACT, ANTI-GLYCAITION FUNCTIONAL FOOD, INCREASES PREGNANCY RATES IN AGED ART REPEATERS. M. Jinno, a M. Takeuchi, a A. Watanabe, a S. Takeshita, b Y. Yamada. aWomen’s Clinic Jinno, Tokyo, Japan; bDepartment of Advanced Medicine, Kanazawa Medical University, Medical Research Institute, Katsunuma, Ishikawa, Japan; cResearch and Development Division, Hayashikane Sangyo Co., Ltd, Shimonomokai City, Yamaguchi, Japan.

OBJECTIVE: Advanced glycation end-products (AGEs) play a pivotal pathogenic role in ageing and diabetes. With IRB approval and informed consents, we showed adverse effects of AGE accumulation on ART outcomes in study I and in study II we improved ART outcomes in aged patients with repeated ART failures by reducing AGEs with Hishi-extract, anti-glycation functional food, which suppresses AGE production and also break down AGEs.

DESIGN: Retrospective analyses and prospective clinical trial (UMIN000017758).

MATERIALS AND METHODS: Study I: Toxico AGE (TAGE), pentosidine (Pent), and carboxymethyl lysine (CML) in blood and follicular fluid (FF) were measured in 157 ART-patients. We analyzed associations of AGE with ART outcomes. Study II: Thirty-two old patients (mean age of 42.2) with repeated (≥3) ART failures received daily 100mg of Hishi-extract (Hayashikane) before and throughout ART. AGEs were measured before and 1-2 months after Hishi-extract.

RESULTS: Study I: TAGE, Pent, and CML in FF, and TAGE in serum correlated with ART outcomes. Study II: Thirty-two old patients (mean age of 42.2) with repeated (≥3) ART failures received daily 100mg of Hishi-extract (Hayashikane) before and throughout ART. AGEs were measured before and 1-2 months after Hishi-extract.

Table 1

<table>
<thead>
<tr>
<th>Age (y)</th>
<th>total amount of gonadotropins (IU)</th>
<th>stimulation length (days)</th>
<th>No. of retrieved oocytes</th>
<th>MII rate (%)</th>
<th>2PN rate (%)</th>
<th>clinical pregnancy rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate ovarian reserve: AMH ≥1.1-4.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Random-start</td>
<td>33.9±3.8</td>
<td>284±511*</td>
<td>10.2±1.1*</td>
<td>7.3±3.5</td>
<td>75.6 (235/311)</td>
<td>60.7 (108/178)</td>
</tr>
<tr>
<td>Conventional-start</td>
<td>35.5±4.0</td>
<td>2409±567*</td>
<td>8.4±1.7*</td>
<td>6.1±3.4</td>
<td>71.7 (1103/1538)</td>
<td>62.3 (917/1471)</td>
</tr>
<tr>
<td>Good ovarian reserve: AMH ≥4.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Random-start</td>
<td>31.8±4.1</td>
<td>2110±589</td>
<td>9.8±1.6*</td>
<td>13.0±6.4</td>
<td>79.7* (572/718)</td>
<td>64.6 (197/305)</td>
</tr>
<tr>
<td>Conventional-start</td>
<td>32.8±3.8</td>
<td>1932±683</td>
<td>8.3±1.6*</td>
<td>11.0±5.2</td>
<td>70.0* (1227/1752)</td>
<td>64.0 (1041/1626)</td>
</tr>
</tbody>
</table>

CONCLUSIONS: Random-start stimulation can be performed as same as conventional-start in patients with moderate or more ovarian reserve (AMH ≥1.1 ng/mL) such as patients who required fresh TESE-ICSI. A prospective study, however, is necessary for final conclusion.
AGE and improvement of pregnancy rate appear to be greater in patients with higher AGE. Detection and reduction of AGE accumulation are novel strategies for infertility treatment.

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TEMPORAL CHANGES IN OOCYTE DONOR TREATMENT REGIMENS IN A REAL-WORLD ANALYSIS OF A US DATABASE OF 7971 DONOR CYCLES OVER 6.5 YEARS. B. Kaplan,* K. S. Richter,* G. L. Motta,† B. Hayward,‡ M. C. Mahony,§ *Fertility Centers of Illinois, Chicago, IL; †Research, Shady Grove Fertility Reproductive Science Center, Rockville, MD; ‡Research, Shady Grove Fertility Reproductive Science Center, Annapolis, MD; §EMD Serono, Inc., Rockland, MA.

OBJECTIVE: To evaluate the real-world use of ovulation triggers in controlled ovarian stimulation (COS) cycles over time in oocyte donors in the US.

DESIGN: Non-randomized, observational, retrospective, large US real-world database analysis.

MATERIALS AND METHODS: Data from all donor oocyte cycles between Jul 2009 and Dec 2015 within a large US clinical dataset were analyzed.

RESULTS: In total, 1726 and 6245 cycles used a GnRH agonist and GnRH antagonist, respectively, to prevent premature luteinizing hormone surges during COS. The percentage of cycles using a GnRH agonist increased over time from 21.5% in Q3 2009 to 95.0% in Q4 2015, while GnRH agonist use decreased. Use of a GnRH agonist (Ag) to trigger ovulation also increased over time, while use of human chorionic gonadotropin (hCG) decreased; by Q4 2015 the former had stabilized at ~70% of cycles. The crossover point for use of an Ag trigger from hCG trigger was Q1 2010; for GnRH antagonist vs agonist treatment, it was Q2 2010. Patients receiving Ag trigger were significantly younger and had a significantly higher antral follicle count (AFC) at first cycle than those receiving hCG trigger after GnRH antagonist use. For 2015, in oocyte donor cycles treated with a GnRH antagonist with Ag trigger, a significantly lower mean total follicle-stimulating hormone dose was used and a greater number of oocytes were retrieved vs GnRH agonist or antagonist cycles that used an hCG trigger (see table). All between-group and over-time comparisons were significantly different (p<0.0001).

CONCLUSIONS: From 2010 through 2015 there was a significant shift from GnRH agonist use to GnRH antagonist use in oocyte donor cycles; the use of Ag trigger in the latter increased while hCG use decreased. The choice of trigger may have been influenced by clinical characteristics, such as age and AFC, and expected outcomes. GnRH antagonist protocols, particularly when combined with an Ag trigger rather than hCG, allow for retrieval of a larger number of oocytes with an assumed reduced risk of adverse consequences related to ovarian hyperstimulation syndrome.

Supported by: Study supported by EMD Serono, Inc., Rockland, MA, USA (a business of Merck KGaA, Darmstadt, Germany).

<table>
<thead>
<tr>
<th>GnRH agonist protocol</th>
<th>Mean (SD) total FSH dose, per cycle, international units</th>
<th>Mean (SD) number of oocytes retrieved, per cycle</th>
</tr>
</thead>
<tbody>
<tr>
<td>hCG trigger</td>
<td>2240.0 (989.3) (n=547)</td>
<td>18.6 (8.9) (n=547)</td>
</tr>
<tr>
<td></td>
<td>3402.5 (1208.3) (n=83)</td>
<td>23.2 (11.7) (n=83)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>GnRH antagonist protocol</th>
<th>Mean (SD) total FSH dose, per cycle, international units</th>
<th>Mean (SD) number of oocytes retrieved, per cycle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ag trigger</td>
<td>2498.8 (958.8) (n=264)</td>
<td>22.2 (9.6) (n=264)</td>
</tr>
<tr>
<td>hCG trigger</td>
<td>2671.3 (1080.3) (n=225)</td>
<td>18.9 (8.5) (n=225)</td>
</tr>
</tbody>
</table>

Ag, GnRH agonist; FSH, follicle-stimulating hormone; GnRH, gonadotropin-releasing hormone; hCG, human chorionic gonadotropin; SD, standard deviation. All between-group and over-time comparisons were significantly different (p<0.0001).

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LOW COST OVARIAN STIMULATION PROTOCOL IS ASSOCIATED WITH LOWER PREGNANCY RATE IN NORMAL RESPONDERS IN COMPARISON TO LONG PROTOCOL. I. El NASHAR,* T. A. FARGHALY,* A. S. ABDALBADIC,* E. BADRAN,* A. A. ABDELALEM,* A. M. ISMAIL,* E. ELSENSOY,* ASSIUT UNIVERSITY, ASSIUT, EGYPT; ‡OBSTETRICS AND GYNECOLOGY, IVF UNIT, ASSIUT UNIVERSITY IVF UNIT, ASSIUT, EGYPT; †OBSTETRICS AND GYNECOLOGY AND ASSIUT IVF UNIT, ASSIUT UNIVERSITY, ASSIUT, EGYPT; §ASSIUT UNIVERSITY IVF UNIT, ASSIUT, EGYPT; ‡OBSTETRICS AND GYNECOLOGY, WOMEN’S HEALTH HOSPITAL, ASSIUT, EGYPT.

OBJECTIVE: To compare Amnoretase Inhibitor (letrozole) with Low dose gonadotrophins as a (Low Cost protocol) versus the standard long protocol for controlled ovarian hyperstimulation in normal responder patients in terms of number of mature oocytes, good quality embryo, endometrial thickness and pregnancy rate.


MATERIALS AND METHODS: This study was conducted in a University fertility center. A selected cohort of normal responder patients including women aged 20-35 years old. Their Body Mass index between 18-29 and classified as Unexplained infertility. AFC more than 5 follicles in one ovary and the Anti- Mullerian Hormone (AMH) more than 1 ng/dl. They were randomized by sealed envelope into two groups. 40 women (study group) received letrozole, 10 mg daily from day 3-7 and FSH 75IU/day from day 5 continuously and GnRH antagonist (orgalantrum 0.25) is given when the follicle size equal to 14 mm till hCG injection. 40 women (control group) received 0.1 decapetyl from day 21 in the previous cycle and continuously stimulated by FSH (150-225IU/day) from day 2. The total dose of FSH injection, number of mature oocytes, good quality embryos, endometrial thickness at the time of hCG trigger as well as Pregnancy rate had been evaluated in both groups. Statistical Analysis was done using Chi- Square and ANOVA tests.

RESULTS: There were a statistically lower significant difference in the pregnancy rate in the Low cost protocol group (12.5 %) if compared to Standard long midluteal protocol group (42.5%) (P = 0.01). No significant difference in mature oocytes and good quality embryos between the groups.

<table>
<thead>
<tr>
<th>[table-1]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low cost</td>
</tr>
<tr>
<td>----------</td>
</tr>
<tr>
<td>Total FSH Dose</td>
</tr>
<tr>
<td>Mature oocyte</td>
</tr>
<tr>
<td>Good quality embryos</td>
</tr>
<tr>
<td>Peak E2</td>
</tr>
<tr>
<td>End. thickness</td>
</tr>
<tr>
<td>Pregnancy rate</td>
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</tbody>
</table>
However, the endometrial thickness and peak E2 is significantly higher in the control group rather than the low cost group (P = 0.001 and 0.0001, respectively). (Table 1)

CONCLUSIONS: Our data showed that we should not offer the low cost protocols to Normal responder patients even in low set resource settings as it is associated with significantly lower pregnancy rate in comparison to standard midluteal long stimulation protocols. It should be for limited use to poor responders patients who are expected to have lower number of oocytes retrieved even if we used the standard protocols.

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OBJECTIVE: Controlled ovarian stimulation (COH) during in vitro fertilization (IVF) cycles involves close monitoring of estradiol (E2) levels and measurements of follicle growth. E2 monitoring can occur multiple times during an IVF cycle and can add to anxiety levels of patients because of repeated blood draws and extra visits to the clinic. In contrast to blood draws, sampling saliva is non-invasive and can be performed remotely. Here, we present a blind validation of a novel saliva-based E2 assay performed in samples collected in 2 independent IVF clinics. The objective was to investigate whether a saliva based E2 assay could replace the use of blood monitoring during a COH cycle.

DESIGN: Blinded sample collection study.

MATERIALS AND METHODS: Concurrent serum and saliva E2 samples were collected from patients who provided between 1 and 7 samples on different days of their COH IVF cycle. Samples were collected in 2 large independent IVF laboratories. Saliva samples were frozen and run blinded in a separate laboratory while Serum E2 values were assessed routinely in the participating IVF clinics. Saliva samples were measured and validated using an immunoassay developed in collaboration with Salimetrics LLC.

RESULTS: One to seven salivary E2 samples were analyzed for each patient (n=63). In clinics A and B, 30 and 33 patients had multiple saliva and serum samples collected. In Clinic A, 129 pairs of saliva and serum E2 were evaluated with a correlation coefficient of 0.91. In Clinic B, 85 pairs were evaluated with a correlation coefficient of 0.88. More than 87% of patients showed an individual within cycle correlation of >0.7 and 66% a correlation of >0.9 (range 0.42-1.0). Patients with discolored saliva samples generally showed poor correlation. This most likely indicated that they failed to follow the instructions for collection.

CONCLUSIONS: Salivary estradiol based hormone testing provides an equivalent alternative to serum based assessment. The ease of saliva sampling is non-invasive and can be performed remotely. Here, we present a blind validation of a novel saliva-based E2 assay performed in samples collected in 2 independent IVF clinics. The objective was to investigate whether a saliva based E2 assay could replace the use of blood monitoring during a COH cycle.

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SHORTENED STIMULATION LENGTH IS ASSOCIATED WITH ADVERSE OUTCOMES IN IVF CYCLES. P. Kovacs, S. Simpson, R. Maxwell, S. R. Lindheim. aKaali Institute IVF Center, Budapest, Hungary; bDept. of OB/GYN, Wright State University, Boonshoft School of Medicine, Dayton, OH; cObstetrics & Gynecology, Wright State University Boonshoft School of Medicine, Dayton, OH.

OBJECTIVE: Ovarian stimulation for 10 days (d) is considered optimal for IVF cycles. However, many require shorter or longer stimulation to achieve an adequate response. Our aim was to assess the impact of stimulation length on IVF outcome using GnRH agonist (a) or antagonist (ant) protocol.

DESIGN: Retrospective chart review.

MATERIALS AND METHODS: This retrospective review evaluated charts from patients undergoing fresh, autologous IVF (n=295) in 2015. Ovulation induction was achieved with rFSH or hMG and pituitary suppression with GnRH-a (n=94) or GnRH-ant (n=201). Demographic data, stimulation characteristics and treatment outcome were collected. At the last ultrasound (up to 3 days prior to hCG) follicles >14 mm were considered. Oocyte yield was calculated by the number of oocytes/follicles at last scan thus involving values > 1. Groups were categorized as short, normal and prolonged stimulation (≤ 9 d, 9-12 d, ≥ 13 d). The main outcome measures were associations between length of stimulation and oocyte yield and pregnancy rate (PR). Comparisons were made for pregnant and non-pregnant cycles and based on cycle length in all cycles and in GnRH-a and GnRH-ant cycles separately. Statistical analysis was done using Pearson’s correlation, Chi square, and ANOVA, with Tukey post-hoc analysis.

RESULTS: The overall PR was 36.3%. In pregnant versus non-pregnant cycles, female age and total gonadotropin dose were significantly lower and the number of follicles, fertilized oocytes, and embryos were significantly higher. However, no differences in the days of stimulation (10.6 vs 10.7 d) and oocyte/follicle count (1.60 vs 1.56) were noted. Egg yield correlated with stimulation duration (r: 0.19, p<0.001). Egg yield, PR for each group for all cycles and based on agonist/ antagonist use are shown in Table I. No differences between groups specific to GnRH-a or GnRH-ant were noted.

Table I. IVF Outcome based on stimulation length

<table>
<thead>
<tr>
<th>Stimulation length</th>
<th>All cycles PR</th>
<th>All cycles oocytes/follicles</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 8 days</td>
<td>17.6%</td>
<td>16.6%</td>
</tr>
<tr>
<td>9-12 days</td>
<td>40.9%</td>
<td>34.7%</td>
</tr>
<tr>
<td>≥ 13 days</td>
<td>28.7%</td>
<td>30.8%</td>
</tr>
</tbody>
</table>

Table II. IVF Outcome based on stimulation length

<table>
<thead>
<tr>
<th>Cycle type</th>
<th>All cycles PR</th>
<th>All cycles oocytes/follicles</th>
</tr>
</thead>
<tbody>
<tr>
<td>GnRH a PR</td>
<td>16.6%</td>
<td>34.7%</td>
</tr>
<tr>
<td>GnRH a oocytes/follicles</td>
<td>30.8%</td>
<td></td>
</tr>
<tr>
<td>GnRH a ant PR</td>
<td>1.0±0.5</td>
<td>1.5±0.9</td>
</tr>
<tr>
<td>GnRH a ant oocytes/follicles</td>
<td>1.9±1.3</td>
<td></td>
</tr>
</tbody>
</table>

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ACTIVATION OF THE COAGULATION SYSTEM DURING IVF CYCLES EXTENDS WELL AFTER OUM Pickup. Y. Cohen, E. Zohav, B. Almoq, A. Cohen, Obestetrics & Gynecology, Lis Maternity Hospital, Tel Aviv Sourasky Medical, Tel Aviv, Israel; 3Lis Maternity Hospital, Tel Aviv Sourasky Medical, Tel Aviv, Israel.

OBJECTIVE: To investigate the changes in the coagulation system during the course of an IVF cycle from baseline to the initial β-hCG test.

DESIGN: Prospective study.

MATERIALS AND METHODS: Patients: Twenty-three women that underwent controlled ovarian stimulation with gonadotropins for IVF. Interventions: The elastic properties of blood clots were measured by thromboelastogram (TEG), providing global assessment of homeostatic function. TEG indices, estradiol (E2), progesterone, PT and PTT were evaluated at four time points: 1. At the beginning of the cycle (corresponding to the lowest levels of E2), 2. Day of hCG administration (maximal stimulation with highest E2 levels), 3. At the day of ovum pickup and 4. At the first β-hCG test (approximately 14 days after ovum pickup). Main outcome measures: TEG indices including R-time: Time until initial fibrin formation. K-time: Time until a 20 mm. amplitude is achieved. Angel: The rate of clot formation. Maximum Amplitude: Strength of the fibrin clot. Coagulation Index (CI): Calculated overall indicator of coagulation. LY30: The percentage decrease in graph amplitude.

RESULTS: Comparison of the different time points showed that R, K, alpha, MA and CI at the time of the first pregnancy test and before hCG administration were significantly higher compared to the baseline measurement before gonadotropins administration, whereas no difference in LY30 was recorded. No correlation was found between E2 levels and TEG indices.

CONCLUSIONS: Our results demonstrate that ovarian stimulation is associated with increased coagulability that extends well after the time of maximal ovarian stimulation. The lack of association between E2 levels and TEG indices suggest that additional factor may have a role in the pathogenesis of increased coagulability in women with ovarian stimulation.

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CONCLUSIONS: Despite similar embryo yield, stimulation ≤8 d was associated with lower PR and oocyte yield from mature follicles when compared to stimulation length between 9-12 d. Beyond the size of the follicles, the length of stimulation should also be considered when hCG is administered prior to retrieval.

References:

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OBJECTIVE: The purpose of this study was to create a model that would determine the most effective ovulation induction method for a patient and to determine the factors that would improve the quality of the oocytes collected. Age, height, weight and number of oocytes data was collected and analysed.

DESIGN: The total number of cases from 2008 to 2015 was 19,578. However, number of cases used in this study is 2,333 because we only used data from cases where patients under 39 years old, used fresh embryos and did not have any missing values. In our model we used the number of oocytes as our objective variable, the ovulation induction method was used as the explanatory variable and these 21 variables were the branch variables. Branch variables: Age, BMI, Day3 Hormone value (E2, LH and FSH), Number of antral follicles, Induction frequency, pre-treatment, infertility factor (tubal factor, endometriosis, anti-sperm antibody-positive, cause unknown, Central ovulation disorders, PCOS, elderly, other, PGD).

MATERIALS AND METHODS: The model was created using the Model-based Recursive Partitioning model. It is called MOB for short. MOB is different from the Tree Structure Model, such as a normal decision tree. It is a technique for creating a model based on branches relationships between two variables. It creates a model by using a combination of structural change and generalized linear models. The branch variable is determined using the structural change model and the condition of each branch variable is analysed using the generalized linear model. In this case Poisson distribution was used for error structure. Also there is no dependency on the data were subjected to cross-validation to build accurate models. We conducted a five-fold cross validation analysis of the P-value which indicates firmness, we repeated it 50 times and we determined the average.

RESULTS: We investigated the relationship between P-value and the prediction accuracy level, a level of three branches, with a P-value of 1.0×10-20 showed the best prediction accuracy level. There were 21 different branch variable candidates but the branch variables that appeared in the highest prediction accuracy level tree structures: number of antral follicles, pre-treatment and FSH hormone level influence the acquisition of good quality oocytes. When the number of antral follicles is low, if there is pre-treatment using Maravel or Planovar and then we use the Long protocol, we can obtain a lot of good quality oocytes.

CONCLUSIONS: We used MOB to develop a model for the selection of the optimum ovulation induction method. The results obtained from the whole data analysis, the cross-validation analysis and from the five randomly divided samples let us identify important variables that affect oocyte quality. We were also able to identify a branch level of three in a tree decision analysis as the branch level that has the highest prediction accuracy level.

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THE COMPETENT FUNCTION OF GRANULOSA CELLS DURING PPOS IN NORMALOVULATORY WOMEN UNDERGOING IVF/ICSI TREATMENTS. L. Zhou, Y. Kuang, W. Chai. Shanghai Ninth People’s Hospital, Shanghai, China.

OBJECTIVE: Our previous study demonstrated that medroxyprogesterone acetate (MPA) is an effective oral alternative for the prevention of premature LH surge in normalovulatory women undergoing controlled ovarian hyperstimulation (COH), and the pregnancy outcomes from FET indicated that the embryos originating from PPOS had similar developmental potential as the short protocol (1). In this study, we investigate the expression related to gonadotropin receptors, sex hormone receptors and steroidogenesis in granulosa cells of normalovulatory women undergoing IVF/ICSI treatments with hMG and MPA protocol.

DESIGN: A translational research study.

MATERIALS AND METHODS: Human granulosa cells (GCs) retrieved from the patients undergoing agonist group and hMG+MPA group were quantitatively compared with qPCR and western blot for the expression of steroidogenic enzymes (sTR, Scc, HSD3B2, aromatase), gonadotropin receptors (FSHR, LHR) and sex hormone receptors (PR, ER). Serum E2 on the trigger day was measured with chemiluminescence.

RESULTS: The cycle characteristics and outcomes show in table. The expression of FSHR and PR, at both the mRNA and protein levels, were significantly higher in hMG+MPA group than agonist group. While the expression of steroidogenic enzymes were similar between the two groups. The serum E2 level on the trigger day in the two groups was 3811.9 pg/ml, 3836.4 pg/ml, respectively, with no statistic significance (p>0.05).

CONCLUSIONS: The results demonstrated that MPA do not impair the gonadotropin activity and steroidogenesis of GCs during the development of follicle in COH.

<table>
<thead>
<tr>
<th>Cycle characteristics and outcomes.</th>
<th>Agonist group</th>
<th>HMG+MPA group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>32.3±3.7</td>
<td>31.3±3.7</td>
</tr>
<tr>
<td>Body mass index(kg/m²)</td>
<td>21.4±2.2</td>
<td>20.9±2.4</td>
</tr>
<tr>
<td>Antral follicle count(n)</td>
<td>10.0±4.5</td>
<td>11.2±3.4</td>
</tr>
<tr>
<td>b FSH(µIU/L)</td>
<td>5.6±1.3</td>
<td>5.7±1.2</td>
</tr>
<tr>
<td>hMG dose(µg)</td>
<td>1489.5±45.8</td>
<td>1865.1±304.4</td>
</tr>
<tr>
<td>Oocytes retrieved(n)</td>
<td>11.0±6.2</td>
<td>13.7±6.3</td>
</tr>
<tr>
<td>MIoocyte(n)</td>
<td>9.3±5.8</td>
<td>12.1±5.6</td>
</tr>
<tr>
<td>Fertilized oocytes(n)</td>
<td>7.5±4.5</td>
<td>9.4±4.9</td>
</tr>
<tr>
<td>Top-quality embryos(n)</td>
<td>3.2±3.6</td>
<td>4.8±3.6</td>
</tr>
<tr>
<td>Cancellation rate(%)</td>
<td>20.0(10/50)</td>
<td>5.8(4/68)</td>
</tr>
<tr>
<td>Clinical pregnancy rate per transfer(%)</td>
<td>0.3(4/16)</td>
<td>0.4(21/51)</td>
</tr>
</tbody>
</table>

References:

Supported by: The Science and Technology Commission of Shanghai Municipality (grant number:15411964500,15411953000) and MerckSerono China Research Fund for Fertility Experts.

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EXTENDING OVARIAN STIMULATION IN PATIENTS WHO ARE SLOW TO RESPOND: DOES PERSISTENCE PAY OFF?. L. Sekhon,a,b J. Rodriguez-Purata,a J. A. Lee,a A. B. Grunfeld,a,b Reproductive Medicine Associates of New York, New York, NY; aObstetrics, Gynecology & Reproductive Science, Icahn School of Medicine at Mount Sinai, New York, NY.

OBJECTIVE: IVF patients with decreased ovarian response often require controlled ovarian hyperstimulation (COH) and late ovulation trigger (OT) on or after cycle day 14. Lengthier COH cycles are often viewed as poor controlled ovarian hyperstimulation (COH), and the pregnancy outcomes from FET indicated that the embryos originating from PPOS had similar developmental potential as the short protocol (1). In this study, we investigate the expression related to gonadotropin receptors, sex hormone receptors and steroidogenesis in granulosa cells of normalovulatory women undergoing IVF/ICSI treatments with hMG and MPA protocol.

DESIGN: A retrospective cohort analysis.

MATERIALS AND METHODS: Patients who underwent COH from September 2002 to April 2016 were included. Donor oocyte and male factor
infertility cases were excluded. COH was initiated on day 3. Criteria for (OT) was ≥ 2 mature follicles ≥ 18mm in size. Patients were stratified by whether OT was < day 14 vs. ≥ day 14. Outcomes of COH and embryo transfer (ET) were compared (Table). Student’s T test, chi square, linear and binary logistic regression were used.

RESULTS: COH was performed in 7839 IVF cycles, with 4850 concurrent ETs in the stimulation cycle and 2786 FET’s in subsequent cycles. Patients with OT < day 14 (n = 6749) vs. ≥ day 14 (n = 1090) were compared according to demographics, cycle characteristics and clinical outcome (Table). Controlling for age and day 3 FSH, increase in cycle day of OT corresponded with decreased ovarian response (-63.3 pg/ml estradiol at trigger), oocytes retrieved (-1.1), fertilized (-0.06), blastocysts developed (-0.4) and delayed endometrial development (TE) biopsy (0.4) and of euploid embryos (p < 0.0001). Increased cycle day of OT was associated with increased odds of not meeting criteria for oocyte retrieval (OR 1.5 [95% CI 1.3-1.7]), <4 oocytes retrieved (OR 1.3 [95% CI 1.2-1.3]), and failed fertilization (OR 1.1 [95% CI 1.1-1.2]) (p < 0.0001), with decreased odds of having a blastocyst available for biopsy (OR 0.9 [95% CI 0.8-0.9]) or transfer (OR 0.9 [95% CI 0.8-0.9]) (p < 0.0001). However, cycle day of OT did not influence odds of having no euploid blastocysts (OR 1.0 [95% CI 0.9-1.1]). Controlling for age, number of embryos transferred and ploidy, odds of implantation and pregnancy loss did not vary with timing of OT.

CONCLUSIONS: Patients who require OT past cycle day 14 are at increased risk of not reaching retrieval, fertilization or blastulation. However, if these hurdles are overcome, overall embryo quality and competence is not hindered. Based on this data, clinicians can counsel slow-responding patients regarding their IVF prognosis, while reassuring them that blastocysts eligible for biopsy and/or transfer are not an increased risk for failed implantation.

OT < 14 vs. ≥ 14 days: Demographics, cycle characteristics and clinical outcome

<table>
<thead>
<tr>
<th>Cycle day of ovulation trigger</th>
<th>&lt; 14</th>
<th>≥ 14</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient age</td>
<td>36.5 ± 4.7</td>
<td>38.3 ± 4.4</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>BMI</td>
<td>24.2 ± 1.1</td>
<td>26.2 ± 6.5</td>
<td>NS</td>
</tr>
<tr>
<td>Day 3 FSH</td>
<td>6.2 ± 2.8</td>
<td>6.5 ± 4.1</td>
<td>NS</td>
</tr>
<tr>
<td>E2 at trigger (pg/ml)</td>
<td>2244.8 ± 114.8</td>
<td>1638.2 ± 976.7</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Oocytes retrieved</td>
<td>15.4 ± 9.5</td>
<td>9.7 ± 7.4</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Mean number of 5 blastocysts</td>
<td>5.1 ± 4.7</td>
<td>2.9 ± 3.7</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Aneuploidy rate</td>
<td>50.3%</td>
<td>49.1%</td>
<td>NS</td>
</tr>
<tr>
<td>Fresh ET</td>
<td>53.4% (2322/4350)</td>
<td>48.8% (244/500)</td>
<td>NS</td>
</tr>
<tr>
<td>Implantation rate</td>
<td>19.4% (845/4350)</td>
<td>20.6% (103/500)</td>
<td>NS</td>
</tr>
<tr>
<td>Fresh ET Early pregnancy loss rate</td>
<td>51.2% (1296/2533)</td>
<td>56.1% (142/253)</td>
<td>NS</td>
</tr>
<tr>
<td>FET Implantation rate</td>
<td>21.8% (551/2533)</td>
<td>19.4% (49/253)</td>
<td>NS</td>
</tr>
</tbody>
</table>

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OBJECTIVE: One of the great controversies of contemporary IVF is whether the traditional usage of gonadotropins to maximally stimulate the ovary subverts natural selection, resulting in lower quality embryos and increasing aneuploidy risk. Modified natural cycle IVF has been proposed as a "patient friendly" alternative approach, resulting in higher quality embryos. While this is an appealing hypothesis, there are limited prospective data to support it. The goal of this study is to determine whether naturally-selected oocytes have intrinsically superior reproductive competence compared to those obtained following stimulation with exogenous gonadotropins, and are less likely to result in aneuploid embryos.

DESIGN: Prospective cohort.

MATERIALS AND METHODS: Between 2013-2015, a single modified natural cycle IVF was offered to all ovulatory infertile women presenting for infertility care. Natural cycles were monitored with ultrasound and endocrine assessment until a dominant follicle was attained. No exogenous gonadotropins or GnRH antagonists were used. Oocyte maturation was induced with both hCG and a GnRH agonist. Following retrieval, mature oocytes underwent ICSI. Embryos were placed into extended culture. Viable blastocytes underwent biopsy for PGS and were then vitrified. Euploid blastocytes were warmed and transferred in a subsequent cycle. A 5-to-1 age- and time-matched control group of infertile women undergoing their first stimulated FET with placed PGS embryos was used for comparisons.

RESULTS: 369 patients with a mean age of 37.3 ± 5.1 underwent IVF and were compared to 1845 patients with a mean age of 37.5 ± 5.1 who underwent stimulated IVF. In an intent to treat analysis comparing all patients undergoing retrieval in both natural and stimulated IVF cycles, 91 (24.7%) did not obtain an oocyte, compared with only 10 (0.5%) patients in stimulated cycles (P < 0.001). The number of patients without a usable blastocyst in natural cycles was 46%, vs. 78% and 46% vs. 66% to transfer, both significantly lower than in stimulated IVF cycles. The overall aneuploidy rate per usable blastocyst were equivalent: 44% of 147 blastocysts in natural cycles vs 42% of 6664 blastocysts in stimulated cycles (P = 0.81). Most importantly, a euploid blastocyst had an equivalent chance of resulting in a delivery whether derived from a natural or stimulated cycle (58.7% vs 59.0%).
CONCLUSIONS: Despite prior speculation that exogenous gonadotropin stimulation results in poorer quality oocytes and embryos, these data indicate that there is no intrinsic performance advantage for oocytes which are naturally selected over those that are obtained in stimulated IVF cycles. While not evaluated here, it should be noted that stimulated cycles often result in supernumerary euploid blastocysts vitrified for future transfer and this would result in a dramatically higher opportunity for pregnancy per retrieval in comparison to natural cycles.

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IS THE LUTEAL-PHASE OVARIAN STIMULATION A FEASIBLE CHOICE FOR ALL PATIENTS? M. Zheng, R. Hu, F. Wang, R. Lu, Ningxia Medical University, Yinchuan, China; Key Laboratory of Fertility Preservation and Maintenance of Ministry of Education, Yinchuan, China; General Hospital of Ningxia Medical University, Yinchuan, China.

OBJECTIVE: To investigate whether the oocytes retrieved during the luteal phase are as competent to mature and fertilized as the oocytes obtained during the follicular phase, to further explore the optimal initiation time of ovarian stimulation. And to study a possible mechanism of follicle stimulating hormone (FSH) regulates the secretion of stem cell factor (SCF) in human granulosa cells (GCs).

DESIGN: Retrospective clinical and experimental study.

MATERIALS AND METHODS: Cycle parameters and outcomes of IV-F-ET cycles from January 2013 to December 2015 were reviewed. The expression of FSHR and SCF in GCs, which obtained from women undergoing the follicular-phase and the luteal-phase ovarian stimulation, was detected. The primary GCs collected from follicular fluid were divided into 5 groups and cultured with 0 IU/L, 10 IU/L, 25 IU/L, 50 IU/L, 100 IU/L of rFSH (Gonal-F) separately. The cultured GCs of intervention group and control group were subjected to treatments with cAMP or an inhibitor of PKA (H-89). The protein and mRNA expression of FSHR and SCF in GCs was detected by using Immunofluorescence, reverse transcription-polymerase chain reaction (RT-PCR), and Western blot.

RESULTS: 107 cycles were analyzed: 58 were performed in the follicular phase (Group 1) and the other 49 cycles were in the luteal phase (Group 2).

There was no difference in the average number of retrieved oocytes between two group (Group 1: 9.81 ± 4.59 vs. Group 2: 10.5 ± 3.72, p>0.05), however, a significant difference of the fertilization rate was observed in follicular phase and luteal phase (90.9% vs. 81.6%, p=0.018). High-quality embryo rate was significantly higher in Group 1 (58.1% vs. 33.0%, p<0.001). FSHR and SCF in GCs derived from the luteal phase were lower secreted than those in GCs derived from the follicular phase. With the rFSH treatments, SCF had a strong expression in primary cultured GCs. SCF was increased by cAMP and H-89 significantly inhibited the effects of both rFSH and cAMP on the expression of SCF mRNA and protein.

CONCLUSIONS: Our research suggests that the luteal phase has no strong potential to produce viable oocytes as the follicular phase. In human GCs, FSH may up-regulate the expression of SCF via the cAMP/PKA pathway to promote the follicle growth and development and the oocytes maturation.

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REPRODUCTIVE OUTCOMES IN POOR-RESPONDER PATIENTS USING SURGICALLY RETRIEVED SPERM. A. Gilman, G. Younes, S. Tannus, W. Son, P. Chan, W. Buckett, McGill University, Montreal, QC, Canada.

OBJECTIVE: Previous studies have examined the use of surgically retrieved sperm in good prognosis female patients, but there is a paucity of studies looking at surgically retrieved sperm in female patients with poor ovarian response to stimulation. This study aims to report reproductive outcomes of ‘poor-responder’ female patients (defined as ≤3 oocytes retrieved at oocyte pick-up) undergoing an in-vitro fertilization (IVF) cycle where surgical sperm retrieval for male partners was performed.

DESIGN: This was a retrospective cohort study comparing all ‘poor-responder’ patients undergoing an IVF cycle at the MUHC Reproductive Centre in Montreal, Canada using surgically retrieved sperm between January 1 2009 and December 31 2015. All cycles meeting the above criteria were included.

MATERIALS AND METHODS: Data was collected through a retrospective chart review and analyzed based on indication for surgical sperm retrieval. These were categorized as non-obstructive azoospermia (NOA), obstructive azoospermia (OA) and repeated IVF failures. Rates of no sperm found with surgical sperm retrieval, fertilization failure, no embryo transfer, clinical pregnancy rate (CPR) and live birth rate (LBR) were examined. Statistical analysis between the three groups was performed using chi-squared and ANOVA testing. Data is presented as mean ± standard deviation or as percentages.

RESULTS: 115 patients met the criteria. There were no significant differences in female and male ages between NOA, OA and repeated failure groups (36.9±4.4 years, 39.1±4.3 years and 38.2±4.1 years respectively; p=0.10 for female age and 46.0±10.5 years, 46.4±8.0 years and 42.9±5.4 years respectively; p=0.22 for male age). Indication for surgical sperm retrieval was NOA in 27.0%, OA in 52.2% and repeated failures in 20.9%. There were no differences in the number of patients where no sperm was found among the three groups (p=0.32). In addition, there was no difference in the number of patients in which there was failed fertilization (p=0.49) and no embryo transfer (p=0.76). CPR were similar between the three groups: 9.7% in NOA, 8.3% for OA and 20.8% in repeated failures (p=0.25) as were LBR: 6.5% in NOA, 10.0% in OA and 8.3% in repeated failures (p=0.85).

CONCLUSIONS: This study compares outcomes in ‘poor-responder’ patients undergoing IVF cycles using surgically retrieved sperm. There were no statistically significant differences in reproductive outcomes between the NOA, OA or repeated failures groups. Although we would expect improvement in rates of sperm retrieval, fertilization, embryo transfer, CPR and LBR among those with a clear indication for surgical sperm retrieval (i.e. OA or NOA) compared to those with repeated IVF failures, none was found. This is potentially due to the underlying poor prognosis in female patients with a poor ovarian response to stimulation. This information should help us in appropriate counseling with respect to realistic success rates for patients within this population. Further study in this area is needed.

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TESTOSTERONE UNDENAMECATE TREATMENT IN WOMEN WITH POOR OVARIAN RESPONSE UNDERGOING IVF: PREGNANCY AND LIVE BIRTH RATES. G. Mskhalya, E. Estlova, M. Malysheva, E. Lubimkina, V. Zaletova, S. Kalinchenko, Andrology and Endocrinology, Center for Reproductive Medicine MAMA, Moscow, Russian Federation; Gynecology, Center for Reproductive Medicine MAMA, Moscow, Russian Federation; ‘People’s’ Friendship University of Russia, Moscow, Russian Federation.

OBJECTIVE: To assess the efficacy of pretreatment with oral form of Testosterone undecanoate (TU) in poor responders undergoing in vitro fertilization (IVF).

DESIGN: Prospective controlled trial.

MATERIALS AND METHODS: 128 women with poor ovarian response, defined according toESHRE consensus/the Bologna criteria of low ovarian response were included. Patients were randomly divided into 2 groups: TU treatment group (77 women) or control group (51 women). For TU group Testosterone undecanoate oral form 40 mg was given daily for at least 40 days (median -51 days) preceding COS for IVF. Primary outcome measures were clinical pregnancy (PR) and live birth (LR) rates. Statistical research was made using a software package statistics (StatSoft Inc. U.S., version 12). Quantitative data is presented as median and quartile range. When comparing the quantitative data of two independent groups Mann-Whitney U test and Fisher exact two-tailed test were used. Values were considered statistically significant if p less than 0.05.

RESULTS: There were no differences in patients’ characteristics between the two groups. There was no significant difference in starting FSH dose or total dose of gonadotropins administered between the groups. There was an increase in number of oocytes retrieved 2 [1; 3] vs 1 [1; 2] in TU group, though it was not significant (p=0.15). The clinical pregnancy rate (per cycle) was significantly higher in TU group (24.7%) than in control group (7.8%), p=0.018. Live birth rate was higher in TU group than in control group 18% vs 5.9%, respectively, though the difference was not statistically significant (p=0.06). The treatment group was divided into 3 subgroups according to age: 1 group - less than 35 years old (20 patients), 2 group - 35-39 years old (20 patients), 3 group included patients 40 years and older (31 women). PR and LR were calculated separately to each age group: 1 group PR -45%, LR 100%, in 2 group PR was 35%, LR - 55.6%, in 3 group - PR -3.2%, LR - 0%.

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CONCLUSIONS: TU pretreatment may be beneficial in women with diminished ovarian response undergoing IVF. PR and LR rate are severely decreased in women 40 years and older, they may need more prolonged pretreatment with TU for better success rate.

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ADJUNCTIVE CLOMIPHENE CITRATE WITH LOW-DOSE GONADOTROPINS VERSUS HIGH-DOSE GONADOTROPINS FOR IN VITRO FERTILIZATION IN POOR RESPONDERS. N. Pereira, J. P. Lekovich, K. Winter, I. Kligman, Z. Rosenwaks. The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: Adjunctive clomiphene citrate (CC) combined with low-dose gonadotropins has been utilized as an alternative to high-dose gonadotropins for in vitro fertilization (IVF) cycles in poor responders. We compare the ovarian stimulation and pregnancy outcomes of IVF cycles in poor responders treated with either combined CC and low-dose gonadotropins or high-dose gonadotropins.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: All poor responders, based on the Bologna criteria, undergoing fresh IVF with GnRH-ant based protocols between 2004 and 2013 were analyzed for inclusion. Group 1 consisted of patients undergoing ovarian stimulation with combined CC (100 mg) between cycle day (CD) 2-6 and low-dose gonadotropins (150 IU recombinant-FSH with 75 IU hMG) beginning CD 5. Group 2 consisted of patients treated with high-dose gonadotropins (450 IU recombinant-FSH with 300 IU hMG or 300 IU recombinant-FSH with 300 IU hMG) beginning CD 2. All patients received luteal estradiol priming. In addition to demographics and baseline IVF characteristics, the total days of ovarian stimulation, total gonadotropins administered (IU), cycle cancellation rate, number of mature oocytes, and fertilization rate was recorded. Biochemical, clinical pregnancy, miscarriage and live birth rates following embryo transfer (ET) were also noted.

RESULTS: 4265 poor responders, with age 41 (40-43) and 3 (2-5) prior IVF cycles, met inclusion criteria. Of these, 448 (11%) and 2660 (62%) patients formed groups 1 and 2, respectively. The remaining 1157 (27%) patients were treated with non-GnRH-ant protocols. The demographics and baseline IVF characteristics of groups 1 and 2 were similar. Group 1 was 1 treated with lesser gonadotropins compared to group 2 (2962.5 IU vs. 5475; P < 0.001). There was no difference in the number of mature oocytes (4 in both groups) or fertilization rate (80.0% vs. 78.7%). The odds of cycle cancellation were lower in group 1 compared to group 2 [0.37 (95% CI 0.16-0.86)]. Following ET of 3 (1-4) embryos, the biochemical (9.59% vs. 9.36%), clinical pregnancy (17.7% vs. 14.7%), miscarriage (3.68% vs. 2.68%), and live birth (14.0% vs. 12.1%) rates were comparable between the groups.

CONCLUSIONS: Our results suggest that a combined CC and low-dose gonadotropin GnRH-ant protocol yields similar ovarian stimulation and pregnancy outcomes as a high-dose gonadotropin protocol in poor responders undergoing IVF. These results are achieved with lesser gonadotropins and a lower cancellation rate in the former group.

| Comparison of Demographics, Baseline IVF Characteristics and Pregnancy Outcomes |
|---------------------------------|---------------------------------|---------------------------------|---------------------------------|
| Parameter                                      | Group 1: CC+Low-Dose Gonadotropins (n=448) | Group 2: High-Dose Gonadotropins (n=2660) | P     |
| Age (years)                                   | 41 (40-43)                                      | 41 (40-43)                                      | NS    |
| Prior IVF Cycles                              | 3 (2-6)                                          | 3 (2-5)                                          | NS    |
| Days of Stimulation                           | 12 (11-13)                                      | 11 (10-12)                                      | <0.001|
| Gonadotropins Administered (IU)               | 2962.5 (2025-4050)                              | 5475 (4500-5475)                                | <0.001|
| Cycles Canceled (%)                           | 6/448 (1.34%)                                   | 9/2660 (3.42%)                                  | NS    |
| Mature (MII) Oocytes (%)                      | 4 (2-7)                                          | 4 (2-6)                                          | NS    |
| Fertilization Rate (2PN/MII, %)               | 80%                                              | 78.7%                                            | NS    |
| Clinical Pregnancy (%)                        | 16 (3.68%)                                       | 72 (2.68%)                                       | NS    |
| Live Birth (%)                                | 63 (14.0%)                                       | 352 (12.1%)                                      | NS    |

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AFFECT OF GNRH AGONIST TRIGGER FOLLOWED BY LOW DOSE hCG ON REPRODUCTIVE OUTCOME IN AT RISK OHSS PATIENTS: A COMPARISON BETWEEN FRESH AND FROZEN TRANSFER. K. D. Nayar, A. Mohan, S. Challet, R. Ahuja, G. Kant, N. Sharma, M. Saxena. Akanksha IVF Centre, Mata Chana Devi Hospital, New Delhi, India.

OBJECTIVE: Utilisation of GnRHa trigger in antagonist cycles to stimulate final oocyte maturation by inducing shorter (34h) surge of gonadotropins leads to luteal phase insufficiency with malfunctioning corpus luteum. Addition of 1500 IU hCG on the day of oocyte retrieval reduces early pregnancy loss rate and provides comparable ongoing pregnancy rate with frozen transfer in subsequent cycle.

DESIGN: A prospective study was conducted on 100 at risk OHSS patients between January 2015 and September 2015 at Akanksha IVF centre. Statistical analysis was performed using SPSS 15.1 version. Categorical values were analysed using Chi-Square and Fisher exact tests. All values were two-tailed with significance level set at p < 0.05.

MATERIALS AND METHODS: One hundred patients at risk of OHSS with serum estradiol levels >2500pg/ml or had >15 follicles ≥12mm in diameter at ultrasound on day of trigger received GnRHa agonist trigger. Patients were further divided into Group A (n=45) with early signs of mild/moderate OHSS (treated as out patients) or where >15 oocytes were retrieved. Embryo transfer was withheld in these patients, all embryos were cryopreserved and transferred in the subsequent cycle. Group B (n=55) comprised of at risk OHSS patients who received GnRHa trigger, did not develop any signs of OHSS and received low dose hCG 1500IU bolus on the day of pick up for luteal support. In these patients, embryos were transferred in the same cycle. Statistical analysis was performed using SPSS 15.1 version. Categorical values were analysed using Chi-Square and Fisher exact tests. All values were two-tailed with significance level set at p < 0.05.

RESULTS: Reproductive outcomes compared between Groups A and B were positive pregnancy test defined as positive βhCG on Day 14 after embryo transfer (40% vs. 36.3%; p=0.36), clinical pregnancy defined as intrauterine gestational sac with a heartbeat after three weeks of positive βhCG test (37.9% vs. 34.5%, p=0.37) and ongoing pregnancy defined as viable pregnancy at 11 weeks (33.3% vs. 29%, p=0.32) and miscarriage defined as pregnancy loss before 24 weeks of pregnancy (11.1% vs 10%, p=0.46). All these parameters were found to be comparable between Group A and Group B with p>0.05.

CONCLUSIONS: GnRHa trigger with a single low dose hCG bolus in selected group of at risk OHSS patients with same cycle transfer gives comparable reproductive outcome than frozen transfer in next cycle.

Reproductive Outcome

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group A (n = 45)</th>
<th>Group B (n = 55)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive hCG per embryo transfer (%)</td>
<td>18/45 (40%)</td>
<td>20/55 (36.3%)</td>
</tr>
<tr>
<td>Clinical pregnancy (%)</td>
<td>17/45 (37.9%)</td>
<td>19/55 (34.5%)</td>
</tr>
<tr>
<td>Ongoing pregnancy (%)</td>
<td>15/45 (33.3%)</td>
<td>16/55 (29.09%)</td>
</tr>
<tr>
<td>Early pregnancy loss (%)</td>
<td>2/20 (10%)</td>
<td>0.456</td>
</tr>
<tr>
<td>(of positive hCG)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>OHSS</td>
<td>0/45</td>
<td>2/55 (mild)</td>
</tr>
</tbody>
</table>

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References:

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OBJECTIVE: To determine in our setting the cut-off value of Progesterone (P) serum levels on the day of human chorionic gonadotropin (hCG) administration that are predictive of a subsequent decrease of the clinical pregnancy rate.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: Fifty-four patients up to 39 years old that performed cycles of IVF/intracytoplasmic sperm injection (ICSI) with fresh embryo transfer between October 2014 and December 2015 were included in the study. All patients used a GnRH antagonist flexible protocol, presented with basal FSH < 20 mIU/ml, had obtained 2 or more MII oocytes in the retrieval and had at least one good quality embryo transferred. The level of P on the day of hCG was measured by electrochemiluminescence immunoassay with the reagent Progesterone II in the Cobas e-411 analyzer (Roche). Pearson’s r coefficient was used to evaluate the correlation between P values and ovarian response variables. ROC curve analysis was used to determine cut-off values of P serum levels for predicting pregnancy rate. Pregnancy rates and patient characteristics were compared between groups. Chi-square test for trend was used for comparing clinical pregnancy rates between groups. Statistical analysis was performed using Medcalc 10.2.0.0, a p value of < 0.05 was considered statistically significant.

RESULTS: Two cut-off values of serum P levels were found, 0.7 and 1.46 ng/ml, dividing the population in three groups: Low P levels: ≤ 0.7 ng/ml (n= 14); Intermediate P levels: 0.7 to 1.46 ng/ml (n=25); and High P levels: >1.46 ng/ml (n=15). There was a significant difference in clinical pregnancy rates between patients from the groups of low, intermediate and high P serum levels (71.4%, 48.0% and 26.7%, p = 0.016 X2 test for trend). P serum levels did not correlate with estrogen levels (r=0.22, p=0.10, 95% CI -0.05 to 0.46), number of follicles (r=0.20, p=0.13, 95% CI -0.06 to 0.45) or oocytes retrieved (r=0.26, p=0.053, 95% CI -0.003 to 0.50).

CONCLUSIONS: Our results support previous studies showing negative IVF/ICSI outcomes with P elevation on day of hCG administration. In our setting this effect starts at a lower threshold than the commonly reported threshold of 1.5 ng/ml. These findings make argument for cryopreservation of embryos as elevated progesterone levels appear to negatively impact in clinical pregnancy rates.

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BASELINE OVARIAN CYST FORMATION FOLLOWING GONADOTROPIN-RELEASING HORMONE ANALOGUES: THEIR PREVALENCE AND IMPACT ON IN VITRO FERTILIZATION OUTCOME. C. Failor, J. F. Knudtson, R. S. Schenken, R. D. Robinson. University of Texas Health Science Center at San Antonio, San Antonio, TX.

OBJECTIVE: One known complication of gonadotropin-releasing hormone (GnRH) agonist treatment for in vitro fertilization (IVF) cycles is the formation of functional ovarian cysts. The effect of baseline ovarian cysts on the outcome of IVF treatment is controversial. No prior studies have compared the prevalence of cyst formation in GnRH agonist versus GnRH antagonist stimulation protocols. Our objective was to determine the prevalence and significance of baseline follicular cysts on the response to controlled ovarian hyperstimulation and the outcome of IVF in women treated with a GnRH agonist versus a GnRH antagonist.

DESIGN: Retrospective case-controlled study.

MATERIALS AND METHODS: Three-hundred and eighteen consecutive IVF cycles performed between January 2010 and December 2014 were analyzed. The subjects were grouped according to stimulation protocol (GnRH agonist vs. GnRH antagonist) and by the presence or absence of baseline ovarian cysts. We compared baseline estradiol levels, total gonadotropin dose used, total number of days of ovulation induction, number of cycle cancellations, number of oocytes retrieved, and the clinical and live birth rates.

RESULTS: There was no significant difference in the prevalence of baseline ovarian cysts using a GnRH agonist versus antagonist protocol (14% vs. 9.5%, p = 0.269). The average time delay to initiate an IVF cycle was 8.9 days for the agonist cycles and 10.2 days for the antagonist cycles (range 0-28 days). The number of oocytes retrieved was lower in the group of patients with a baseline cyst treated with the antagonist protocol (4.7 with a cyst vs. 10.2 without a cyst, p = 0.039) as well as a significantly higher cycle cancellation rate (36% vs. 8.4%, p = 0.028, OR 6.16, 95% CI 1.51-25.12). This effect was not seen with the GnRH agonist protocol. There was no difference in the number of ampules of gonadotropins used for stimulation or total days of stimulation for either protocol. Finally, there was no significant difference between the groups according to the clinical pregnancy rate or live birth rate.

CONCLUSIONS: The presence of a baseline ovarian cyst delays the time to initiate an IVF cycle; however, there is no significant difference in the prevalence of cyst formation between GnRH agonist and GnRH antagonist protocols. Although presence of a baseline ovarian cyst was associated with a lower number of oocytes retrieved and higher cycle cancellation rate, there is no negative impact on pregnancy rates when compared to cycles without cyst formation. Larger prospective studies are needed to confirm these findings.

References:

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LUTEAL ESTRADIOL PRIMING ISN'T SUPERIOR TO CONVENTIONAL GnRH-ANTAGONIST PROTOCOL IN POOR RESPONDER PATIENTS WITH DIFFERENT ANTI-MULLERIAN HORMONE LEVELS. A. P. Cil, Y. Sahin, S. Kahraman. Assisted Reproductive Technologies and Reproductive Genetics Center, Istanbul Memorial Hospital, Istanbul, Turkey.

OBJECTIVE: To determine whether the luteal estradiol priming protocol (EPP) increase pregnancy outcomes in poor responder patients with different AMH levels compared to conventional GnRH antagonist protocol?

DESIGN: Retrospective data analysis.

MATERIALS AND METHODS: We retrospectively identified all GnRH antagonist (ICSI cycles n=72) and without (n=442) prior Estradiol priming in the previous luteal phase between May and November 2015 from a private IVF center database. Patients having previously undergone at least one controlled ovarian stimulation (COS) cycle fulfilling the criteria of POR according to AMH level of lower than 1.3ng/ml defined by updated Bologna poor responder criteria were included in the analysis. In Estradiol priming protocol, patients received one 0.1 mg transdermal E2 patch every other day starting 10 days after LH surge until menses, followed by conventional GnRH-antagonist protocol. The patients were subgrouped into three groups according to their AMH levels of 0.0-0.1ng/ml (Group1); 0.2-0.5ng/ml (Group2) and 0.6-1.3ng/ml (Group3), respectively. Statistical comparisons were done with student’s t-test or chi-square test where appropriate.

RESULTS: Mean age, BMI, AMH levels, and number of embryos transferred were similar between the two protocols within each AMH group. Despite the use of significantly higher gonadotrophine dose and having longer days of stimulation, patients using EPP in group 1 and group 2 yielded only one more mature oocyte resulting in similar ongoing pregnancy success compared to conventional GnRH-antagonist protocol. Oocyte yield and cycle outcomes were similar between the two protocols in group 3.

CONCLUSIONS: We did not find any increased benefit of using EPP in any poor responder patient group except yielding one more mature oocyte in patients with AMH<0.5ng/ml. However, this increase in mature oocyte number did not result in higher ongoing pregnancy rate. Therefore one should take into account the increase in gonadotrophine dose, the cost of ART and stimulation days when considering EPP in poor-responder patients.
THE ROAD TO THE LAST ABDOMINAL ULTRASOUND USE IN IVF. A. Revel, G. Karavany, Y. Shufaro, J. Hyman, A. Ben-Meir.

OBJECTIVE: To compare patient pain and discomfort, sonographic visualization and procedure efficacy in the conventional trans-abdominal (TA) to trans-vaginal (TV) sonographic guidance embryo transfer (ET).

DESIGN: Prospective randomized controlled study.

MATERIALS AND METHODS: Patients undergoing fresh ET were randomly assigned to the study group (TV sonographic guidance, n=30) or the control group (TA sonographic guidance, n=50). Following ET each patient filled out a visual analogue scale (VAS) based questionnaire evaluating pain and discomfort before, during and after the procedure. The physician also assessed quality of sonographic visualization. Follow up lasted 12 months and included data regarding pregnancy rates. The primary outcomes were pain and discomfort before, during and after ET procedure. Secondary outcomes were visualization of the ET location, pregnancy and delivery rates.

RESULTS: Pain sensation assessed by VAS before, during and after the procedure was significantly lower in the study group compared to the control group (5.61 vs. 1.45, 5.08 vs. 2.38 and 2.87 vs. 1.5, respectively; P<0.05 for all comparisons). Visualization of the uterus and the embryo transfer location were significantly better in the TVUS group (9.67 vs. 8.54; P<0.01). Implantation and live birth rates were significantly higher in the TVUS group (30% vs. 15%, OR=2.24; 95% CI. 1.13-5.36; p<0.05 and 36% vs. 18%, OR=2.56; 95% CI. 1.02-6.46; p<0.05, respectively).

CONCLUSIONS: TV US guidance to facilitate ET is superior to TA US in visualization of ET location, pain and discomfort to the patients. Trans-vaginal US is not inferior to trans-abdominal US in terms of procedure efficacy.

REFERENCES:

OBJECTIVE: Twins are at higher risk for fetal growth restriction and stillbirth compared to singleton gestations. Dichorionic twins, conceived spontaneously or by IVF, often have discordant growth as a consequence of defective trophoblast invasion or impaired development of uteroplacental circulation. Significant birthweight (BW) discordance is associated with poor perinatal outcome. Recently, controlled ovarian hyperstimulation (COH) followed by fresh embryo transfer (ET) has been linked to defective placentation, evidenced by lower BW compared to pregnancies conceived from frozen embryo transfer (FET). While this notion has been demonstrated in studies of singleton gestations, there is limited data examining the effect of ovarian stimulation on growth and prematurity in twin gestations.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: All fresh or frozen ET cycles in which patients had ≥2 blastocysts transferred from November 2002 to July 2015, resulting in live twin birth at ≥24 weeks gestation, were included. Cycles with spontaneously/selectively reduced twin gestations were excluded. Main outcome measures included gestational age at delivery, twin BW, BW discordance and the incidence of prematurity and poor growth (low/very low/extremely low BW). Student’s t-test, chi-square and linear regression analysis were used.

RESULTS: Nine hundred and fifty-eight patients delivered dichorionic twins after fresh (n=772) and frozen ETs (n=186). Patient demographics, cycle characteristics and perinatal outcomes are listed in Table 1. Fresh ET twins had a significantly lower mean average BW (2127.8g vs. 2314.8g, <0.005) than the FET group. For every 1pg/ml increase in peak estradiol there was a 0.06g decrease in the averaged twin BW (<0.0001). The degree of BW discordance and prematurity were similar among groups.

CONCLUSIONS: Similar to what is reported in singleton pregnancies, dichorionic twins conceived after fresh ET had lower BW compared with their FET cohort. However, the adverse effects on proper trophoblast invasion and placental appearance to be mild as they did not translate into increased BW discordance, prematurity or BW <2500g. Further studies incorporating additional perinatal outcomes (ie. preeclampsia) are required to better understand the role of the endometrial hormonal milieu on placentaion.

Patient demographics, cycle characteristics & perinatal outcome

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Fresh ET Twins</th>
<th>FET Twins</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient’s age at ET</td>
<td>33.4 ± 4.0</td>
<td>33.3 ± 3.9</td>
<td>NS</td>
</tr>
<tr>
<td>BMI</td>
<td>24.5 ± 5.0</td>
<td>23.9 ± 4.1</td>
<td>NS</td>
</tr>
<tr>
<td>Endometrial Thickness at transfer (mm)</td>
<td>11.7 ± 3.2</td>
<td>10.3 ± 6.1</td>
<td>NS</td>
</tr>
<tr>
<td>Peak E2</td>
<td>3415.0 ± 1508.9</td>
<td>648.4 ± 564.5</td>
<td>NS</td>
</tr>
<tr>
<td>Number of Embryos</td>
<td>3.5 ± 0.5</td>
<td>2.2 ± 0.5</td>
<td>NS</td>
</tr>
<tr>
<td>Transferred Gestational age at delivery (wks)</td>
<td>34.8 ± 2.5</td>
<td>34.6 ± 2.5</td>
<td>NS</td>
</tr>
<tr>
<td>Length at birth (average of twins) (cm)</td>
<td>18.3 ± 1.5</td>
<td>18.3 ± 1.7</td>
<td>NS</td>
</tr>
<tr>
<td>Mean averaged birthweight of twins (g)</td>
<td>2127.8 ± 841.1</td>
<td>2314.8 ± 673.5</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>Mean birthweight difference (g)</td>
<td>304.2 ± 281.7</td>
<td>306.8 ± 253.8</td>
<td>NS</td>
</tr>
<tr>
<td>Birthweight discordance &gt;=1 twin with low birthweight (&lt;2500g)</td>
<td>11.9%</td>
<td>11.8%</td>
<td>NS</td>
</tr>
<tr>
<td>66.5% (513/772)</td>
<td>65.1% (121/186)</td>
<td>NS</td>
<td></td>
</tr>
</tbody>
</table>

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OBJECTIVE: While ongoing pregnancy rates (OPR) have been shown to be enhanced in women with supernumerary blastocysts, it is unknown how the use of preimplantation genetic screening (PGS) at transfer selection and the presence of supernumerary euploid embryos (SEEs) affect IVF cycle outcome. This study sought to determine how SEE counts affect euploid, single blastocysts transfer cycle outcome.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: All patients who underwent a euploid SET between July 2011 and April 2016 were included. Cohorts were split into “Implanted” and “Non-Implanted” groups. Patients with <2 euploid embryos at the time of SET were excluded. Ongoing pregnancy rates (OPR) were correlated with SEE counts and corrected for age and diagnosis. Student’s t-test, linear and binary logistic regression analyses were performed.

RESULTS: One thousand ninety-nine cycles were included in the study. Patient demographics did not differ between study cohorts. Overall, patients achieved a 60.6% implantation and 55.5% OPR. Patients who had successful implantation and an ongoing pregnancy (n=610) had similar numbers of oocytes retrieved (17.3 +/-9.8) and blastocysts biopsied (5.9+ 4.3) to those who did not (OR 1.008 [95% CI 0.996-1.020], p=0.19 and OR 1.015 [95% CI 0.992-1.039], p=0.21, respectively). SEEs were similar between cohorts (Implanted: 3.70 +/- 3.02; Non-Implanted: 3.57 +/- 3.11) (OR 1.008 [95% CI 0.97-0.049], p=0.68). When the total of SEEs in the Implantation cohort was analyzed, the OPR was significantly increased from 46.0% to 58.9% when patients had >4 embryos (p=0.0043).

CONCLUSIONS: Patients with at least one SEE are likely to have a higher ongoing clinical pregnancy rate than patients with only one available embryo. This rate increases with the increased number of vitrified SEEs. Although patients who incorporate PGS prior to embryo selection during an IVF cycle have high success rates, a boost in supernumerary euploid counts further enhances positive outcome probability.
**RESULTS:** Demographic variables of patients in the REs transfer and in the trainee transfer groups were comparable (patients age, smoking), although infertility duration was longer and patients BMI was higher in the trainee group. Number of collected oocytes, available blastocysts and quality of transferred embryos were similar. Transfers performed by trained REs resulted in higher pregnancy and clinical pregnancy rates than those by trainees (58.7% vs 52.1%, p=0.02; 49.2% vs 41.8%, p=0.01, respectively). When trainees were grouped into junior and senior trainees, the pregnancy and clinical pregnancy rates after transfer by senior trainees and trained REs were comparable (Table 1). However, pregnancy rates after transfers by trained REs outperformed those done by junior trainees (58.7% vs 51%, p= 0.03).

**CONCLUSIONS:** Both first and second year trainees have good implantation and clinical pregnancy rates. Although the rates in first year trainees are slightly lower, by second year, they are comparable with trained REs.

<table>
<thead>
<tr>
<th>Age (yrs)</th>
<th>Senior trainees</th>
<th>Trained REs</th>
<th>P Value</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infertility duration</td>
<td>3.7 ± 3.1</td>
<td>3.1 ± 2.2</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>BMI (Kg/M²)</td>
<td>25.4 ± 5.6</td>
<td>24.5 ± 5.3</td>
<td>0.012</td>
<td></td>
</tr>
<tr>
<td>Smoking (%)</td>
<td>10.6</td>
<td>8</td>
<td>0.3</td>
<td></td>
</tr>
<tr>
<td>MII oocytes (n)</td>
<td>9.5 ± 4.8</td>
<td>9.3 ± 4.8</td>
<td>0.56</td>
<td></td>
</tr>
<tr>
<td>Fertilization rate (%)</td>
<td>78 ± 17</td>
<td>77 ± 19</td>
<td>0.82</td>
<td></td>
</tr>
<tr>
<td>Total # blast (n)</td>
<td>2.9 ± 2</td>
<td>2.9 ± 1.8</td>
<td>0.81</td>
<td></td>
</tr>
<tr>
<td>Good quality embryos (Grade 1-2)</td>
<td>72.1</td>
<td>68.6</td>
<td>0.3</td>
<td></td>
</tr>
<tr>
<td>Pregnancy rate (%)</td>
<td>52.9</td>
<td>58.7</td>
<td>0.12</td>
<td></td>
</tr>
<tr>
<td>Clinical pregnancy rate (%)</td>
<td>42</td>
<td>49.2</td>
<td>0.06</td>
<td></td>
</tr>
</tbody>
</table>

**Table 1. Senior trainee vs. trained REs transfers- demographic, cycle and outcome characteristics**

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**P-258 Tuesday, October 18, 2016**

**PATIENTS OF ADVANCED MATERNAL AGE SHOULD ONLY TRANSFER ONE EUPLOID BLASTOCYST: A COMPARATIVE ANALYSIS.** C. Gordon, a J. B. Whitney, b I. Hatch, c R. E. Anderson, d M. C. Schewe, e OB/GYN, University of California Irvine Medical Center, Orange, CA; b ART Lab, Ovation Fertility, Newport Beach, CA; c Southern California Fertility Center, Irvine, CA; d Southern California Center for Reproductive Medicine, Newport Beach, CA.

**OBJECTIVE:** To determine the efficacy of single embryo transfer (SET) compared to dual embryo transfer (DET) in advanced maternal age patients (age ≥38). Second, to assess the proper number of embryos to transfer on a patient’s first attempt using a preimplantation genetic screened (PGS) BL.

**DESIGN:** Retrospective cohort analysis of 140 vitrified-warmed euploid blastocyst transfers of patients ≥38 years old. All transfers represented the patients first transfer attempt using PGS. Implantation and live birth results were evaluated and compared using chi-square to determine differences (p<0.05).

**MATERIALS AND METHODS:** Vitrified euploid embryo transfer cycles (January 2013 to June 2015) were included from two clinics using a single laboratory. Patients had all embryos laser hatched on Day 3, blastocysts cultured to Day 5/6 for trophoblastic (TE) biopsy and vitrified utilizing the microSecure method. All TE biopsy samples were analyzed using NGS or aCGH. All frozen embryo transfers used standard HRT protocols and blastocysts were thawed and transferred within 4 hours post-warming.

**RESULTS:** A total of 140 patients, average age 39.7, achieved a collective clinical pregnancy of 83% (116/140) and a live birth rate of 80% (112/140). SET achieved a live birth rate of 79.5% (97/122) similar to DET (15/18, 83.3%). Although pregnancy outcome comparisons were not different (Table 1), a trend (p<0.10) toward higher implantation for SET was observed. Most significantly, the twinning rate was appreciably higher (p<0.001) with DET at 73% (11/15) compared to 1% for SET (1/97).

**CONCLUSIONS:** A patient’s age is a key factor when deciding the optimal number of untested embryos to transfer. Whereas, when evaluating euploid blastocysts, both SET and DET resulted in identical live birth outcomes for advanced maternal age women. Most importantly, the risk of twins was exceptionally high at 73.3% when transferring two euploid blastocysts. Clearly, single euploid ET has excellent pregnancy outcomes. In turn, the conventional wisdom of increasing the number of transferred embryos to increase take home baby rates warrants reconsideration. Independent of age, when using euploid blastocysts we believe that SET, for the first attempt, should be adopted as a standard of care practice for clinics applying PGS. Furthermore, it is evident that SET can reduce potential embryo wasteage.

**CONCLUSIONS: Both first and second year trainees have good implantation and clinical pregnancy rates. Although the rates in first year trainees are slightly lower, by second year, they are comparable with trained REs.**
Live singleton births after fresh vs. frozen SET: Demographics, cycle characteristics and outcome

<table>
<thead>
<tr>
<th></th>
<th>Fresh SET Pregnancy</th>
<th>Frozen SET pregnancy</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>34.4 ± 4.7</td>
<td>35.9 ± 4.6</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>BMI</td>
<td>22.9 ± 3.6</td>
<td>22.8 ± 3.8</td>
<td>NS</td>
</tr>
<tr>
<td>Endometrial thickness at ET (mm)</td>
<td>9.7 ± 2.4</td>
<td>9.0 ± 1.8</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>Trophoderm biopsy</td>
<td>20.4% (26/127)</td>
<td>52.4% (65/124)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Gestational hypertension/Preeclampsia</td>
<td>10.2% (13/127)</td>
<td>6.5% (8/124)</td>
<td>NS</td>
</tr>
<tr>
<td>Gestational diabetes</td>
<td>6.3% (8/127)</td>
<td>4.8% (6/124)</td>
<td>NS</td>
</tr>
<tr>
<td>Placenta previa</td>
<td>3.1% (4/127)</td>
<td>0.8% (1/124)</td>
<td>NS</td>
</tr>
<tr>
<td>Preterm delivery (&lt;37 weeks)</td>
<td>11.0% (14/127)</td>
<td>6.5% (8/124)</td>
<td>NS</td>
</tr>
<tr>
<td>Birthweight (g)</td>
<td>3154.1 ± 590.1</td>
<td>3385.5 ± 570.7</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>Macrosomia (&gt;4500g)</td>
<td>0.8% (1/127)</td>
<td>1.6% (2/124)</td>
<td>NS</td>
</tr>
<tr>
<td>Cesarean section delivery</td>
<td>48.0% (61/127)</td>
<td>54.8% (68/124)</td>
<td>NS</td>
</tr>
</tbody>
</table>

**P-260 Tuesday, October 18, 2016**

**SHOULD WE CONSIDER DAY-2 AND DAY-3 EMBRYO MORPHOLOGY BEFORE DAY-5 TRANSFER WHEN BLASTOCYSTS REACH A SIMILAR GOOD QUALITY?**. C. Heremont,a N. Sermondade,b L. Cedrin,a M. Grynberg,a C. Sifer,a “Biologie de la Reproduction - Hospital Jean Verdier, Bondy, France; bService Biologie de la Reproduction - CECOS, Hopital Jean Verdier, Bondy, France; cHospital Jean Verdier, Bondy, France; Reproductive Medicine, Hôpital Jean Verdier, Bondy, France; IVF Unit, University Hospital Jean Verdier, Bondy, France.

OBJECTIVE: Recently, extended culture strategy has considerably spread, as a consequence of advances in culture media. Blastocyst transfer improves implantation rates (IR), as a result of the synchronization between embryonic stage and endometrial receptivity, and the possibility to improve embryo selection. Actually, the efficiency of this strategy has been demonstrated in good prognosis population. However, almost nothing is known upon the impact of blastocyst transfer morphology before day-5 transfer when blastocyst(s) reach a similar good quality. Therefore, the aim of the present study was to compare clinical outcomes of good-quality blastocyst transfers according to the quality at D2 and D3 of the transferred blastocyst(s).

DESIGN: This is a retrospective analysis of prospectively collected data, including 226 Day 5 blastocyst transfers performed between January 2012 and June 2015 in the ART unit of Jean Verdier University Hospital.

MATERIALS AND METHODS: Patients were included according to the following criteria: (i) female age <37 years; (ii) first or second IVF/ICSI cycle; (iii) quality of the transferred blastocyst: blastocele ≥ B3, inner cell mass A/B; trophectoderm A/B (according to Gardner and Schoolcraft’s criteria) (i); (iv) known implantation outcome for each transferred blastocyst (including double blastocyst transfers when IR was 0 or >100%). Blastocysts were sorted into two groups according to their quality at D2 and D3: good-quality embryo (GQE) or poor-quality embryo (PQE). IR, clinical pregnancy rate (CPR), miscarriage rate (MR) and live birth rate (LBR) were compared between both groups.

RESULTS: The quality of the transferred blastocysts was similar whatever the morphological aspects they showed at D2. Besides, IR (38.3% vs. 45.2%; p=0.40), CPR (53.2% vs. 57.1%; p=0.60), MR (16.3% vs. 16.6%; p=0.97) and LBR (36.4% vs. 42.9%; p=0.43) were comparable in both D2-GQE and D2-PQE groups. Similarly, when considering the morphology at D3 of the transferred blastocysts, no significant difference was found in both biological and clinical outcomes.

CONCLUSIONS: The present investigation failed to find any significant difference in the IR, CPR and MR between the transfers of good-quality blastocysts derived either from GQE or PQE at D2 and D3. Taking those results into account, good-quality blastocyst transfer should be performed irrespectively of embryo quality at cleavage stage, since it may not compromise success rates in a good prognosis population.

References:

**P-262 Tuesday, October 18, 2016**

**IS THE INCIDENCE OF RETAINED EMBRYOS SIMILAR IN FRESH VERSUS FROZEN ETs?**. J. Rodriguez-Purata,a L. Sekhon,a,b J. A. Lee,a M. C. Whitehouse,a E. Cervantes,a M. Luna,a T. Mukherjee,a,b A. B. Copperman,a,b A. Sandler,a,b “Reproductive Medicine Associates of New York, New York, NY; 2Obstetrics, Gynecology and Reproductive Science, Icahn School of Medicine at Mount Sinai, New York, NY.”

OBJECTIVE: The presence of a retained embryo(s) in the embryo transfer (ET) catheter is an uncommon event, occurring in 1-8% of all ART treatment cycles. Although a fresh IVF cycle approach has been the first line approach for many clinics, extended embryo culture and preimplantation screening is supporting the implementation of freeze-all strategies. Increased embryo manipulation and expansion could theoretically alter normal morphokinetics and adhesion and thereby affect the incidence of retained embryos. This study sought to evaluate the incidence of embryo retention in fresh versus cryopreserved embryo transfers.

DESIGN: Retrospective.

MATERIALS AND METHODS: Patients undergoing an IVF cycle with PGD (qPCR-based CCS) from July 2010 to February 2016 were included. Patients were segregated into Fresh and FET groups. Only the first cycle of each patient was included. Only euploid embryos were transferred. The
SEQUENTIAL EMBRYO SCORING SYSTEM CAN SUBSTITUTE FOR TIME LAPSE MONITORING SYSTEM. Y. Kim,1 H. Sun,2 H. Chi,2 S. Kim,1 K. Lee,1 S. Kwak,1 J. Park,1 C. Yoo1, J. Kim2.1Babydream Research Center, Mamapapa & Baby OBGY Clinic, Ulsan, Korea, Republic of;2Mamapapa & Baby OBGY Clinic, Ulsan, Korea, Republic of.

OBJECTIVE: Time lapse scoring system has an advantage in selecting the best embryo by evaluating embryo’s continuous development at certain time points.

In our laboratory, we investigated if the sequential embryo-scoring system could exhibit positive effects in selecting embryos by replacing the time-lapse function with cleavage stage embryos, including early-cleavage assessment. [1] If transfer of a euploid embryo fails to progress to a clinical pregnancy on the second transfer as compared to those that did not, the risk of maternal and neonatal morbidity associated with multiple gestation. [1] If transfer of a euploid embryo fails to progress to a clinical pregnancy on the second transfer as compared to those that did not, the risk of maternal and neonatal morbidity associated with multiple gestation. [1] If transfer of a euploid embryo fails to progress to a clinical pregnancy on the second transfer as compared to those that did not, the risk of maternal and neonatal morbidity associated with multiple gestation. [1] If transfer of a euploid embryo fails to progress to a clinical pregnancy on the second transfer as compared to those that did not, the risk of maternal and neonatal morbidity associated with multiple gestation.

RESULTS: During the study period, we identified 464 fresh and 1558 FET cycles. Overall, age (36.8±4.4 vs. 36.6±4.2), FSH (6.0±3.0 vs. 6.2±3.5), AMH (3.2±2.7 vs. 3.8±4.4), BMI (23.6±4.2 vs. 23.2±4.1) and ET count (1.3±0.4 vs. 1.2±0.4) were similar between fresh and FET cycles, respectively. Embryo retention was statistically lower during a FET cycle when compared to a fresh cycle (0.4 vs. 2.4%), interpreted as 85% less probability for a screened embryo(s) to be retained in the catheter during a FET cycle (OR 0.15 (95% CI 0.1 - 0.4), p<0.001) compared to that of Group (2) (41.6% and 31.6%, respectively).

CONCLUSIONS: Our study evaluated the continuous developmental process of the embryo through the sequential embryo scoring system. We found that embryos with scores higher than 16 points resulted in a significantly higher pregnancy rate. Therefore, the sequential embryo scoring system is effective in predicting high pregnancy rates.

Support: by Mamapapa & baby OBGY clinic.
CONCLUSIONS: Lower pregnancy rates might be expected after an initial failed transfer cycle, as the number of good quality blastocysts available is reduced. However, clinical pregnancy rate with a second STEET following an initial failed cycle was similar to the pregnancy rate seen for all first transfers in our population, providing hope for couples. A thicker endometrial echo and younger maternal age at transfer were associated with increased ability to achieve clinical pregnancy in a second STEET after previous failure, indicating a possible underlying uterine or embryologic factor. Further research is needed to identify other potential contributions to pregnancy failure with STEET in order to increase utilization of single embryo transfer.

References:

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IMMEDIATE AMBULATION AFTER EMBRYO TRANSFER HAS NO EFFECT ON ONGOING PREGNANCY RATES IN FRESH OR FROZEN IVF CYCLES WITH OR WITHOUT COMPREHENSIVE CHROMOSOMAL SCREENING. A. Frankel,a T. A. Molinaro,b P. A. Bergh, aNursing, Reproductive Medicine Associates of NJ, Basking Ridge, NJ; bReproductive Medicine Associates of New Jersey, Eatontown, NJ; cRMA, Basking Ridge, NJ.

OBJECTIVE: Objective: Determine whether immediate ambulation following embryo transfer has an adverse effect on ongoing pregnancy rates.

DESIGN: Design: Retrospective cohort study.

MATERIALS AND METHODS: Materials and Methods: Analysis of patients undergoing In Vitro Fertilization (IVF) with fresh or frozen embryo transfer from January 2014 to December 2014. Embryo implantation rates and ongoing pregnancy rates were compared for patients who ambulated immediately following transfer versus patients who had 20 minutes of bed rest following transfer. The analysis was limited to one cycle per patient to avoid confounding. Demographics and outcomes were compared using student’s t test or chi square where appropriate.

RESULTS: Results: 2092 cycles were available for analysis comprised of 1086 transfers with twenty minutes of bedrest and and 1006 transfers where immediate ambulation was allowed. There was no statistically significant difference in the mean age, use of comprehensive chromosomal screening (CCS) or proportion of fresh and frozen transfers between groups. The no ambulation group had a slightly higher mean number of embryos transferred (1.39 vs 1.32) that was statistically different, but not likely clinically significant. The ambulation group had similar implantation rates (65.9%) and ongoing pregnancy rates (60.3%) compared with the no ambulation group (65.2% and 59.0% respectively). (TABLE 1).

CONCLUSIONS: Conclusion: Bed rest after embryo transfer is not needed to achieve high implantation or ongoing pregnancy rates. This conclusion holds true in fresh and frozen cycles with and without Comprehensive Chromosomal Screening.

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PROSPECTIVE, RANDOMIZED, CLINICAL TRIAL TO COMPARE TWO ENDOMETRIAL PREPARATION PROTOCOLS. P. Ferrer Molina, a C. Calatayud Liiso, b R. Carreras Collado, c M. Munoz Garcia, d M. Diaz Bachiller, e J. Blanes Espi, f M. Checa, g Crea Medicina de la Reproduccion, Gynecologist, Valencia, Spain; h Crea Medicina de la Reproduccion, Doctor, Valencia, Spain; i Hospital del Mar, Gynecologist, Barcelona, Spain; j Hospital del Mar, Barcelona, Spain.

OBJECTIVE: The aim of this study is to confirm that the transdermal way is equal or superiorthan the oral way for the estrogensadministration in endometrial preparation cycles for embryos transfer, taking as principal variable the number of days necessary for obtaining a triple line endometrium thicker than 7mm. As secondary variables, we evaluate comfort and patient’s satisfaction, plasmaic levels of estradiol as well as pregnancy, miscarriage and delivery rates.

DESIGN: We outlined a prospective, randomized control trial.

MATERIALS AND METHODS: In this study, 140 patients who are going to undergo an embryo transfer cycle are randomized in 2 groups: group I will follow a protocol with pills of estradiol hemihydrate.Endometrial thickness will be measured by transvaginal ultrasound on day 10 of the cycle. Should the lining not measure more than 7mm, a second measurement will be performed on day 15 of the cycle. A blood analysis of estradiol level will be performed when the lining is thicker than 7mm. Patients will complete a satisfaction survey to evaluate treatment’s comfort and side effects.

RESULTS: Patients of group II reached a significantly thicker endometrium on the day of first control compared to group I’s patients (7.59 mm vs 7.01 mm; p<0.026), with lower level of estradiol in blood (159.16 pg/ml vs 237.14 pg/ml; p<0.000). Patients of group I found their treatment more comfortable than patients of group II. In group II more cases of mastalgia and dermatitis were detected. No significant differences were found in terms of pregnancy, miscarriage and birth rates.

CONCLUSIONS: Treatment with transdermal estrogens allows to reach a higher endometrial thickness in less days, with lower plasmatic levels of estradiol, although it is worst tolerated by patients (ClinicalTrials.gov: NCT01430650).

References:
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PREGNANCY OUTCOMES OF SINGLE VERSUS DOUBLE EMBRYO TRANSFER IN WOMEN WITH A CONGENITAL UNICORNOATE UTERUS. X. Li, a Y. Ouyang, b Y. Yi, b Reproductive and Genetic Hospital of CITIC-Xiangya, Chang-sha, China; 3Institute of Reproductive & Stem Cell Engineering, Central South University, Changsha, China.

OBJECTIVE: To investigate the effects of single embryo transfer (ET) and double ET on pregnancy outcomes in women with a unicornuate uterus.

DESIGN: Retrospective analysis.

MATERIALS AND METHODS: The pregnancy outcomes of 300 infertility patients with a unicornuate uterus and got clinical pregnancy via in vitro fertilization (IVF)-ET from January 2012 to May 2015 were analyzed. The rates of embryo implantation, live birth, transfer cycle pregnancy, clinical pregnancy and multiple pregnancy were compared between single and double ET using chi-squared test; comparisons of pregnancy outcomes were made between singleton pregnancy via single ET (A group) and via double ET (B group), and between singleton pregnancy of A group and twin pregnancy via double ET (C group) using two-sample t-test, chi-squared test or fisher exact test.

RESULTS: There were a total of 377 transfer cycles in the 300 cases, including 53 single ET cycles which contained 23 cases of singleton pregnancy, and 324 double ET cycles which obtained 126 cases of singleton pregnancy, 74 cases of twin pregnancy and 3 cases of triple pregnancy. 35 cases of spontaneous/selective reduction were excluded from analysis. Comparison of the IVF treatment outcomes based on single or double ET, the rates of transfer cycle pregnancy (43.4%(23/53) vs. 62.7%(203/324), p=0.008), clinical pregnancy (46.8%(22/47) vs. 76.7%(194/253), p=0.001) and multiple pregnancy in single ET were all significantly lower. While the rates of embryo transplantation (43.4%(23 /53) vs. 43.1%(279/648), p=0.962) and live birth (37.7%(20/53) vs. 48.4%(157/324), p=0.147) had no significant differences. There were no significant difference in pregnancy outcomes between A and B group (p=0.741). When comparing the pregnancy outcomes of A and C group, the differences were significantly different (P=0.002): the rates of early pregnancy loss (8.7%(2/23) vs. 14.3%(6/42)), late miscarriage (4.5%(1/23) vs. 16.7%(7/42), and preterm delivery (13.0%(3/23) vs. 42.9%(18/42) in A group were all lower; in addition, the gestational weeks at delivery (38.1±1.9 vs. 35.2±2.9; p<0.001) and birth weight (3.1±0.5vs. 2.2±0.6 kg; p<0.001) in A group were both significantly higher. Although the rates of term low birth weight infant (0 (0/17) vs. 18.2%(4/22); p=0.118) and perinatal mortality (0 (0/20) vs. 10.7%(6/56); p=0.331) were both lower in A than C group but didn’t reach significant level (Table).

CONCLUSIONS: Single ET could obtain similar rates of embryo implantation and live birth as double ET. Singleton pregnancy via single ET can not only gain better pregnancy outcomes than twin pregnancy via double ET, but also reduce the risk of multiple pregnancy. Therefore, single ET is recommended in women with a unicornuate uterus during IVF-ET.

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ELECTIVE SINGLE EMBRYO TRANSFER CRITERIA SHOULD BE APPLIED TO FROZEN EMBRYO TRANSFER CYCLES. M. R. Freeman, a M. Hinds, a K. G. Howard, b J. Howard, b G. Hill, a Ovation Fertility, Nashville, TN; aNashville Fertility Center, Nashville, TN.

OBJECTIVE: To evaluate the outcomes for eSET (elective single embryo transfer) and eDEt (elective double embryo transfer) in frozen embryo transfer cycles.

eSET vs. eDET in FET cycles

<table>
<thead>
<tr>
<th>Patient Group</th>
<th># Embryos transferred</th>
<th># Transfers</th>
<th>Ongoing/transfered (delivery)</th>
<th>Ongoing/transfered (%)</th>
<th>Ongoing/transfered (singleton)</th>
<th>Ongoing/transfered (multiple)</th>
<th>Implantation (rate)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PGS Patients</td>
<td>1</td>
<td>76</td>
<td>38 (50)</td>
<td>37</td>
<td>1 (3)</td>
<td>39/76 (51)</td>
<td>3/76 (4)</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>42</td>
<td>27 (64)</td>
<td>16</td>
<td>12 (44)</td>
<td>40/84 (48)</td>
<td>1/12 (8)</td>
</tr>
<tr>
<td>Non-PGS Patients</td>
<td>1</td>
<td>79</td>
<td>41 (52)</td>
<td>40</td>
<td>1 (2)</td>
<td>42/79 (53)</td>
<td>1/42 (2)</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>194</td>
<td>117 (60)</td>
<td>79</td>
<td>38 (32)</td>
<td>155/388 (40)</td>
<td>5/155 (3)</td>
</tr>
<tr>
<td>Negative, biochemical, or miscarriage in fresh cycle</td>
<td>1</td>
<td>20</td>
<td>10 (50)</td>
<td>7</td>
<td>0</td>
<td>10/20 (50)</td>
<td></td>
</tr>
<tr>
<td>Pregnant &amp; delivered in fresh cycle</td>
<td>2</td>
<td>129</td>
<td>73 (57)</td>
<td>51</td>
<td>22 (30)</td>
<td>95/258 (37)</td>
<td></td>
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<tr>
<td></td>
<td>1</td>
<td>41</td>
<td>22 (54)</td>
<td>21</td>
<td>1 (5)</td>
<td>23/41 (54)</td>
<td>1/23 (4)</td>
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<tr>
<td></td>
<td>2</td>
<td>38</td>
<td>23 (61)</td>
<td>15</td>
<td>8 (35)</td>
<td>31/76 (41)</td>
<td>2/31 (6)</td>
</tr>
</tbody>
</table>

Fisher’s Exact Test: P=0.176 7P=0.0001 8P=0.75 5P=0.225 6P=0.0001 7P=0.034 7P=1.0 6P=0.056 5P=0.24 6P=0.65 4P=0.022 12P=0.124

DESIGN: Retrospective study.

MATERIALS AND METHODS: Data analysis of ongoing pregnancy and live birth rates, multiple pregnancy rates, and implantation rates (+fetal heart motion# embryos transferred) of patients who qualified for eSET (<35 years old at the time of cryopreservation; > 1 cryopreserved blastocyst in storage) and who self-elected either eSET or eDET in 391 frozen embryo transfer (FET) cycles occurring between 2011 and 2015. FET outcomes were evaluated according to the patients’ election to have preimplantation genetic screening (PGS) or not (PGS patient; non-PGS patient) or fresh cycle outcome (negative outcome; pregnant and delivered in fresh cycle). Proportion data were analyzed using Fisher’s exact test; P< 0.05 was considered to be statistically significant.

RESULTS: There were no statistically significant differences observed in ongoing pregnancy and live birth rates in FET for eSET vs. eDET in any of the patient groups evaluated. Multiple pregnancy rates were significantly decreased in all eSET groups (0 - 5%), compared to eDET groups (30 - 44%). Implantation rates were significantly higher for eSET vs. eDET in non-PGS patients (53% vs. 40%), but failed to reach a significant difference in the other groups.

CONCLUSIONS: Similar ongoing pregnancy and live birth rates can be maintained while reducing the occurrence of multiple gestations with eSET compared to eDET in FET cycles. This is important since fewer fresh embryo transfers are being done due to the increase in PGS and IVF cycle management. If two or more cryopreserved blastocysts are available, eSET in FET cycles will provide additional future FET attempts while decreasing multiple pregnancy complications and fetal loss. Furthermore, eSET represents a significant potential cost savings since current estimates for delivery of twins is five times, and triplets is 20 times the cost of delivery of a singleton.

References:

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STRATEGIC IMPLEMENTATION OF EXTENDED CULTURE RESULTS IN DIFFERENT CLINICAL OUTCOMES COMPARED TO ROUTINE BLASTOCYST CULTURE IN DONOR CYCLES. V. Libby, a S. Babayev, a B. G. Reed, a K. Doody. a UT Southwestern Medical Center, Dallas, TX; bCenter for Assisted Reproduction, Bedford, TX.

OBJECTIVE: This study aims to compare laboratory and clinical outcomes in donor cycles between clinics that use an algorithm to determine whether cleavage embryos versus blastocyst stage embryos will be used versus clinics that do all blastocyst transfers.

DESIGN: Retrospective Cohort Study

MATERIALS AND METHODS: All fresh and frozen donor embryo transfers in the SART database from 2004 to 2013 were reviewed. Years were separately analyzed for each clinic. Clinics were grouped according to the percentage of blastocyst transfers with greater than or equal to 95% termed “Day 5” clinics and those with <95% as algorithm-based clinics. Among algorithm-based clinics, 45,296 patients underwent fresh and 22,592 underwent frozen donor embryo transfers from 298 distinct clinic-years. Among algorithm-based clinics, 45,296 patients underwent fresh and 22,592 underwent frozen embryo transfers from 5,080 clinic-years. Patient and cycle characteristics and birth outcomes were included in the analysis. The main outcome measures were pregnancy, live birth, multiple gestation, birth weight, neonatal death, and gender rates.
RESULTS: Age was higher for algorithm-based clinics while weight and BMI were higher for Day 5 clinics in all cycles. The overall pregnancy rate was higher for Day 5 fresh and frozen cycles. Miscarriage rate was similar between groups. The multiple gestation rate was higher for Day 5 transfers in fresh donor cycles, but higher for algorithm clinics in frozen cycles. However, mononygotic twinning rate was similar between groups. Live birth rate was higher for Day 5 in fresh and frozen cycles. Live birth weight and gender proportions for singletons and multiples were similar between all groups.

CONCLUSIONS: Pregnancy and live birth rates were higher for Day 5 fresh and frozen donor cycles when compared to algorithm-based clinics.

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OLD HABITS DIE HARD: USE OF CORTICOSTEROIDS AND ANTIBIOTICS PRIOR TO EMBRYO TRANSFER. L. A. Kaye,a C. B. Bartels,a A. Bartolucci,a B. L. Maslow,a J. Nulsen,a C. A. Benadiva,b *University of Connecticut, Farmington, CT; bCenter for Advanced Reproductive Services, Farmington, CT.

OBJECTIVE: To evaluate clinical and ongoing pregnancy rates in embryo transfer cycles with and without corticosteroid and oral antibiotic administration.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Fresh and frozen embryo transfers performed at a university-affiliated in vitro fertilization (IVF) center between 2014-2015 were identified based on whether they received oral doses of methylprednisolone and doxycycline and 434 embryo transfers after the discontinuation of routine corticosteroids and oral antibiotics prior to embryo transfer, except for cleavage stage embryo transfer with assisted hatching when implantation rates improved without the use of these medications. With advances in IVF culture, technique, and success rates, the historical justification for use of these medications has lost relevance, even for intrauterine sperm injection or cleavage stage embryos with assisted hatching.

RESULTS: During 1385 fresh transfer cycles, 14 patients were diagnosed with EP. The EP to clinical pregnancy rate was 3.3% in the standard protocol group versus 0.9% in the modified protocol group. After adjusting for confounding factors, the incidence of EP was significantly lower with the modified technique for embryo catheter loading. There were insignificant differences for the implantation, pregnancy and miscarriage rates in GI & GII and they were as follow; (23.9% vs 25.8%), (9.1% vs 9.7%).

CONCLUSIONS: Our results showed that there is an association between the incidence of EP and the procedure for embryo catheter loading that modifies the technique of ET. We assume that both, the gentle embryo deposition due to the presence of a column of free medium which acts as a buffer shoulder against forcible ejection and the absence of air brackets, may minimize the embryo migration inside the uterine cavity which could be an explanation for the lower incidence of EP reported with the modified protocol for EL.

P-271 Tuesday, October 18, 2016

CANC EMBRYO CATHETER LOADING HAVE AN INFLUENCE ON THE INCIDENCE OF ECTOPIC PREGNANCY IN IVF/ET CYCLES?. M. E. Eid. Obst/Gyne, Professor of Obst/Gyne, Cairo Univ., Egypt, Dubai, United Arab Emirates.

OBJECTIVE: Compared with natural conception, ectopic pregnancy (EP) rate is 2.5-5 fold higher after IVF/ET. Among the different steps in embryo transfer (ET) technique, less attention has been given to the embryo loading (EL) procedure. Thus, it may be necessary to optimize the EL technique in order to minimize the drawbacks and unwanted outcomes. In the present study, we questioned whether the column of the embryo-containing medium may affect the incidence of EP. In this investigation, we compared the EP rates of women who conceived from the transfer of embryos loaded by two different EL techniques (standard & modified).

RESULTS: We analyzed 442 embryo transfers with the routine use of methylprednisolone and doxycycline and 434 embryo transfers after the discontinuation of routine steroid and antibiotic usage. The clinical pregnancy rate with the routine use of methylprednisolone and doxycycline prior to embryo transfer was 55.9% compared to 61.5% after discontinuation of these medications (p=0.09). Ongoing pregnancy rates were 47.5% with medications versus 51.4% without medications (p=0.25). Clinical miscarriages occurred in 14.6% (36/247) of clinical pregnancies with medications compared to 16.5% (44/267) of pregnancies without medications (p=0.64).

CONCLUSIONS: There is no statistically significant difference in IVF outcomes was noted after the discontinuation of routine corticosteroids and oral antibiotics.
References:

P-272 Tuesday, October 18, 2016
EFFECT OF PGS ON IVF OUTCOMES FOLLOWING ELECTIVE SINGLE EMBRYO TRANSFER (ESET) IN OOCYTE DONATION IN THE UNITED STATES: 2005 TO 2013. D. H. Baral,a,b S. Darmon,a V. A. Kushnir,a,c E. Lazzaroni-Tealdi,a Q. Wang,d D. Albertini,a,b N. Gleicher,a,b Center for Human Reproduction, New York, NY; Albert Einstein College of Medicine, Bronx, NY; Wake Forest School of Medicine, Winston-Salem, NC; University of Kansas Medical Center, Kansas City, KS; Rockefeller University, New York, NY.

OBJECTIVE: Since ESET is widely considered an indication for PGS, we assessed the effect of PGS on on live birth rates in ESET cycles following initial fresh oocyte donation (OD) with or without PGS.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: To explore trends in third party reproduction, we obtained data from the Assisted Reproductive Technology Database developed by SART on all donor oocyte cycles performed in the United States from 2005 through 2013. Live births after initial fresh oocyte donation cycle, PGS and ESET of a single blastocyst were calculated to provide estimates of live birth rates.

RESULTS: 3,449 patients underwent a fresh ESET first oocyte donation cycle during the study period. PGS was performed in 203 (6%) while 2016 (94%) were performed without PGS (nPGS). Live birth rates in ESET cycles were 52% with PGS and 59% with nPGS, almost reaching significance (P = 0.053). Clinical pregnancy rates were significantly lower in the PGS group 63% vs. 70% (P = 0.031). Use of PGS in patients who underwent ESET did not reduce the chance of miscarriage (PGS 17% vs nPGS 16%, p = 0.68), and when the analysis was limited to the last two years (2012 and 2013), there were no differences in outcomes between PGS and nPGS group (Table).

CONCLUSIONS: Though utilization of PGS in association with ESET is widely recommended under the assumption that PGS improves clinical pregnancy and live birth rates and reduces miscarriage rates, national data over 8 years do not demonstrate any beneficial effects.

<table>
<thead>
<tr>
<th></th>
<th>2005-2013</th>
<th>2012-2013</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PGS</td>
<td>nPGS</td>
</tr>
<tr>
<td>Clinical pregnancies (%)</td>
<td>631</td>
<td>701</td>
</tr>
<tr>
<td>Live births (%)</td>
<td>522</td>
<td>592</td>
</tr>
<tr>
<td>Miscarriages (%)</td>
<td>17</td>
<td>16</td>
</tr>
</tbody>
</table>

References:

P-274 Tuesday, October 18, 2016
INNER CELL MASS AND TROPHOCTODERM QUALITY AS PREDICTIVE PARAMETERS OF PREGNANCY AND IMPLANTATION. L. Inarugui,a F. Ayerd,i M. Ferrando,a F. Quintana,a Z. Larreguelegui,a IVI Bilbao, Leioa, Spain; Andrology Laboratory, IVI Bilbao, Leioa, Spain.

OBJECTIVE: The development of sequential media has enabled the blastocyst transfer to be the most used strategy when optimizing embryo selection. The most commonly used method for the blastocyst selection is the morphological assessment of the: blastocoele expansion, size and compaction of the inner cell mass (ICM) and the cohesion and number of cells of the trophoeoderm (TE). Some authors have reported the value of each one, although the most extended practice is considering the ICM as the most important factor. In the present study we want to check the value of the trophoderm morphology on single embryo transfers (SET) carried out in our center. The goal of the study is to define the potential of the TE for predicting pregnancy and implantation.

DESIGN: We analyzed and compared the results of SET from IVF/ICSI (own and donor oocytes) and thawed embryo transfer cycles of two different groups: Group 1: optimal ICM (‘a’ quality) and medium TE (‘b’ or ‘c’ quality)- Group 2: optimal TE (‘a’ quality) and medium ICM (‘b’ or ‘c’ quality).

The assessment of the embryo quality has been made following ‘Asociación de la reproduccion’ (ASEBIR) guidelines.

OBJECTIVE: To examine if individual components of a Gardner’s blastocyst grade or a summarized score are predictive of implantation for multiple but not single EMBRYO TRANSFERS. J. E. Gray,a M. A. Fritz,a,b D. S. Berger,c,d UNC Fertility, Raleigh, NC; Obstetrics and Gynecology, University of North Carolina Chapel Hill, Chapel Hill, NC; Penn Fertility Care, Philadelphia, PA.

OBJECTIVE: To examine if individual components of a Gardner’s blastocyst grade or a summarized quantitative score derived from blastocyst grade are predictive of the implantation rate of the embryos transferred.

DESIGN: Retrospective study.

MATERIALS AND METHODS: Women undergoing fresh Day 5 embryo transfers at UNC Fertility from 2013 to 2015 were included in our study. Embryos were assessed by Gardner’s blastocyst grading scale and implantation was measured by fetal cardiac activity. Individual components of the Gardner’s grade including expansion, inner cell mass (ICM), and trophoeoderm (TE) were analyzed for their relationship with implantation rate by a SAS general linear model (GLM) and p values less than 0.05 were considered significant. Additionally a summarized score of the Gardner’s blastocyst grade was generated by converting letter components of the ICM and TE to numeric (A to 3, B to 2, C to 1), normalizing the 1 to 6 scale of the numeric expansion score to the ICM and TE scale by multiplying by 0.75, and then summing the numbers from the three components. Embryos transferred on day 5 at developmental stages preceding blastocyst were given zeros for all metrics.

RESULTS: A total of 276 day 5 embryo transfers including 434 embryos were examined. 139 of these transfers were elective single embryo transfer (eSET). Higher values of all three components of the Gardner’s blastocyst grade and the summarized score associated significantly with higher implantation rates when all transfers were included (see table above), but none of the components of the Gardner grade were significantly associated with implantation when only eSET were analyzed. No differences were present in mean age or cycle number with respect to any of the Gardner score groupings (p > 0.05), but the mean number of embryos significantly increased as embryo quality decreased (p < 0.0001).

CONCLUSIONS: Our data indicate that high quality in vitro embryo development evidenced by good grades in any aspect of a Gardner blastocyst grade is predictive of implantation in embryo transfers involving multiple embryos. Practice guidelines regarding the application of eSET to only good quality embryos may likely allow our detection of differences amongst grades in implantation rates and leads to decreased average number of embryos transferred in these categories. Our data support the inclusion Gardner grades as a factor to determine number of embryos transferred on Day 5 and application of eSET only when high quality blastocyst development occurs in culture.

<table>
<thead>
<tr>
<th>Expanded Grade</th>
<th>4</th>
<th>3</th>
<th>2</th>
<th>1</th>
<th>0</th>
<th>GLM p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Implantation Rate</td>
<td>54%</td>
<td>51%</td>
<td>35%</td>
<td>26%</td>
<td>21%</td>
<td>0.02</td>
</tr>
<tr>
<td>ICM Grade</td>
<td>A</td>
<td>B</td>
<td>C</td>
<td>No Blast</td>
<td>GLM p value</td>
<td></td>
</tr>
<tr>
<td>Implantation Rate</td>
<td>57%</td>
<td>45%</td>
<td>21%</td>
<td>21%</td>
<td>0.0004</td>
<td></td>
</tr>
<tr>
<td>TE Grade</td>
<td>C</td>
<td>No Blast</td>
<td>GLM p value</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Implantation Rate</td>
<td>58%</td>
<td>46%</td>
<td>39%</td>
<td>21%</td>
<td>0.003</td>
<td></td>
</tr>
<tr>
<td>Summarized Score</td>
<td>9-6</td>
<td>6-4</td>
<td>4-2</td>
<td>2-0</td>
<td>GLM p value</td>
<td></td>
</tr>
<tr>
<td>Implantation Rate</td>
<td>53%</td>
<td>44%</td>
<td>24%</td>
<td>21%</td>
<td>0.002</td>
<td></td>
</tr>
</tbody>
</table>

References:
to be higher too. This study shatters the belief about that the ICM has a bigger contribution on the implantation and shows that an optimal TE predicts higher implantation and pregnancy rates. Therefore, trophodermal cohesion and morphology should preferentially be used as the most important factor in choosing the best embryo for transfer.

**P-275 Tuesday, October 18, 2016**

**TIMING OF EMBRYO TRANSFER AFTER HYSTEROSCOPIC POLYPECTOMY DOES NOT EFFECT PREGNANCY RATES.** Z. Diken, A. Rodriguez, Y. Lin, J. Crochet. OB GYN, UTMB, Galveston, TX; University of Texas Medical Branch, Galveston, TX; Center of Reproductive Medicine, Webster, TX.

OBJECTIVE: To determine if timing of embryo transfer after hysteroscopic polypectomy effects outcomes.

DESIGN: Retrospective chart review.

MATERIALS AND METHODS: A retrospective chart review was performed. Women who underwent polypectomy with subsequent ET from September 2012 to June 2015 was included. Women utilizing donor oocytes or those with prior uterine surgery were excluded. Age, gravidity, parity, body mass index (BMI), cycle type (fresh or frozen), number of embryos transferred, and pregnancy outcomes were collected for each subject. The control group included women proven to have a normal uterine cavity who underwent ET. The experimental groups consisted of women who had ET within 90 days of polypectomy (Group 1) and women who had ET ≥90 days after polypectomy. The pregnancy rate (PR), clinical pregnancy rate (CPR), and ongoing pregnancy rates (OPR) were calculated for each group and compared by chi-square testing with significance set at p < 0.05.

RESULTS: 408 women were included in the study. There were no differences in the baseline characteristics of each group. There were no differences in regards to PR, CPR, or OPR amongst the three groups (table 1).

CONCLUSIONS: This is one of the first studies to examine the timing of ET after hysteroscopic polypectomy, and these data suggest that the timing of ET does not impact outcomes. Given that it takes at least 60 days for the endometrium to heal, these findings are somewhat unexpected. Our data did not allow for a comparison at 60 days. We do find it interesting that all women who achieved pregnancy after ET within 90 days of polypectomy had an ongoing pregnancy, while there were 4 losses (3 missed abortions, 1 chemical pregnancy) in the group that had ET ≥90 days after polypectomy. Prospective studies looking specifically at the 60-day timeframe may help clarify the effect of timing of ET after hysteroscopic polypectomy.

<table>
<thead>
<tr>
<th>Outcomes by Group</th>
<th>No Polypectomy (N=299)</th>
<th>Group 1 ≤90 Days (N=42)</th>
<th>Group 2 ≥90 Days (N=67)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnancy</td>
<td>190 (63.5% )</td>
<td>24 (57.1% )</td>
<td>39 (58.2% )</td>
<td>0.5677</td>
</tr>
<tr>
<td>Clinical pregnancy</td>
<td>180 (60.2% )</td>
<td>24 (57.1% )</td>
<td>37 (55.2% )</td>
<td>0.7289</td>
</tr>
<tr>
<td>Ongoing pregnancy</td>
<td>174 (58.2% )</td>
<td>24 (57.1% )</td>
<td>35 (52.2% )</td>
<td>0.6728</td>
</tr>
</tbody>
</table>

References:

**P-276 Tuesday, October 18, 2016**

**DIFFICULTY OF EMBRYO TRANSFER DOES NOT PREDICT FAILED ATTEMPT AT VAGINAL DELIVERY IN SINGLETON PREGNANCIES.** E. Barnard, T. L. Jones, L. E. Vaughan, K. Mara, C. Doddington. “Mayo Clinic, Rochester, MN; Reproductive Endocrinology and Infertility, Mayo Clinic, Rochester, MN; Division of Biomedical Statistics and Informatics, Mayo Clinic, Rochester, MN.

OBJECTIVE: Patients utilizing assisted reproductive technologies undergo multiple exams assessing the ease of traversing the cervix for embryo transfer. While previous studies have found an association between the difficulty of transfer and the ability to achieve pregnancy, no prior studies have looked at the difficulty of transfer as a predictor of subsequent obstetric outcomes. Our objective was to evaluate whether difficult embryo transfer attempts portend poor obstetric outcomes, in particular failed attempt at vaginal delivery in singleton pregnancies.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Our study population included women undergoing in vitro fertilization at Mayo Clinic from 2013-2015. Institutional review board approval was obtained. Exclusion criteria included multiple gestations, women who delivered at outside institutions, and those who underwent cesarean section prior to the onset of labor for indications such as elective repeat, placenta previa, or breech presentation. Statistical analysis was performed using the T-test and Wilcoxon rank sum test for continuous variables and chi-square and Fisher exact tests for categorical variables.

RESULTS: Our cohort included 176 women. After chart review, 81 met inclusion criteria and were included in the final analysis. Women were assessed based on difficulty of embryo transfer: easy versus intermediate/difficult. Results are presented in Table 1. Baseline characteristics including age, parity and body mass index were similar between groups. Difficult transfer did not predict a higher rate of induction, did not experience protracted labor, and did not have a higher risk of cesarean section. If validated in a larger population, this information may be reassuring for patients after achieving pregnancy via assisted reproductive technology.

| Baseline Data and Obstetric Outcomes Comparing Easy and More Challenging Mock Transfers |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|
| Easy Mock Transfer (N=52) | Intermediate/Difficult Mock Transfer (N=29) | Total (N=81) | p Value |
| Age (Mean(SD)) | 34.2 (5.2) | 33.2 (3.9) | 33.8 (4.8) | 0.42 |
| Body Mass Index (Mean(SD)) | 25.5 (4.7) | 22.5 (5.3) | 25.4 (4.9) | 0.68 |
| Induction | 27 (51.9%) | 11 (37.9%) | 38 (46.9%) | 0.23 |
| Length of Phase of Labor (min) | Median 245.5 | Median 145.5 | Median 201.5 | 0.016 |

| Active Phase of Labor (min) | Median 245.5 | Median 145.5 | Median 201.5 | 0.016 |

References:
ENDOMETRIUM

P-277 Tuesday, October 18, 2016

ADENOMYOSIS IS ASSOCIATED WITH DIMINISHED ENDOMETRIAL EXPRESSION OF BONE MORPHOGENETIC PROTEINS BMPR1B AND SMAD4. E. G. Richards,* S. A. El-Nashar,* J. K. Schooilmee,* M. R. Hopkins,* A. O. Famuyide,* G. S. Daftary,* 1Department of Obstetrics and Gynecology, Mayo Clinic, Rochester, MN; 2Division of Female Pelvic Medicine and Reconstructive Surgery, University Hospitals Case Medical Center Case Western Reserve University, Cleveland, OH; 3Department of Laboratory Medicine and Pathology, Mayo Clinic, Rochester, MN.

OBJECTIVE: Adenomyosis remains an enigmatic, recalcitrant, highly prevalent uterine disease. We comprehensively screened 56 adenomyosis and 264 matched control samples to identify dysregulated critical signaling pathways within our overall strategy of developing novel therapeutic options directed against these using in vivo and in vitro testing paradigms.

DESIGN: Samples from 56 patients with adenomyosis and 264 matched controls who underwent hysterectomy at Mayo Clinic were plated on tissue microarrays to facilitate high throughput immunohistochemistry screening for expression of critical signaling pathways. We present here our results from the canonical BMP signaling pathway (ligands BMP2, 6, 7; receptors BMPR1A, BMPR1B, and downstream SMAD proteins 4, 6, 7).

MATERIALS AND METHODS: Clinical correlation of the immunohistochemistry derived expression analysis was accomplished with data abstracted from medical records, including age at procedure, ethnicity, BMI, reproductive history, and recent hormone treatment. Review of staining was completed by a pathologist who was blinded to the clinical information. Statistical analysis of composite scores was performed using JMP 9.0 (SAS INC, Cary, NC).

RESULTS: BMPR1B and SMAD4 expression was significantly decreased in glandular endometrial tissue of adenomyosis samples compared to controls (BMPR1B mean H-score 83.5 vs 109.9, p = 0.0019; SMAD4 mean H-score 98.7 vs 123.2, p = 0.0022). The mean age of adenomyosis patients was higher than controls (52.6 vs 44.4, p < 0.0001) and fewer reported abnormal bleeding (30.4% vs 47.6%, p = 0.0170). Otherwise there was no difference in ethnicity, BMI, or recent hormone treatment.

CONCLUSIONS: Adenomyosis was associated with decreased canonical BMP pathway expression. Patients with adenomyosis and diminished BMP expression are older and have less dysfunctional bleeding, yet required hysterectomy for other pelvic symptoms. Like endometriosis, adenomyosis is clinically heterogeneous. It is therefore critical to identify individual patient-specific gene dysregulation in order to administer effective therapy.

Supported by: Resident research funding.

P-278 Tuesday, October 18, 2016

UBIQUITIN-PROTEASOME PATHWAY IS INVOLVED IN THE DECREASE OF ESTROGEN RECEPTOR-α BY CLOMIPHENE CITRATE IN HUMAN ENDOMETRIAL CELLS. M. Amita,* H. Saito,* T. Takahashi.1 Division of Reproductive Medicine, National Center for Child Health and Development, Setagaya, Tokyo, Japan; 2Fukushima Medical Center for Children and Women, Fukushima Medical University, Fukushima-City, Fukushima, Japan.

OBJECTIVE: Clomiphene citrate (CC) has been widely used as the first-line treatment for anovulatory infertile women. Although CC restores ovulation in about 80% of anovulatory women, the subsequent pregnancy rate is only about 20–40%. The cause of this low pregnancy rates have been thought to be the anti-estrogenic effects of CC on the uterine endometrium, which have been explained by two mechanisms: competition with estrogen and reduction of the number of estrogen receptors (ERs). We previously showed that CC inhibited estrogen-induced ERα transactivation by inhibiting the recruitment of steroid receptor coactivator-1 in both human endometrial cancer cell lines and endometrial epithelial cells. However, the mechanism by which CC reduces the number of ERs has not been determined. In this study, we demonstrate that CC induces ubiquitination and subsequent degradation of ERα in a human endometrial cancer cell line.

DESIGN: We examined how CC reduces ERα in a human endometrial cancer cell line.

MATERIALS AND METHODS: We performed the following experiments by using Ishikawa human endometrial cancer cell lines. Experiment 1: We examined the effects of estradiol (E2), CC, and the pure anti-estrogen, ICI182780 (ICI) on the ERα protein and mRNA expression in Ishikawa cells, by western blot and real-time quantitative PCR. Experiment 2: We examined the effects of E2, CC, and ICI on the expression of ubiquitinated ERα, by immunoprecipitation of ERα followed by immunoblotting with an anti-ubiquitin antibody. Experiment 3: We examined whether CC decreases ERα through proteasomal degradation, by co-treatment with MG132, a proteasome inhibitor, and E2, CC, or ICI. Multiple group comparisons were made by one-way ANOVA followed by Scheffe’s F-test. Significant differences were defined as those with P < 0.05.

RESULTS: Experiment 1: The expression levels of ERα protein after treatment with E2, CC, and ICI were significantly decreased within 3 h compared to those before treatment. On the other hand, the expression levels of ERα mRNA were not significantly different compared to vehicle alone. Experiment 2: E2, CC, and ICI significantly increased the levels of ubiquitinated ERα compared to vehicle alone. Experiment 3: Co-treatment with MG132 and ICI decreased the expression of ERα caused by the ligands only.

CONCLUSIONS: These results suggest that CC induces the decrease in ERα protein levels through the ubiquitin-proteasome pathway in Ishikawa endometrial cancer cells.

Reference:

P-279 Tuesday, October 18, 2016

EFFECTS OF SUPRAPHYSIOLOGIC LEVELS OF ESTRADIOL ON ENDOMETRIAL DECIDUALIZATION AND HOXA10 EXPRESSION. H. Cottrill,* J. Spencer,* N. Sidell,* A. Rajakumar,* Emory Reproductive Center, Atlanta, GA; Division of Research, Department of Gynecology and Obstetrics, Emory University School of Medicine, Atlanta, GA.

OBJECTIVE: Supraphysiologic levels of estradiol associated with controlled ovarian hyperstimulation (COH) and in vitro fertilization (IVF) prior to fresh embryo transfers may alter implantation and placentation, and increase the risk for obstetric complications such as pre-eclampsia. We therefore elevated levels of estradiol in vitro alters endometrial decidualization. Prior studies have observed a reduction in HOXA10 expression when endometrial stromal cells (ESCs) are decidualized in culture. We therefore also measured endometrial receptivity by quantifying HOXA10 gene expression.

DESIGN: Controlled laboratory study.

MATERIALS AND METHODS: Primary ESCs were obtained from reproductive age women undergoing gynecologic surgery without evidence of endometrial disease. ESCs were grown and treated according to previously published protocols. For this study, cells were treated with a decidualization cocktail consisting of 100 nM medroxyprogesterone acetate, 0.5 nM dibutyryl cAMP, and three different doses of 17β-estradiol 10 nM, 100 nM, or 1000 nM (E2). The culture medium was collected and replaced on day 4, day 8, with the final medium and cell collection on day 12. ESCs were morphologically evaluated for decidualization. To assess the effects on decidualization markers, prolactin (PRL), insulin-like growth factor binding protein 1 (IGFBP-1), and vascular endothelial growth factor (VEGF) were measured by ELISAs. In addition, RNA was extracted from the cells and HOXA10 expression was analyzed by quantitative reverse transcription-polymerase chain reaction (qRT-PCR).

RESULTS: Decidualization markers PRL, IGFBP-1, and VEGF significantly increased when ESCs were treated at the three E2 cocktail concentrations. While IGFBP-1 and VEGF levels did not change with increasing E2 concentrations, PRL decreased with 1000 nM E2 (7.2 ng/ml +/- 2.4 SEM), when compared to 10 nM E2 (17.9 +/- 2.9) and 100 nM E2 (16.7 +/- 5.3) on day 8. A similar trend in decreased PRL levels with 1000 nM E2 was observed at day 12. Morphological examination on day 8 and 12 showed signs of decidualization in all treatment conditions. HOXA10 expression was lower at 10 nM E2 (40%) and 100 nM E2 (60%) as expected, but did not change with 1000 nM E2 compared with untreated control cells on day 12.

CONCLUSIONS: Supraphysiologic levels of estradiol not typically seen in vivo, may reduce in vitro decidualization of endometrial stromal cells. While prolactin levels did increase with 1000 nM E2, it was 2.5 fold lower than the cells in the 10 nM and 100 nM E2 decidualization cultures. Furthermore, reduced HOXA10 expression was not observed in the decidualization
culture with 1000 nM E2. These results suggest that E2 levels following fresh embryo transfers after COH and IVF may alter the endometrial environment at the time of placentation. Further study is needed to elucidate how these markers are related to obstetric risks observed after fresh IVF cycles.

References:

Supported by: Abraham J. & Phyllis Katz Foundation.

P-280 Tuesday, October 18, 2016

MIRNA EXPRESSION IN RECEPTIVE VERSUS POST-RECEPTIVE ENDOMETRIUM IN PATIENTS UNDERGOING IVF. F. P. Rodrigues, a,b T. C. Bonetti, b C. V. de Carvalho, b F. Vigo, b R. Frialet, a F. Villela, c E. Motta, c Clinical, Huntington Medicina Reprodutiva, Sao Paulo, Brazil; Scientific, Huntington Medicina Reprodutiva, Sao Paulo, Brazil; Department of Urology, Human, Sao Paulo Federal University, Sao Paulo, Brazil; Fundacion IVI / INCLIVA, Paterna, Spain; Department of Obstetrics and Gynecology, Fundacion Instituto Valenciano de Infertilidad (FIVI), Instituto Universitario IVI/INCLIVA, Valencia University, School of Medicine, Stanford University, Paterna, Spain; Huntington Medicina Reprodutiva, Sao Paulo, Brazil.

OBJECTIVE: The functional genomic has been widely investigated and endometrial gene expression signature has been recently used to screen the implantation window. Endometrial microRNAs have been identified in recent years, during the mid-secretory phase, and it is speculated to regulate cell proliferation and differentiation, which could affects embryo implantation, but their exact role is not yet understood. The aim of this study was to investigate microRNA (miRNA) differentially expressed in receptive compared to post-receptive endometrium diagnosed by Endometrial Receptivity Array in natural cycles of infertile patients undergoing in vitro fertilization (IVF).

DESIGN: Prospective cohort study including 12 good prognosis infertile women undergoing ERA test during a natural cycles prior to IVF treatment, at Human Reproduction University Center from July 2012 to December 2013.

MATERIALS AND METHODS: Women underwent endometrial biopsy, during the implantation window, at post-ovulatory day +7, in a natural menstrual cycle. The endometrial samples were submitted to RNA purification and were analyzed by miRNA PCR-array (miRscript miRNA PCR Array, Qia-gen) and by customized Endometrial Receptivity Array (ERA) (Igenomix, Spain).

RESULTS: The ERA analysis identified 5 receptive and 7 post receptive endometrium samples. When comparing receptive versus post receptive endometrium, none downregulated miRNA was observed. However, in receptive samples eight miRNAs were found upregulated with fold change higher than 3.0. Among those, two upregulated miRNAs were statistically significant: has-miR-374a-5p (fold: 8.9, p=0.03) and has-miR-17-5p (fold: 8.9, p=0.03). In spite of non-significant, two other miRNA had a high fold change, as has-miR-30a-5p (fold: 9.7, p=0.116) and has-miR-103a-3p (fold: 10.5, p=0.125).

CONCLUSIONS: We identified eight miRNAs differentially overexpressed in receptive endometrium by ERA assay and may be considered new potential biomarkers candidates for endometrial receptivity. Recent studies suggest that miR-374a and members of miR-103 family are miRNAs related to cell proliferation, mainly in cancer, while members of miR-17 and miR-30 families were identified in the uterine cavity, during the implantation window and could be associated with the endometrium receptivity.

Supported by: “Fundação de Amparo à Pesquisa do Estado de São Paulo”, Brazil (FAPESP) Proc. number 2012/16911-0. Fundación Instituto Valenciano de Infertilidad (FIVI), Spain

P-281 Tuesday, October 18, 2016

EXOGENOUS GONADOTROPINS UPREGULATE PRIMARY ENDOMETRIAL STROMAL CELL DECIDUALIZATION IN FRESH IN VITRO FERTILIZATION CYCLES. M. M. Schulte, a C. S. Stephens, b K. Moley, c Ob/Gyn, Washington University in St Louis, St. Louis, MO; OB/GYN, Washington University School of Medicine, St. Louis, MO; OB/GYN, Washington University in St. Louis, St. Louis, MO.

OBJECTIVE: There is much debate in our field surrounding the best mode of embryo transfer in In Vitro Fertilization (IVF) cycles - transferring an embryo in a “fresh” cycle or adopting a “freeze all policy” and transferring embryos in a subsequent frozen embryo transfer cycle (FET). Proponents of FET claim that the endometrium is in a more “natural” state and thus is more likely to be receptive to a blastocyst; however there is a lack of scientific evidence to support this idea. The objective of this study was to compare endometrial stromal cell decidualization in a standard IVF cycle when exposed to exogenous gonadotropins, to a natural cycle in the same patient.

DESIGN: Basic Science in vitro experiment using primary human endometrial stromal cells.

MATERIALS AND METHODS: Women undergoing fresh IVF cycles with planned preimplantation genetic screening and “freeze all policy” were enrolled at time of ultrasound guided follicle aspiration (USFA). An endometrial biopsy was obtained at time of USFA and endometrial stromal cells (ESCs) were isolated. Each sample was split into two, half the cells were plated within twenty four hours and considered to mimic a “fresh” IVF cycle. The other sample was cultured for 14 days in order to “washout” any remaining exogenous hormonal effect, and mimicking a natural cycle. Both samples were again split into a control and decidualized group and the decidualized group was exposed to 1 mM medroxyprogesterone acetate (MPA) and 0.5 mM cAMP for nine days to decidualize in vitro. The mRNA expression levels for prolactin (PRL) a known marker of decidualization, was measured by quantitative RT-PCR. The fold change in gene expression between control and decidualized samples for each patient was calculated for both groups. This way, the patient served as her own control. The relative fold change for each patient from the “natural cycle” to the “fresh” cycle was compared.

RESULTS: Three patients were enrolled in the study. The ESCs in the fresh cycle group after being exposed to exogenous gonadotropins had prolactin fold change increases of 3 fold, 10 fold and 25 fold compared to the other patients following a standard long agonist protocol (10 fold and 2 fold).

Patient Age   Diagnosis           Stimulation Protocol | Number of Oocytes Retrieved | Number of Oocytes Fertilized | Number of Blastocysts | Endometrial Fold Change Increase in Prolactin
30            Recurrent Pregnancy Loss | Long Agonist            | 11 | 9 | 5 | 2 Fold
40            Male Factor            | Long Agonist            | 18 | 9 | 1 | 10 Fold
40            Ovulatory Dysfunction   | Flare                   | 5  | 4 | 1 | 25 Fold

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ACTIVATING TRANSCRIPTION FACTOR 3 (ATF3) FACILITATES DECIDUAL PROLACTIN SECRETION IN HUMAN ENDOMETRIAL STROMAL CELLS BY INCREASING FORKHEAD BOX 01 (FOXO1) EXPRESSION. X. Cheng, C. Huang, Q. Yan, J. Shen, R. Jiang, Z. Dao, L. Ding, X. Zhen, G. Yan, H. Sun. The Affiliated Drum Tower Hospital of Nanjing University Medical School, Nanjing, China.

OBJECTIVE: To explore the specific regulating mechanisms of ATF3 involved in the process of human endometrial decidualization. 

DESIGN: Human endometrial stromal cells (hESCs) were infected with Ad-LacZ or Ad-ATF3 adenovirus, otherwise stimulated with 0.5 mM 8-Br-cAMP and 1 μM hydroxyprogesterone acetate (MPA) after knocking down ATF3 or being transfected with miR-135b, all treated hESCs were applied for 3 days and 6 days. Expression of ATF3 was studied in endometria of successful conceived women with once embryo transplantation (n=31) and repeated implantation failure (RIF) patients (n=29).

MATERIALS AND METHODS: 8-Br-cAMP and MPA were demonstrated to induce hESC decidualization. The expression of ATF3, FOXO1 were analyzed by Western blot and Q-PCR, meanwhile, the expression of miR-135b was detected by Q-PCR. The secretion of decidual prolactin (dPRL) was examined by ELIFA. FOXO1 was identified as the target gene for miR-135b via luciferase reporter assay. Chip-PCR was performed to examine the interaction between ATF3 and miR-135b. Moreover, immunofluorescent assay was applied to inspect hESC’s morphology. The invasion assay of BeWo spheroids to hESCs was performed to measure embryo invasion in vitro.

RESULTS: ATF3 was up-regulated whereas miR-135b was down regulated in a time-dependent manner in hESCs when stimulated with both 8-Br-cAMP and MPA for 24 h. As expected, human early pregnancy decidualization (n=8) demonstrated higher expression of ATF3 (P<0.001) and lower expression of miR-135b (P<0.01) when compared with secretory phase endometria from women with normal menstrual cycle (n=10). MiR-135b directly targeted FOXO1 3’UTR and suppressed its protein expression, subsequently decreased dPRL secretion. ATF3 depressed miR-135b activity by specifically binding to its promoter region, increasing FOXO1 expression, and consequently facilitating dPRL secretion during decidualization (P<0.001). On the contrary, knockdown of ATF3 in hESCs observably reduced dPRL secretion induced by 8-Br-cAMP and MPA (P<0.001). Furthermore, overexpression of ATF3 in hESCs markedly drove hESCs morphologically transformed from fibroblast-like to decidual cell-like and accelerated BeWo spheroid invasion in vitro. Moreover, ATF3 was aberrantly decreased in endometrial samples of RIF patients compared with fertile women (P<0.001). The low dPRL secretion of hESCs isolated from RIF patients’ endometria was recovered by ATF3 to a normal level.

CONCLUSIONS: This study first illustrates that transcription factor ATF3 facilitates decidual prolactin expression in hESCs by increasing FOXO1 expression during decidualization induced by 8-Br-cAMP and MPA in vitro.
MATERIALS AND METHODS: Women with regular menses, proven fertility and exclusion criteria of endometriosis were enrolled at the time of elective tubal ligation. Patients underwent an endometrial biopsy and each sample was cultured for nine days to rid any endogenous hormone effect and then a histological and decidualized group were revealed. The decidualized group were exposed to 1 mM medroxyprogesterone acetate and 0.5 mM cAMP for nine days. The mRNA expression levels of Prolactin (PRL) and Insulin Like Growth Factor Binding Protein 1 (IGFBP1) were measured by quantitative RT-PCR. The fold change in gene expression between control and decidualized samples was calculated. Patients were categorized into obese (BMI ≥ 30) and lean (BMI < 30). A Students t-test was used for statistical analysis and a stratified analysis was performed to control for race. Western blot analysis was then performed measuring accumulation of cytoplasmic LC3-II which determines autophagic flux.

RESULTS: Thirty seven patients were enrolled with twenty three obese patients and fourteen lean patients. The fold change in gene expression of both markers of endometrial decidualization, PRL and IGFBP1, were significantly (p<0.05) lower in obese patients compared to lean. Western blot analysis comparing autophagic flux in obese vs lean race matched patients revealed impaired autophagic flux in obese patients compared to lean.

CONCLUSIONS: By controlling the in vitro hormonal environment and measuring markers of endometrial decidualization we found that ESCs from obese women have lower mRNA expression levels of PRL and IGFBP1, indicating a reduced ability to undergo normal decidualization. Impaired autophagy may be one mechanism responsible for the decrease in decidualization. A novel therapy that targets improving this mechanism such as Niacin could alleviate poor decidualization and ultimately poor pregnancy outcomes in this population.

The NICHD Grant R01 HD 065435. Supported by: ASRM/REI Fellow Research Grant 2015.

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A NEW WAY TO DETERMINE UTERINE RECEPTIVITY BY MOLECULAR PROFILING OF ENDOMETRIAL BIOPSYs. S. V. Dambaeva,1, A. D. Katukurundage,1, L. Wu,2 N. Sung,2 M. D. Salazar Garcia,3, A. Skariah,4 A. Gilman-Sachs,1 J. Kwak-Kim,2 K. Beaman1. 1Dept. Microbiology and Immunology, Clinical Immunology Laboratory, Rosalind Franklin University of Medicine and Science. 2Division of New Jersey Reproductive Medicine, Roseland, NJ, IL; 3Dept. of Obstetrics and Gynecology, Reproductive Medicine Center, Chicago Medical School, Rosalind Franklin University of Medicine and Science, North Chicago, IL.

OBJECTIVE: A unique gene expression pattern in the endometrium is vital for successful implantation and placentation. Aberrant gene expression, both increased and decreased, of uterine derived growth factors contributes to recurrent pregnancy loss (RPL) and infertility (IF). The objective of this study was to determine cellular and secreted factors involved in pathogenesis of RPL and IF by molecular analysis of endometrial biopsy samples.

DESIGN: Patients with unexplained RPL and IF were enrolled in the Reproductive Medicine Center. Endometrial biopsies were collected in mid-luteal phase.

MATERIALS AND METHODS: mRNA was extracted from endometrial samples, converted into cDNA and analyzed by quantitative RT-PCR (qRT-PCR) for factors important for tissue homeostasis (IL-18, IL-15, IL-22, IL-22 receptor (IL-22R), fibroblast growth factor-inducible 14 (Fn14), serum cytokinococlutidinase 1 (SGK1)). The level of NK cells was quantitated by mRNA of CD56, CD57 and CD16b (also expressed by neutrophils). The ratio of CD16b/CD56 was used to determine relationship between CD56bright endometrial NK cells and CD16b positive cytotoxic NK cells and/or neutrophils.

RESULTS: The initial evaluation of the endometrium of RPL (n=11) and IF (n=8) women revealed differential expression of cN14. RPL samples had significantly higher levels of Fn14 mRNA than samples from women with IF (4.4±1.7 and 1.5±0.3 correspondingly). There was a direct correlation between expression of Fn14 and IL-18, IL-15, IL-22R in samples from women with IF. In all specimens, the CD16b/CD56 ratio negatively correlated with CD56 mRNA (r = -0.792, p<0.02). Interestingly, mRNA levels of CD16b paralleled the mRNA levels of CD57 (cytotoxic NK cell marker) in RPL samples but not in IF samples, indicating a measurable neutrophil increase in IF endometrium. High CD16b/CD56 ratio correlated with low values of SGK1 mRNA expression and vice versa (r = -0.677, p<0.01).

CONCLUSIONS: The analysis of endometrial tissue by qRT-PCR can be important for the evaluation of uterine receptivity and for embryo implantation. The initial results show that specimens from women with RPL and IF have different patterns of cellular and growth factor expression.

Support: Clinical Immunology Laboratory at Rosalind Franklin University, North Chicago, IL.

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THE UTILITY OF ENDOMETRIAL AND UTERINE VASCULARITY MEASUREMENT BY TRANSVAGINAL ULTRASONOGRAPHY IN PREDICTING PREGNANCY OUTCOME DURING FROZEN-THAWED EMBRYO TRANSFER CYCLES. K. Lee, J. Joo, S. Kim, S. Lee. Pusan National University Hospital, Busan, Korea, Republic of.

OBJECTIVE: An appropriate endometrial condition and vascular supply are usually known as essential for implantation of embryo. This study was performed to assess the role of endometrial and uterine vascular status measurement in predicting pregnancy outcome during frozen-thawed embryo transfer (FET) cycles.

DESIGN: Total 70 infertile women were recruited with controlled ovarian stimulation (COS) followed by oocytes retrieval. After IVF or ICSI, embryos were cultured to blastocysts and blastocysts with good quality were selected for cryopreservation.

MATERIALS AND METHODS: After endometrial preparation, vitrified blastocysts were thawed and assisted hatching by zona dissection was performed. On the day of embryo transfer (ET), endometrial thickness (EMT), resistance index (RI) and pulsatility index (PI) of sub-endometrial artery (SEA) and uterine artery (UA) were obtained by transvaginal sonography (TVS). All women were divided into pregnant or non groups, and these variables were compared between 2 groups.

RESULTS: Patients’ general demographic characteristics weren’t different statistically between pregnant and nonpregnant groups. The overall implantation rate, clinical pregnancy rate, and ongoing pregnancy rate were 31.1%, 41.4% and 28.6%, respectively. 29 Patients who conceived had average EMT, RI of SEA, PI of SEA, RI of UA, and PI of UA values of 9.15mm, 0.91, 2.42, 0.95, and 3.37, respectively. 41 Patients who didn’t conceive had average EMT, RI of SEA, PI of SEA, RI of UA, and PI of UA values of 9.31mm, 1.01, 2.56, 0.94, and 3.00, respectively. In two groups, all variables were not statistically different (p > 0.05).

CONCLUSIONS: Measurement of endometrial thickness and blood flow index of uterus and endometrium by transvaginal sonography during frozen-thawed embryo transfer (FET) cycle can’t seem to predict the pregnancy outcome. But endometrial receptivity is thought to be still important factor in successful implantation of FET cycle and many studies agree that high degrees of endometrial perfusion shown by Doppler sonogram suggests more receptive endometrium.

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OBJECTIVE: While it is apparent that an endometrial thickness <7 mm is associated with diminished outcomes in assisted reproduction (lower implantation, clinical and ongoing pregnancy rates), we know that pregnancies do occur in patients with thin endometrial linings. There is no data, however, on obstetric outcomes in these patients following IVF treatment. This analysis was performed to determine if endometrial thickness <7 mm is associated with adverse obstetric outcomes compared to patients with a thicker endometrium.

DESIGN: Retrospective cohort

MATERIALS AND METHODS: FETs from 2010-2016 at a single center were included. All transferred embryos were at the blastocyst stage of development. Cycles were divided into 2 groups based on endometrial thickness measured the day before transfer (<7 mm vs. >7 mm). Outcomes including live birth rate (LBR), maternal complications (abruption, bleeding, gestational diabetes, infection, pregnancy induced hypertension, placenta previa, retained products of conception), estimated gestational age (EGA) at delivery, birth weight (grams), and mode of delivery were compared between the 2 groups. Statistical analysis was performed using a χ2 test of proportions or student t-test. Alpha error less than 0.05 was significant.
RESULTS: 392 FETs with an endometrial thickness <7 mm and 8057 FETs with an endometrial thickness ≥7 mm were included. The mean number of embryos transferred was 1.4 blastocysts. 3888 transfers utilized preimplantation genetic screening (46.0%). The only patient demographic measured that was different between the 2 groups was body mass index (BMI) which was 24.7±5.0 kg/m² in patients with a lining <7 mm compared to 25.8±5.8 kg/m² in control patients (p = 0.0006). Adverse obstetric outcomes were compared between groups (table 1).

Table 1: Preterm delivery and low birth weight occur more often in FETs <7 mm.

<table>
<thead>
<tr>
<th>Endometrial thickness</th>
<th>≤ 7 mm</th>
<th>≥ 7 mm</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LBR</td>
<td>35.2%</td>
<td>41.4%</td>
<td>0.0005</td>
</tr>
<tr>
<td>Maternal complications</td>
<td>8.7%</td>
<td>12.1%</td>
<td>0.7184</td>
</tr>
<tr>
<td>EGA</td>
<td>34.7±3.3 weeks</td>
<td>35.5±3.2 weeks</td>
<td>0.006</td>
</tr>
<tr>
<td>Birth weight (grams)</td>
<td>2948±7±708.9</td>
<td>3178.7±1222.6</td>
<td>0.0003</td>
</tr>
<tr>
<td>Low birthweight</td>
<td>24.8%</td>
<td>34.1%</td>
<td>0.0055</td>
</tr>
<tr>
<td>(&lt;2500 gram)</td>
<td>71.2%</td>
<td>79.1%</td>
<td>0.4857</td>
</tr>
</tbody>
</table>

CONCLUSIONS: In frozen embryo transfers, patients with an endometrial thickness <7 mm demonstrate a higher proportion of preterm delivery and low birth weight. In addition to counseling these patients on reduced pregnancy rates, patients should also be counseled on risk of preterm birth.

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HUMAN ENDOMETRIAL RECEPTIVITY-ASSOCIATED miRNAS: BEYOND THE GENES. C. Innocenti,³ D. Haouzi,⁵ B. Drissenecek,³ Y. Antoine,⁷ F. Entezami,² L. Delarcohe,¹ C. Brunet,² S. Havamah,⁷ Unite 1203 IRMB Montpellier, Montpellier, France; U1203 - IRMB - CHRU Montpellier, Montpellier, France; INSERM U1203, Human Early Embryonic Development and Pluripotency, Montpellier, France; U1203-IRMB, Clermont-l'Heraud, France; IVF Laboratory Eylau-UNILABS, Clinique de La Muette-Ramsay GDS, Paris, France; Eylau-Unilabs IVF Laboratory, Neuilly-sur-Seine, France; Endocrinologist, Montpellier, France; ART/PGD Department, Arnaud de Villeneuve Hospital, Montpellier, France.

OBJECTIVE: Beyond the genes, do miRNAs are associated to endometrial receptivity status during the expected implantation windows?

DESIGN: Endometrial biopsies were collected during the implantation windows under hormone replacement therapy (6 to 9 days after progesterone administration). Then RNAs were extracted for mRNA and miRNA purification to perform the Win-Test and the miRNA expression profile, respectively. The Win-test consists of measuring the expression level of 13 transcripts associated to the endometrial receptivity by RT-qPCR. The miRNAs profile was evaluated with the Affymetrix® miRNA 4.1 Array Strips.

MATERIALS AND METHODS: Endometrial biopsies were obtained from 20 patients with repeated implantation failure during IVF/ICSI cycles. The endometrial receptivity status was determined using the Win-test allowing to classify endometrial samples as receptive or non-receptive. Then, miRNA expression profiles between the two groups of patients, receptive (n=15) and non-receptive (n=5), were performed.

RESULTS: Using 3 distinct statistical analyses, we identified five miRNAs differentially expressed between receptive and non-receptive endometrium [miR-1 (x-4.9, FDR<0.0001), miR-2 (x-2.5, FDR<0.0001), miR-3 (x-3.6, FDR<0.0001), miR-4 (x-3.9, FDR<0.0001), miR-5 (x-2.1, FDR<0.0001)]. All of them were down-regulated in receptive endometrium tissues and associated with the over-expression of the 13 specific genes biomarkers of the Win-Test. These 5 miRNAs target 165 over-expressed miRNAs during the implantation windows, including the 13 specific genes biomarkers of the implantation window, that reached to several biological functions that play a crucial role during implantation.

CONCLUSIONS: The identification of miRNAs in endometrial tissues associated to endometrial receptivity opens new perspectives in poor implanted patient.

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CDKN1C (P57): THE DETERMINANT OF HUMAN ENDOMETRIAL STROMAL CELL DECIDUALIZATION. L. Wang, L. Huang, H. Zhang, K. Qian. Tongji Hospital, Tongji Medical College. Huazhong University of Science and Technology, Reproductive Medical Center, Wuhan, China.

OBJECTIVE: Uterine decidualization, characterized by human endometrial stromal cells (hESCs) differentiation into decidual cells with distinct morphological appearances, unique biosynthetic and particular secretory phenotypes, is of great significance to the establishment as well as the maintenance of pregnancy (1, 2). However, the exact cell cycle arrest mode and the exact molecular mechanism underlying hESCs decidualization are still not fully elucidated. We aim to confirm that the cyclin-dependent kinase inhibitors, p57, plays an important role in the decidualization of human hESCs.

DESIGN: Basic experimental study using human samples.

MATERIALS AND METHODS: Human uterine endometrial stromal cells were collected and decidualized by progesterone and cAMP. The cell cycle distribution during hESCs decidualization was analyzed by flow cytometry. Several cell cycle related genes were confirmed up- or down-regulated after decidualization by microarray technique and immunohistochemistry staining. And their roles in hESCs decidualization was analyzed by RNAi, flow cytometry, chemiluminescence assay and transmission electron microscope.

RESULTS: We confirmed a typical cell cycle distribution mode during hESCs decidualization characterized by a cell cycle arrest at G0/G1 phase. By microarray and immunohistochemistry staining, the decreased expression of CyclinD1, CDK2 and the CDC2 as well as the increased expression of p57 and p15 were observed during hESCs decidualization. We found that down-regulation of p57 but not p15 significantly impaired the process of decidualization, manifesting in both cell morphological and secretory alteration of the hESCs as well as an inhibition of cell cycle arrest in G1/G0 phase.

CONCLUSIONS: P57 plays a determinant role in the process of decidualization by promoting terminal withdraw of hESCs from cell cycle.

References:

Supported by: National Natural Science Foundation of China (Grant No. 815171464 and Grant No. 81170583).

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ENDOMETRIAL VASCULARITY AND INCREASING ENDOMETRIAL THICKNESS CAN PREDICT LIVE BIRTH: A RETROSPECTIVE ANALYSIS OF 1575 FET CYCLES. H. Konar,⁵ S. Sharma,⁶ P. Chakraborty,⁷ I. Saha,⁵ R. Chattopadhyay,⁵ S. Ghosh,⁵ B. Chakravarty.⁵ ¹Professor, Obstetrics & Gynecology, Kolkata, India; ²Inferility, Scientist, Kolkata, India; ³Reproductive Medicine, Embryologist, Kolkata, India; ⁴Assisted Reproduction, Consultant, Kolkata, India; ⁵Reproductive Medicine, Director, Kolkata, India.

OBJECTIVE: To evaluate the implication of increasing endometrial thickness and/or evidence of subendometrial blood flow in prediction of live birth in frozen embryo transfer (FET) cycles.

DESIGN: Retrospective analysis.

MATERIALS AND METHODS: 1575 FET cycles excluding donor oocyte recipients and gestational carriers were analysed. The endometrium was prepared using oral estradiol 6-12mg daily, started on day 2 or 3 of cycle ultrasound was done from day 12 onwards to measure endometrial thickness. Once endometrial thickness was ≥ 8 mm, doppler study of endometrial blood flow was conducted. Embryo transfer (ET) was done once endometrial thickness ≥ 8 mm and or presence blood flow in the subendometrial region after 3days of progesterone administration. Patients were stratified into 3 groups (Group A (n=929): have increasing endometrium and subendometrial blood
flow; Group B (n=394): with increasing endometrial thickness only; Group C (n=252): with static endometrium) All frozen embryo transfers were performed at D3 embryo stage. Luteal support of estrogen and progesterone were continued and serum β-hCG was done 14 days after ET. Clinical pregnancy was confirmed by using transvaginal sonography after 4 weeks. Clinical pregnancy and live birth rate were the main outcome measures. Statistical analyses were done by chi-square and comparisons between groups were measured by odds ratio (OR).

RESULTS: The overall pregnancy rate was 33.9%. Pregnancy rate was significantly high (p<0.001) in group A (n= 398) (42.84%) in comparison to group B (n=98) (24.87%) and group C (n=38) (15.07%). Significantly higher live birth rate (OR: 2.218; 95% CI: 1.65-2.87, p=0.001) was observed in Group A (36.06%) in comparison to Group B (20.56%) and Group C (11.11%).

CONCLUSIONS: An increasing endometrium and vascularity of endometrium might cue towards a favorable outcome in FET cycles. Our findings A (36.06%) in comparison to Group B (20.56%) and Group C (11.11%).

MATERIALS AND METHODS: Endometrial biopsies were obtained from 10 patients with repeated implantation failures. The endometrial receptivity status was asserted. Fresh or frozen-thawed embryo transfer has been performed according to the Win-Test result allowing successful pregnancy.

RESULTS: Endometrial biopsies (n=10) were collected during the implantation windows under hormone replacement therapy (6 to 9 days after progesterone administration). Then RNAs were extracted for mRNA and miRNA purification to perform RT-qPCR gene expression and the miRNA expression profile, respectively. The RT-qPCR gene expression consists of measuring the expression level of 13 transcripts associated to the endometrial receptivity by RT-qPCR.

OBJECTIVE: Are there miRNAs in endometrial tissue during the implantation windows predicting miscarriage of the attempt?

RESULTS: ER Map test can predict endometrial receptivity status by qRT-PCR using a new panel of 48 genes. These genes allowed accurate classification of samples into different receptivity status. Using a discriminant model, 100% cases were correctly classified in both groups, fertile and infertile patients. Expression analyses of 192 genes involved in endometrial receptivity and immune response were performed. All patient samples were additionally tested with an independent endometrial receptivity assay (ERA) to verify their endometrial status. Endometrial receptivity of an independent group of 182 patients was then tested using ER Map so that the precise moment and duration of their WOI could be established.

RESULTS: The endometrial volume was significantly higher in the pregnant cycle (2.58 +/- 1.32 and 2.05 +/- 1.08, p<0.007). Also, PI of ESVs was significantly higher in the pregnant cycle (2.32 +/- 0.86, 1.96 +/- 0.62 mL, p=0.007). Also, PI of ESVs was significantly higher in the pregnant cycle (2.58 +/- 1.32 and 2.05 +/- 1.08, p<0.007).

RESULTS: The endometrial volume was significantly higher in the pregnant group (2.32 +/- 0.86, 1.96 +/- 0.62 mL, p=0.007). Also, PI of ESVs was significantly higher in the pregnant cycle (2.32 +/- 0.86, 1.96 +/- 0.62 mL, p=0.007).

RESULTS: The endometrial volume was significantly higher in the pregnant group (2.32 +/- 0.86, 1.96 +/- 0.62 mL, p=0.007). Also, PI of ESVs was significantly higher in the pregnant cycle (2.32 +/- 0.86, 1.96 +/- 0.62 mL, p=0.007).
OBJECTIVE: It is well established that high levels of endogenous estrogen mediate endometrial thickening in patients with increased body fat. However, the relative contribution of BMI on the endometrial response to exogenous estrogen supplementation is less understood. This study seeks to assess whether patients with extremely low BMIs are able to achieve adequate endometrial thickness and optimal clinical outcome in response to exogenous endometrium in synthetic ART cycles.

DESIGN: Retrospective cohort analysis

MATERIALS AND METHODS: All patients undergoing endometrial preparation for euploid embryo transfer (ET) in a synthetic cycle from 2005-2016 were included. Patients with uterine-factor infertility (ie. history of Asherman’s syndrome, submucosal fibroid or uterine septum) were excluded. Patients were stratified by WHO’s BMI categories (≤17, 18-19, 20-21, 22-24, ≥25). Maximal endometrial thickness achieved and numbers of days of estrogen supplementation required before ET were analyzed. Clinical outcomes included implantation, clinical pregnancy rate and the rate of pregnancy loss. Kruskal-Wallis, Pearson correlation, linear and binary logistic regression were used.

RESULTS: A total of 3858 synthetic cycles were evaluated. Baseline demographics and cycle characteristics are shown (Table). Controlling for age, for each unit decrease in BMI there was a 0.06 mm decrease in peak endometrial thickness (r² = 0.41; p = 0.05). The hypoestrogenization: of mice and men. Semin Reprod Med. 2010;28:17-26.

CONCLUSIONS: Patients with extremely low BMI attain lower maximal endometrial thickness compared with normal BMI patients who received a similar duration of exogenous estrogen supplementation. The hypoestrogenized state of very thin patients may lead to a marked reduction in estrogen receptor induction within the endometrium, limiting the effect of exogenous estrogen. However, it is reassuring that this phenomenon was not seen to adversely impact the probability of achieving clinical pregnancy.

Patients stratified by BMI: Demographics/cycle characteristics

<table>
<thead>
<tr>
<th></th>
<th>≤=17</th>
<th>18-19</th>
<th>20-21</th>
<th>22-24</th>
<th>≥=25</th>
<th>P value</th>
</tr>
</thead>
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<tr>
<td>Euploid FET cycles</td>
<td>47</td>
<td>224</td>
<td>326</td>
<td>436</td>
<td>315</td>
<td></td>
</tr>
<tr>
<td>n=1348</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age at stimulation</td>
<td>32.8 ± 3.8</td>
<td>35.0 ± 4.8</td>
<td>35.2 ± 4.0</td>
<td>35.8 ± 4.0</td>
<td>36.2 ± 4.8</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Age at ET</td>
<td>34.6 ± 4.8</td>
<td>36.2 ± 4.5</td>
<td>36.3 ± 4.1</td>
<td>36.7 ± 4.0</td>
<td>37.4 ± 4.6</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Days estrogen supplementation</td>
<td>18.6 ± 4.1</td>
<td>36.2 ± 4.5</td>
<td>36.3 ± 4.1</td>
<td>36.7 ± 4.0</td>
<td>37.4 ± 4.6</td>
<td>NS</td>
</tr>
<tr>
<td>E₂ at surge (pg/ml)</td>
<td>871.5 ± 1122.0</td>
<td>510.8 ± 301.9</td>
<td>515.7 ± 381.1</td>
<td>527.9 ± 397.5</td>
<td>536.0 ± 435.3</td>
<td>NS</td>
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<td>Endometrial thickness (mm)</td>
<td>8.3 ± 6.1</td>
<td>8.6 ± 1.4</td>
<td>8.8 ± 1.5</td>
<td>9.0 ± 1.5</td>
<td>9.4 ± 1.7</td>
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<tr>
<td>(6.4-12.0)</td>
<td>(5.9-12.0)</td>
<td>(6.0-14.0)</td>
<td>(6.0-14.0)</td>
<td>(6.0-16.0)</td>
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<tr>
<td>Correlation with endometrial thickness</td>
<td>r=0.41</td>
<td>r=0.013</td>
<td>r=0.05</td>
<td>r=0.06</td>
<td></td>
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<tr>
<td>Number of blastocysts transferred</td>
<td>P&lt;0.03</td>
<td>P&lt;0.98</td>
<td>P&lt;0.33</td>
<td>P&lt;0.29</td>
<td>P&lt;0.27</td>
<td></td>
</tr>
<tr>
<td>Implantation rate</td>
<td>59.6% (28/47)</td>
<td>58.4%</td>
<td>(131/224)</td>
<td>(193/326)</td>
<td>(264/436)</td>
<td>(173/315)</td>
</tr>
<tr>
<td>Clinical pregnancy rate</td>
<td>53.2%</td>
<td>54.9%</td>
<td>52.7%</td>
<td>56.0%</td>
<td>48.5%</td>
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</tr>
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<td>(25/47)</td>
<td>(123/224)</td>
<td>(172/326)</td>
<td>(244/436)</td>
<td>(153/315)</td>
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<td></td>
</tr>
<tr>
<td>Early pregnancy loss rate</td>
<td>29.8% (14/47)</td>
<td>17.0% (38/224)</td>
<td>17.5%</td>
<td>22.7% (99/436)</td>
<td>22.2% (70/315)</td>
<td>NS</td>
</tr>
</tbody>
</table>

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OBJECTIVE: This assay aims to study the function of FHL1 in embryo adhesion

DESIGN: Endometrial tissue samples were collected from fertile controls (n=14) and patients with recurrent implantation failure (RIF) (n=14). Mice uterus samples of different pregnancy days were obtained. Protein and mRNA were extracted to detect expression levels of FH1L. HEK293T cells, BeWo and Ishikawa cells were used to investigate the molecular mechanism in vitro assay.

MATERIALS AND METHODS: Detection of FHL1 expression in endometrial cell controls, patients with RIF and those in pregnancy stage. Mice uterus was performed through western blotting and real-time PCR assay. Association between FHL1 and HOXA10 was confirmed by co-immunoprecipitation, western blotting and luciferase reporter assays. The effect of FHL1-Hoxa10 interaction on embryo adhesion was evaluated with BeWo spheroid attachment assay.

RESULTS: HomeoboxA10 (HOXA10), a key transcription factor, plays a critical role in embryonic adhesion by regulating the expression of downstream target genes, such as β3-integrin (ITGB3). HOXA10-interacting proteins induce embryo adherent effects, and the identification of new HOXA10-binding partners may provide mechanistic insights into the regulation of gene expression during embryo adhesion. We first demonstrated that FHL1 is a HOXA10-associated protein by co-immunoprecipitation assay. FHL1, a member of HIF protein family, whose mRNA and protein levels were revealed to be up-regulated in the mice uterus on Day 4.5 of pregnancy, the window of mice embryo implantation, and overexpression of FHL1 in the Ishikawa cells increased the BeWo spheroids adhesion by 50% (p<0.05). More importantly, we found that FHL1 mRNA and protein in the endometrium from patients with RIF dramatically decreased compared with fertile controls (p<0.05). Secondly, enhanced FHL1 expression in Ishikawa cells promoted endogenous HOXA10 and its target gene ITGB3 expression. Finally, luciferase assay demonstrated that FHL1 overexpression not only improved ITGB3 expression by 50% (p<0.05), but also promoted HOXA10 mediated ITGB3 expression by 30% (p<0.05), and short interfering RNA (siRNA)-mediated FHL1 protein knockdown reduced HOXA10 and ITGB3 expression dramatically. While the endogenous Hoxa10 was silenced, the promotion of FHL1 on ITGB3 transcription was undetected.

CONCLUSIONS: The association between FHL1 and HOXA10 is involved in the regulation of HOXA10-dependent transcription of endomtrial genes, which contributes to embryo adhesion.

References:

Supported by: National Nature Science Foundation of China (31571189, H.X.S.).

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IDENTIFICATION OF HUMAN ENDOMETRIAL MICRONAS ASSOCIATED WITH REPEATED IMPLANTATION FAILURES. D. Haouzi, L. Drissennek, A. Antoine, F. Entezami, A. Gala, T. Mullet, C. Vincens, H. Hamamah. U1203 - IRMB - CHRU Montpellier, Montpellier, France; U1203-IRMB, Clermont-l’Héroult, France; JVF Laboratory Elylau-UNILABS, Clinique de La Muette, Paris, France; CHU Montpellier, Montpellier, France; CHU ADV, Montpellier, France.

OBJECTIVE: Can we identify microRNAs from endometrial biopsies involved in repeated implantation failures?

CONCLUSION: Endometrial biopsies (n=20) were collected during the implantation windows under hormone replacement therapy (6 to 9 days after progesterone administration). The RNAs were extracted for mRNA and miRNA purification to perform RT-qPCR gene expression and the miRNA expression profile, respectively. The RT-qPCR gene expression consists of measuring the expression level of 13 transcripts associated to the endometrial receptivity (Window Implantation Test; Patent EP10305561.2). The miRNA profile was evaluated with the Affymetrix® miRNA 4.1 Array Strips.

MATERIALS AND METHODS: Endometrial biopsies during the implantation windows were obtained from 20 patients with RIF (≥ 5) during IVF/ICSI cycles. At first, endometrial receptivity status was evaluated by the RT-qPCR gene expression. Then, miRNA expression profiles were evaluated in receptive patients (n=15) with a βhCG− (n=5) or βhCG+ (n=10) after embryo replacement.

RESULTS: Using 3 distinct statistical analyses, we identified six microRNAs differentially expressed in receptive patients, with or without implantation failures. These six microRNAs were all over-expressed in receptive endometrium from patients with a negative βhCG [miR-1 (x2.5, FDR<0.004), miR-2 (x5.9, FDR<0.0001), miR-3 (x5.8, FDR<0.0001), miR-4 (x6.5, FDR<0.0001), miR-5 (x6.1, FDR<0.0001) and miR-6 (x4.7, FDR<0.0001)]. Two of them are members of the let-7 family that have been previously reported to play a crucial role in angiogenesis and maintain of pregnancy. The relevance of these biomarkers is being validated in independent large cohort of patients.

CONCLUSIONS: The identification of endometrial microRNAs associated to implantation failures open new perspectives in RIF patient care management.

Supported by: This work was partially supported by a grant from the Ferrering Pharmaceutical Company.

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POTENTIAL MECHANISM BY WHICH GLUCOSE REGULATES DECIDUALIZATION IN HUMAN ENDOMETRIAL STROMAL CELLS. H. Tamura N. Sugino. Obstetrics & Gynecology, Yamaguchi University Graduate School of Medicine, Ube, Japan.

OBJECTIVE: We recently reported that decidualization stimuli activate the insulin signaling pathway in human endometrial stromal cells (ESCs). Five genes that belong to the insulin signaling pathway: IRS1, IRS2, INSR, MAPK10, and AKT3 increased in human ESCs during decidualization. Those genes are reported to be involved in insulin actions. In fact, glucose uptake was increased by decidualization with the induction of pro-lactin (PRL) and IGFBP-1, specific markers of decidualization. On the other hand, the increase of PRL or IGFBP-1 induced by decidualization stimuli was inhibited by incubating ESCs under the environment of low-glucose concentration. Those results suggest that decidualization stimuli activate the insulin signaling pathway, which in turn contributes to decidualization through the increase of glucose uptake. However, it is unclear how glucose is involved in decidualization in human ESCS. Therefore, the present study was undertaken to investigate the mechanism by which glucose regulates decidualization in human ESCs.

DESIGN: experimental study

MATERIALS AND METHODS: ESCs isolated from the proliferative endometrial tissue were incubated under the environment of low-glucose concentrations (0 and 5 mM) + medroxyprogesterone acetate (10^-8 M) + medroxyprogesterone acetate (10^-6 M) (E+MPA) (14 days culture) or cAMP (0.5 mM) (4 days culture). E+MPA or cAMP was used to induce decidualization, and decidualization was evaluated by mRNA expression of PRL and IGFBP-1.

RESULTS: mRNA levels of PRL and IGFBP-1 were remarkably increased by E+MPA or cAMP, but this increase was significantly inhibited under the low-glucose concentration. To examine the mechanism by which low-glucose inhibits decidualization, we focused on FOXO1, which is a well-known transcription factor that induces decidualization. Knockdown of FOXO1 by siRNA significantly inhibited the increases in PRL and IGFBP-1 induced by decidualization stimuli, indicating that FOXO1 is involved in decidualization of ESCs. FOXO1 expression was increased by decidualization, but this increase was significantly suppressed under the low-glucose concentration. Then, to investigate the regulation of FOXO1 expression by glucose, we examined the status of histone H3K27 acetylation (H3K27ac), which is related with active transcription, of the proximal promoter region of FOXO1 by ChiP assay. The H3K27ac status of the FOXO1 promoter was increased by decidualization under the normal-glucose concentration (24 nM), but this increase was significantly inhibited under the low-glucose concentration, suggesting that glucose increases the H3K27ac status of the FOXO1 promoter.

CONCLUSIONS: The glucose uptake is increased by decidualization stimuli, and the glucose increases FOXO1 expression by making the histone modification status of the promoter active, which in turn contributes to decidualization in human ESCs.

Supported by: Scientific Research from the Ministry of Education, Science, and Culture, Japan.

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KISSPEPTIN REGULATES THE MOTILITY OF HUMAN DECIDUAL ENDOMETRIAL STROMAL CELLS: EFFECT ON EMBRYO IMPLANTATION AND PREGNANCY BEYOND THE BRAIN. H. Wu, H. Huang, H. Wang, Y. Soong. Department of Obstetrics and Gynecology, Chang Gung Memorial Hospital Linkou Medical Center, Taoyuan, Taiwan.

OBJECTIVE: Kisspeptin-signaling system beyond the brain was demonstrated that kisspeptin have the roles in embryo implantation and placentaion at several peripheral sites. Endometrial stromal cells play an important role on decidual programming of human pregnancy. Motile behavior and invasive potential of decidual endometrial stromal cells have been considered of critical importance for embryo implantation and programming of human pregnancy. In the present study, we examined the action of kisspeptin-regulated cell motility of human decidual endometrial stromal cells and the mechanisms of the action, indicating the role of kisspeptin in embryo implantation and pregnancy beyond the brain.

DESIGN: In this in vitro study, we examined the expression, actions and signaling of kisspeptin and kisspeptin receptor in human decidual endometrial stromal cells, indicating the role of kisspeptin in embryo implantation and pregnancy.

MATERIALS AND METHODS: Human decidual endometrial stromal cells were isolated from the decidual tissue after informed consent. Kisspeptin agonist and antagonist were synthetic peptides. Cell motility was estimated by invasion and migration assay. Immunoblot analysis was performed to investigate the expression of kisspeptin receptor, FAK, Src, ERK1/2, MMP-2 and MMP-9. ERK1/2 inhibitor was pretreated for 30 min to evaluate the effects of ERK. MMP-2 inhibitor and MMP-9 inhibitor were pretreated for 30 min to evaluate the effects of MMP-2 and MMP-9 in cell motility. Human Kisspeptin receptor, FAK, and Src siRNA were used to knock down the expression of Kisspeptin receptor, FAK, and Src signaling.

RESULTS: The Kisspeptin receptor was expressed in human decidual endometrial stromal cells. The kisspeptin agonist and antagonist regulated cell motility and the phosphorylation of FAK, Src, and ERK1/2 signaling. Kisspeptin analogues-regulated cell motility was changed in cells pretreated with inhibitors and siRNA. Moreover, inhibition of MMP-2 and MMP-9 with MMPs inhibitor suppressed cell motility in response to kisspeptin. Kisspeptin analogues-mediated cell motility was suppressed by knockdown of endogenous FAK and Src with siRNA.

CONCLUSIONS: Our results demonstrate that kisspeptin and kisspeptin receptor are present in human decidual tissues and stromal cells, indicating the kisspeptin signaling in human decidual tissues and stromal cells beyond the brain. This study demonstrates that kisspeptin analogues-mediated the cell motility of human decidual endometrial stromal cells through the peripheral kisspeptin receptor and the phosphorylation of FAK, Src, and ERK1/2-dependent activation of MMP-2 and MMP-9. Our findings represent a new...
BCL6 AND SIRT1 EXPRESSION IN UNEXPLAINED INFERTILITY VERSUS UNEXPLAINED RECURRENT PREGNANCY LOSS.
C. W. Fox, a S. L. Young, b J. Jeong, c W. A. Palomino, d B. A. Lessey. a OB/GYN, Greenville Health System, Greenville, SC; b Obstetrics & Gynecology, UNC School of Medicine, Chapel Hill, NC; c Obstetrics, Gynecology and Reproductive Biology College of Human Medicine, Michigan State University, Grand Rapids, MI; d Obstetrics & Gynecology, University of Chile, Santiago Chile, Chile; e Obstetrics and Gynecology, Reproductive Endocrinology and Infertility, Greenville, SC.

OBJECTIVE: The purpose of the study is to compare BCL6 and SIRT1 expression in women with unexplained infertility and unexplained recurrent pregnancy loss to determine if these proteins can explain why one group gets pregnant and the other does not.

DESIGN: Retrospective case control

MATERIALS AND METHODS: Human endometrial samples were collected from patients with unexplained infertility, unexplained recurrent pregnancy loss, and fertile controls with laparoscopically proven normal pelvic anatomy. Immunohistochemical staining was performed on these samples to determine the level of nuclear expression of BCL6 and SIRT1. The degree of nuclear expression was assessed using the H-score semiquantitative assessment.

RESULTS: In women with proven endometriosis, SIRT1 and BCL6 were found to co-localize in the secretory phase. In women with unexplained infertility, a positive correlation was noted between BCL6 and SIRT1 expression. In contrast, no correlation was observed between BCL6 and SIRT1 in patients with uRPL. Higher levels of SIRT1 expression were demonstrated in endometrial samples from patients with UI which were not seen in the fertile control population or with women with uRPL.

CONCLUSIONS: BCL6 and SIRT1 nuclear expression appear to be biomarkers of progesterone resistance. We found BCL6 and SIRT1 expression has a positive correlation in patients with UI, but not in women with uRPL. While BCL6 is a marker of inflammation and is expressed in patients with endometriosis, it is up-regulated in uRPL and low in fertile controls without endometriosis. SIRT1 was elevated in UI but not consistently elevated in uRPL and may be a determining factor for progesterone resistance and explain why patients with UI do not implant. These results suggest a role for the BCL6/SIRT1 complex as a potential diagnostic and/or therapeutic target in women with uRPL and may account for the difference in UI versus uRPL.

Supported by: This study was funded in part by NIH R01 HD067721 (to S.L.Y and B.A.L.)

FEMALE REPRODUCTIVE SURGERY

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IMPACT OF THE FOOD AND DRUG ADMINISTRATION (FDA) SAFETY COMMUNICATION ON MORCELLATION ON SURGICAL PRACTICE AND PERIOPERATIVE MORBIDITY FOLLOWING MYOMECTOMY. N. C. Stenz, a L. Cooney, a M. D. Samuel, b D. K. Shah. a Reproductive Endocrinology & Infertility, University of Pennsylvania, Philadelphia, PA; b Biostatistics and Epidemiology, Univ. of Pennsylvania, Perelman School of Medicine, Philadelphia, PA.

OBJECTIVE: To compare incidence, surgical approach, operative time, and perioperative morbidity following myomectomy before and after the FDA safety communication regarding power morcellation

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: After IRB approval, data were abstracted from the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) database on women undergoing myomectomy between April-December 2013 (before FDA communication (pre-FDA), N=1823) and April-December 2014 (after FDA communication (post-FDA), N=690). Time points were selected based upon the increased scrutiny of power morcellation by the lay press and professional societies starting in mid-December 2013. Cases performed between January-March 2014 were excluded as a washout period to allow for changing practices. Myomectomies along with their respective approach and fibroid burden were determined based upon CPT coding. Incidence of myometromies per quarter was modeled using a generalized linear model. Surgical approach, operative time, and perioperative morbidity were compared between those operated on before and after the FDA communication using chi2 and two sample t-tests. Adjusted odds ratios (AOR) with 95% confidence intervals (CI) were calculated using multivariable logistic regression adjusting for age, race, ethnicity, BMI and myoma burden.

RESULTS: Myometromy rates decreased by 63.9% following the FDA communication (p<0.001). The magnitude of this decrease varied by surgical approach and was significantly more pronounced for laparoscopic as compared to abdominal myomectomies (70.9% vs. 56.3%, p<0.001 respectively). Myometromies post-FDA were more likely to be abdominal (57.1%) than laparoscopic (42.9%), as compared to myometromies pre-FDA which were more likely to be laparoscopic (52.8%) than abdominal (47.2%) (p<0.001). There was no change in the relative disease burden of myometromies performed before or after the FDA communication (p=0.28). Models adjusting for myoma burden showed an increased risk of sepsis (AOR 4.11; 95% CI 1.15, 14.61) in myometromies completed post-FDA though absolute rates were <1% in both groups. No significant changes were noted in operative time or other perioperative morbidity

CONCLUSIONS: The FDA safety communication on power morcellation was associated with marked changes in the practice of myomectomy. Significantly fewer myometromies were performed following the FDA communication, particularly using the laparoscopic approach. This substantial change in surgical practice may be associated with a small but significant increase in sepsis but is otherwise not accompanied by significant changes in morbidity. These findings will be expanded with inclusion of 2015 data when available.

P-301 Tuesday, October 18, 2016

LAPAROSCOPIC RESECTION AND REPAIR OF UTERINE ISTHMOCOELE. C. E. Miller, a C. Steller, b A. Cholkeri-Singh, c K. Sasaki. a The Advanced IVF Institute, Naperville, IL; b Advocate Lutheran General Hospital, Park Ridge, IL; c Gynecology, The Advanced Gynecologic Surgery Institute, Naperville, IL; c Advanced Gynecologic Surgery Institute, Naperville, IL.

OBJECTIVE: To present our experience with laparoscopic resection and repair of uterine isthmocoele.

DESIGN: This is an observational study of 21 patients who have undergone a laparoscopic resection and repair of uterine isthmocoele from January 2014 through January 2016.

MATERIALS AND METHODS: Data was collected via retrospective chart review.

RESULTS: Of the twenty-one patients who had a resection and repair of uterine isthmocoele, all but five (23.8%) presented with infertility. Fifty percent of the patients have no residual isthmocoele on post-operative imaging, and 44.4% have only a small nodule that measured ≤6mm. Fifteen patients have attempted pregnancy, of which 12 have achieved pregnancy (80%). Approximately 42% of those conceived spontaneously. Four pregnancies ended in a first trimester miscarriage, six are ongoing, and two delivered, one at term with a repeat cesarean section and the second underwent a 31 week repeat cesarean section due to preterm labor. Patients who initially presented with pain and abnormal uterine bleeding had complete resolution of their symptoms. Two patients initially presented with an ectopic pregnancy

Pregnancy Outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Count</th>
<th>Percentage</th>
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</thead>
<tbody>
<tr>
<td>Achieved pregnancy</td>
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<td>80%</td>
</tr>
<tr>
<td>Ongoing</td>
<td>6</td>
<td>50%</td>
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<tr>
<td>Method of Conception</td>
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</tr>
<tr>
<td>IVF</td>
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<tr>
<td>IU</td>
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<td>83%</td>
</tr>
<tr>
<td>Spontaneous</td>
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<td>41.7%</td>
</tr>
</tbody>
</table>

FERTILITY & STERILITY®
in their isthmuscule that was removed in conjunction with a resection and repair of the isthmuscule. Both had uncomplicated follow up and one went on to achieve successful pregnancy.

CONCLUSIONS: Laparoscopic resection and repair of uterine isthmuscule is a feasible and successful technique resulting in improved symptoms and improved fertility rates.

P-302 Tuesday, October 18, 2016
AIR INFUSED SALINE FOR PREDICTING TUBAL PATENCY WITH FLEXIBLE OFFICE HYSTEROSCOPY IS CORRELATED WITH POST-HYSTEROSCOPY CHANGES IN CUL-DE-SAC FLUID VOLUME. J. Aldred,a D. M. Riche,a W. May,b S. E. Wilson,a J. M. Shwayder,a J. P. Parry,b OB/GYN, University of Mississippi Medical Center, Jackson, MS; Pharmacy Practice, School of Pharmacy, UMMC, Jackson, MS; School of Health Related Professions, UMMC, Jackson, MS; OB/GYN-REI, UMMC, Jackson, MS.

OBJECTIVE: Air infused saline during flexible office hysteroscopy (the Parryoscope technique) has been an accurate predictor of tubal patency when correlated with laparoscopy. However, the association between the rate with which air bubbles traverse the ostia and post-procedural sonographic cul-de-sac (CDS) fluid volume has never been studied, even though this could concurrently affirm office hysteroscopy findings.

DESIGN: Retrospective chart with cross-over components.

MATERIALS AND METHODS: Patients undergoing sonography with flexible office hysteroscopy including hysteroscopic evaluation of tubal patency in a university setting. CDS fluid volume over time (in minutes) was calculated for comparisons. Chi-square test was used for dichotomous data, while a t-test was used for continuous data with a priori of 0.05.

RESULTS: 436 women met inclusion criteria and agreed to participate in the study. 92% of women with hysteroscopic evaluation had no meaningful shift in fluid in the CDS post-procedurally. When increases were observed in spite of hysteroscopic occlusion, these occurred in the context of elevated initial CDS fluid. There was a significantly decreased rate of CDS fluid accumulation in patients with unilateral or bilateral known or suspected tubal disease (-0.13 cm²/min), known risk factors for adhesions (-0.16 cm²/min), and sonographic identification of adhesions through the sliding sign (-0.23 cm²/min) vs. those with no history of hysteroscopic surgery (-0.34 cm²/min; p < 0.0001) and by office hysteroscopy (-0.52 cm²/min; p < 0.0001).

CONCLUSIONS: Though post-hysterectomy CDS fluid volume cannot address the laterality of patency and may be misleading with high initial volumes, post-procedural sonographic assessment has multiple interdependent and complimentary roles that validate hysteroscopic evaluation. Flexible hysteroscopy combined with ultrasound can be used as an effective alternative to hysterosalpingograms and sonosalpingography for office tubal patency assessment.

P-303 Tuesday, October 18, 2016
HYSTEROSCOPIC SURGERY AS A SURROGATE MARKER FOR LOCAL ENDOMETRIAL INJURY IN FRESH IVF CYCLES. A. M. Abdelmageed,a O. S. Abdelmageed,a A. Abbas,a T. A. Farghaly,a M. K. Ali,a A. A. Nasar,a S. A. Shazly,a D. M. Habib,a Obstetrics and Gynecology, Women Health Hospital, Assiut University, Assiut, Egypt; Obstetrics and Gynecology, Mayo Clinic, Rochester, MN.

OBJECTIVE: Biopsy induced local endometrial injury has been shown to improve endometrial receptivity among IVF women. This study tested the hypothesis that hysteroscopic resection of the endometrial lesions represents indirect means of endometrial injury and aimed to compare the effect of uterine flushing by fluid (through SIS or OH) to that of endometrial trauma (induced by hysteroscopic surgery) on IVF outcome.

DESIGN: Prospective cohort study

MATERIALS AND METHODS: Infertile women prior to enrollment in In-Vitro Fertilization (IVF), were categorized into 3 groups based on the interventions utilized to improve their uterine receptivity. Group 1 and 2 comprised women with normal findings on saline infusion sonography (SIS) and office hysteroscopy (OH) respectively. While group 3 included women who underwent hysteroscopic surgery for endometrial lesions within 90 days or less prior to IVF. The outcome measures compared among the groups were endometrial thickness at day of trigger (ET), implantation (IR) and clinical pregnancy rates (CPR). Wilcoxon rank sum test, Chi-square test and logistic regression were used for comparisons.

RESULTS: A total of 378 women were included and categorized into groups 1 (n=189), 2 (n=130), and 3 (n=59). The 3 groups were similar in age, antral follicle count, AMH, number of oocytes retrieved and, number and quality of embryos transferred. However, women in group 3 were more likely to have a higher BMI (mean ± SD) 29.9 ± 6.7 vs. 25.8 ± 4.4, respectively, (p < 0.005). ET ≥ 11 mm was significantly more prevalent among women in group 3 than groups 1 and 2 (56% vs. 37% vs. 43.9%, respectively, p = 0.02). In a multivariate regression analysis, after adjustment to other confounders, ET ≥ 11 mm was a predictor for IVF success (aOR = 1.95; CI = 1.2-2.9, P = 0.003). Furthermore, a conditional logistic regression model revealed that the probability of achieving ET ≥ 11 mm was related to applying hysteroscopic surgery (Wald statistics = 6.8, OR = 1.5, 95% CI = 1.1-1.9, P = 0.009). Nevertheless, the 3 groups have comparable IR and CPR (Groups 1 vs. 2; 3% vs. 21% vs. 26%, respectively, p = 0.05 and 43% vs. 40% vs. 49.1%, respectively, p = 0.05). In a subgroup analysis, in women with ET < 11 mm a comparable trend for CPR was demonstrated among the 3 groups (Groups 1 vs. 2: 2.5% vs. 17.7% vs. 15.3%, respectively, p = 0.05); however, there was a trend toward a negative correlation between the CPR and the higher BMI in group 3 (r = -0.3p = 0.02). But in ET ≥ 11 mm, higher CPR occurred in group 3, compared to groups 1 and 2 (33.8% vs. 18.5% vs. 23%, respectively, p = 0.02).

CONCLUSIONS: Endometrial traumatization during hysteroscopic surgery could be considered a surrogate mean for endometrial injury as reflected by ET. Uterine flushings during SIS or OH has no favorable effect on ET.

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IMPACT OF PRIOR REPRODUCTIVE SURGERY ON HEALTH RELATED QUALITY OF LIFE AMONG IVF WOMEN. A. M. Abdelmageed,a O. S. Abdelmageed,a A. A. Abdelaleem,a T. A. Farghaly,a E. Badran,a S. A. Shazly,a M. K. Ali,a I. Elnashar,a A. Abbas,a Obstetrics and Gynecology, Women Health Hospital, Assiut University, Assiut, Egypt; Obstetrics and Gynecology, Mayo Clinic, Rochester, MN.

OBJECTIVE: Different infertility treatments have been shown to affect the psychological state of the infertile women. This study aimed to examine the effect of prior reproductive surgery on the health related quality of life among infertile women planned for IVF.

DESIGN: Prospective cohort study

MATERIALS AND METHODS: Infertile women scheduled for IVF were counseled to complete RAND SF-36 (HRQOL) questionnaire in their first visit, and prior to enrolling in pre-IVF work up. SF-36 questionnaire is an instrument that comprised 8 subscores and 2 major component scores; physical (PCS) and mental (MCS) component scores. Women were categorized into 3 groups based on their history of prior reproductive surgery. Group 1 comprised women who did not undergo any reproductive surgery before; group 2 included women with history of one reproductive surgery; while group 3 included subjects with history of 2 or more surgeries. The HRQOL scores were compared among the 3 groups. Enrolled women who completed the questionnaire were followed up to their IVF cycle outcome. Comparisons between groups were evaluated using the t-test, Wilcoxon rank sum test, chi-square test and logistic regression as appropriate.

RESULTS: Two hundreds forty women completed the questionnaire. 50% of them had prior failed IVF. There was a significant trend for lower scores among the 8 subscales of SF-36 with increased number of surgeries (p = 0.000). Women in group 3 (n = 57; 23.8%) had significant lower MCS and PCS, compared to groups 2 (n = 124; 51.7%) and 1 (n = 59;24.5%) (45.9±20 vs. 60.5±25 vs. 67.7±25, respectively, p = 0.000; 40 ±20 vs. 63.8±20 vs. 72.9±20, respectively, p = 0.000). In multivariate regression analysis adjusted to the other confounders, compared to groups 1 and 2 (Median (IQR); 26 (7.3) vs. 24(6.3) vs. 24(6), respectively, p = 0.025), ET ≥ 11 mm was significantly more prevalent among women in group 3 than groups 1 and 2 (56% vs. 37% vs. 43.9%, respectively, p = 0.02). In a multivariate regression analysis, after adjustment to other confounders, ET ≥ 11 mm was a predictor for IVF success (aOR = 1.95; CI = 1.2-2.9, P = 0.003). Furthermore, a conditional logistic regression model revealed that the probability of achieving ET ≥ 11 mm was related to applying hysteroscopic surgery (Wald statistics = 6.8, OR = 1.5, 95% CI = 1.1-1.9, P = 0.009). Nevertheless, the 3 groups have comparable IR and CPR (Groups 1 vs. 2; 3% vs. 21% vs. 26%, respectively, p = 0.05 and 43% vs. 40% vs. 49.1%, respectively, p = 0.05). In a subgroup analysis, in women with ET < 11 mm a comparable trend for CPR was demonstrated among the 3 groups (Groups 1 vs. 2: 2.5% vs. 17.7% vs. 15.3%, respectively, p = 0.05); however, there was a trend toward a negative correlation between the CPR and the higher BMI in group 3 (r = -0.3p = 0.02). But in ET ≥ 11 mm, higher CPR occurred in group 3, compared to groups 1 and 2 (33.8% vs. 18.5% vs. 23%, respectively, p = 0.02).

CONCLUSIONS: Endometrial traumatization during hysteroscopic surgery could be considered a surrogate mean for endometrial injury as reflected by ET. Uterine flushings during SIS or OH has no favorable effect on ET.

OBJECTIVE: Optimization of the function and anatomy of reproductive organs either by medications or surgery is the main target of many clinicians prior to IVF in order to get favorable cycle outcomes. Our objective was to evaluate the prevalence of reproductive surgery in women scheduled for IVF, and to correlate the baseline characteristics of these women to the probability of undergoing a reproductive surgery.

DESIGN: Prospective cross-sectional cohort.

MATERIALS AND METHODS: Through one-year cross sectional survey, infertile women scheduled for IVF were categorized into 3 groups based on their history of prior reproductive surgery. Group 1 comprised women who did not undergo any reproductive surgery before; group 2 included women with history of one reproductive surgery; while group 3 included subjects with history of 2 or more surgeries. The 3 groups were compared as regards their baseline demographic and clinical characteristics. Statistical methods used for comparisons included t-test, Chi-square test, Wilcoxon rank sum test and logistic regression.

RESULTS: 244 women accepted to participate in the study; 76% of them (n=185) reported prior reproductive surgery. Women in group 3 (n=59) were more likely to have a longer duration of infertility (Mean±SD: 5.8±3 vs. 5.2±3.2 vs. 4.5±3; p=0.009), and comprised more women with endometriosis (50.8% vs. 21.4% vs. 19%; p=0.000) and tubal block (22% vs. 11.1% vs. 3.4%; p=0.000), when compared to groups 2 and 1 respectively. The total number of surgical procedures in the whole cohort was 238 surgical procedures. Out of them; 29.4%, 18.9%, and 16.4% were procedures for endometriosis, uterine procedures, and diagnostic laparoscopies, respectively. In stepwise multivariate regression analysis, after adjustment of other variables; longer duration of infertility (aOR = 1.2, 95% CI=1.04-1.3, P=0.007), having moderate endometriosis (aOR = 12.1, 95% CI=5.6-26.4, P=0.000), and having tubal disease (aOR = 6.7, 95% CI=2.7-16.6, P=0.000) were significantly associated with likelihood of an IVF woman to have 2 surgical reproductive procedures through her infertility treatment.

CONCLUSIONS: Reproductive surgeries are common among IVF women presenting a sort of financial burden. Women with endometriosis have substantial probability of undergoing a high order reproductive surgery.

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THE EVOLUTION TO ROBOTIC SALPINGOGRAMY FOR MANAGEMENT OF ECTOPIC PREGNANCY. S. A. Singer J. P. Shepherd. Department of Obstetrics, Gynecology, & Reproductive Sciences, UPMC-Magee Womens Hospital, Pittsburgh, PA.

OBJECTIVE: To determine cost-effectiveness (CE) of robotic salpingostomy (RS-ost) in women with ectopic pregnancy in a single remaining tube and desiring future pregnancy compared to laparoscopic salpingostomy (LS-ost), salpingectomy (LS-ect), and methotrexate (MTX).

DESIGN: Cost-effectiveness analysis (CEA).

MATERIALS AND METHODS: We created multiple CEA models accounting for appropriateness of MTX, availability of vitro fertilization (IVF), and impact of 5 age groups on subsequent spontaneous and assisted fertility. Surgical costs were based on Medicare physician fee schedules. Robotic costs were 160.7% of laparoscopy from published gynecologic studies. Successful completion of RS-ost was varied from 50-100% to compare differential success versus LS-ost (baseline success 76%). CE of RS-ost was calculated in cost per subsequent intrauterine pregnancy. Willingness-to-pay (WTP) was based on age-specific IVF success.

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DEVELOPMENT OF A NEW TUBAL RECANALIZATION METHOD USING THE COMBINATION OF HYSTEROSCOPE AND LAPAROSCOPE IN THE TREATMENT OF OBSTRUCTED FALLOPIAN TUBES. A. Tanaka, M. Nagayoshi, I. Tanaka, T. Miki, T. Yamaguchi. Saint Mother Hospital, Kitakyusyu, Japan.

OBJECTIVE: The Falloposcopic tuboplasty (FT) catheter system for the reconstructive surgery was developed to treat the obstruction of the fallopian tubes. Using this treatment the fallopian tubes can be recanalized and many natural pregnancies have been achieved. However, the fact that a visual confirmation that the catheter has been properly inserted in the fallopian tube is not so easy and the short durability of the catheter are the weak points of this method. In order to overcome these problems we developed a new strategy to conduct reconstructive surgery of the tubes using a combination of hysteroscope and laparoscope.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: The equipment used was a laparoscope (VISERAELITE Olympus), a hysteroscope (EHY-110s Pentax) and a T-ERUMO catheter (RF-GY35183). 67 Childless couples with unilateral or bilateral fallopian tubal obstructions without other infertility factors were selected from January 2012 to December 2015. The catheter (0.89mm diameter double lumen Kitazato Co.) was inserted into the opening of fallopian tube and moved it forward slowly under the laparoscopic observation. When the tip of catheter hit the wall of the fallopian tube especially at the bend, it became almost impossible to move forward any further so it was useful to hold the embriated end with forceps laparoscopically and stretch it to make the bend straight for further progression.

RESULTS: From Jan. 2012 to Dec. 2015, 37 cases of both fallopian tubes blockage and 30 cases of obstruction in one of the tubes, making a total of 67 cases, were treated using this method. Four weeks after treatment a fallopian tubes and HSG (hysterosalpingography) was conducted after four times of additional hydrotubations. The recanalization of the fallopian tubes was confirmed in 25 out of 37 cases of bilateral tubal blockage, and in 24 of 30 cases of a single tubal blockage. Up to this date spontaneous pregnancy rates and miscarriage rates obtained were 28.6% (14/49), 21.4% (3/14) and 8 healthy babies have been born, remaining 3 cases are ongoing.

CONCLUSIONS: This method is useful as a treatment for fallopian tubes obstruction and opens the possibility of achieving a natural pregnancy in cases of blockage of both fallopian tubes that until now only have had ART as a treatment method.
RESULTS: CE of RS-ost is summarized in Table 1. When MTX was not an option, RS-ost was cost-effective when successfully completed in >77.6-78.6% for different age/IVF categories. RS-ost was dominant (less expensive, more effective, and therefore preferred) when successfully completed in >75.5-81.0% of different age categories if IVF was available. Compared to LS-ost success of 76%, RS-ost has to be successful 1.6-2.6% more often in order to reach CE, and 2.9-5.0% more often to be dominant. LS-ost was dominant for RS-ost success <76%, but no evidence suggests reduced success with RS-ost compared to LS-ost. LS-ect was never preferred. When MTX was reasonable, it was dominant when RS-ost success was <89.7-89.8% for all age/IVF categories. RS-ost achieved CE only when success was >93.0-99.7%, a potentially unattainable differential success over LS-ost of >17.0-23.2%. LS-ost and LS-ect were never preferred when MTX was an option.

CONCLUSIONS: MTX is the preferred strategy if clinically reasonable. When MTX is not an option, RS-ost is cost-effective with modest differential success over LS-ost. With slightly larger but still modest differential success, it is dominant. Age and IVF availability do not impact our CEA. LS-ect was never preferred, but remains a reasonable choice in real-life scenarios. Given our results, the different CLs were delivered of randomized or observational data, it is reasonable to consider RS-ost in treatment of ectopic pregnancy.

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HYSTEROSCOPIC POLYPECTOMY ON THE DAY OF EGG RETRIEVAL FOLLOWED BY EMBRYO TRANSFER ON DAY 3 OR DAY 5 DOES NOT SEEM TO NEGATIVELY AFFECT IMPLANTATION: A CASE SERIES. J. P. Rouleau, R. Garcia, J. Hernandez, A. Palumbo. Reproductive Endocrinology, Centro de Asistencia a la Reproducción Humana de Canarias, La Laguna, Spain.

OBJECTIVE: To evaluate the effect of hysterectomy performed on the day of egg retrieval on subsequent implantation after embryo transfer during the same cycle.

DESIGN: Case series in a private infertility center.

MATERIALS AND METHODS: Three patients undergoing ovarian stimulation for IVF and one patient undergoing endometrial preparation for oocyte donation had a translavaginal ultrasound suggestive of endometrial polyp around the time of egg retrieval. All patients had a previous diagnosis of endometrial polyp by saline infusion sonohysterography (SIS) within the previous 3 months. Hysteroscopy had been performed by their referring gynecologist. The possible effect of the polyp on implantation was discussed with the patient and the decision was taken to perform hysteroscopy on the day of egg retrieval. Hysteroscopy confirmed the presence of endometrial polyp(s) in all cases. Polypectomy using a polyp grasper though a 3.8 mm hysteroscope (Wolf, Germany) was performed. Postoperatively, patients reported no discomfort and vaginal bleeding was minimal. As expected, translavaginal ultrasound performed immediately post-hysteroscopy showed the presence of intracavitary fluid. On the following day, there was no bleeding and a translavaginal ultrasound revealed a trilaminar endometrium with no intracavitary fluid. Embryo transfer was performed under ultrasound guidance on day 3 (3 IVF patients) or day 5 (one oocyte donation patient).

RESULTS: Case 1. 35 year old woman with premature ovarian failure. Polypectomy was performed on the day of the donor’s egg retrieval. Two blashocysts were transferred 5 days later and a twin gestation resulted. Two healthy babies were delivered by cesarean section at 36 weeks’ gestation without complications.

Case 2. 41 year old patient with poor ovarian reserve. Hysteroscopy was performed at the time of egg retrieval and two polyps were removed. One embryo was transferred on day 3 resulting in a singleton gestation. A healthy baby was delivered vaginally at 40 weeks gestation without complications.

Case 3. 36 year old patient who had polypectomy performed on the day of egg retrieval. Two embryos were transferred on day 3 and the result was a biochemical pregnancy.

Case 4. 40 year old patient who had polypectomy performed on the day of egg retrieval. After transfer of one embryo on day 3, no pregnancy ensued.

CONCLUSIONS: Hysteroscopic polypectomy may be performed around the time of egg retrieval in patients who unexpectedly present with endometrial polyp during stimulation. Gentle endometrial manipulation and polyp removal does not seem to have a negative effect on implantation.

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OBJECTIVE: The objective of this study is to assess the effects of the type of female genital mutilation (FGM) verified by physical examination on the sexual function of Sudanese women living in Jeddah, Saudi Arabia using the Arabic Female Sexual Function Index (ArFSFI).

DESIGN: Cross-sectional study.

MATERIALS AND METHODS: This study was performed between August 2014 and February 2016 at Erfan and Bagedo Hospital, Jeddah, Saudi Arabia after obtaining IRB approval. The inclusion criteria were: 1). age 18 to 55 years; 2). muslim; 3). married; 4). sexually active women; and 5). able to read and speak Arabic. The exclusion criteria were: 1). menopause; 2). pregnancy; 3). and having psychological or chronic medical diseases that may affect the sexual function. All participants signed the written informed consent and were given a self-administered anonymous questionnaire. It included questions on demographics, FGM status (“Sunna”, Pharoni, and others) and the ArFSFI. Complete physical examination including speculum and bimanual vaginal examinations were done by a single senior gynecologist experienced with FGM to document the type of FGM.

RESULTS: A total of 140 Sudanese women were approached to participate in the study. Of these, 113 (81%) women completed the questionnaire. Ten (7%) women refused to participate and 17 (12%) women were excluded because they were post-menopausal. Women with type III were older, more parous and had low level of education. On gynecological examination, 42 (37%) women had had type I, 27 (24%) women had had type II, and 44 (39%) had had type III. There were statistical significant differences in the six domains and the full scale score of the ArFSFI between type I, type II, and type III (Table 1). The full scale scores for type I, type II, and type III were lower than the cutoff point (28.1) for the ArFSFI.

CONCLUSIONS: Sexual dysfunction is associated with type I, type II, and type III FGM.

Table 1: Relation between FSFI score and FGM types

<table>
<thead>
<tr>
<th>Variable</th>
<th>Type I</th>
<th>Type II</th>
<th>Type III</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Desire</td>
<td>3.9 ±0.4</td>
<td>3.3 ±0.5</td>
<td>2.2 ±0.5</td>
<td>0.27</td>
</tr>
<tr>
<td>Arousal</td>
<td>4.1 ±0.4</td>
<td>3.3 ±0.4</td>
<td>1.9 ±0.8</td>
<td>0.041</td>
</tr>
<tr>
<td>Lubrication</td>
<td>4.6 ±0.5</td>
<td>3.8 ±0.6</td>
<td>2.6 ±1.3</td>
<td>0.025</td>
</tr>
<tr>
<td>Orgasm</td>
<td>4.8 ±0.4</td>
<td>3.8 ±0.5</td>
<td>2.7 ±1.4</td>
<td>0.026</td>
</tr>
<tr>
<td>Satisfaction</td>
<td>4.8 ±0.7</td>
<td>3.9 ±1.0</td>
<td>3.3 ±0.8</td>
<td>0.012</td>
</tr>
<tr>
<td>Pain</td>
<td>4.5 ±0.5</td>
<td>3.5 ±0.8</td>
<td>2.1 ±1.2</td>
<td>0.039</td>
</tr>
<tr>
<td>Full scale score</td>
<td>28.6 ±1.9</td>
<td>21.6 ±2.8</td>
<td>14.7 ±5.5</td>
<td>0.010</td>
</tr>
</tbody>
</table>

Supported by: This work was supported by the Deanship of Scientific research (DSR), King Abdulaziz University, Jeddah under grant number (140-873-D1435). The authors, therefore, gratefully acknowledge the DSR technical and financial support.

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HIDDEN ENDOMETRIAL ABNORMALITIES IN WOMEN AGED 35 YEARS OR MORE AND SCHEDULED FOR IVF: HOW THEIR UTERI WILL BEHAVE AFTER RESECTION OF THE ABNORMALITIES? A. M. Abdelmagied, A. Abbas, T. A. Farghaly, A. A. Abdalaleem, E. Badran, M. K. Ali, d. m. habib, O. S. Abdalmageed, I. Elnashar. Obstetrics and Gynecology, Women Health Hospital, Assiut University, Assiut, Egypt.

OBJECTIVE: Evaluation of the endometrial cavity is a critical step prior to IVF. Higher female age has been described before as a risk factor for acquiring cavity lesion (CL) that may impair implantation. Our objective was to evaluate the prevalence of cavity lesions (CLs) among IVF women aged 35 years or more, and the effect of resection of these lesions before IVF on live birth rate (LBR).

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: Infertile women scheduled for IVF with prior normal hysterosalpingography (HSG) were examined by office hysteroscopy (OH) to detect possible CLs. Only women aged 35 or more were considered for enrollment. All CLs diagnosed by OH were treated prior to IVF cycle. OH findings, IVF related data, implantation rate (IR), clinical pregnancy rate (CPR), and live birth rate (LBR) were reported for all women.
OBJECTIVE: To determine the reproductive outcome after hysteroscopic metroplasty in women with deep-septated and T-shaped uterus.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Patients with deep uterine septum (≥3 cm) and T-shaped uterus were included. The study population included 200 women with recurrent miscarriage/previous miscarriage/preterm delivery/previous infertility. The surgeries were performed under general anesthesia with an operative hysteroscope, fitted with a monopolar hook cautery.

RESULTS: A total of 96 patients with deep uterine septum and 78 patients with T-shaped uterus were included in the study. The median ages of the patients were 31 years in both groups. The mean follow-up periods of the patients were 2 years. The majority of patients were nulliparous (75%). Similarly, in the cohort with T-shaped uterus the live birth rate was increased from 6% (6 per 75 pregnancies) to 75.6% (28 per 37 pregnancies) after hysteroscopic metroplasty (P < 0.001).

CONCLUSIONS: Hysteroscopic metroplasty improves the live birth chance significantly in patients with deep uterine septum and T-shaped uterus with a history of primary infertility/recurrent miscarriage/preterm delivery. It seems that the prognosis after metroplasty for T-shaped uterus is as good as metroplasty for deep uterine septum.

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THE REPRODUCTIVE OUTCOME AFTER HYSTEROSCOPIC METROPLASTY IN PATIENTS WITH DEEP UTERINE SEPTUM AND T-SHAPED UTERUS. Y. Şeker,1 Y. Bakır,2 M. M. Seval,1 M. Sonmez,1 B. Berker,1 C. S. Atabekoglu1 1Obstetrics and Gynecology, Ankara University, Ankara, Turkey; 2Obstetrics and Gynecology Assistant, Ankara, Turkey.

OBJECTIVE: To determine the reproductive outcome after hysteroscopic metroplasty in women with deep-septated and T-shaped uterus.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Patients with deep uterine septum (≥3 cm) and T-shaped uterus with a history of primary infertility/recurrent miscarriage/preterm delivery and underwent hysteroscopic metroplasty at a university based infertility clinic between January 2008 and December 2015 were included. The surgeries were performed under general anesthesia with an operative hysteroscope, fitted with a monopolar hook cautery.

RESULTS: A total of 96 patients with deep uterine septum and 78 patients with T-shaped uterus were included in the study. The median ages of the patients were 31 years in both groups. The mean follow-up periods of the patients were 2 years. The majority of patients were nulliparous (75%). Similarly, in the cohort with T-shaped uterus the live birth rate was increased from 6% (6 per 75 pregnancies) to 75.6% (28 per 37 pregnancies) after hysteroscopic metroplasty (P < 0.001).

CONCLUSIONS: Hysteroscopic metroplasty improves the live birth chance significantly in patients with deep uterine septum and T-shaped uterus with a history of primary infertility/recurrent miscarriage/preterm delivery. It seems that the prognosis after metroplasty for T-shaped uterus is as good as metroplasty for deep uterine septum.
consecutive cases were made during IVF of sperm, oocytes, ICSI procedures, zygotes, cleavage stage embryos, and blastocysts at 400x–960x magnification. Images were viewed and scored in on a 55 inch 4k ultraHD monitor providing additional magnification factors. Specialized hardware/software allowed real-time full motion full resolution viewing of videos. High frame rate capture (96 fps) was used to digitally slow the movement of individual sperm. All videos were reviewed by two embryologists.

RESULTS: The system was successfully able to image gametes and embryos at 5k ultra HD. Images viewed at full resolution/high magnification provided enhanced structural clarity and detail. See Table for results by cell type.

<table>
<thead>
<tr>
<th>Structure</th>
<th>Image Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sperm</td>
<td>Motile sperm morphology is comparable to IMSI. High frame rate recording digitally slowed motion increasing morphologic detail and simplifying selection</td>
</tr>
<tr>
<td>Oocyte</td>
<td>Ultrasound analysis superior to standard microscopy including differentiation of zona pellucida, cytoplasm and polar body. No new structures were identified.</td>
</tr>
<tr>
<td>Zygote</td>
<td>Very detailed PN with increased definition of symmetry and nucleoli. Increased definition of polar bodies and small fragments. Increased definition of morphological alterations including cytoplasm intrusions, perivitelline space, zona pellucida, cytoplasmic halo, and vacuoles , and halo.</td>
</tr>
<tr>
<td>Cleavage Embryo</td>
<td>Image resolution superior to standard microscopy with increased visualization of nuclei, multinucleation, the zona as a sphere, vacuoles and granularity of cytoplasm. On compacted morula cell limits are well-defined.</td>
</tr>
<tr>
<td>Blastocyst</td>
<td>Superior visualization and all individual cells of trophoectoderm and ICM are easily delineated. On expanded blastocysts, a novel observation noted was nuclei from all blastomeres were visible.</td>
</tr>
</tbody>
</table>

CONCLUSIONS: It is possible to video image living human gametes and embryos at extreme magnification in ultra high definition “5K” resolution. Cellular structural detail and image quality surpassed that of standard methods and could replace traditional microscopy. Images can be digitally slowed to arrest the motion of living sperm, potentially improving sperm selection at ICSI. For eggs and embryos, resolution and magnification did not identify new morphological features. However, the ability to visualize and quantify individual cells, intracellular structures, and nucleation in blastocysts could be a novel mechanism for embryo assessment. Further validation studies are underway.

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ROLE OF THREE DIMENSIONAL ENDOMETRIAL VOLUME AND THICKNESS IN PREDICTING THE OUTCOME OF IVF CYCLES. N. Singh, A. Yadav, V. Perumal. Department of Obstetrics & Gynaecology, All India Institute Of Medical Sciences, Delhi, India.

OBJECTIVE: To study the role of endometrial thickness and 3D endometrial volume in predicting the endometrial receptivity in fresh non donor IVF cycles.

DESIGN: Prospective observational study.

MATERIALS AND METHODS: A total of 59 patients undergoing non donor oocyte fresh IVF cycles were enrolled in the study; with mean±SD of age (31.2±3.9 years ) and BMI (25.3±3.3 kg m-2). Endometrial thickness and endometrial volume were taken on the day of HCG trigger and on 7th day of embryo transfer by single trained observer using GE E8 3D ultrasound machine with transvaginal scan using voluson software. Outcome measures were implantation rate and pregnancy rate.

RESULTS: The overall pregnancy rate was 13.5% (8/59). Mean±SD of endometrial thickness on the day of trigger among pregnant women (11.0±2.7 mm) and non-pregnant women (9.9±1.9 mm) was not statistically significant (P=0.166). Similarly, the corresponding values on 7th day of embryo transfer (14.6±3.8 and of 12.7±3.8) were also not significant (P=0.197). Mean endometrial volume on the day of trigger among pregnant women (5.2±1.6 ml) was significantly (P=0.037) higher than that of non-pregnant women (4.0±1.5 ml). Similar trend was observed on 7th day of embryo transfer (10.9±6.6 ml vs 7.4±3.5; P=0.029). Logistic regression analysis was carried out to find out significant factors that enhance pregnancy outcome. After adjusting for age and BMI, endometrial volume on trigger day and on 7th day was found to be significant factor for pregnancy rate. Adjusted odds ratio (AOR) on the day of trigger was 2.5 (95% CI: 1.04-6.0). The corresponding value on 7th day of embryo transfer was 1.3 (95% CI: 1.01-1.7). ROC analysis for endometrial volume on trigger day revealed that area under curve (AUC) was 0.743 (P=0.028) and cut-off value of 4.5 was obtained for an optimum sensitivity and specificity of around 75%. AUC for endometrial volume on 7th day of embryo transfer was 0.710 (P=0.058) and for a cut-off value of 8.5, optimum sensitivity and specificity was about 63%.

CONCLUSIONS: Endometrial volume is found to be a significant predictor in determining the endometrial receptivity and the IVF cycle outcome.

References:

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INCREASED ARREST PRIOR TO COMPACTION IN EMBRYOS DERIVED FROM TESTICULAR SPERM. P. K. Gill N. Desai. OB-GYN/Women’s Health Institute, Cleveland Clinic, Beachwood, OH.

OBJECTIVE: Sperm play an essential role in embryonic genome activation and embryonic progression to blastocyst. The purpose of this study was compare morphokinetics of embryonic development in IVF-ICSI cycles in which sperm were retrieved from the epididymis by percutaneous aspiration (PESA) or else through surgical extraction from the testis (TESE).

DESIGN: A retrospective analysis of the effect of epididymal and testicular sperm on early embryonic development.

MATERIALS AND METHODS: Kinetic data and cycle outcomes were retrospectively analyzed for 76 azoospermic patients undergoing an IVF/ICSI cycle with percutaneous epididymal aspiration (PESA) or a testicular sperm extraction (TESE). Normally fertilized zygotes (n=389) were cultured in the EmbryoScope time lapse incubator at 37° C with 6% O2 and 6% CO2. Time lapse videos were viewed and annotated for cell division and cleavage anomalies. The incidence of multinucleation, reverse cleavage and direct uneven cleavage was monitored. Clinical pregnancy rate (CPR), implantation rate (IR) and blastulation rate were also calculated. The chi square and Student t-test were used as appropriate to compare PESA and TESE cycle outcome data and embryo morphokinetics. P values <0.05 were considered significant.

RESULTS: Clinical pregnancy and IR with TESE derived embryos (51% and 31%, respectively) was similar to that with PESA (57% and 37%, respectively). Embryos in the TESE group were however significantly slower in reaching early kinetic endpoints (t2,t4,t8). Table 1 contrasts growth kinetics between the two treatment groups. The main day 3 cell count was lower with TESE (7.69 ± 2.09) vs PESA (8.65 ± 2.73; p=0.03). embryos. Furthermore,
an increased percentage of embryos in the TESE group failed to compact (TESE 31.0%, P < 0.0001) and time to compaction was greater. Despite early differences, tM, tSB and tEBL timings for embryos from both treatments were similar. We did however find that a significantly lower percentage of TESE embryos formed expanded blastocysts (TESE 54% vs PESA 52%; P < 0.001).

CONCLUSIONS: Delayed developmental times were observed in embryos derived from testicular sperm up until the stage of compaction, one of the early indicators of embryonic genomic activation. Compaction is a critical transition point for continued embryo development. It is interesting that embryos from the TESE group arrest at a higher rate prior to this stage but once over the hurdle, have similar kinetics as PESA derived embryos. Prospective studies examining the severity of testicular dysfunction and sperm quality in TESE patients and its relationship to embryo kinetics may help to further elucidate these results.

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INTRACYTOPLASMIC SPERM INJECTION (ICSI) OUTCOME USING IMMOTILE SPERMATOZOA EVEN AFTER PENTOXIFYLLINE ADMINISTRATION IN NON-OBSTRUCTIVE AZOOSPERMIC PATIENTS. S. Mizuta,a K. Yamaguchi,b R. Nishiyama,a Y. Takaya,a K. Iizuya,a H. Matsumabayashi,a T. Ishikawa. Reproductive Clinic Osaka, Osaka, Japan;bIshikawa Hospital, Urology, Himeji, Japan.

OBJECTIVE: To select testicular sperm extraction (TESE)-retrieved viable spermatozoa for ICSI, pentoxifylline administration or hypo-osmotic swelling test (HOST) were often used. However, we have often observed the non-obstructive azoospermia (NOA) patients whose testicular spermatozoa are immotile only even after pentoxifylline administration. To evaluate capability of immotile testicular spermatozoa even after pentoxifylline administration, we assessed embryonic development and clinical outcome for TESE-ICSI.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: We performed microdissection TESE (micro TESE) in 459 cases with NOA patients including after orchidopexy, Klinefelter syndrome, cryptozoospermia, mumps orchitis, azoospermia factor (micro TESE) in 459 cases with NOA patients including after orchidopexy, Klinefelter syndrome, cryptozoospermia, mumps orchitis, azoospermia factor (AZF) microdeletion and unexplained NOA and 204 couples had 342 patients with NOA whose testicular spermatozoa are obstructive azoospermia (NOA) patients whose testicular spermatozoa are immotile only even after pentoxifylline administration. To evaluate capability of immotile testicular spermatozoa even after pentoxifylline administration, we assessed embryonic development and clinical outcome for TESE-ICSI.

CONCLUSIONS: We have had three successful pregnancies and one live birth derived from embryo with immotile sperm injection, although embryonic development and clinical outcomes were very low even after artificial oocyte activation. These result suggests sperm motility is the most important to achieve even in TESE-ICSI.

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ICSI HAS SIGNIFICANTLY INCREASED THE PREGNANCY RATE COMPARED TO THE CONVENTIONAL IVF IN THE PATIENTS WITH HIGH SPERM DNA FRAGMENTATION INDEX. J. Park,a K. Lee,a H. Sun,a H. Chi,a S. Kwak,a S. Kim,a Y. Kim,a J. Kim,a C. Yoo.a Mamapapa&baby OBGY Clinic, Ulsan, Korea, Republic of; bMamapapa&baby OBGY, Ulsan, Korea, Republic of.

OBJECTIVE: Sperm DNA fragmentation has been associated with adverse clinical outcomes such as low fertilization rate, poor embryo development, repeated IVF failure, and recurrent miscarriage. Although a few of studies reported that ICSI showed a beneficial effect on clinical outcomes in the patients with high sperm DFI, the beneficial effect of ICSI is still controversial, and the reason of the beneficial effect has not been clearly identified, yet. The purpose of this study was to assess the beneficial effect of ICSI in the patients with high sperm DNA fragmentation index (DFI).

DESIGN: The study included 458 patients who underwent IVF cycles from January 2015 to November 2015.

MATERIALS AND METHODS: 458 semen samples were divided into two groups according to the sperm DNA fragmentation index (DFI); Low group (DFI ≤ 50%, n = 397), High group (DFI ≥ 51%, n = 61). Conventional semen analysis was performed according to the guidelines of WHO 2010. Halp sperm test was used for sperm DNA integrity determination. Both the Low and High groups were divided into conventional IVF and ICSI subgroups according to the method of fertilization.

RESULTS: There were no differences between the Low and High groups in the characteristics of the patients; mean age of the patients (36.5 ± 3.9 vs. 36.7 ± 3.8) and male (38.2 ± 4.2 vs. 38.5 ± 3.6), mean number of retrieved oocytes (8.7 ± 5.1 vs. 8.7 ± 5.6), endometrial thickness (10.0 ±1.2 vs. 10.3 ±2.1), and mean number of ET (1.9 ± 1.0 vs. 1.9 ± 1.0). No difference was observed between the two groups in the clinical outcomes; fertilization rate (76.9 vs. 80.1%), pregnancy rate (44.3 vs. 49.2%), and abortion rate (11.1 vs. 13.1%). In the Low group, the pregnancy and implantation rates (44.5 and 27.8%) of ICSI group were not different from the rates (42.9 and 26.1%, respectively) of conventional IVF group. However, in the High group, the pregnancy and implantation rates (55.3 and 34.4%) of ICSI group were significantly higher than the rates (28.6 and 16.0%, respectively, P < 0.001) of conventional IVF group.

CONCLUSIONS: ICSI significantly increased the pregnancy rate and implantation rates in the patients with high sperm DFI. The beneficial effect of ICSI may be resulted from the selection of the sperm with rapid motility. Therefore, ICSI will be a practical and efficient strategy to overcome infertility in men with high sperm DFI.

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REPRODUCTIVE OUTCOMES FOLLOWING SURGICAL SPERM RETRIEVAL IN COUPLES WITH OBSTRUCTIVE AZOOSPERMIA (OA), NON-OBSTRUCTIVE AZOOSPERMIA (NOA) AND REPEATED IN VITRO FERTILIZATION (IVF) FAILURE. G. Younes, A. Gilman, S. Tannus, W. Son, P. Chan, W. Buckett. McGill University, Montreal, QC, Canada.
OBJECTIVE: To evaluate reproductive outcomes of IVF cycles with surgically retrieved sperm in couples with OA, NOA and repeated IVF failures.

DESIGN: A retrospective comparative study.

MATERIALS AND METHODS: Charts of all patients who underwent surgical sperm retrieval at the MUHC Reproductive Centre in Montreal, Canada from January 1, 2009 - December 31, 2015 were reviewed retrospectively. 802 cycles were found in the database. All patients had one of the following procedures: testicular sperm extraction (TESE), microTESE, testicular sperm aspiration, percutaneous or microsurgical epididymal sperm aspiration. The patients were divided into 3 groups based on indication for procedure: NOA, OA and repeated IVF failures. 21 cycles did not meet these indications and were excluded. Demographics, treatment characteristics and outcomes were analyzed using the Kruskal-Wallis test.

RESULTS: 781 cycles were included in the analysis: 362 with OA, 226 with NOA and 193 with at least one previously failed IVF cycle, included cases with, oligo-turatoasthenospermia, high DNA fragmentation, or repeated failures with normal spermograms. Mean male age was higher in OA as compared to NOA and the repeated failures' group. (43.1±7.8, 40.7±8.8, 41.9±5.8 respectively, p<0.0001). Mean female age was higher in the repeated failure group (35.9±4.8, 34.8±4.5, 37.1±4.0, p<0.0001). Male FSH level was significantly higher in NOA (p<0.0001). The chance of finding sperm and likelihood of having an embryo transfer were significantly lower in this group (p<0.0001). There were more embryos fertilized in OA 5.79±4.4 compared to NOA 5.2±4.4 and 4.6±4.2 in repeated failures (p=0.003). There was no difference in the number of embryos transferred. Patients with OA were more likely to have a positive pregnancy test (37%, 27%, 28.5% respectively, p=0.02). However there was no difference in the clinical pregnancy rate (31.8%, 23.9%, 25.4% respectively, p=0.07) or in live birth rate (20.4%, 17.7%, 15.5% respectively, p=0.3). There was no statistically significant difference in miscarriage rate between the groups (35.7%, 25.9%, 38.7% respectively, p=0.33).

CONCLUSIONS: Surgical sperm retrieval has revolutionized treatment in men with OA and NOA, however there has been some debate as to whether surgically retrieved sperm is preferable to ejaculate in other populations, such as repeated failures. This study found that the likelihood of finding sperm, the number of fertilized embryos and the likelihood of embryo transfer were significantly lower in NOA. However, the clinical pregnancy rate and live birth rate were not statistically significantly different in all groups. An interesting finding is the higher than average miscarriage rate in the repeated failure group as well as a lower live birth rate, although this is not statistically significant. Age might be a contributor to this. Further study is needed to determine the benefit of surgically retrieved sperm in this group.

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EFFECTS OF SPERM QUALITY ON THE SUCCESS OF INTRACYTOPLASMIC SPERM INJECTION (ICSI) WITH TESTICULAR SPERM VS WITH EJACULATED SPERM. B. Herrero, M. Lusignan, W. Son, W. Bucket, P. Chan, McGill University Health Centre, Montreal, QC, Canada; McGill University, Montreal, QC, Canada.

OBJECTIVE: To evaluate whether sperm quality as determined by routine semen analysis and sperm chromatin integrity affects ICSI outcomes using testicular sperm in couples with recurrent ICSI failure with ejaculated sperm.

DESIGN: Retrospective analysis using electronic medical record from 2010 to 2015 in a university-based reproductive center evaluating ICSI outcomes using testicular sperm (T-ICSI) in a consecutive cohort of couples (n=77) with primary infertility with at least two failed attempts of ICSI. Comparison was made with data from a second cohort of cases: ICSI cycles (E-ICSI) from a separate cohort of consecutive couples (n=68) from the same center and study period with primary infertility with at least two failed attempts of ICSI.

MATERIALS AND METHODS: Population parameters including ages of partners, semen parameters, sperm chromatin structure assay (SCSA) and terminal deoxynucleotide transferase-mediated dUTP nick-end labeling (TUNEL) scores, and numbers of previous failed ICSI cycles were recorded and compared. ICSI outcomes including the number of MII oocytes retrieved, fertilization rate, pregnancy rates per embryo transfer (PR/ET) and live birth rates (LB) were recorded and compared. Two-tailed t-tests for unequal variance (α = 0.05) were used for comparison of means. Proportion data were analyzed with Barnard’s tests (α = 0.05).

RESULTS: The median ages of the male (40.4 vs 40.1) and female partners (36.6 vs 36.8) were similar between T-ICSI and E-ICSI groups. The median sperm concentrations (37.6±10/ml vs 51.3±10/ml) and percentage forward motility (23.5 vs 23.2), but not percentage normal morphology (4.2 vs 4.6) of the T-ICSI and E-ICSI groups differed significantly. The mean number of previous failed ICSI cycles (2.6 vs 2.8), average number of MII oocyte collected per cycle (6.5 vs 6.5) and mean fertilization rates (62.7% vs 63.6%) were similar. Overall, T-ICSI group had a significantly higher PR/ET (27.9% vs 10%) and LB (23.4% vs 5.0%). Further, mean with abnormal semen parameters (LB: 32% vs 7%) or abnormal TUNEL (≥36%) (LB: 21% vs 0%) or SCSA (DFI≥25) scores (LB: 20% vs 9%) had significantly better ICSI outcomes when using testicular sperm for ICSI.

CONCLUSIONS: To our knowledge, this is the first and largest series in the literature evaluating the impact of sperm quality on the efficacy of testicular sperm for ICSI in men with recurrent failure of ICSI with ejaculated sperm. We believe that, rather than comparing to the outcomes of these couples’ own previous failed ICSI cycles, comparison of the T-ICSI outcomes to E-ICSI outcomes of a separate cohort of couples with a similar history of ICSI failure avoided inflation of the efficacy of T-ICSI. Our results indicated that in these couples, particularly those with abnormal ejaculated sperm parameters or chromatin quality as determined by TUNEL and SCSA, the use of testicular sperm yields significantly better ICSI outcomes.


Supported by: This study was supported by an operating to PC by the Canadian Institutes of Health Research (MOP-86636).

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OBJECTIVE: Few studies have used comprehensive chromosomal screening (CCS) to evaluate impaired spermatogenesis contribution to aneuploidy rate and cycle outcome. This study examines male factor infertility in IVF couples to understand if it lowers euploid embryo rates and/or compromises pregnancy outcome.

DESIGN: Retrospective.

MATERIALS AND METHODS: All patients who underwent IVF-CCS and had ≥1 embryo biopsied from July 2002 to April 2016 were included. Couples without male factor infertility were considered controls. To control for aneuploidy incidences associated with advanced age, females >40 were excluded. The rate of euploidy per embryo biopsied was calculated. The effect of male factor on euploidy rate and pregnancy outcome was modeled by logistic and multivariate logistic regression, accounting for male/female age, sperm concentration and morphology (alone and combined). A second analysis grouped couples by male factor type (A: oligozoospermia; B: azoospermia; C: oligozoospermia + azoospermia; D: None) using Chi-square analysis. Further analysis compared Groups A, B, and C (as a combined “male factor” group) with group D (“non-male factor”).

RESULTS: In all couples evaluated (n=550), neither male age nor any combination of male factor parameters was associated with euploidy rate when controlling for female age. In couples who underwent SET with a euploid embryo (n=503), both euploidy rate and sperm concentration (p<0.05) were positively correlated with pregnancy rates, and neither was correlated with early pregnancy loss. No significant differences in euploidy rate or pregnancy outcome were observed among male factor groups A, B, C or D. There was a significantly lower incidence of miscarriage in the male factor than the non-male factor group (p<0.05). No significant differences between the male factor and non-male factor groups were found in euploidy rate or other pregnancy outcomes.

CONCLUSIONS: When controlled for oocyte age, couples with male factor infertility appear to have a similar rate of euploidy per embryo biopsied as compared to couples without male factor. In patients with at least one euploid embryo available for transfer, the rate of pregnancy appears to be correlated
with both ejaculated per biopsy rate and sperm concentration; however, there is no effect on other pregnancy parameters. The rate of miscarriage after IVF-CCS with SET appears to be lower in couples with male factor infertility as compared to those with non-male factor etiologies, however this may be related to the incidence of PCOS and other etiologies of infertility in the non-male factor patients. Overall, the utility of IVF-CCS is a positive driver for cycle success in couples faced with male factor infertility.

References:
2. Coates A et al. Use of suboptimal sperm increases the risk of aneu-

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DETECTING Y-CHROMOSOME MICRODELETIONS USING NEXT GENERATION SEQUENCING (NGS) DATA. R. Shraga,a M. C. Akana,b S. L. Bristow,a A. Manoharan,a O. Puig,a,b Recombine, New York, NY;cLab, Recombine, New York City, NY.

OBJECTIVE: Male factor is at least partly responsible for infertility in approximately 50% of couples. Microdeletions in the Y-chromosome are identified in 5-13% of men with otherwise unexplained infertility.1 However, the incidence of micr
edeletions can be both complicated and expensive, and testing is not routinely performed. Our objective was to develop an assay that allows for detection of Y-chromosome microdeletions via Next Generation Sequencing (NGS).

DESIGN: We designed a sequencing capture system with probes in the Y-chromosome AZFa and AZFb regions, covering the exonic segments of all genes in the two regions. Samples were sequenced using Illumina Next-Seq 500 and reads were mapped to the human genome using standard GATK pipeline.

MATERIALS AND METHODS: We computed average depth per sample interval and ran several normalization procedures to remove variation in depth due to non-biological noise. This protocol corrected for sample variability, batch effects, bias in GC content in the sequences, and other technical biases. After normalization, a copy number estimate per interval was computed by comparing each sample’s normalized depth per interval to the median normalized depth. Deletions were then called by running the Circular Binary Segmentation algorithm on the interval estimates.

RESULTS: DNA samples from the Coriell repository were sequenced at different depths (100-300X). We detected unambiguously Y-chromosome microdeletions in all index cases. Deletions ranged in size from 2.3 to 7.7 Mbp. Data modeling indicates that microdeletions are detected confidently with an average sequencing depth of ~100X, which is routinely used in clinical sequencing as recommended by the American College of Medical Genetics and Genomics guidelines. Further validation of the algorithm with additional clinical samples is ongoing.

CONCLUSIONS: These results demonstrate that NGS is an inexpensive, accurate, and comprehensive method to detect Y-chromosome microdeletions. The advantage of NGS is that multiple mutations and chromosomal abnormalities can be screened in a single assay, enabling simultaneous analysis of various contributions to male infertility. Identifying the genetic basis for male infertility can guide decision-making around treatment, such as surgical intervention, use of ICSI, or use of donor sperm.

Reference:

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EPIGENOME ANALYSIS USING INFINUM 450K BEADCHIP ARRAYS IDENTIFIES ABERRANT DNA METHYLATION IN SPER-
MATOZOA OF MALES WITH UNEXPLAINED INFERTILITY. M. M. Lajunen,a Y. A. Alkhaleed,a S. Tierling,a J. Walter,b M. E. Hammadah,a,b Obstetrics & Gynecology, Saarland University, Germany, Homburg, Germany;cGenetik/Epigenetik, Saarland University, Germany, Saarbruecken, Germany.

OBJECTIVE: To determine whether DNA methylation at CpG dinucleo-
tides is different in sperm DNA of subfertile and fertile male.

DESIGN: Human semen samples were collected during the period be-
tween August 2014 to May 2015 from males who developed idiopathic infertility and underwent intracytoplasmic sperm injection.

MATERIALS AND METHODS: Infinium 450K BeadChip arrays were used to identify genomic regions that show differences in sperm DNA methylation patterns between subfertile and fertile males from couples that have idiopathic infertility and underwent intracytoplasmic sperm injection.

RESULTS: In this study 22 CpG dinucleotides have been found to be significantly and consistently different (between 19.33% and 86.46%; \( \text{fdr-adj.p} < 0.155 \)) in the DNA methylation level in sperm samples of 3 subfertile and 3 fertile males. Only 7 of those (DNA methylation difference between 19.33% and 78.58%) do not overlap common annotated SNPs. 4 CpGs were found to be directly linked to the genes UBE2G2, ALDH3B2, PTGIR, ADAMTS14. 3 CpGs were located in intergenic DNAasi clusters. Currently, these results are under validation through local deep bisulfite sequencing and are planned to be tested on a larger sample cohort.

CONCLUSIONS: The present study identified 7 consistently altered CpG dinucleotides in sperm, which may represent novel candidates related to idio-
pathic infertility. If detectable in a larger sample cohort these CpG sites might serve as a future diagnosing tool for male infertility.

Supported by: Department of Obstetrics & Gynecology, University of Saarland.

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DOES SEVERE TERATOZOOSPERMIA IS CORRELATED WITH EMBRYONIC ANEUPLOIDY RATES?. J. Rodriguez-Purata,a L. Sekhon,a,b J. A. Lee,a M. C. Whitehouse,a R. Sliifkin,a E. Flisser,a M. Duke,a A. B. Copperman,a,b,b N. Bar-Chama,a,b Reproduc-
tive Medicine Associates of New York, New York, NY;cObstetrics, Gynecol-
ogy and Reproductive Science, Icahn School of Medicine at Mount Sinai, New York, NY; dObstetrics and Gynecology, RMANY-Mount Sinai, New York, NY.

OBJECTIVE: Sperm volume, motility, and morphology are generally accepted as predictors of in vivo and in vitro fertilization. Kruger et al. demonstrated that microscopic assessment of morphology plays an integral role in evaluating a male patient. This study aims to determine if extremely low percentages of structurally normal sperm is correlated with increased rates of embryonic aneuploidy in couples who utilize IVF with preimplanta-
tion genetic screening (PGS).

DESIGN: Retrospective.

MATERIALS AND METHODS: Couples who underwent an IVF cycle and PGS from July 2010 to October 2015 were included. Sperm were assessed by Kruger’s strict criteria. Proportion of Kruger morphology was analyzed for male age (A: 10.4%; B: 12.4%; C: 26.0%; D: 21.9%; E: 37.2%; \( \text{p} < 0.05 \)). Fertiliza-
tion rates of embryonic aneuploidy for each female age group and per study group was calculated, with 95% confidence inter-
vals calculated by Clopper-Pearson method. Chi-square was used to test significance, established at \( p<0.05 \).

RESULTS: Couples consisted of females (21.4-70.3 years) who underwent 1105 autologous fresh IVF cy-
cles with PGS. Trophoectoderm biopsy was performed on 7927 embryos, of which 38.8% (n=3077) were found aneuploid. The percentage of male patients with a morphology count \( \leq 1 \) increased with male age (A: 10.4%; B: 12.4%; C: 26.0%; D: 21.9%; E: 37.2%; \( \text{p}<0.05 \)). Fertiliza-
tion rate was similar between group in each female age group. Aneu-
ploidy rate was higher in couples where male Kruger morphology was \( \leq 1 \) in each female age group, although it did not reach statistical sig-
nificance (Table 1).

CONCLUSIONS: Multiple studies have shown semen samples with poor Kruger morphology have similar fertilization and pregnancy rates to normal morphology when IVF/ICSI is utilized. In the present study, morphol
ogy was identified between teratozoospermic specimens and increased incidence of embryonic aneuploidy. Male partners with sperm
defects have shown teratozoospermia can be reassured that they do not have an increased incidence of producing chromosomally abnormal embryos. Further large randomize control trials are needed to confirm these findings.
MESA was conducted. Scrototomy is usually performed under general anesthesia. In the case of lower positive ratio (<30%). This test is based on the principle that viable spermatozoa have intact membranes which shows swelling of the cytoplasmic space and yellowish regions at the head of epididymis through insertion of a glass pipette with a sharp angle. It is easy to collect a large volume of sperm by selecting the available spermatozon.

OBJECTIVE: Kartagener triad syndrome consists of dextrocardia, bronchoectasia and chronic bronchitis. It is often associated with completely immotile sperm with structurally abnormal tails. However, we observed that about half of Kartagener syndrome cases show obstructive azoospermia (10ml of 1% Lidocaine + Anapeine in equal quantities). High quality sperm is retrieved from whitish regions and low quality sperm from yellowish regions at the head of epididymis through insertion of a glass pipette with a sharp angle. It is easy to collect a large volume of sperm from the white regions.

RESULTS: We summarized clinical outcome of Kartagener syndrome in Table.

CONCLUSIONS: Kartagener syndrome is now regarded as one type of primary ciliary dyskinesia (PCD) which is accompanied with ultrastructural or functional defects of cilia (flagellum) and higher probability of conception by selecting the available spermatozoon.

SUCCESSFUL TREATMENTS FOR KARTAGENER SYNDROME WITH COMPLETELY IMMOTILE SPERM OR AZOOSPERMIA. A. Tanaka, M. Nagayoshi, I. Tanaka, T. Miki, T. Yamaguchi. Saint Mother Hospital, Kitakyusyu, Japan.

OBJECTIVE: Kartagener triad syndrome consists of dextrocardia, bronchoectasia and chronic bronchitis. It is often associated with completely immotile sperm with structurally abnormal tails. However, we observed that about half of Kartagener syndrome cases show obstructive azoospermia.

RESULTS: We summarized clinical outcome of Kartagener syndrome in Table. We report successful cases of Kartagener syndrome with completely immotile sperm or obstructive azoospermia.

DESIGN: Retrospective case series.

MATERIALS AND METHODS: Viability of completely immotile sperms was investigated with eosin-negroin test. We conducted HOST to choose the viable spermatozoon when the positive ratio was over 30%. This test is based on the principle that viable spermatozoa have intact membranes which shows swelling of the cytoplasmic space and curling of the sperm tail. The spermatozoon with HOST positive was available for use in ICSI. In the case of lower positive ratio (<30%), MESA was conducted. Scrototomy is usually performed under general (Propofol + Fentanyl citrate) or loco-regional (cord block) anesthesia.
DESIGN: This retrospective cohort study was conducted in a private IVF clinic between August 2011 and December 2015. A total of 550 non-obstructive azoospermic males underwent microdissection testicular sperm extraction (MicroTESE). Over a four-year period the same couples applied for IVF and ICSI was performed using either fresh testicular spermatozoa or frozen-thawed testicular spermatozoa, according to the clinical evaluation of the patients.

MATERIALS AND METHODS: In the stated time-period, 248 and 150 embryo transfers were derived from fresh microTESE and frozen-thawed microTESE samples, respectively. A sperm cryopreservation medium containing TEST-yolk buffer was used for sperm freezing. Embryos were transferred either on day 3, 4 or 5 according to embryo development and the number of embryos to be transferred (one or two). Fourteen and sixteen days after pick-up, serum β-hCG was assessed. On 7th week, clinical pregnancy was defined as foetal heart beat seen by transvaginal ultrasonography.

RESULTS: The first ICSI cycle with fresh testicular spermatozoa resulted in a clinical pregnancy rate (CPR) of 49.2% and an ongoing pregnancy rate (OPR) of 42.3% with a clinical miscarriage rate of (CMR) 13.9%. For the consecutive cycles using frozen-thawed testicular spermatozoa, these rates were; CPR: 47%; OPR: 38.4% and CMR: 18.3%, respectively (p=0.67; p=0.43 and p=0.41, respectively). Differences in outcomes were found in the days of embryo transfer, which obviously reflect the quality of gametes and embryos. OPRs varied from 18.97% to 56.62% in the fresh miTESE group and from 17.31% to 57.38% in the frozen-thawed group.

CONCLUSIONS: No significant differences were found between outcomes using fresh or frozen-thawed microTESE samples. Cryopreserved sperm obtained by microTESE can be used as an effective sperm source in ICSI cycles. These results suggest that cryopreservation of testicular spermatozoa is as suitable as fresh testicular spermatozoa for ICSI and thus can avoid the need for repeated microTESE. Differences in outcomes reside in the quality of embryos, therefore the quality of the extracted sperm is crucial to predict the pregnancy outcome.

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OBJECTIVE: To evaluate if elevated sperm DNA fragmentation is related to embryo euploidy and blastulation rates.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: 56 IVF cycles in couples where the male partner had a TUNEL assay performed on unprocessed semen samples from 1/2011-12/2015 were analyzed for percent blastulation and results of comprehensive chromosomal screening (CCS) by trophectoderm biopsy. Only cycles, in which the partner underwent a prior semen evaluation for DNA fragmentation with the Terminal deoxynucleotidyl transferase-mediated dUTP nick end labeling (TUNEL) assay were included for analysis. Donor egg cycles were excluded. Results were analyzed according to whether TUNEL results were normal or abnormal (≥7%). Data was further stratified according to female age categories. Fisher exact test and Chi-square were used to analyze data and p<0.05 was considered significant.

RESULTS: Mean age of patients in the study cohort was 36.8 ± 5.1 for the female and 43.2 ± 10.2 for the male partner. Ninety-one percent of the embryos were fertilized with ejaculated sperm and the remaining with surgically retrieved sperm. Of 678 embryos evaluated, 305 reached the blastocyst stage and 93% of blastocysts underwent PGS. The mean TUNEL result in the study cohort was 8.9 ± 7.4%. Overall, the rate of euploidy in the PGS group according to age was 64% (age ≤ 37), 32.8% (age 38-40), 16.6% (age 41), and 6.8% (age ≥ 42). There was no correlation between the rate of euploidy and abnormal TUNEL result except for women of age ≤ 37 years, p=0.003. Overall blastulation rates were 64.7% (age ≤ 37), 52.9% (age 38-40), 48.4% (age 41), 30.6% (age ≥ 42), which did not correlate with normal TUNEL for any age group.

CONCLUSIONS: Elevated sperm DNA fragmentation may correlate with decreased euploidy for younger women ≤ 37 undergoing IVF, but does not likely correlate with blastulation rates. The relationship between sperm DNA fragmentation and early IVF outcomes of embryo development and ploidy should be further evaluated in studies powered to detect a difference in outcomes. Sperm DNA fragmentation may affect pregnancy and ongoing pregnancy rates through mechanisms beyond early embryo development.

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OBJECTIVE: To evaluate the influence of female age and ovarian reserve on the outcomes of ICSI cycles with either fresh or frozen-thawed testicular spermatozoa retrieved from non-obstructive azoospermic patients when compared to a large cohort who had undergone ICSI with either fresh or frozen-thawed ejaculated or aspirated sperm.

DESIGN: This retrospective cohort study was conducted in a private IVF clinic between August 2011 and December 2015. A total of 550 non-obstructive azoospermic males underwent microdissection testicular sperm extraction (MicroTESE). Over a four-year period, some of the same couples applied for IVF and ICSI was performed using either testicular spermatozoa or frozen-thawed testicular spermatozoa, according to the clinical evaluation

<table>
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<th>Age</th>
<th>Tunel</th>
<th>Euploid</th>
<th>Aneuploid</th>
<th>p-value</th>
<th>Blastocyst</th>
<th>No Blastocyst</th>
<th>p-value</th>
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<td>≤ 37</td>
<td>% embryos abnormal TUNEL</td>
<td>n=135</td>
<td>n=76</td>
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<td>n=242</td>
<td>n=132</td>
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<td>% embryos normal TUNEL</td>
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<tr>
<td>≥ 41</td>
<td>% embryos abnormal TUNEL</td>
<td>47.1%</td>
<td>52.9%</td>
<td>58.1%</td>
<td>41.9%</td>
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<td>43.9%</td>
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<tr>
<td>% embryos normal TUNEL</td>
<td>27.7%</td>
<td>72.3%</td>
<td>45.9%</td>
<td>43.9%</td>
<td>0.26</td>
<td>n=68</td>
<td>n=117</td>
</tr>
</tbody>
</table>

*statistical significance.
of the patients. In the same period 10086 couples applied for IVF and ICSI was performed with either fresh or frozen-thawed ejaculated or aspirated sperm.

MATERIALS AND METHODS: In the stated time-period, 248 and 150 embryo transfers were derived from fresh microTESE and frozen-thawed microTESE samples, respectively. A total of 8299 embryo transfers derived from either fresh or frozen-thawed ejaculated or aspirated sperm. Embryos were transferred either on day 3, 4 or 5 according to embryo development and the number of embryos to be transferred (one or two). Seventeen and sixteen days after pick-up, serum β-hCG was measured. At 7 weeks, a transvaginal ultrasound was performed to monitor early pregnancy. Clinical pregnancy was defined as a fetal heart beat seen by transvaginal ultrasonography.

RESULTS: No statistically significant differences were found between the microTESE and ejaculated/ aspirated sperm groups regarding the number of retrieved cumulus-oocyte complexes (COCs) for the five distinct categories (1-5; 6-10; 11-15; 16-20; >20). Clinical pregnancy rates (CPR) varied from 36.9 to 58.1% in the microTESE group for the first and last group, whereas CPR were of 34.35 and 47.7, in the same categories (p=0.59 and p=0.26, respectively). On the other hand, female age was causing a decrease of 4.5 to 6.5% in the CPR of the microTESE group when compared to the ejaculated/ aspirated sperm group for all age categories analyzed (<30; 30-34; 35-37; 38-40; 41-42 and 43 >). The trend in the age-dependent decline was significant (p=0.0158 and p<0.0001, respectively). The CPR was calculated as 56.1 and 50.8% in the ejaculated/ aspirated sperm group and microTESE group for <30 years of age, respectively.

CONCLUSIONS: No significant differences were found between the ejaculated/ aspirated sperm group and microTESE group regarding CPR in all COC or female age categories. The female age-related decline was significant in both groups and was causing a 4.5 to 6.5% decline in the CPR of the microTESE group. Therefore, microTESE should not be regarded as a factor which aggravates IVF success rates once an embryo transfer could be planned.

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OBJECTIVE: ICSI is indicated in severe oligo-asthenoteratozoospermia (OAT) and azoospernia. There is no evidence of differences in the clinical outcomes and development of children after ICSI with testicular or ejaculated sperm from severe OAT. There is evidence in the literature that OAT has adverse effects on sperm viability, DNA fragmentation and ROS (Reactive Oxygen Species) production. Therefore, extracted testicular sperm could have less DNA fragmentation than ejaculated sperm. However, it has been shown that ICSI outcomes per transfer are similar between testicular extracted sperm and severe OAT sperm. It has also been demonstrated that certain oocyte cytoplasmic factors in young women are able to repair DNA sperm damage. The aim of this study is to evaluate the ICSI outcomes in a selected population of woman with good reproductive prognosis depending on the semen origin and characteristics.

DESIGN: Retrospective study.

MATERIALS AND METHODS: A total number of 164 selected ICSI cycles performed from January 2009 to December 2015 were evaluated. Thirty cycles were performed using extracted testicular sperm (TS) from azoospermic men, 98 using ejaculated sperm from moderate OAT (MOAT: < 10 million/ml) and 66 with sperm from severe OAT (SOAT: < 1 million/ml). Only the first cycle performed in a selected population of woman less than 36 years old with no identifiable infertility etiology and with 2 selected embryo transfer of day-2 were included. Cycles with donor sperm were excluded. The following clinical factors, including age, number of oocytes retrieved, normal fertilization rate, embryo quality, clinical pregnancy rate (PR), implantation rate (IR), miscarriage rate (MR), twin pregnancy rate (TPR) and live birth rate (LBR) per transfer after ICSI depending on the semen origin were evaluated.

RESULTS: PR, IR, MR, TPR and LBR per transfer, showed no significant differences between groups (PR: MOAT 52%; SOAT 56%; TS 47%; p=0.6863; IR: MOAT 31%; SOAT 35%; TS 35%; p=0.3311; MR: MOAT 16%; SOAT 16%; TS 0%; p=0.2744; TPR: MOAT 12%; SOAT 14%; TS 50%; p=0.3120; LBR: MOAT 34%; SOAT 42%; TS 40%; p=0.5128. The outcomes for pregnancy, implantation rate and live birth rate were similar between the groups. However for testicular sperm cycles, no abortion was obtained and twin pregnancies rate was 50%.

CONCLUSIONS: There is no evidence of differences in the clinical outcomes after ICSI with testicular sperm in azoospermia patients compared to ejaculate sperm from moderate and extreme severe OAT. Oocyte cytoplasm in young woman with no sterility cause could repair sperm DNA damage. Testicular sperm determines low incidence of miscarriage and increase the twin pregnancy risk. In cases of repeated implantation failure with extreme OAT, testicular sperm recovery should be explored.

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ABSTRACT WITHDRAWN
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TOTAL MOTILE COUNT IS MORE PREDICTIVE OF CLINICAL PREGNANCY AT OLDER MATERNAL AGE. E. B. Mankus,1 J. F. Knudson,2 A. E. Holden,3 R. S. Schenken.4 Obstetrics and Gynecology, University of Texas Health Science Center at San Antonio, San Antonio, TX; 2Epidemiology and Biostatistics, University of Texas Health Science Center at San Antonio, San Antonio, TX.

OBJECTIVE: To determine live birth rates in relation to semen analysis parameters on day of intrauterine insemination (IUI).

MATERIALS AND METHODS: Couples undergoing fresh, non-donor IUI at UTHSCSA from 2010-2014 were included. The main outcome was live birth rate (LBR). The secondary outcome was clinical pregnancy rate by maternal age groups. Categorical variables were assessed by chi-square with a p-value <0.05 considered significant. Multivariable logistic regression was used to analyze covariates.

RESULTS: There were 655 cycles in 311 patients. In all cycles, there was no difference in LBR in relationship to TMC (p=0.1). No live births occurred with TMC under 2 million. The duration of infertility or parity did not affect LBR (p=0.44, 0.663). Using 37yo as the age cutoff, ROCs for TMC and live birth (AUC=0.754, yielding 83% sensitivity and 87% specificity) revealed a break point at 10.9 million for LBR (p=0.04) but not for live birth (p=0.07). LBR by maternal age groups were 11.8% (<30yo), 11.7% (30-36.9y) and 3.4% (37y+). ROCs analysis for LBR revealed a morphology cutoff of 20.5% with a 66% sensitivity and 61% specificity (p=0.02).

CONCLUSIONS: TMC above 11 million was more predictive for clinical pregnancy in women above the age of 37yo. The LBR for women over 37y with IUI should not be offered for any age group if pregnancy in women above the age of 37yo. The LBR for women over 37y was 20.5% with a 66% sensitivity and 61% specificity (p=0.02). ROCs analysis for LBR revealed a morphology cutoff of 20.5% with a 66% sensitivity and 61% specificity (p=0.02).

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PATERNALLY DERIVED EMBRYONIC ANEUPLOIDY IS COMMON BUT NOT ASSOCIATED WITH MALE FACTOR INFERTILITY. M. Shah,1 R. Lathi,2 M. Eisenberg.3 “Stanford University, Palo Alto, CA; 2REI, Stanford University, Stanford, CA; 3Urology, Stanford University, Stanford, CA.

OBJECTIVE: To study whether there is a correlation between semen analysis parameters and paternally derived embryonic aneuploidy.

MATERIALS AND METHODS: All patients who underwent pre-implantation genetic screening (PGS) using a SNP array platform were included. Patients underwent in vitro fertilization with PGS between from 2009 to 2015 at a single academic center. PGS information was obtained using Natera’s Spectrum™ PGS platform, which allows for detection of parental source of aneuploidy. All semen parameters were obtained on the day of insemination, with the exception of morphology which was obtained from the most recent semen analysis.

RESULTS: A total of 452 embryos were biopsied, of which 239 (47%) were aneuploid. 8% were paternally derived, 21% were of mixed maternal and paternal origin, and 71% were maternally derived. Among the paternally derived aneuploid embryos, 21% were sex chromosome aneuploides, while the remaining 79% were autosomal chromosome aneuploides. Of the 15 couples with paternally derived aneuploid embryos, 47% underwent PGS/PGD for single gene disorders, 27% for diminished reserve and 20% for male factor infertility, of which 2 men had undergone prior vasectomies and used TESE derived sperm for insemination. ICSI was performed on all cases with paternal aneuploidy. Paternal age and semen parameters did not differ between maternally and paternally derived aneuploid embryos (table 1).

CONCLUSIONS: Paternally derived embryonic aneuploidy is common, accounting for 29% of aneuploidy in our study. Semen parameters do not appear to correlate with paternally derived aneuploidy. Larger studies are needed to determine whether other factors, such as male lifestyle habits, medical history, or prior exposures increase risk of male derived aneuploidy.

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IMPACT OF PATERNAL AGING WITH OR WITHOUT SEMINAL ABNORMALITIES ON OOCYTE DONOR CYCLES OUTCOMES. A. G. Castaneda,1 A. Davila,2 E. A. Amaro,3 C. R. Chapa,1 P. Galache,1 P. Patrizio.4 1IECH Fertility Center, Monterrey, Mexico; 2Reproductive Medicine and Clinical Andrology, Instituto para el Estudio de la Concepccion Humana, Monterrey, Mexico; 3IECH Fertility Center, Cuautltemoc, Mexico; 4IE.C.H Fertility Center, Monterrey, Mexico; 5Obstetrics, Gynecology & Reproductive Sciences, Yale Fertility Center & Fertility Preservati, New Haven, CT.

OBJECTIVE: To assess the influence of paternal age with or without severe male factor on oocyte donation cycles outcomes.

MATERIALS AND METHODS: 427 donor/recipient cycles were analyzed between Jan 2009 and Dec, 2015. Two main groups were formed according to male age: Group 1, males ≤40 yo and Group 2, males ≥40 yo. Another two subgroups were also analyzed according to male age and the presence of severe male factor (defined as a sperm concentration <15 mill/ml and motility <20%) (Group 1A ≤40yo, and Group 2A patients ≥40 yo). Data were expressed as mean ± SD. SPSS software version 20.0 was used for statistical analysis. Comparisons were performed using ANOVA Test, with p<0.05.

RESULTS: Overall the 427 recipients had a mean age of 39.2±5.1 y, basal FSH 22.8±28.1 and estradiol 49.1±58.0. The mean number of oocytes retrieved per cycle was 12.6±6.2, mature and ICISed oocytes were 10.8±6.3. Fertilization rate was 58% and the mean total embryos transferred per cycle were 2.3±0.6. Male age was 34.5±5.4 vs 45.4±4.9 for group 1 (n=275) and 2 (n=152), respectively (p<0.001). Sperm parameters are shown in table 1. For group 1, fertilization rate was 65% (1880/2910), cleavage and blastocyst yield were 78% and 32%, respectively. For Group 2, fertilization rate was 62% (1017/1642), cleavage and blastocyst yield were 80% and 31%, respectively. Pregnancy rate was 50% and clinical/ongoing pregnancy was 38%. These rates were not different. Analysis of the subgroups with severe male

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group 1</th>
<th>Group 2</th>
<th>P Value</th>
<th>Subgroup 1A</th>
<th>Subgroup 2A</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>vol.</td>
<td>3.3±2.8ml</td>
<td>2.9±1.4ml</td>
<td>NS</td>
<td>5±4.1ml</td>
<td>3.4±1.6ml</td>
<td>NS</td>
</tr>
<tr>
<td>Total count.</td>
<td>77.1±50.8mill/ml</td>
<td>72.3±54.5mill/ml</td>
<td>NS</td>
<td>6.7±6.02mill/ml</td>
<td>5±5.7mill/ml</td>
<td>NS</td>
</tr>
<tr>
<td>TMS</td>
<td>44.0±13.0mill</td>
<td>40.7±13.1mill</td>
<td>0.01</td>
<td>20.84±16.5mill</td>
<td>20±16.8mill</td>
<td>NS</td>
</tr>
<tr>
<td>Normal forms</td>
<td>5.2±7.6%</td>
<td>6.3±25.9%</td>
<td>NS</td>
<td>1.1±1.7%</td>
<td>1.2±2.3%</td>
<td>NS</td>
</tr>
</tbody>
</table>

Semen parameters for paternally vs. maternally derived aneuploid embryos

<table>
<thead>
<tr>
<th>Age</th>
<th>Paternally derived</th>
<th>Maternally derived</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>37.3 years</td>
<td>100%</td>
<td>96%</td>
<td>0.57</td>
</tr>
<tr>
<td>Volume</td>
<td>3.2 mL</td>
<td>3.5 mL</td>
<td>0.72</td>
</tr>
<tr>
<td>Concentration</td>
<td>35 mill/mL</td>
<td>49 mill/mL</td>
<td>0.66</td>
</tr>
<tr>
<td>% Motile</td>
<td>54%</td>
<td>53%</td>
<td>0.41</td>
</tr>
<tr>
<td>Morphology</td>
<td>16%</td>
<td>13.7%</td>
<td>0.22</td>
</tr>
</tbody>
</table>
factor (group 1A, males <40 years old) showed a fertilization rate of 56%, cleavage and blastocyst development of 81% and 18%, pregnancy rates of 42% and clinical/ongoing rates 26%. Group 2A (males >40 years old), showed a fertilization rate of 50% not significantly different compared with Group 1A, 81% and 27% for cleavage and blastocyst development with pregnancy and clinical/ongoing pregnancy rates of 47% and 26%, respectively.

CONCLUSIONS: Male aging does not seem to compromise ART outcomes when using oocyte donor cycles. However in the subgroups of severe male factor, blastocyst yield and final outcomes (pregnancy and clinical/ongoing pregnancies) are diminished independently of age.

References:

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SPERM DNA FRAGMENTATION HAS A NEGATIVE CORRELATION WITH PROGRESSIVE MOTILITY AND STRICT MORPHOLOGY. C. Alvarez Sedo, D. Lorenzo, M. Bilinski, H. Uriondo, F. Fulco, G. Alvarez, S. Papier. CEGYR (Reproductive Medicine and Genetics), Buenos Aires, Argentina.

OBJECTIVE: In the last decade, the evaluation of sperm DNA fragmentation has become more important as a method to assess semen quality. Several authors have reported a negative correlation between high DNA fragmentation levels and assisted reproductive technology (ART) outcomes. Considering a population with male factor, we have previously reported that elevated sperm DNA damage is associated with advance male age and oxidative stress (1) (2). The aim of this study, including a non-selected population of infertile men, was to establish which seminal parameter has a greater relationship with DNA fragmentation.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Three hundred and eighty patients who were undergoing ART were selected. Samples were collected by masturbation after sexual abstinence for 2-5 days. After semen liquefaction (30-60 minutes), semen analysis was performed (concentration, progressive motility, vitality, and morphology) and polymorphonuclear neutrophils, and motile sperm were selected by swim-up according to the procedures established by the World Health Organization (2010). Sperm DNA fragmentation was assessed over motile sperm by TUNEL assay. For statistical analysis Pearson’s correlation and ANOVA were performed.

RESULTS: The correlation between TUNEL - sperm concentration was R=0.21, sperm motility R=0.49, strict morphology R=0.41 and PMN R=0.16. All of the correlations were statistically significant (p<0.05). When correlations were compared, sperm motility and morphology were significantly higher than the others, but no different between them.

The results of the comparison between groups (oligo, terato, asthenozoospermia) and normozoospermic patients are depicted in Table 1 (* p<0.05).

CONCLUSIONS: Within an unselected male population who attend an IVF center to assess their seminal quality, it was shown that strict morphology and motility had a higher negative correlation with DNA fragmentation in compared with concentration and PMN. Both groups had higher levels of DNA damage in compared with normozoospermic and oligozoospermic men.

References:

OUTCOMES OF INTRACYTOPLASMIC SPERM INJECTION IN MEN WITH OLIGOASTHENOSPERMIA AND BACTERIOSPERMIA. L. Li, Y. Zhang, S. W. Li. Reproductive Medical Center, West China Second University Hospital, Sichuan University, Chengdu, China.

OBJECTIVE: To determine the impact of bacteriospermia in men with oligoasthenospermia on the outcomes of intracytoplasmic sperm injection (ICSI) and thereby provide more information that will enable patients to make informed choices about ICSI.

DESIGN: Case-control study.

MATERIALS AND METHODS: We recruited 60 couples with male oligoasthenospermia. ICSI outcomes including rates of fertilization, cleavage, good quality embryo, clinical pregnancy and implantation in the study group of 30 men with oligoasthenospermia and bacteriospermia were compared with those in a control group of 30 matched men with oligoasthenospermia but no bacteriospermia (1:1 pair case-control study).

RESULTS: The rate of fertilization (63.49% vs. 79.03%) was significantly lower in the study group than in the control group (P<0.05). There were no significant differences in the rates of cleavage, good quality embryo, clinical pregnancy and implantation in the study group than in the controls (all P>0.05).

CONCLUSIONS: Men with oligoasthenospermia and bacteriospermia had lower fertilization rate in ICSI than men with oligoasthenospermia but no bacteriospermia. While there were no significant differences in potential ability of embryo development and implantation in fertilized eggs. Detailed information should be provided to patients with oligoasthenospermia and bacteriospermia so that they can make informed choices about ICSI.

References:

Table 1

<table>
<thead>
<tr>
<th></th>
<th>Normozoospermia</th>
<th>Oligozoospermia</th>
<th>Asthenozoospermia</th>
<th>Teratozoospermia</th>
<th>PMN</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>131</td>
<td>17</td>
<td>18</td>
<td>56</td>
<td>16</td>
</tr>
<tr>
<td>Age</td>
<td>38.1±6.6</td>
<td>38.1±5.2</td>
<td>41.0±7.6</td>
<td>37.0±6.8</td>
<td>39.4±7.4</td>
</tr>
<tr>
<td>Volume (mL)</td>
<td>3.1±1.3</td>
<td>2.9±1.5</td>
<td>2.5±1.2</td>
<td>2.8±1.2</td>
<td>2.9±1.7</td>
</tr>
<tr>
<td>Concentration (mill/mL)</td>
<td>72.3±34.3</td>
<td>7.3±4.6a</td>
<td>68.9±42.0</td>
<td>64.6±42.9</td>
<td>86.3±62.8</td>
</tr>
<tr>
<td>Progressive motility (%)</td>
<td>55.8±9.5</td>
<td>47.9±11.4</td>
<td>24.3±6.8a</td>
<td>49.3±9.8</td>
<td>50.6±9.8</td>
</tr>
<tr>
<td>Total motility (%)</td>
<td>60.6±9.4</td>
<td>53.5±11.1</td>
<td>30.6±7.1a</td>
<td>54.8±10.4</td>
<td>56.9±9.8</td>
</tr>
<tr>
<td>Vitality (%)</td>
<td>70.1±8.6</td>
<td>57.2±18.4</td>
<td>57.9±11.5</td>
<td>68.1±9.7</td>
<td>63.5±15.7</td>
</tr>
<tr>
<td>PMN (mill/mL)</td>
<td>0.2±0.2</td>
<td>0.1±0.1</td>
<td>0.3±0.3</td>
<td>0.2±0.2</td>
<td>1.5±0.6a</td>
</tr>
<tr>
<td>Swim-up (mill/mL)</td>
<td>18.8±15.7</td>
<td>9.2±11a</td>
<td>5.5±7.7a</td>
<td>9.7±4.8</td>
<td>11.8±8.0</td>
</tr>
<tr>
<td>Strict morphology (%)</td>
<td>9.1±2.3</td>
<td>6.7±1.7</td>
<td>6.6±2.2</td>
<td>2.3±0.8a</td>
<td>7.0±2.8</td>
</tr>
<tr>
<td>DNA fragmentation (%)</td>
<td>9.2±6.1</td>
<td>16.7±8.3</td>
<td>21.8±7.5a</td>
<td>18.9±5.1a</td>
<td>14.4±9.2</td>
</tr>
</tbody>
</table>

P-335 Tuesday, October 18, 2016

**EUPLOID BLASTOCYST TRANSFER IS A VIABLE CLINICAL OPTION FOR MALE FACTOR INFERTILITY WITH HIGH SPERM DNA FRAGMENTATION.** J. M. Stevens, A. Schneiderman, K. Maruniak, B. Findley, W. B. Schoolcraft, M. Katz-Jaffe. Colorado Center for Reproductive Medicine, Lone Tree, CO.

**OBJECTIVE:** A significant association has been reported between sperm DNA fragmentation and sperm chromosome abnormalities. The objective of this study was to evaluate the clinical efficacy of euploid frozen blastocyst transfer for male factor (MF) infertility patients with high sperm DNA fragmentation.

**DESIGN:** Retrospective analysis of IVF cycles with high sperm DNA fragmentation compared to maternal age matched controls.

**MATERIALS AND METHODS:** A consecutive cohort of 49 MF infertility patients with high sperm DNA fragmentation (range 16-35%; mean 23.6±5.8) who underwent an IVF cycle were analyzed in comparison to maternal age matched controls with normal semen analysis (cycling during the same time period 2014-2015). DNA fragmentation was assessed using the In Situ Cell Death Detection Kit with modifications (Roche). Oocytes were fertilized by intracytoplasmic sperm injection and all embryos were routinely cultured to the blastocyst stage and biopsied for comprehensive chromosome screening prior to vitrification. Standard protocols for a hormone replacement frozen embryo transfer were employed. Statistical analysis comparing the groups included Fisher’s exact and Student’s t-test, with significance at P<0.05.

**RESULTS:** MF infertility patients with high sperm DNA fragmentation (n=49; mean maternal age = 35.8±4.0 years) had comparable IVF cycle outcomes to maternal age matched controls with normal semen analysis including: oocytes retrieved (21.2±9.0 vs. 20.6±9.6; ns), zygotes fertilized (12.8±8.0 vs. 11.8±6.9; ns) and good quality blastocysts (6.3±3.8 vs. 6.1±4.9; ns). Higher blastocyst aneuploidy rates were observed for the MF infertility patients with high sperm DNA fragmentation although these were not significantly different (45% vs. 38% controls; ns). A total of 38 euploid frozen blastocyst transfers have been performed with excellent clinical outcomes for high sperm DNA fragmentation MF patients, comparable to controls; clinical pregnancy with fetal heart tone = 84.2%, miscarriage = 6.3% and live birth = 79.0%.

**CONCLUSIONS:** The likelihood of an ongoing viable pregnancy for MF infertility patients with high sperm DNA fragmentation following a euploid blastocyst transfer was considerably high, despite a trend towards an increased blastocyst aneuploidy rate. Additionally, the miscarriage rate for these couples was markedly low despite the hypothesis that high sperm DNA fragmentation is associated with increased risk of pregnancy loss.

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**OBJECTIVE:** To evaluate the percentage of euploid embryo development in patients with obstructive and non-obstructive azoospermia.

**DESIGN:** Retrospective data analysis.

**MATERIALS AND METHODS:** From March 2013 to April 2016, 36 azoospermic men underwent 45 cycles of ICSI-PGS cycles with blastocyst biopsy for comprehensive chromosomal screening using high density oligonucleotide microarray comparative genomic hybridization. 30 cycles used testicular sperm from obstructive azoospermia men with prior vasectomy, 9 cycles were non-obstructive, and 6 cycles were from azoospermic men with unknown causes. The results were compared with 621 In-Vitro Fertilization (IVF) patients that used ejaculated sperm during the same time period. 3,475 blastocysts were generated and underwent trophectoderm biopsy and PGS.

**RESULTS:**

<table>
<thead>
<tr>
<th>Age group</th>
<th># ICSI Cycle</th>
<th># MII eggs ICSI'd</th>
<th>#2PN(Fert rate)</th>
<th>Blastocyst # (rate)</th>
<th>Euploid #(rate)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;37TESE 38</td>
<td>38</td>
<td>446</td>
<td>341 (76.5%)</td>
<td>206 (60.4%)</td>
<td>133/163 (81.6%)</td>
<td>P=0.6</td>
</tr>
<tr>
<td>&lt;37TESE 401</td>
<td>401</td>
<td>4372</td>
<td>3096 (70.8%)</td>
<td>3271/5361 (61.0%)</td>
<td>1911/2491 (76.7%)</td>
<td>P=0.4</td>
</tr>
<tr>
<td>38-42TESE 7</td>
<td>7</td>
<td>54</td>
<td>48 (88.5%)</td>
<td>19 (39.6%)</td>
<td>10/19 (52.5%)</td>
<td></td>
</tr>
<tr>
<td>38-42TESE 220</td>
<td>220</td>
<td>1044</td>
<td>885/1044 (84.8%)</td>
<td>771/1537 (50.2%)</td>
<td>306/802 (38.2%)</td>
<td></td>
</tr>
</tbody>
</table>

**CONCLUSIONS:** Our data demonstrate that testicular sperm from azoospermic patients have comparable fertilization, blastocyst formation and euploid rates compared to cycles using ejaculated sperm. These comparable rates of fertilization, blastocyst formation and rates of euploid embryos with the use of testicular sperm requires further study but may be due in part to female partners with more favorable fertility potential.

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**THE DOWN EXPRESSION OF NPAS2 PREDICTS LOW TESTOSTERONE LEVELS DUE TO DECREASED EXPRESSION OF STAR.** A. S. Herati, C. Cengiz, D. J. Lamb. *Urology, Baylor College of Medicine, Houston, TX.*

**OBJECTIVE:** Male hypogonadism is defined as the inability of the testis to produce testosterone and/or spermatozoa due to a dysfunction of the hypothalamic-pituitary-gonadal axis. Within Leydig cells of the testis, cholesterol is converted in a series of reactions to form testosterone as part of the steroid pathway. This pathway is regulated by several mechanisms, many of which are extra-testicular. It is well established that circadian genes can modulate the reproductive system; however, the exact mechanism by which this occurs is still unknown. Neuronal PAS domain protein 2 (NPAS2) is a circadian rhythm gene that exhibits both central and peripheral expression. We hypothesize that NPAS2 regulates testosterone production via modulation of the steroid acute regulatory protein (Star) protein. The objective of our study, therefore, was to elucidate the expression of NPAS2 in the male reproductive tract and determine its effects on steroidogenesis.

**DESIGN:** Laboratory Research Study.

**MATERIALS AND METHODS:** Testis specific expression NPAS2 was determined using Boun’s fixed sections of testis obtained from 10-week old mice. Immunohistochemistry (IHC) was performed using a commercially available NPAS2 antibody (Santa Cruz Biotechnology, Tx, USA). Additionally, co-immunofluorescence (co-IF) staining with 3-Beta-Hydroxysteroid Dehydrogenase (3B-HSD) was performed on adjacent sections of testis. To characterize the impact of NPAS2 on steroidogenesis, transfection studies were performed using NPAS2 siRNA (GEDharmacon,USA), using lipofectamine (Thermo, USA) on an immortalized mouse Leydig (TM3) cell line (ATCC, Virginia, USA). The expression of Star was quantified using a Taq-Man (Thermo, USA) based qPCR assay. The efficiency of knock-down was analyzed using Western blot analysis, as well as qPCR.

**RESULTS:** Testis NPAS2 expression was visualized in the seminiferous tubules as well as in the interstitial cells of the testis. Co-IF studies revealed that the Leydig cells within the interstitial cells were stained. Using qPCR, a (60%) reduction of Star mRNA levels was observed in siRNA treated TM3 cells compared to controls.

**CONCLUSIONS:** In this study NPAS2 expression was localized within mouse testis seminiferous tubules and Leydig cells. Silencing of NPAS2 gene expression results in decreased testosterone production.

**MALE REPRODUCTION AND UROLOGY - RESEARCH**

P-335 Tuesday, October 18, 2016

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THE EFFECT OF ADHD MEDICATIONS ON SEMEN ANALYSIS IN SUB-FERTILE COUPLES. 

B. Patel,1  E. B. Johnstone,2  A. Presson,1  C. Zhang,1  T. Jenkins, 1, K. I. Aston,1  D. T. Carrell,3  J. M. Hotaling,1  Obstetrics & Gynecology, University of Utah, Salt Lake City, UT;2Epidemiology, University of Utah, Salt Lake City, UT;3Urology, University of Utah, Salt Lake City, UT.

OBJECTIVE: Three million Americans take stimulants to treat Attention Deficit Hyperactivity Disorder but their effects on sperm quality are largely unknown. One study has indicated that they may increase sperm motility.1 We sought to determine if ADHD stimulants improve sperm motility in a population of infertile men.

DESIGN: We performed a retrospective review of semen analyses collected by the University of Utah from 2002 to 2016. We recorded the age of the patient and medication use for a minimum of three months at the time of collection. Patients taking a stimulant were compared to controls taking no medications, and the interaction of stimulants and known spermatotoxic medications was also examined.

MATERIALS AND METHODS: Semen parameter outcomes included ejaculate volume, concentration, total sperm count, total progressive motility, progressive motility and total motile sperm count. Linear mixed effects regression models were used to assess the effect on semen parameters controlling for patient age. Root transformations were used to achieve approximate normality for regression analysis. All results were reported in the millions. Coefficients, 95% confidence intervals (CIs) and p-values were reported. Statistical significance was evaluated at p<0.05 and all tests were two-tailed.

RESULTS: There were 86 samples in the stimulant group, 678 in the spermatotoxic group, and 11165 controls. Use of stimulant was associated with a statistically significant decrease in all parameters except ejaculate volume (p=0.59) and progressive motility (p=0.09). Results were as follows: concentration -1.2 (CI: -2.2 to -0.2, p=0.015), total sperm count -2.4 (CI: -4.1 to -0.6, p=0.008), total progressive motility -2.8 (CI: -4.9 to -0.6, p=0.012), total motile sperm count -1.3 (CI: -2.3 to -0.2, p=0.015). Using a spermatotoxic medication was associated with a decrease in all parameters (p<0.05) except for ejaculate volume (p=0.63). Only total sperm count achieved statistical significance in the spermatotoxic medications and stimulants combined group, where it had a paradoxical increase (5.8, CI: 0.5 to 11.2, p=0.033).

CONCLUSIONS: This study suggests that the use of stimulants adversely affects sperm counts and motility. A possible mechanism of action is decreased body weight. Leydig cell concentration and testosterone production.7 The protective effect from stimulants and spermatotoxic medications may be due to confounding or a previously unknown mechanism requiring further studies. Proper identification and possible temporary cessation of stimulant medications may improve sperm counts. This work demonstrates that the mechanisms for stimulants impacting sperm parameters in a population setting may be distinct from those in the laboratory.

References:
Family 1 | Cystic fibrosis transmembrane conductance regulator (CFTR) | Chr7:117171011 | C>T | P111L | CFTR variants are well known causes of male infertility, but this variant has not been previously reported.

Family 2 | Outer dense fiber of sperm tail gene (ODF3) | Chr11:199381 | G>A | A183T | Functions to add stiffness, elastic recoil and protection against shearing forces during sperm movement.

Family 3 | Testis-expressed 14 gene (TEX14) | Chr17:56700391 | C>A | R85L | In mice, tex14(-/-) spermato genesis arrest before completion of first meiotic division, resulting in absence of mature sperm; it is likely due to evolutionary conservation that the role of the TEX14 gene is the same in humans and is disrupted by this mutation.

Family 4 | Early endosome antigen 1 (EEA1) | Chr12:93172897 | A>C | A>C | A component of a tubulobular complex at the apical junction between Sertoli cells and spermatids.

**DESIGN:** Observational prospective study. Study population included 4 families. Each family had at least 2 infertile siblings diagnosed with NOA and one fertile sibling.

**MATERIALS AND METHODS:** DNA is obtained from blood samples of parents and affected and non-affected family members. DNA is fragmented, exons coding for proteins are captured and sequenced. Sequence data is analyzed for inheritance of genetic variants (recessive or dominant), whether the gene is expressed in tissues and possible effect on protein function.

**RESULTS:** By using exome sequencing to identify rare, severe protein-altering variants segregating with disease, we have found novel mutations in all families that have a high likelihood of being responsible for the phenotype. One of these is a novel mutation in the cystic fibrosis transmembraneceptor (CFTR), a known infertility gene, while the other mutations are in genes that may function in essential spermatogenesis pathways (e.g. Sonic Hedgehog signaling, Notch signaling and ciliary proteins). (Table 1)

**CONCLUSIONS:** We believe our approach of identifying familial cases of this globally sporadic disease may yield better insights into genes responsible for male infertility, and therefore provide new therapeutic targets to increase reproductive success.

**References:**

**P-344** Tuesday, October 18, 2016

**ABSTRACT WITHDRAWN**

**P-345** Tuesday, October 18, 2016

**INFERTILE MEN HAVE A REDOX IMBALANCE THAT DISTINGUISHES THEM FROM FERTILE MEN.**

**OBJECTIVE:** Homologous chromosome pairing (synapsis) and DNA exchange (recombination) during meiosis govern chromosome segregation. Our recent work showed the correlation of a lack of recombination on the sex chromosomes (XY) with increased XY disomy in the sperm of infertile men. Carriers of XY abnormalities may face more segregation errors due to errors in XY pairing, possibly leading to increased levels of aneuploid sperm, which may not be suitable for use in ICSI. This study aims to investigate the meiotic behavior and sperm aneuploidy rates in three infertile men with mosaic or abnormal sex chromosomal karyotypes.

**DESIGN:** We obtained ejaculate sperm from a 47,XY infertile man and testicular tissue from a 45,X(X0)%/46,XY and a 47,XY(10%)/46,XY infertile man. Testicular tissue from ten 46,XY fertile men undergoing vasectomy reversal was used as control.

**MATERIALS AND METHODS:** We used fluorescence immunostaining to visualize the synaptonemal complex and MLH1 proteins in order to assess the chromosome pairing and global recombination, respectively. We also analyzed the meiotic XY patterns. Sperm aneuploidy rates were determined using fluorescence in situ hybridization, Mann-Whitney Test and Fisher Test were used for statistical analysis. The meiotic transcriptional activity of the XY body was also examined using immunostaining in the 45,X/46,XY man.

**RESULTS:** 22% of spermocytes (n=45) in the 47,XXY man were 46,XY, where 50% had unpaired XY. 78% of spermocytes were 47,XXY. In the 45,X/46,XY man, 75% of spermocytes (n=101) were 46,XY, where...
16% had unpaired XY. Only 25% of spermatocytes were 45.X. The unpaired XY in the 45,X/46,XY man had abnormal transcriptional inactivation. On the other hand, all of the spermatocytes in the 47,XX/46,XY man were 46,XY. The mosaic carriers showed normal synapt and recombination rates compared to controls (P<0.05, Mann-Whitney Test). All three carriers showed elevated rates of XY disomy and sex nullisomy in the sperm compared to controls (P < 0.01, Fisher Test).

CONCLUSIONS: We are the first to study meiotic behaviors in depth in a 45,X/46,XY man. We unprecedentedly noted unpaired XY in the 45,X/46,XY and 47,XX/46,XY men, suggesting a new mechanism for arrest of these cells. We found that the meiotic cell composition in carriers of XY abnormalities may be different than the somatic karyotype, potentially due to cell arrest pre-meiosis. The increased rates of sperm aneuploidy in the carriers were within the range found in 46,XY infertile men 1-9. The important clinical relevance of our work is that infertile men with XY abnormalities may produce sperm with primarily normal chromosomal constitution, which makes the extraction of normal sperm for ICSI possible in men with similar karyotypes.

References:

Supported by: This study was funded by Canadian Institutes of Health Research.

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OBJECTIVE: Nitric oxide (NO), produced by an inducible synthase (iNOS), is known to directly affect Sertoli cell (SC) function and indirectly affect germ cell development and sperm production. Our recent studies showed that multiple SC signalling proteins are altered in time-dependent manner by inhibiting SUMOylation. Whether inhibition of this biochemical process may trigger rapid intracellular changes associated with NO signalling is unknown.

DESIGN: Primary rat Sertoli cell model; treatment with Ginkgolic Acid (GA) to inhibit E1-SUMO activating enzyme required during the process of SUMOylation. To determine whether inhibiting SUMOylation can regulate function through the NO pathway, SCs were treated with GA +/- hormones.

MATERIALS AND METHODS: SCs isolated from testes of 18-day-old SD rats were purified then established in primary culture (≥95% pure) in defined serum-free media. On day 3 ex vivo, SCs were pretreated with GA (25µM; 1h) to inhibit new SUMOylation or matched-vehicle control. Androgen testosterone (T;100nM) or 7α-methyl-19-nortestosterone (MNT;100nM), or gonadotropin FSH (300ng/ml) was added for an additional 1h. Nuclear and cytoplasmic proteins were analyzed by sequential Western blotting with activity-specific immune reagents. Each phosphorylated (p) protein was normalized to its pan-protein in the same lane. In addition, intracellular NO was analyzed by quantitative Flow Cytometry. SCs were pre-loaded with DAF-FM diacetate (20min; 34°C) and treated with GA or matched-vehicle control (1h). Either a hormone or its vehicle-blank control was next added for an additional 1h. Single cell-associated fluorescence was measured with 20,000 individual events, 4 replicates for each primary SC experiment (4). Statistical significance, p≤0.05.

RESULTS: GA treatment alone, or in combination with hormone, significantly affected the steady-state activities of specific SC signalling pathways compared to matched-controls +/- hormones. Nuclear (N) and cytoplasmic (Cy) iNOS protein decreased significantly following GA. Significant increases in activity of CREB, INK, and mTOR were observed in N and Cy. In contrast, inhibition of SUMOylation reduced N and Cy p42/44 MAPK and pAkt activities. Inhibition of SUMOylation was associated with decreased p-tyrosine and p-serine STAT3 in both cell compartments, whereas N levels of AR and ERβ increased. Intracellular NO was significantly induced by GA.

CONCLUSIONS: Taken together, these data provide evidence consistent with the hypothesis that acute inhibition of SUMOylation can affect SC function by regulating the activity of multiple survival pathways including rapid intracellular NO signalling.

Supported by: Reproductive Health Program, Population Council and The F.M. Kirby Foundation.

P-346 Tuesday, October 18, 2016

MALE INFERTILITY AND FSHR GENE POLYMORPHISMS IN IVF. L. Zhyliyova*, O. Feskov,* Karazin National University, Kharkiv, Ukraine; *Center of Human Reproduction, Kharkiv, Ukraine.

OBJECTIVE: Some studies suggest male infertility may be linked to single nucleotide polymorphisms (SNP) of gene of FSH receptor (FSHR). We analyzed two FSHR gene polymorphisms (FGP), G919A (Ala307Thr) and A2039G (Asn680Ser), for correlations with semen parameters of IVF patients.

DESIGN: Controlled study in a single IVF clinic with in-house genetic laboratory.

MATERIALS AND METHODS: During 6-month period in our clinic, all IVF couples of age 35 < with primary diagnosis as male infertility (MI) excluding azoospermia (AZS) agreed to participate in our study (N=51). After IRB approval, prior to IVF, the blood (10mL) of 51 males was drawn, chromosome samples were obtained from lymphocytes, and extracted DNA was processed by RT-PCR for further finding of FGP as in 1. DNA fragmentation index (DFI) was measured in sperm, and patients were then categorized by DFI of greater or less 20%. As a comparison, we used genetic passports of all male patients who were diagnosed with AZS in our clinic in the last four years (41 total). Chi-squared test was used to statistically analyze differences between groups.

<table>
<thead>
<tr>
<th>AZS patients; normal karyotype (N=34)</th>
<th>Non-AZS patients; normal karyotype (N=51)</th>
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<tbody>
<tr>
<td>* Normal genotype Polymorphic</td>
<td>* Normal genotype Polymorphic</td>
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<tr>
<td>Obstructive = 0</td>
<td>Obstructive = 13</td>
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<tr>
<td>Non-obstruct. = 3</td>
<td>Non-obstruct. = 18</td>
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<td>DFI &gt; 20% = 1</td>
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<td>DFI &gt; 20% = 18</td>
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<td>DFI &lt; 20% = 7</td>
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* Normal genotype is GGAA among all variants of SNP pair of G919A and A2039G.
6-month trial for non-AZS infertile men was performed from Sep 2012 to Mar 2013.
Genetic passports for AZS patients were accumulated from Mar 2012 to Mar 2013.
RESULTS: 37/41 AZS patients but only 25/51 non-AZS infertile patients appeared polymorphic in G919A or A2039G (p<.001). Normal karyotype was expressed in 34 of 41 AZS cases and in all 51 non-AZS cases (see Table). In non-AZS trial, low-damage sperm (DFI<20%) allowing better blastocyst formation was observed in 25/26 normal genotype patients, but only in 7/25S polymorphic (p<.001). Among 21 patients with non-obstructive AZS, the presence of alternative alleles of G919A was associated with increased level of FSH in blood: 9/15 patients with alternative alleles had FSH > 25 mIU/mL, compared to only 1/6 patients with GG-normal allele (p=0.072). It is possible that FSH was actively secreted, but the presence of alternative allele changed the FSH receptor’s ability to bind FSH, thereby affecting spermatogenesis.

CONCLUSIONS: Adding to previous studies of SNP [2, 3], we present three novel findings regarding the role of FGP of G919A/A2039G in male infertility. First, 90% AZS vs 49% non-AZS patients have FGP. Second, we observe a correlation of FSH level with presence of alternative alleles of G919A among patients diagnosed with non-obstructive AZS. Third, in non-AZS cases, normal-genotype patients much more often express an un hurt or low-damage DNA in sperm and have a better chance for IVF success, compared to polymorphic patients. Further studies are needed to understand why links between MI and FGP exist. We hypothesize that the PGD of embryos and further transfer of ones without FGP might reduce a risk of inheritance of reproductive function’s abnormality.

References:

P-347 Tuesday, October 18, 2016

AN EFFICIENT ANDROGEN RESPONSE, ANTIOXIDANT DEFENSE AND PROTEOSOMAL PATHWAY MAINTAIN FERTILITY IN DONORS WITH ROS-POSITIVE SPERM. L. Samanta,a,b A. Agarwal,R. Sharma,a K. Kothandaraman,a N. Swain,a,b Redox Biology Laboratory, School of Life Sciences, Ravenshaw University, Orissa, India; bAmerican Center for Reproductive Medicine, Department of Urology, Cleveland Clinic, Cleveland, OH.

OBJECTIVE: Reactive oxygen species (ROS) in spermatozoa involves electron leakage from the sperm mitochondria resulting organelle damage and the initiation of an intrinsic apoptotic cascade. This results in the loss of motility, DNA damage, and viability and subsequently the cells undergo apoptosis. Our results in the eukaryotic cell line of ph-chromaphage in the which may facilitate the silent phagocytosis of these cells in the aftermath of insemination. This process influence the female tract immune response to sperm antigens and fertility. The objective of this study was to identify the molecular mechanisms by which some men with high ROS levels remain fertile utilizing high throughput proteomic analysis.

DESIGN: The study design involved proteomic analysis of spermatozoa from ROS-positive and ROS-negative fertile donors.

MATERIALS AND METHODS: Spermatozoa from fertile men with low ROS levels (control group, n=17, <500RLUs/10⁶ sperm) and high ROS levels (experimental group, n=14, >500 RLUs/10⁶ sperm) were used in this study. Following normalization of protein concentration, samples were pooled, and proteins were extracted and separated by 1-D gel (n=3). Protein bands were digested and loaded on an LTQ-Orbitrap Elite hybrid mass spectrometer. The functional annotations of proteins were obtained using bioinformatics tools and pathway databases.

RESULTS: There was overexpression of transcript variants of NADH dehydrogenase and antioxidant defense (superoxide dismutase, glutathione peroxidase, glutathione reductase, thioredoxin reductase 2, peroxiredxin 4, Apolipoprotein A1 and tests specific glyceraldehyde-3-phosphate dehydrogenase). Mitochondrial thioredoxin-dependent peroxide reductase and thioredoxin-related transmembrane protein 4 were uniquely expressed in the group with high ROS providing additional defense. Overexpression of Apolipoprotein D suggests better androgen response. Pathway analysis of differentially expressed proteins indicated that in the low ROS group, the net protein turnover was regulated by an efficient molecular chaperone system while in the high ROS group, the general protein turnover was regulated by an efficient ubiquitin-proteosome pathway along with proteins involved in maintenance of morphology and motility of spermatozoa.

CONCLUSIONS: An efficient androgen response, antioxidant defense and proteosomal pathway are responsible for maintaining fertility in donors with ROS-positive sperm.

P-348 Tuesday, October 18, 2016

CIGARETTE SMOKING AND ASSOCIATED EFFECTS ON THE RATE OF AGING IN SPERM DNA METHYLATION PATTERNS. T. Jenkins, D. T. Carrell, J. Hotaling, K. L. Aston. University of Utah, Salt Lake City, UT; Surgery (Urology), University of Utah School of Medicine, Salt Lake City, UT; Surgery (Urology), University of Utah, Salt Lake City, UT.

OBJECTIVE: To understand the impact of long-term cigarette smoking in altering the rate at which sperm undergo typical age associated DNA methylation modifications.

MATERIALS AND METHODS: 40 human sperm samples from our tissue bank were selected based on exposure to cigarette smoke. Inclusion criteria required that individuals consumed a minimum, on average, of ½ a pack of cigarettes per day and also had been smoking for at least 10 years. We analyzed average DNA methylation via Illumina’s 450k methylation array, and selectively targeted genomic regions previously identified to have age associated DNA methylation perturbations in healthy donors who do not smoke. Regression analyses (age vs. average regional fraction methylation) at 20 of the most highly age-associated regions were performed. The slope of the line of best fit and r values were assessed to determine differences in the rate of “sperm aging” resultant from cigarette consumption.

RESULTS: Our results indicate that, in general, regardless of the level of consumption or time of cigarette smoke exposure, virtually no affect is seen on the rate of age-associated methylation alterations (slope) in sperm. Specifically, we found that the average slope at genomic sites most highly modified with age was approximately -0.0035, while the average slope at the same sites in the smoking group was not statistically different at -0.0031 based on a two tailed t-test (p = 0.4493). This finding confirms the remarkable consistency of methylation modification with age in sperm that has been reported in multiple cohorts. Interestingly however, the r values of these regression lines were significantly lower in the smoking group, though still significant in most cases based on regression analysis, as compared to the donor group with average values of 0.123 and 0.521 respectively (p < 0.0001).

CONCLUSIONS: Our data support the concept that “sperm aging” occurs in remarkably consistent patterns as has been previously identified in multiple cohorts. Interestingly, while smokers displayed the same rate of modification with age at these regions of known age-associated change there appeared to be more variability in this association as identified by a lower average correlation coefficient of methylation values. This suggests that, while on average sperm DNA methylation signatures are altered at the same rate in all individuals independent of cigarette smoke exposure, these regions of known change may become less stable in those who smoke and thus display increased variability. Further analysis is required to fully assess the mechanism for the increased variability seen in this study.

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NEILL AND CTDSPL: NOVEL GENETIC FACTORS PREDISPOSING TO PEYRONIE’S AND DUPUYTREN’S DISEASES. A. W. Pastuszak, J. Bournat, Y. Cabeza-Arvelaz, L. I. Lipshultz, D. J. Lamb. Scott Department of Urology, Baylor College of Medicine, Houston, TX; Baylor College of Medicine, Houston, TX; Center for Reproductive Medicine, Baylor College of Medicine, Houston, TX; Urology/Center for Reproductive Medicine/MB, Baylor College of Medicine, Houston, TX.

OBJECTIVE: Peyronie’s disease (PD) results in abnormal inflammation and fibrotic plaque development in the penile tunica albuginea (TA), and thus can limit sexual intercourse. Several genetic factors predisposing to PD are unknown. We sought to identify genes involved in PD, and herein present data implicating NEILL1, a secreted growth factor involved in fibrosis and inflammation, and CTDSPL, a phosphatase involved in the TGF-β pathway and inflammation, in Peyronie’s and Dupuytren’s diseases (DD).

DESIGN: Genomic study comparing men with both PD and DD and controls.

MATERIALS AND METHODS: Blood-derived genomic DNA from 19 men with both PD and DD and 4 controls was used for array comparative
medications for PD, predicted to negatively affect protein function, and associated with both PD and DD. A 4.4 kb microdeletion on chromosome 3p22.2 encompassing the CTDSPL gene was identified in 1/19 (5.3%) men. Men with PD, predicted to negatively affect protein function, and associated with Crohn’s disease and ankylosing spondylitis. No mutations predicted to affect CTDSPL function were identified. Overexpression of NELL1 and CTDSPL in TA fibroblasts from PD and control males downregulated proinflammatory and upregulated antiinflammatory genes. Penis from Nell1-deficient mice exhibited higher hydroxyproline content than controls.

CONCLUSIONS: Microdeletions in both NELL1 and CTDSPL were identified in men with both PD and DD. Both genes are involved in TGF-β signaling pathway. In A549 fibroblasts, overexpression of NELL1 and CTDSPL modulates expression of fibrotic pathway markers, and Nell1-deficient mouse penis is enriched in hydroxyproline, indicating that Nell1-deficient mice may be predisposed to fibrosis. These results support roles for NELL1 and CTDSPL in fibrosis in men with PD and DD.

References:

Supported by: Supported in part by the NScal, Nist, and a Urology Care Foundation Russell Scott, Jr., Resident Research Award. AWP is a National Institutes of Health (NIH) K12 Scholar supported by a Male Reproductive Health Research Career (MRHR) Development Physician-Scientist Award (HD073917-01) from the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) Program (to DJL).

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IDENTIFICATION OF LIVE SPERM BY FLOW CYTOMETRY USING VISIBLE SPECTRUM, MEMBRANE PERMEABLE SYTO RED NUCLEIC ACID STAINS. A. Bolyakov, a, S. Mital, a, A. Lovett, a, M. Veliciano, a, C. N. Schlegel, a, D. Paduch, a, Weill Cornell Medicine, New York, NY; aUrology, New York Presbyterian/Weill Cornell Medicine, New York, NY; aUrology, Weill Cornell Medical College, New York, NY; aDept of Urology, Weill Cornell Medical College, New York, NY.

OBJECTIVE: Seminal fluid is comprised of a mixture of cells, various proteins and other substances. Traditional sperm isolation using light microscopy is limited as it is able to examine only certain cells at a time. The advent of flow cytometry allows for rapid analysis of a vast number of cells for specific characteristics. Most cellular stains require permeabilization of the membranes rendering identified sperm not usable for artificial reproductive techniques. Our goal was to identify the optimal DNA-stain which would allow for the highest differentiation of haploid and diploid cells from a semen sample using visible light spectrum fluorophores without permeabilization of the cell membrane.

DESIGN: BD Accuri C6 flow cytometer was used to test a variety of cell membrane permeable nucleic acid stains on seminal fluid to determine the optimal stain for haploid cell analysis.

MATERIALS AND METHODS: 9 normal ejaculated sperm samples were collected. White blood cells were isolated from peripheral blood to be used as controls of diploid cells. All samples were centrifuged at 800g for 10 minutes to collect a pellet. The pellets were re-suspended & aliquoted in 300 ul with 0.9% NaCl. Each sample was stained separately with 3.3 uM of SYTO 17, 59-64, and 25 ug/ml of Propidium Iodide (PI), then incubated for 60 min in room temperature. SYTO 59-64 dyes generally show cytoplasmic or mitochondrial staining as well as nuclear staining. Forward scattered light, and side scattered light in a logarithmic scale was collected from the cells based on relative fluorescence (PI: 585/40 nm; SYTO: 765/25 nm). All flow cytometry analysis was done using BD C6 Software Version 1.0 and FlowJo v10.

RESULTS: The permeable, nucleic acid stains SYTO allow for quantification of haploid cells using flow cytometry. Haploid cells were separated from diploid cells (WBCs) both in log and linear presentation 100% of time. SYTO 17 has highest degree of specificity for haploid cells in seminal fluid with 100% of specificity & sensitivity for detection of as low as 800 sperm per 100,000 events (0.8%). SYTO17 has unique staining of nuclear nucleic acids in comparison to other SYTO stains which have higher affinities to cytoplasmic and/or mitochondrial stains. We uncovered novel method of initial gating of sperm based on FSCH & SSC logarchic scale as optimal method of gating to accommodate unique size and shape of spermatozoon.

CONCLUSIONS: Our study shows feasibility and high level of reproducibility of selecting live sperm using visible light spectrum fluorochrome thus providing tool for isolation of sperm from seminal fluid and ultimately testicular specimen tissues. This technique in conjunction with fluorescence activated cell sorting may change the paradigm of identifying and isolating spermatozoi men with a variety of pathologic conditions.
significantly in the majority of men prescribed CC. However, PSA levels should be monitored due to the small number of men who do develop abnormalities.

P-352 Tuesday, October 18, 2016
IDENTIFYING DIFFERENTIAL MRNA & MiRNA EXPRESSION PATTERNS IN MICROSCOPICALLY ISOLATED INDIVIDUAL SEMINIFEROUS TUBULES REVEALS UNIQUE “NICHE” FOR SPERMATOGENESIS IN MEN WITH SEVERE FORMS OF INFERTILITY. S. Mittal,1 A. Melnik,1 A. Bolyakov,1 P. N. Schlegel,2,3 D. Paduch.1 1Urology, New York Presbyterian / Weill Cornell Medical College, New York, NY; 2Urology, Weill Cornell Medical College, New York, NY; 3Dept of Urology, Weill Cornell Medical College, New York, NY.

OBJECTIVE: Non-obstructive azoospermia (NOA) is a cause of male infertility secondary to genetically driven defects in spermatogenesis. Testicular sperm extraction (TESE) is successful in identifying small number of sperm in 50% of men with NOA. During TESE, predominantly collapsed seminiferous tubules (ST) are identified with rare areas of dilated STs that are more likely to harbor viable sperm. Hence we hypothesize that miRNA regulated control of mRNA expression along STs leads to optimal environments for spermatogenesis within the human testis.

DESIGN: Seminiferous tubules from individuals were isolated and differential mRNA and miRNA expression profiles were determined to show heterogeneity within the same patient.

MATERIALS AND METHODS: STs were obtained from 7 patients, including 3 with NOA, and 2 patients with Sertoli-cell only (SCO). In the three NOA patients, single STs were cut based on the differences in diameter along the same ST into: full/dilated or empty/collapsed tubules. Quantitative PCR was performed on all tubules for GDNF and GFRα1 and values expressed per vimentin and clusterin. ACTB was used as a housekeeping gene. Expression of GFRα1 was corrected for number of Sertoli cells (vimentin/clusterin). MiRNA expression profiles were determined for each segment of STs and normalized to let-7a. GenEx software was used to identify differentially expressed miRNAs using adjusted p < 0.0007 and minimum of 2-fold difference.

RESULTS: Quantitative PCR showed a statistically significant decrease in the relative expression of GFRα1 between dilated and collapsed STs (p < 0.001) indicating an abnormal expression of spermatogonial stem cells (SSC) or spermatagonia. A set of 22 miRNA were identified to be differentially expressed and linked to known signaling pathways in Sertoli cells and SSCs. CONCLUSIONS: Our data supports the hypothesis that unique miRNA profiles support normal SSC division that correlate into islands of spermatogenesis, especially in men with NOA. This data in conjunction with previous observations that SSCs are likely present in patients with SCO offers new targets for further research and possible therapeutic intervention.

P-353 Tuesday, October 18, 2016
SIGNIFICANT IMPACT OF BODY MASS INDEX ON A MODIFIED SPERM MOTILITY-MORPHOLOGY ALGORITHM. W. Roudbash1 L. K. Hill.1 Biomedical Sciences, University of South Carolina School of Medicine Greenville, Greenville, SC; 2Regional Urology, Greenville Health System, Greenville, SC.

OBJECTIVE: Body mass index and semen parameters have both been of interest for predicting pregnancy outcomes. No one semen parameter has been found to be highly diagnostic of male subfertility. We have previously reported that sperm motility index (SMI), which accounts for both velocity and linearity, can describe sperm motility more specifically than simply sperm concentration, percent sperm motility, percent sperm morphology (normal forms). Sperm motility-morphology index (SMMI) was calculated as follows: SMMI = (percent motility* sperm progression* percent morphology).

RESULTS: Mean BMI was 27.5 and the mean sperm motility-morphology index (SMMI) was 8.9. Regression analysis showed a significant (P = 0.027) relationship between BMI and the SMMI.

CONCLUSIONS: Increased body mass indices have a negative impact on the sperm motility-morphology index. Additional research is warranted to see how this association between BMI and sperm motility-morphology index impacts pregnancy outcomes.

P-354 Tuesday, October 18, 2016
CAPACITATION DEFECTS ARE COMMON IN MEN QUESTIONING THEIR FERTILITY AND ARE INDEPENDENT OF STANDARD SEMEN ANALYSIS PARAMETERS. A. J. Travis,a C. Cardona,a A. Simpson,b M. A. Moody,c E. Seaman,c G. C. Ostermeier,b cUniversity of Illinois, Champaign-Urbana, IL; aAndrovia LifeSciences, Mountainside, NJ; bUrology, University of Illinois at Chicago, Chicago, IL.

OBJECTIVE: Semen analysis fails to diagnose defects in capacitation. Sperm must capacitate to be able to fertilize. Localization of the ganglioside Gd3 (Cap-Score167) identifies cells capable of capacitating, providing a bioassay for sperm fertilizing ability (Panizza et al., ASRM 2014). However, those data were obtained solely from men seeking fertility treatment. The objectives of this study were to compare the Cap-Scores of men seeking fertility work ups versus men with known fertility, and to evaluate if Cap-Score provided novel functional data or merely tracked with standard semen analysis parameters.

DESIGN: Cohort comparison between presumed fertile (cohort 1, pregnant or recent father) and potential subfertile/inferile men (cohort 2, men questioning fertility). Relationships between Cap-Score and traditional semen measures were also explored.

MATERIALS AND METHODS: All studies approved by WIRB (20152233). Semen samples were liquefied, washed, and incubated under non-capacitating and capacitating conditions. Sperm were fixed overnight and Cap-Score determined via fluorescence microscopy. Semen quality measures were evaluated according to WHO. T-Test, ANOVA and correlation analyses were done using MS Excel (2013) and XLSTAT (2015).

RESULTS: The mean Cap-Score for cohort 1 was 35.3 (SD = 7.7%; n = 76 donors; 187 collections). Cap-Scores were lower for cohort 2 (31.6 ± 8.1%; p = 1.0E-03), with 33.6% (41/122) having Cap-Scores > 1 SD below the mean for cohort 1, versus an expected 16%. For cohort 2, no relationship was observed between Cap-Score and morphology (p = 0.28), motility (p = 0.14) or concentration (p = 0.67). 93.4% (114/122) of men in cohort 2 exhibited normal motility, yet 30.7% (35/114) of them had Cap-Scores > 1 SD below the mean for cohort 1. Similarly, 101 of 122 men (82.7%) exhibited normal concentration with 32.6% (33/101) having Cap-Scores > 1 SD below the mean for cohort 1.

CONCLUSIONS: These results show that capacitation defects are common in men having difficulty conceiving and that Cap-Score provides functional data complementing traditional semen analysis. Because capacitation is required for fertilization, the Cap-Score can provide an important functional complement to standard semen analysis and may help in choosing the most appropriate fertility treatment.

Supported by: Androvia LifeSciences.

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TESTOSTERONE TO ESTRADIOL RATIO CORRELATES WITH SPERM CONCENTRATION IMPROVEMENT IN HYPOGONADAL OLIGOZOSPERMIC PATIENTS TREATED WITH ANASTROZOLE. N. Abhyankar,a O. Shoshany,a C. Niederberger,b aUrology, University of Illinois at Chicago, Chicago, IL; bUniversity of Illinois at Chicago, Chicago, IL.

OBJECTIVE: To investigate predictors of semen parameters improvements in oligozoospermic subfertile men.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: We reviewed all subfertile men prescribed anastrozole at a male infertility clinic from December 2009 till March 2016. Indications for anastrozole were low bioavailable testosterone (<155ng/dl) and either a relatively elevated estrogen, a contraindication to clomiphene citrate or a ratio of testosterone to estrogen (T/E) < 10. Exclusion criteria were: a history of exogenous testosterone or a sex chromosome disorder. Data on demographics, clinical & laboratory characteristics were recorded. To reduce regression to the mean bias, we selected the best pretreatment semen analysis. Paired t-test was used to compare pre and post

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treatment parameters. Age and FSH adjusted linear regression was used to identify predictors of improvement in semen analysis.

RESULTS: Out of 58 patients on anastrozole, 20 were oligozoospermic. Median age was 36 years (IQR 32–41), mean length of infertility was 43.8 months (±4.3 months). After one month of anastrozole therapy, mean total testosterone increased by 240 ng/dl and mean estradiol level decreased by 16.1 pg/ml (both p<0.0001). These levels were maintained 4 months in therapy. Sperm concentration and total motile count increased after 4 months of treatment (4.9±1.2 ml/ml to 13.6±2.9 ml/ml, p=0.001 and 4.8±1.37 million to 12±3.6 million, p=0.01, respectively). Predictors of improvements in seminal parameters were post-treatment T/E ratio (p<0.0001) and changes in T/E ratio (p<0.0001).

CONCLUSIONS: A larger increase in sperm concentration and TMC was correlated with a larger increase in post-treatment T/E ratio and percentage change in T/E ratio during treatment. Our results may suggest that correction of T/E ratio is important in improving semen parameters. A prospective controlled study is required to assess the hypothesis generated by this retrospective study.

P-355 Tuesday, October 18, 2016


OBJECTIVE: One mechanism by which sperms initiate the process of degradation (senesence) may be due in part to down regulation of antioxidant capacity which inducing changes in membrane permeability and subsequent apoptosis. Other Factors present in the semen such as white blood cells (WBC), defective sperms (DS) and oxidative stress (OS) may accelerate the sperm degradation. The aims of this study were to (i) determine whether WBC, DS and OS act as agents that induce sperm degradation as measured by levels of lipid peroxidation (LP), apoptosis (AP) and (ii) how these levels change over time.

DESIGN: Retrospective.

MATERIALS AND METHODS: Semen samples from 50 men were obtained by masturbation after 2-5 days of sexual abstinence and were evaluated at three time points 1, 26 and 34 hrs post collection to determine: sperm concentration (×10⁶/ml), total motility (%), oxidative stress (OS) may accelerate the sperm degradation. The statistical analysis indicated that the samples with low WBC had levels of LP significantly different until 34hr (NZS 0.5± 0.55 vs 4.55±0.46 and TZS 3.58 ± 0.63 vs 5.01±0.61) and the AP values were significantly different both in time and category at 26hr (NZS 5.23 ± 0.61) and at 34hr (NZS 5.35 ± 0.38 and TZS 5.9 ± 0.56) and the levels of AP at 1hr (NZS 14.4±7.6 and TZS 15.01 ± 5.41, 26hr (NZS 46.7±5.99 and TZS 67.13 ± 7.27) and 34hr (NZS 69.49 ± 6.12 and TSZ 80.62 ± 9.3). The increased LP and AP levels were associated with decreased sperm function and increased sperm morphological abnormalities such as nuclear fragmentation, chromatid dispersion, and cellular agglutination.

CONCLUSIONS: Markers of OS, namely LP and apoptosis, are elevated in circumstances associated with semen senescence such as increased WBC, defective sperms, or extended periods of time of sperm outside the body. These data support the hypothesis that semen senescence is driven in part by OS and those men with OS from WBC and or DS (Teratozoospermia) may have impaired sperm function.

References:
1. Edna Tirado; Michele Marquette; Donna Kinzer; Benjamin Leader Brent Barrett; Alan Penzias Antioxidants Prevents sperm damage from reactive oxygen species: An in vitro comparison of 5 antioxidants cocktails. J of Andrology Suppl March-April 2011- p 88.

Supported by: ReproSource Inc.

P-357 Wednesday, October 19, 2016

THE RELATIONSHIP BETWEEN BREAST DENSITY & BONE MINERAL DENSITY IN NEVER USERS OF POSTMENOPAUSAL HORMONE THERAPY. B. Seckin, M. Kuru Pekcan, H. A. Inal, C. Gulerman. "Zekai Tahir Burak Women’s Health Research and Education Hospital, Ankara, Turkey; "IVF Unit, Konya Education and Research Hospital, Konya, Turkey.

OBJECTIVE: Estrogen is known to affect both mammographic breast density (1) & bone mineral density (BMD) (2), but there are inconsistent results about the association of these density measurements in postmenopausal women. Furthermore, there are scarce data on the relationship between breast density & BMD in never users of postmenopausal hormone therapy (3). In this study we examined the relationship between mammographic breast density & BMD in postmenopausal women who were never hormone replacement therapy users.

DESIGN: Cross-sectional study.

MATERIALS AND METHODS: A total of 293 postmenopausal women were enrolled in this study. Mammograms and BMD measurements for density purposes were obtained. Assessment of mammographic breast density was performed by using Breast Imaging-Reporting and Data System (BI-RADS) classification. The bone mineral density was measured using dual energy X-ray absorptiometry (DEXA) of the lumbar spine and femoral neck.

RESULTS: Grade 1 breast density was observed in 64 women (21.8%), grade 2 in 113 women (38.6%) and grade 3 and 4 in 116 (39.6%) women. Breast density decreased with increasing age and body mass index (BMI). Meanwhile, no significant differences were detected in BMD measures of the hip (p=0.14) and lumbar spine (p=0.29) among the breast density categories. After adjusting for age and BMI, the differences in the mean BMD at the hip and lumbar spine across the breast density categories remained insignificant (p=0.26 and 0.11, respectively).

CONCLUSIONS: There is no evidence of a relationship between mammographic breast density and bone mineral density in postmenopausal women who had never used hormone replacement therapy.

References:

P-358 Wednesday, October 19, 2016

RESTORATION OF YOUNG OVARIAN FUNCTION TO POSTREPRODUCTIVE FEMALE MICE SIGNIFICANTLY INFLUENCED GLUCOSE METABOLISM AND IMMUNE FUNCTION. J. B. Mason. School of Veterinary Medicine, Utah State University, Logan, UT.

OBJECTIVE: Our objective was to determine if restoration of reproductive function in postreproductive female mice would mimic the beneficial effects on metabolism and immune function seen with dietary restriction.

DESIGN: Postreproductive mice had their senescent ovaries replaced with new ovaries from young, actively-cycling mice.

MATERIALS AND METHODS: At 12 months of age, female CBA/J mice had their endogenous ovaries removed and replaced with a pair of donor
ovaries from a 60-day-old mouse. Control and transplant recipients were assessed at 16 months of age. Immune function was assessed with a FACS-based T-cell immunoassay. Metabolic changes were assessed with a Glucose Tolerance Test.

RESULTS: The results showed that glucose metabolism and immune function in 16-month-old postreproductive mice with young ovaries was not different from six-month-old mice and was significantly improved compared with 16-month-old, non-transplanted postreproductive mice.

CONCLUSIONS: In summary, our novel results indicate that restoration of young ovarian function to postreproductive female mice significantly influenced metabolism and immune function as measured by glucose tolerance test and T-cell immunoassay. These observations are important because they imply that, in our model, the presence of young ovarian cells may mimic the positive health span effects seen with dietary restriction. These results also support a potential link between the spectacular advances in health span due to reproductive manipulation in primitive species and dietary restriction in mammals.

Supported by: This research was supported by Utah State University Research Initiation Funds and a Utah State University Research Catalyst Program Grant to JM.

P-359 Wednesday, October 19, 2016

RETROSPECTIVE ANALYSIS OF THE EFFICACY OF ART AND REPRODUCTIVE OUTCOMES IN FEMALES WITH FRAGILE X ASSOCIATED PRIMARY OVARIAN INSUFFICIENCY. L. Tan,1,2 L. Krichevsky,3 E. Greenblatt,3 R. Casper3, C. A. Laskin,3 S. Sierra,3 T. Hannam,3 M. F. Karnis,2 C. L. Librich,5 P. A. Sharma,4 Obstetrics & Gynaecology, University of Toronto, Toronto, ON, Canada; 2Faculty of Medicine, University of Toronto, Toronto, ON, Canada; 3Division of Reproductive Endocrinology & Infertility, Women’s College Hospital, University of Toronto, Toronto, ON, Canada; 4Ob/Gyn, NYU Medical Center, New York, NY; 5Ob/Gyn, NYU Langone School of Medicine, New York, NY.

OBJECTIVE: Fragile X premutation (55-200 CGG repeats) is the most common genetic cause of 46,XX primary ovarian insufficiency (POI) [1,2]. There is currently no published literature regarding the reproductive outcomes and efficacy of artificial reproductive technology (ART) in females with Fragile X associated primary ovarian insufficiency (FXPOI) making counseling about reproductive treatment a challenge. Much of the data regarding FXPOI patients were extrapolated from studies of women with other causes of POI. Trial and error in these women can be avoided by calculating time to conception as well as substantiating cost to the patient. This study aimed to determine whether ART treatment options and success rates differ between females with FXPOI and those with POI due to other causes.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: We performed a retrospective chart review of patients with POI from seven fertility centers in Ontario from 2007 to 2015. The study group consisted of FXPOI patients, younger than 40 years old (n=19). The control group consisted of females younger than 40 years old who were diagnosed with POI or approaching POI, with no Fragile X premutation (n=76). The FXPOI and control patients were grouped and matched by age (<30, 30-34, and 35-39 years old) and by their ovarian reserve assessment utilizing AMH testing (AMH <2.0 pmol/L and AMH = 2.0-6 pmol/L).

RESULTS: 19 FXPOI patients who underwent a total of 51 treatment cycles and 76 control patients who underwent a total of 172 treatment cycles were identified. When comparing the FXPOI and control groups as a whole (stimulated and natural cycles combined), the pregnancy rate per cycle was nearly the same in both groups (24% versus 21%) respectively. However, the pregnancy rate per cycle was significantly lower in the AMH <2.0 pmol/L FXPOI group (6.3%) compared to the control group (20.8%). Ovulation induction with clomiphene citrate was the most efficacious method in the FXPOI group with a 23% pregnancy rate per cycle versus 5.9% in the control group.

CONCLUSIONS: FXPOI females with very low ovarian reserve (AMH <2.0 pmol/L) have significantly lower chance of pregnancy success compared to their age matched counterparts with POI due to other causes. This group will benefit from early diagnosis and targeted treatment with milder ovarian stimulation (e.g. clomiphene citrate). While this study is limited by its small sample size, the data seems to suggest that clomiphene citrate may potentially play an important first line ovulation induction therapy for women with FXPOI.

Supported by: This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (grant number: H1515019).

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OBJECTIVE: This study investigated the cytoprotective effects and molecular mechanism of Evoxidae Fructus (EF) extracts against 4-vinylcyclohexene diepoxide (VCD)-induced ovotoxicity in CHO-K1 ovary cells.

METHODS AND MATERIALS: Cells were plated, pretreated with EF for 2 h and continuously treated with 1.5 mM VCD for 24h. Cell viability was assessed by MTT assay. Protein levels were assessed by western blot.

RESULTS: VCD significantly suppressed cell viability and induced apoptosis at 1.5 mM in CHO-K1 cells. EF dose-dependently blocked the ovotoxicity induced by treatment with VCD. Furthermore, EF significantly activated Akt and its downstream effectors such as mTOR and GSK-3β. The ability of EF to prevent cytotoxicity by VCD was antagonized by pretreatment of LY294002, a PI3K/Akt inhibitor.

CONCLUSIONS: We demonstrated that EF has the ability to protect ovary cells against VCD-induced ovotoxicity, which may be associated with Akt activation. These results suggest that the beneficial effects of EF may be used to improve premature ovarian failure or unexplained infertility caused by environmental factor.

References:

Supported by: This research was supported by a grant from the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (grant number: H1515019).

P-361 Wednesday, October 19, 2016

LEAN MASS IS A MODIFIABLE RISK FACTOR FOR VERTEBRAL FRACTURE IN POSTMENOPAUSAL WOMEN. A. W. Tiesgs,1 R. J. Meislin,2 N. M. Sachdev,3 M. J. Nachtigall,4 L. E. Nachtigall4,5 OB/GYN, NYU Langone School of Medicine, New York, NY; 2NYU School of Medicine, New York, NY; 3Obstetrics and Gynecology, New York University Fertility Center, New York, NY; 4OB/Gyn, NYU Medical Center, New York, NY; 5Obstetrics and Gynecology, NYU School of Medicine, New York, NY.

OBJECTIVE: Vertebral fracture is the most common clinical manifestation of osteoporosis and is significantly associated with an increased risk of future fractures. Bone mineral density has traditionally been the best predictor of fragility fractures, however, lean mass may have a greater contribution to the risk of fracture than previously understood. Dual-energy X-ray
absorptiometry (DXA) allows for highly accurate measurements of bone mass as well as both fat and lean body mass. The primary objective of this study is to determine if there is an association between lean body mass and the incidence of vertebral fragility fractures in postmenopausal women. The presence of an association between number of vertebral fractures and T-score, Z-score, body mass index (BMI), muscle mass index (lean mass kg/height m^2), and fat mass are secondary outcome measures.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: All women between the ages of 40 and 100 years, who underwent body composition and bone density testing using DXA scan at the NYU Bone Density and Body Composition Unit from May 2011 to November 2014 were identified. All indications were included. Pa- tients with DXA that did not include a lateral vertebral assessment were excluded. Parametric variables were confirmed by Shapiro-Wilk testing and compared by analysis of variance (ANOVA). Chi-square testing was used for nominal variables.

RESULTS: A total of 358 women met inclusion criteria. The average age was 70.2 years (Range 46 to 93 years), average weight was 139.6lbs ± 25.9 (Range 50 to 267 lbs) and average body mass index (BMI) was 25.0 ± 4.5 kg/m^2 (Range 16.7 to 42.3). A total of 124 vertebral fractures were identified in 85 patients (23.7%), with an average of 0.35 (±0.7) vertebral fractures per patient. Both lean body mass and Z-score were noted to have an inverse association with number of vertebral fractures (p = 0.03 and p = 0.02, respectively). Women without vertebral fractures had an average lean mass of 62.4 lbs (±8.5) (average BMI 24.9 ±4.5), while women with at least one vertebral fracture had an average lean mass of 59.5 lbs (±8.7) (average BMI 26.0 ±4.5). Women with at least one vertebral fracture were more likely to have an average T-score of at least −0.8 (±1.5), but T-score was not found to be significantly associated with number of fractures (p = 0.26). Additionally, fat mass (p = 0.82), BMI (p = 0.19), and muscle mass index (p = 0.36) did not prove to be predictive of vertebral fracture in this population.

CONCLUSIONS: Irrespective of BMI, a lean mass of greater than 62.4lbs was associated with lower incidence of vertebral fracture in our population. These results suggest the importance of assessing lean mass in postmeno- pausal women, as it is a modifiable risk factor for osteoporotic fractures.

Reference:

REPRODUCTIVE ENDOCRINOLOGY - CLINICAL

P-362 Wednesday, October 19, 2016

HIGHER 25-HYDROXYVITAMIN D (25(OH)D) IS ASSOCIATED WITH INCREASED FECUNDABILITY. A. Z. Jukic,a C. R. Weinberg,b A. Z. Steiner.c aYale School of Public Health, New Haven, CT; bNational Institute of Environmental Health Sciences, Durham, NC; cUniversity of North Carolina, Chapel Hill, NC.

OBJECTIVE: In rodents, vitamin D deficiency has been associated with dramatic reductions in fertility and supplementation with vitamin D improves reproductive success. (1). In women undergoing fertility treatment, vitamin D sufficiency has been associated with improved success rates, how- ever, no studies have prospectively examined vitamin D status and sponta- neous conception in women with no known fertility problems.

DESIGN: We used data from a prospective community-based cohort study of time to pregnancy. The Ovary to Conceive, to examine the association of vitamin D status with fecundability.

MATERIALS AND METHODS: Fecundability was measured by the number of menstrual cycles required to conceive a clinical pregnancy. Women between the ages of 30-44, with no known fertility problems, were enrolled in Time to Conceive early in their attempt to become pregnant. Women between the ages of 30-44, with no known fertility problems, were enrolled in Time to Conceive early in their attempt to become pregnant.

RESULTS: Results of regression analyses are shown in table 1

CONCLUSIONS: This is the largest study to compare predictors of ovarian reserve in women with UI against a well-characterized control popula- tion. Contrary to our hypothesis, women with UI did not show evidence of decreased markers of ovarian reserve. Our findings suggest that ovarian reserve in women with UI against a well-characterized control population.

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Adjusted Association between Markers of Ovarian Reserve in Controls vs. UI

Outcome | B-Coeff (95% CI) | Control vs. Unexplained Infertility | p-value
--- | --- | --- | ---
AMH | -1.6 (-5.8, 2.5) | NS
AFc | -3.1 (-8.0, 1.8) | NS
AMH:AFc ratio | -0.2 (-3.2, 28) | NS
VALIDATION OF THE ACCESS AMH ASSAY & ITS COMPARISON WITH LABCORP ULTRASENSITIVE ASSAY. A. Younis, K. C. Hawkins, W. J. Butler. Fertility Institute, Navicent Health & OB/GYN Dept., Mercer University School of Medicine, Macon, GA.

OBJECTIVE: AMH is the best currently available measure of ovarian reserve. In the USA, most fertility clinics get AMH values from Labcorp or Beckman Access. A study was done at Ashd Labs, the first outpatient laboratory to validate and implement the Beckman Access AMH assay in USA. The objective of this study was to evaluate the performance of the Access AMH assay using patient serum samples and directly compare results with Labcorp AMH levels.

DESIGN: Prospective AMH assay evaluation in a fertility outpatient laboratory.

MATERIALS AND METHODS: Coefficients of variation, precision, stability, linearity, and inter-laboratory comparison were determined using recombinant AMH quality control and patient serum samples. Patients were consented and made aware that AMH assay will be based on materials designed by manufacturer as research-use-only (RUO). Blood were collected for AMH on the day of the first office visit for fertility workup. Serum AMH level of 30 women (age 20-44 yrs) were assessed locally using Access2 analyzer and at Labcorp using their ultra-sensitive AMH assay. Inter-laboratory correlation study was performed on 75 patient samples in which AMH values were first obtained using a UniCell DXI analyzer at an independent outside laboratory (Pathology Associates Medical Laboratories, Spokane WA). The serum samples were frozen and shipped in dry ice to our location where they were thawed and analyzed in Access2 analyzer using similar reagent kit lots. All statistical evaluation was performed using SPSS.

RESULTS: The Access AMH assay demonstrated excellent performance across the measuring range for both intra-assay and inter-assay coefficients of variation (2.1 % and 1.8 %, respectively). The assay was linear over the six ranges recommended by the manufacturer, and no strong bias was observed. AMH values ranged from 0.015 to 20.01ng/mL with the Labcorp and 0.011 to 25.40ng/mL with Access AMH. Values between fresh and frozen samples using Access AMH assay revealed no impact of sample freezing and storage. The Access AMH and Labcorp ultrasensitive assay types were highly correlated (R² = 0.97, Slope= 0.96), and no statistical differences were observed between the two methods. Inter-laboratory comparison results showed that the two systems were statistically identical (R² = 0.998 and 0.997 for Access2 and UniCell DXI respectively).

CONCLUSIONS: We have validated and now routinely measure serum AMH levels in-house using the Access automated assay. Regression analysis demonstrates high correlation across the measuring range between the results obtained on two different analyzers located in different geographical locations. The findings of our correlation studies demonstrate strong agreement between the results generated by the Access AMH and Labcorp ultrasensitive assay indicating that the two methods are interchangeable.

P-365 Wednesday, October 19, 2016

CO-PRESENCE OF INCREASED ANTRAL FOLLICLE COUNT AND HYPERANDROGENISM PREDICTS THE MANIFESTATION OF IMMUNE INFLAMMATORY RESPONSES. M. D. Salazar Garcia, a S. Kwon, a K. Nguyen, a N. Sung, a L. Wu, a A. M. Skariah, a S. V. Dambaeva, b A. Gilman-Sachs, b K. Beaman, b J. Kwak-Kim. a Obstetrics and Gynecology, Rosalind Franklin University of Medicine and Science, Vernon Hills, IL; bMicrobiology and Immunology, Rosalind Franklin University of Medicine and Science, North Chicago, IL.

OBJECTIVE: To investigate the association between antral follicle count and immune inflammatory markers.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: A total of 60 infertile women (age 34.6±5.0, BMI 26.2±7.2) were enrolled. Patients were divided in three groups according to number of antral follicles (measuring >2-9 mm) per ovary; antral follicle count 1-5 (n=22), 6-11 (n=22) and ≥12 (n=22). Antral follicle count, metabolic and immune inflammatory markers were investigated. Hyperandrogenism was defined as dehydroepiandrosterone sulfate levels >231µg/dL, total testosterone levels >45µg/dL and/or free testosterone levels >6.4pg/dL. The statistical analysis was performed using SPSS software package. One way ANOVA, two way ANOVA and Pearson product-moment correlation coefficient were utilized to analyze the relationship between antral follicle count and various anthropometric, metabolic and immune inflammatory markers.

RESULTS: Levels of serum soluble form of the receptor for advanced glycation end products (sRAGE), total testosterone and antinullerian hormone (AMH) were significantly higher in patients with ≥12 follicles when compared to patients with 1-5 follicles (1450.3±559.9 vs. 1022.8±413.7, P<0.03; 18.0±2.3 vs. 18.1±1.5, P=0.048 respectively). A significant main effect for the interaction between antral follicle count and hyperandrogenism was found for VCAM and adiponectin levels (P=0.020 and 0.001 respectively). Soluble RAGE levels were negatively correlated with the levels of glucose (r=0.290, P=0.026), protein C (r=-0.402, P=0.002), protein S (r=-0.341, P=0.012) and BMI (r=-0.319, P=0.014). TNFα/IL-10 producing T helper cell ratios and serum IL-10 levels were significantly different between patients with and without hyperandrogenism (P=0.025 and 0.011 respectively).

CONCLUSIONS: Serum sRAGE levels are associated with ovarian antral follicle count. Co-presence of ultrasonographic polycystic ovarian changes and hyperandrogenism is associated with inflammatory immune responses. It is speculated that a possible protective role of sRAGE may be attenuated by the presence of hyperandrogenism in patients with polycystic ovary.

Supported by: Reproductive Medicine, Department of Obstetrics and Gynecology, Clinical Immunology Lab at Chicago Medical School at RFUMS.

P-366 Wednesday, October 19, 2016

THE IMPACT OF SERUM VITAMIN D LEVEL ON IN VITRO FERTILIZATION OUTCOME: A PROSPECTIVE OBSERVATIONAL STUDY. Z. Bu, a L. Hu, a Y. Sun, a Reproductive Medicine Center, First Affiliated Hos, Zhezhong, China; aReproductive Medical Center, the First Affiliated Hospital of Zhezhong Univers, Zhezhong, China.

OBJECTIVE: To explore the impact of serum vitamin D (VD) level on in vitro fertilization and embryo transfer (IVF-ET) outcome.

DESIGN: A prospective cohort study was conducted in a university affiliated hospital from April 2015 to September 2015. Serum vitamin D level, as well as the age of patients, body mass index (BMI), antral follicle count (AFC), number of embryos transferred, were analyzed to explore their relationship with ongoing pregnancy rate in IVF.

MATERIALS AND METHODS: In total, 298 patients (age from 21 to 40 years old, FSH < 10 mIU/mL) with their first standard GnRH-a long protocol were included into this study. Of these, 248 patients underwent embryo transfer eventually. According to serum VD level on the day of hCG administration, patients were divided into three groups: Deficient, VD < 20 ng/mL; Normal, 20 ng/mL ≤ VD < 30 ng/mL; Replete, VD ≥ 30 ng/mL.

RESULTS: In general, patients in Deficient group were with significantly older than those in the other two groups (33.7 ± 3.5 vs 32.4 ± 63.8 vs 31.2 ± 3.6; P=0.006), and the duration of infertility was longer. BMI, AFC, Gn duration, number of oocytes retrieved were comparable between three groups. In bivariate correlation analysis, VD level was negatively correlated with age (r = -0.218; P < 0.01). For patients with embryo transfer, ongoing pregnancy rates in the three groups were 56.3% (27/48), 60.3% (91/151), and 57.1% (28/49), respectively. However, in multivariate logistic regression analysis, only age and number of embryos transferred were associated with ongoing pregnancy rate. VD level had no association with pregnancy outcome [adjusted OR = 1.62 (95% CI: 0.68-3.88), P = 0.28, for Normal group; adjusted OR = 1.57 (95% CI: 0.78-3.19), P = 0.21, for Replete group. Reference = Deficient group].

CONCLUSIONS: VD level is negatively correlated with age. It seems that VD level has no impact on pregnancy outcome.

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IMPROVED LIVE BIRTH RATE FOLLOWING ANTIANTIBiotic TREATMENT FOR CHRONIC ENDOMETRIOSIS IN INFERTILE WOMEN WITH A HISTORY OF REPEATED IMPLANTATION FAILURE. K. Kitaya, a H. Matsubayashi, a Y. Takaya, a K. Yamaguchi, b Urology, Ishikawa Hospital, Himeji, Japan; aReproduction Clinic Osaka, Osaka, Japan; bUrology, Ishikawa Hospital, Himeji, Japan.

OBJECTIVE: The aim of this prospective study was to evaluate the prevalence of chronic endometritis (CE) in infertile women with a history of repeated implantation failure (RIF) and the effect of the antibiotic treatment on reproductive outcome in these patients.

DESIGN: RIF was defined as consecutive negative serum pregnancy tests on the 11th day after transfer of day 3 embryos or the 9th day after transfer of day 5 blastocysts (grade 1 or 2 according to Veeck’s classification) despite
transfer of three or more morphologically good day 3 embryos and/or day 5 blastocysts (3BB or above according to Gardner scoring system).

MATERIALS AND METHODS: The infertile women with a history of RIF underwent endometrial biopsy. CE was histopathologically diagnosed using immunohistochemistry for the placental marker CD138. Following the antibiotic treatment for CE, second-look/third-look endometrial biopsy and immunohistochemistry was performed to assess histopathologic cure rate. The cumulative live birth rate in the following embryo transfer cycles were prospectively compared between the treated RIF/CE group and the RIF/non-CE group (infertile women with RIF but not CE).

RESULTS: Three hundred thirty-five women met the diagnostic criteria of RIF: CE was diagnosed in 34.6% (116/335) of infertile women with a history of RIF. Of them, 115 patients (99.1%) desired for antibiotic treatment. The cumulative histopathologic cure rate of CE was 92.2% (106/115) following the first-line treatment (oral doxycycline, 200 mg/day, 14 days), and 99.1% (114/115) following the second-line treatment (a combination of oral metronidazole, 500 mg/day, 14 days and oral ciprofloxacin 400 mg/day, 14 days). The cumulative live birth rate in the first embryo transfer cycle (p = 0.044, odds ratio 1.69) and three embryo transfer cycles (p = 0.039, odds ratio 1.67) was significantly higher in the treated RIF/CE group (32.2%, 36/115 and 37.4%, 43/115, respectively) than in the RIF/non-CE group (22.0%, 45/205 and 26.3%, 54/205, respectively).

CONCLUSIONS: In this prospective observational study, we found CE in about one-third of infertile women with a history of RIF. The histopathologic cure rate and live birth rate following antibiotic treatment are encouraging in these patients.

P-368 Wednesday, October 19, 2016

DIFFERENTIAL EFFECT OF OVARIAN HYPERSTIMULATION ON THE SERUM PROGESTERONE LEVEL, EMBRYO QUALITY AND PREGNANCY RATES: AN ANALYSIS OF 3,767 IVF CYCLES. O. Oktem, a,b K. Yakin, a,b A. Isiklar, a,b A. Balaban, a,b B. Urman. a Obsterics and Gynecology, Koe University School of Medicine, Istanbul, Turkey; bWomen’s Health Center Assisted Reproduction Unit, American Hospital, Istanbul, Turkey.

OBJECTIVE: To investigate if there is any differential subgroup effect of ovarian stimulation on serum progesterone (P) level at ovulation trigger, embryo quality and pregnancy rates.

METHODS: A non-interventional, retrospective cohort data of a single center.

MATERIALS AND METHODS: 3,767 IVF cycles with GnRH agonist long protocol were included. Of these 2,971 were fresh and the remaining 796 were frozen ET IVF cycles. Nine different evenly spaced intervals were constructed for serum P level on the hCG day (<0.5 to 1.9 ng/mL), 2-2.4/2.5-2.9/3-3.4/3.5-3.9/4-4.5ng/mL). Then, the IVF cycles in these intervals were further divided into low (< 6 oocytes), normo (6-12 oocytes) and high-responders (>12 oocytes).

RESULTS: The CPR [from 45.7% to 23% (p = 0.033) and IR [from 17.1% to 7.6% (p < 0.001)] declined in a gradual and continuous fashion with the progressive rise of serum P on the hCG day from <0.5 to the 4.0-4.4ng/mL interval in the fresh cycles. Such a decrease was not observed in the CPR (61.5% vs. 65.4%, 54.5% vs. 44.3%, 15.6% vs. 15.0%, and IR (24.8% vs. 22.4%, 24.2% vs. 24.2%, 15.0% vs. 15.0%) of the frozen cycles. Serum P was significantly associated with the success of pregnancy (OR [95%CI]: 0.80 (0.73-0.88), p < 0.001) in the fresh but not in the frozen cycles (0.88 (0.75-1.31), p = 0.05). In the subgroup analysis of the fresh cycles, elevation of serum P level from <0.5 to the 4.0-4.4mg/mL interval caused a drastic decline in the CPR of the normo-responders (57% vs. 16.6%, respectively, p = 0.02) but not in the high-responders (52.1% vs. 33.2%, respectively, p = 0.04). In the low-responders, a smaller rise from <0.5 to 2.0-2.4mg/mL was sufficient to decrease the CPR from 24.2% to zero. On multivariate logistic regression analysis the threshold intervals detrimental to the pregnancy success were 1.5-1.9 for the low-responders, and 2.0-2.4 and 3.0-3.4 ng/mL for the normo and high-responders, respectively. The high-responders continued to produce grade-1 embryos in increasing numbers until serum P reaches the 3.0-3.4ng/mL interval whereas the corresponding intervals for the low and normo-responders were 2.0-2.4 and 2.5-2.9 ng/mL, respectively. Overall, there was a positive impact of the number of good-quality embryos transferred (up to 3) on the chance of pregnancy [(OR [95%CI]: 1.25 (1.17-1.34), p < 0.001)]. This effect was gradually diminished with rising serum P level and finally was lost at 3.0-3.4 ng/mL in the high-responders, and 2.5-2.9 and 2.0-2.4 ng/mL intervals in the normo and low-responders, respectively.

CONCLUSIONS: The detrimental effect of premature rise in serum P on the endometrial receptivity may begin gradually and still allow the implantation of good-quality embryos. This may also explain why high-responders are more capable of deterring the deleterious effect of premature rise in serum P on the pregnancy success than low and normo-responders.

P-369 Wednesday, October 19, 2016

FACTORS IMPACTING ENDOMETRIAL THICKNESS (EMT) AND OUTCOMES IN LETROZOLE INTRAUTERINE INSEMINATION (IUI) CYCLES. K. A. Green, a,b M. Evans, a I. Sasson, a,b C. S. Vale, a,b DeCherney, a,b K. Devine, a E. A. Widra, a M. J. Hill, a,b NIH- NICHD, Bethesda, MD; bOklahoma State University, Broken Arrow, OK; bShady Grove Fertility of PA, Wayne, PA; bLankenau Medical Center, Wynnewood, PA; bShady Grove Fertility Center, Washington, DC.

OBJECTIVE: To examine the effects of letrozole IUI cycle characteristics on EMT and clinical pregnancy.

METHODS: Letrozole IUI cycles from 2014-2015 in which letrozole was used alone or in combination with gonadotropins were identified. Analyzed variables included: letrozole alone vs. in combination with gonadotropins, exogenous estrogen use for endometrial development, patient age, serum estradiol (E2) concentration, number of follicles >14mm on day of hCG trigger, and postwash total motile sperm (TMS) count. The relationships between these variables and both EMT and clinical pregnancy were assessed. Statistical associations were determined using GEE models and ROC curves.

RESULTS: Of 890 cycles analyzed, 533 had EMT measured two days before IUI. The number of follicles >14mm was positively associated with EMT (P = 0.003) and exogenous estrogen use was negatively associated with EMT (P < 0.001), likely because patients with a thin endometrium were given supplementation. Serum E2 was not associated with EMT. Adjusted models demonstrated a positive association between both the number of follicles >14mm (OR 1.36, P = 0.009) and TMS (OR 1.01, P = 0.02) with clinical pregnancy. ROC curves showed that follicle number predicted clinical pregnancy (AUC = 0.6, P = 0.008), whereas EMT (AUC = 0.52) and serum E2 (AUC = 0.54) did not. In adjusted GEE models, age, serum E2, EMT, estrogen use, and gonadotropin use were not associated with clinical pregnancy. Clinical pregnancy rates were similar at any EMT >4mm, regardless of whether exogenous estrogen or gonadotropins were administered in addition to letrozole (Table). The sample size for EMT ≤4mm was too small to make any conclusions within this subgroup.

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FERTILITY OUTCOMES IN WOMEN WITH HYPOPITUITARISM (HP) WHO UNDERGO ART TREATMENT. J. Rodriguez-Purata,a L. Sekhon,a,b J. A. Lee,a M. C. Whitehouse,a A. B. Copperman,a,b B. Sandler,a,b aReproductive Medicine Associates of New York, New York, NY; aObstetrics, Gynecology and Reproductive Science, Icahn School of Medicine at Mount Sinai, New York, NY.

OBJECTIVE: Patients with HP face many reproductive challenges. A number of studies evaluating these patients reported sub-optimal outcomes both in terms of PRs and pregnancy outcome. While new-age fertility advancements have been thought to improve treatment outcome for these
Hypopituitarism (n=91) Controls (n=1235)

Age 33.9±4.6 (95% CI 32.9 – 34.8) 33.9±4.6 (95% CI 33.1 – 34.5)

BMI 21.7±4.5 (95% CI 20.5 – 22.8) 25.0±5.9 (95% CI 24.5-25.5)

Day +16 E2 905.4 (95% CI 433.4 – 948.1) 428.6±578.3 (95% CI 392.6-464.6)

Endometrium at surge 9.2±1.7 (95% CI 9.0 – 9.7) 10.2±1.6 (95% CI 10.1-10.3)

E2 at surge 2260.4±2201.6 (95% CI 2201.6-2319.2) 2173.9±2130.4 (95% CI 2130.4-2260.4)

Gestation age 38.0±3.3 (95% CI 37.1 – 38.8) 37.3±2.2 (95% CI 36.9-37.7)

P4 at surge 0.7±0.4 (95% CI 0.6 – 0.8) 1.0±0.6 (95% CI 1.0-1.0)

Preterm (<29 weeks) 29.3% (24/82) 31.1% (380/1235)

P4 3.7±1.9 (95% CI 2.7 – 3.5) 3.7±1.9 (95% CI 3.5-3.9)

Stim duration 10.6±2.3 (95% CI 10.1-10.9) 8.6±2.6 (95% CI 8.2-9.0)

<2500 gr) 52.7% (48/91) 51% (631/1235)

LH ±16 182.6±136.4 (95% CI 153.2 – 212.1) 188.5±143.2 (95% CI 144.0-156.1)

Day +1 LH 122.1±98.0 (95% CI 114.0-135.6) 128.3±95.2 (95% CI 120.5-136.1)

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FOLLICULAR TRACKING UNDER ULTRASOUND REVEALED OVULATION DEFECTS IN UNEXPLAINED INFERTILITY DURING NATURAL CYCLE. F. Guo. Center of Reproductive Medicine, Nantong University Affiliated Hospital, Nantong, China.

OBJECTIVE: Unexplained infertility (UI) was thought to have normal ovulation. To investigate if this is true, ovulation status of UI women were monitored by transvaginal ultrasonography (TVU) during natural cycle.

DESIGN: Prospective study.

MATERIALS AND METHODS: 567 UI women diagnosed with basic infertility were recruited to have TVU follicle tracking at an academic infertility center. Their menstrual cycle were all 26 to 30 days. The entire follicle development was monitored from day 10 of the cycle to the time of follicle rupture or to day 20 of the cycle. Follicle size was measured and recorded.

RESULTS: 421 out of 567 UI women finished 629 natural cycles follicle tracking. In addition to normal follicle size ovulation, three types of abnormal follicular development were observed: 1) no follicular growth in 28 cycles (4.5%); 2) ovulation with small follicles (OSF, follicle ovulate at less than 15 mm) in 65 cycles (10.3%); and 3) luteinated unruptured follicles (LUF) in 34 cycles (5.4%). A total of 127 abnormal ovulation cycles were observed in this study, accounting for 20.2% of 629 UI cycles. Based on follicle tracking and timed intercourse, in 502 normal follicle size ovulation cycles 74 women became pregnant while in 65 OSF cycles only 2 became pregnant. The pregnancy rate was 14.7% vs 3.1% (P <0.01). There was no pregnancy in the 34 LUF and 28 no follicle growth cycle.

CONCLUSIONS: This study shows ovulation dysfunction existed in UI patients. TVU Follicle tracking is a reliable way to monitor follicle development and ovulation. One cycle of TVU to evaluate ovulation status make the UI diagnosis more precise.

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THE FREQUENCY OF A SLIGHTLY INCREASED SERUM PROGESTERONE (P) RANGE OF 1.6 TO 1.9 NG/ML AT PEAK FOLLICULAR MATURATION PRIOR TO THE LUTEINIZING (LH) SURGE IN NATURAL CYCLES. J. H. Cheek1 J. R. Liss2.1 Dept. OB/GYN, Cooper Medical School of Rowan University, Melsrose Park, PA; Cooper Institute for Reproductive Hormonal Disorders, P.C., Mt. Laurel, NJ.
OBJECTIVE: Recently high powered studies from well known in vitro fertilization (IVF) centers have presented data showing that if the serum P is in the range of 1.6 to 1.9 ng/mL immediately prior to the human chorionic gonadotropin (hCG) injection, the pregnancy rates following embryo transfer (ET) will be reduced. The objective of the present study was to determine how frequent does this subtle rise in P occurs in natural cycles and does this range of P, presumably by advancing the window of implantation, have a negative impact on pregnancy outcome.

DESIGN: Prospective observational study.

MATERIALS AND METHODS: Beginning 18 days before expected menses serum estradiol (E2), P, and LH were measured on a daily basis in infertile women with regular menses until 2 days after the LH surge.

RESULTS: There were only 2 cases where the serum P exceeded 1.5 ng/mL in 80 cycles evaluated (2.5%). The P levels were 1.71 and 1.64 ng/mL. The woman with the higher P level conceived with just luteal phase support with vaginal P. She has successfully completed her second trimester.

CONCLUSIONS: Premature luteinization with serum P exceeding 2 ng/mL before the LH surge occurs but is uncommon. It was not known how common this more subtle rise in P occurs and whether it could be a cause of unexplained infertility. These data show that if such a range could cause occult infertility in natural cycles, it is uncommon. Furthermore, the fact that 1 of 2 had a successful pregnancy, despite attaining this P range, brings into question whether advancing the window of implantation related to a subtle rise in P is a cause of infertility at least on natural cycles. Based on these data, the study, which initial power analysis suggested 300 cases to be evaluated, was terminated at this point since it did not seem to be clinically important.

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OBJECTIVE: The biological actions of prolactin (PRL), a polypeptide hormone, are mostly related to lactation and reproduction. Hyperprolactinemia is associated with suppression of hypothalamic-pituitary-gonadal axis through the inhibition of the pulsatile secretion of gonadotropin releasing hormone (GnRH). Is one of the most common endocrine disorders causing female infertility and occurs in 30-40 % of infertile women (1,4). A monomer of 23 kDa is the bioactive fraction. However, there are others isoforms with low or absent bioactivity, as dimer or big-PRL (50 kDa) and macroprolactin (MPRL, 150-170 kDa)(5). Several clinical studies have demonstrated that macroprolactinemia occurring in 10-42 % of all cases of hyperprolactinemia (1). Usually, treated with dopamine agonists without discriminating whether the presence of MPRL, producing a sharp decrease of PRL levels. But it is unknown if a hypoprolactinemia could affect ovarian stimulation and embryo implantation (6,7). The objective of this work was to evaluate the prevalence of MPRL in infertile female patients.

DESIGN: Prospective observational study.

MATERIALS AND METHODS: 195 infertile women were screened for hyperprolactinemia and only serum PRL levels greater than 26 ng/mL were further studied for the presence of MPRL. The free PRL (f-PRL) was analyzed by a precipitation with polyethylene glycol (PEG) precipitation assay(8,9). We calculated the percentage of recovered prolactin (PRL-r%). The determination of PRL was performed by ECLIA ROCHE-(EIGH). Patients with risk factors for hyperprolactinemia were excluded. The results were expressed in percentage.

RESULTS: The age media was 35 (20-45). 18% of evaluated patients shown hyperprolactinemia. After precipitation of MPRL, 46% of diagnosed by hyperprolactinemia shown f-PRL <26 ng/mL. The median percentage of prolactin recovered was 71%. The prevalence of MPRL in infertile women was 8%.

CONCLUSIONS: MPRL presence is a significant cause of misdiagnosis, unnecessary investigation, and inappropriate treatment in patients with suspected hyperprolactinemia. PEG precipitation is useful to screen all patients with high PRL levels. As the bioactivity of MPRL is low or absent, the evaluation of f-PRL will be recommended. Further studies with larger groups of patients are needed to confirm these findings.

References:

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ACADEMIC PRODUCTIVITY IN THE CLINICAL RESEARCH/REPRODUCTIVE ENDORCINE SCIENTIST TRAINING PROGRAM (CREST): A 10-YEAR APPRAISAL. N. Santoro, a R. S. Usadi, a A. Christy, a A. J. Polotskys, a H. Zhang, a Obstetrics and Gynecology, University of Colorado School of Medicine, Aurora, CO; bReproductive Endocrinology and Infertility, Carolinas Healthcare, Charlotte, NC; cContraception Discovery and Development Branch, NIH, Rockville, MD; dUniversity of Colorado, Aurora, CO; eYale School of Public Health, New Haven, CT.

OBJECTIVE: To determine the academic productivity of Scholars who have completed the CREST Program.

DESIGN: Comparison of publication rates of CREST Scholars graduates based on current employment.

MATERIALS AND METHODS: 50 CREST Scholars who completed the program from 2006-2015 are included in the analysis. Scholar publications were culled from PubMed (editors and Letters to the Editor were removed). Comparisons were made between Scholar publications before and 2 years after completion of the program, and sorted by whether or not the Scholar had a current position in private practice or at an academic medical center. STATA version 10.1 was used to perform data analysis. Comparisons were performed using Wilcoxon matched pairs sign rank testing and t testing. Data are expressed as mean +/-SEM.

RESULTS: Overall Scholar productivity prior to CREST enrollment was 8.1 +/- 1.1 publications, and 5.9 +/- 1 publication afterwards. The rate of publications per year were also similar before and after completion of the program (0.83 vs 0.83 respectively). Of the 23 CREST Scholars who are currently in private practice, publication productivity after completion of the program was significantly reduced, with only 4 Scholars producing more publications after the program than before (P=0.0054). The 27 CREST Scholars who are currently in academic practice had similar numbers of publications before and after the CREST program (P=0.9234). There was a trend for Scholars who are in academic practice to have more publications prior to CREST compared to those in private practice (9.6 +/- 1.8 vs 6.4 +/- 1.3; P=0.17). After completion of CREST, Scholars in academic practice produced a mean of 9.3 +/- 1.6 publications, whereas those in private practice produced a mean of 1.9 +/- 0.7 publications (P=0.0002).

CONCLUSIONS: Being in academic practice appears to be a strong predictor of publication productivity after completion of the CREST program. The relatively high rate of pre-program publications likely reflects a burst of publications associated with fellowship training. There is opportunity to improve CREST program graduate productivity by providing more support to Scholar graduates who are in private practice positions.

Reference:
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VALIDATION OF THE ESTRADIOL ASSAY BY USE OF MASS SPECTROMETRY AND FOLLICULAR VOLUME. M. Peavey, N. Akbas, W. E. Gibbons, S. Devara. P. W. Zarutskie. Reproductive Endocrinology and Infertility, Ob/Gyn, Baylor College of Medicine, Houston, TX; Pathology and Immunology, Texas Childrens Hospital, Houston, TX. OBJECTIVE: The ability to accurately determine estradiol concentrations is important for clinicians to monitor ovarian stimulation and determine patient outcomes during IVF cycles. Estradiol values are a crucial component of clinical decisions, but there are limited studies demonstrating successful techniques for optimization of estradiol assays. The aim of this study is to compare estradiol values obtained with the current platform (ADVIA Centaur® CP Immunoassay system) to Abbott Architect i1000® Immunoassay system, using mass spectrometry (LC/MS/MS) as a gold standard, with correlation to parameters used in clinical decisions.

DESIGN: A total of 37 serum estradiol samples were prospectively collected from 10 patients undergoing ovarian stimulation for IVF.

MATERIALS AND METHODS: Total follicular volume (volume = 4/3πr²; r = radius of follicle) was calculated and serum estradiol measured using Centaur® and Architect i1000® assays, with LC/MS/MS as the gold standard. Comparison studies of estradiol to total follicular volume as well as estradiol follicular volume were performed. Regression fit (RF) and percent bias (PBIAS) were determined for Centaur® and Architect i1000® systems to report the average tendency of the simulated estradiol values to be larger or smaller than their observed value. Age, anti-Mullerian hormone level, and Society for Assisted Reproductive Technology (SART) diagnosis were also recorded.

RESULTS: Average patient age and AMH value were 34.5 (±2.9) yrs and 2.4 (±1.4) ng/mL, respectively. Reported estradiol ranged from 124 to 4000 pg/mL. When the comparison of estradiol to total follicular volume was performed via RF, Architect i1000® demonstrated a nearly perfect fit with the gold standard LC/MS/MS, while Centaur®CP consistently showed significantly higher estradiol values and slope. Furthermore, when considering the ratio of estradiol to follicular volume, Centaur®CP had a significant positive bias of 23.8%, while the Architect i1000® had a negligible 1.2% positive bias.

CONCLUSIONS: Optimization of an estradiol assay can be achieved with prospective collection and comparison across platforms, using LC/MS/MS as the gold standard. This study highlights the need for clinical awareness in evaluation of estradiol assays, supporting the recent Endocrine Society statement encouraging mass spectrometry for reliable estradiol measurement1. For clinicians, attention to assay quality assurance via mass spectrometry can improve estradiol accuracy, thus allowing more informed clinical decisions for improved patient outcomes.

Reference:

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OBJECTIVE: Expression of vascular endothelial growth factor (VEGF), produced by many tissues including the endometrium, ovary and trophoblast, is essential for proper embryo implantation and development of the placenta. To determine if the mode of fertilization influenced VEGF production at the time of embryo implantation we compared the release of VEGF into the systemic circulation shortly after embryo transfer in women whose oocytes were fertilized by ICSI or by conventional in-vitro fertilization (IVF).

DESIGN: Retrospective case-control study.

MATERIALS AND METHODS: Sera obtained 9-11 days after embryo transfer (cycle day 28) from 311 women who underwent an IVF cycle at our institution, 222 who had fertilization by ICSI and 89 with conventional in-vitro fertilization, were tested for VEGF, growth factors and cytokines by ELISA. Both groups underwent comparable stimulation protocols. The only criteria for sample selection was the availability of sera for analysis and complete clinical data including cycle outcome. Mediator levels as well as clinical variables in the two groups were compared by the Mann-Whitney and chi-square test.

RESULTS: Median serum VEGF levels were 117.4 (0-887) pg/ml in women whose oocytes were fertilized by ICSI as compared to 89.2 (0-602) pg/ml in women who underwent conventional IVF (p = 0.0188). Analyzing only women who became pregnant, median VEGF was 120.9 pg/ml vs. 93.1 pg/ml in the two groups (p = 0.0207). There were no differences between the two groups in maternal age, causes of infertility, number of oocytes harvested or fertilized and number of embryos transferred to the uterus. Pregnancy outcomes were also comparable in both groups. There were no differences in the concentration of any other mediator - interleukin (IL) -1 beta, IL-11, IL-13, insulin-like growth factor (IGF)-1, IGF binding protein-1, secretary leucocyte protease inhibitor, brain-derived neurotrophic factor - between the two groups.

CONCLUSIONS: The selective elevation in serum VEGF around the time of embryo implantation in women whose oocytes were fertilized by ICSI suggests that the direct injection of a spermatozoon into an oocyte may alter subsequent functions of the early stage embryo. This may be manifested by increased VEGF production and release by fetal trophoblasts and/or by an elevated ability of the preimplantation embryo to induce VEGF production by maternal endometrial cells. Further investigations are necessary to differentiate between these two possibilities. Elevated VEGF levels after IVF have been associated with ectopic pregnancy. However, the prevalence of this outcome was similar in both groups indicating that elevated VEGF as a result of ICSI is not a risk factor for ectopic pregnancy.

REPRODUCTIVE ENDOCRINOLOGY - RESEARCH

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INSULIN INDUCES OSCILLATING EXPRESSION OF CIRCADIAN GENE PER2 AND STEROIDAL ACUTE REGULATORY PROTEIN GENE IN HUMAN GRANULOSAL CELLS. M. Chen, Y. Xu, B. Miao, H. Zhao, J. Gao, C. Zhou. The First Affiliated Hospital of Sun Yat-sen University, Guangzhou, China; The Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, China.

OBJECTIVE: To explore the temporal effect of insulin on expression of circadian genes and steroidogenesis related genes in human luteinized granulosa cells.

DESIGN: Basic research.

MATERIALS AND METHODS: Human luteinized granulosa cells from patients who underwent in vitro fertilization treatment were purified and cultured in vitro for 9 days until they reach confluence prior to any treatment. Cells were exposed to insulin with a concentration of 4 IU/mL for 2 h and then cultured in serum-free medium until harvest. Samples were harvested every 4 h from the beginning of treatment until 48 h. The patterns of mRNA expression of the circadian genes CLOCK, PER2, and BMAL1, and the steroidogenesis-related genes STAR, CYP11A1, HSD3B2, and CYP19A1 in cultured human luteinized granulosa cells were analyzed over the course of 48 h after insulin treatment by quantitative polymerase chain reaction.

RESULTS: After insulin stimulation, expression of PER2 showed an oscillating pattern, with two peaks occurring at the 24th and 40th hour; expression of CLOCK increased significantly to the peak at the 24th hour, whereas expression of BMAL1 decreased to the bottom at the 20th h then increased to the peak at the 40th h over time in human luteinized granulosa cells. Among the four steroidogenesis-related genes evaluated, only STAR displayed an oscillating expression pattern with two peaks occurring at the 24th and 40th hours after insulin stimulation.

CONCLUSIONS: Our data point to a role of the insulin in the modulation of circadian rhythms in human luteinized granulosa cells. Moreover,
circadian clock may be related with steroidogenesis in human granulosa cells. Supported by: This work was supported by grants from the National Basic Research Program of China (2013CB94700), the Scientific Project of Health Industry (201002013) and the Science and Technology Planning Project of Guangdong Province, China (2008A030201028).

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RASD1 REDUCTION IS ASSOCIATED WITH REPEATED IMPLANTATION FAILURE. Y. Choi, M. Park, K. Choi, E. Han, E. Kim, H. Kwon, D. Choi.

OBJECTIVE: This study aimed to look into the expression of RASD1 in the uterine endometrium of RIF patients and its regulatory mechanism by estrogen in the uterus.

DESIGN: Experimental study using human sample and animal model.

MATERIALS AND METHODS: Blood and endometrial samples were collected from RIF patients and control women to check hormonal level and gene expression files for microarray analysis. Semi-quantitative RT-PCR was performed to verify its expression in human tissues. Adult ICR mice were used to look into expression of RASD1 using RT-PCR and western blotting analysis. Adult female mice were ovarioctomized and treated for examining the effect of hormones 17β-estradiol and progesterone by subcutaneous injection for various duration.

RESULTS: The expression of RASD1 was significantly reduced in the uterine endometrium of RIF patients compared to that of controls. RASD1 transcripts were highly expressed in female reproductive tissues including the uterus. The expression of RASD1 was significantly elevated in endometrial epithelium at the proestrus stage of the estrous cycle. The signal of RASD1 in the uteri of ovarioctomized mice was increased by estrogen (E2) treatment, but not by progesterone (P). Its expression was rapidly induced with the highest level at 2 hours after E2 treatment and significantly decreased by pretreatment of a nuclear estrogen receptor (ER) antagonist, ICI 182,780 in ovariectomized mice. The rapid expression of RASD1 was mediated by ER-ERK1/2 non-genomic signaling pathway.

CONCLUSIONS: Our results imply that RASD1 plays an important role in uterine modulation during the cycle and RASD1 expression is regulated by ER-ERK1/2 pathway during the cycle. Our findings will give us better understanding of the dynamic change of uterine remodeling during the estrous cycle and unknown RIF etiology.

References:

DO CHANGES IN STRICT KRUGER MORPHOLOGY AFTER SPERM PREPARATION FOR INTRAUTERINE INSEMINATION CHALLENGE ANYTHING TO PREDICTING CYCLE OUTCOME? C. F. Roman-Rodriguez, N. Virji, N. Fahmy, B. Pacaud, M. Bray, L. Sung, Obstetrics and Gynecology, Nassau University Medical Center, East Meadow, NY; Reproductive Specialists of New York, Mineola, NY; Reproductive Specialists of New York, Brooklyn, NY.

OBJECTIVE: To determine if improvement in morphology after sperm processing for intrauterine insemination changes outcome.

DESIGN: Prospective Study.

MATERIALS AND METHODS: Data was collected prospectively for 60 couples undergoing 101 cycles of intrauterine insemination (IUI). Criteria included women ≤40 years of age, day 3 AMH ≥1 and FSH ≤15, absent tubal disease, and absent endometriosis. Semen collected from the male partners was analyzed for sperm count, motility and morphology before and after sperm processing. Motile sperm were obtained by one-layer density gradient centrifugation and the pellet was washed and re-suspended in sperm wash. Only men who had a total motile sperm count(TMSC) ≥5 million and who were not on any sperm-enhancing medications were included. Clinical pregnancy (CPR) was confirmed by the presence of an intrauterine sac documented by ultrason. The categorical variables were compared with Pearson Chi-square tests, and binary logistic regression analysis was performed.
The effect of iron deposition on the ovary: iron suppresses granulosa cell proliferation and arrest cell cycle through regulating P38 MAPK/P53/P21 pathway. M. Chen, C. Chou, J. Yang, S. Chen, H. Ho, Y. Yang. Obstetrics and Gynecology, National Taiwan University Hospital, Taipei, Taiwan; National Taiwan University Hospital, Taipei, Taiwan; Obstetrics and Gynecology, National Taiwan University Hospital, Taipei, Taiwan.

Objective: Iron is an essential nutrient, but might be toxic when accumulated in the tissue causing cellular dysfunction. Little is known regarding the effect of iron load on gonadal function. In this study, we aimed to investigate the effect of iron on the ovarian follicle and granulosa cell proliferation.

Design: Human ovarian tissue sections and mice granulosa cell culture studies.

Materials and Methods: Forty-eight ovaries of 24 women derived from gynecologic surgeries were all sectioned for iron deposition detection by Prussian Blue staining and immunohistochemistry staining. Using primary mouse non-lutenized granulosa cells for in-vitro studies.

Results: Iron deposition around the ovarian follicles of the ovaries were more commonly seen in women with higher baseline body mass index (BMI) levels and history of oligomenorrhea and/or polycystic ovary syndrome (PCOS). Fe2+, but not Fe3+ that released from the iron depot significantly suppress the granulosa cell proliferation and arrest the cell cycle at G2/M phase. The increased expression of P21 and P53 by Fe2+ treatment in granulosa cell culture could be significantly suppressed by the treatment with P53 siRNA and P38 MAPK inhibitor, separately. Besides, using ROS inhibitor could down-regulate the enhanced P38 MAPK expression that was induced by Fe2+ in granulosa cells.

Conclusions: Iron depot could exist in the ovaries of women without primary iron overload syndrome. Obesity and history of PCOS/oligomenorrhea associate with the presence of iron deposition on ovaries. Fe2+ that released from the iron depot could directly arrest the cell cycle and inhibit the granulosa cell proliferation through regulating the ROS-mediated P38 MAPK/P53/P21 pathway. Our findings substantiate that the iron load in women may directly affect the gonadal function.

References:

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WESTERN-STYLE DIET (WSD) IN THE PRESENCE AND ABSENCE OF ELEVATED CIRCULATING ANDROGEN ALTERS OVARIAN STRUCTURE-FUNCTION IN YOUNG ADULT RHESUS MONKEYS. C. V. Bishop, T. Reiter, R. L. Stouffer. Division of Reproductive & Developmental Sciences, Oregon National Primate Research Center, Beaverton, OR; Obstetrics & Gynecology, Oregon Health & Science University, Portland, OR.

Objective: To evaluate the effects of chronic consumption of WSD in the absence and presence of mildly elevated testosterone (T) on ovarian structure-function after puberty.

Design: 2 by 2 factorial cohort; nonhuman primate model.

Materials and Methods: Female rhesus monkeys were either fed a normal balanced diet (n=20) or a WSD (n=20 [1]) from time of menarche (2.5 y of age) to 5.5 y of age. Estradiol (E2) levels were elevated by T (C vs T; P<0.016). There were no differences in the AUC of the E2 peak, or all E2 patterns, ovarian structure at menses by 3D/4D ultrasound (US [3]), and in a subgroup (n=6 group) vascular parameters of the corpus luteum (CL) at mid-luteal phase by contrast-enhanced US [4]. All data were analyzed by Linear Models function of SAS (v9.4).

Results: Ovarian size at menses tended to increase with exposure to WSD. Diet (P<0.07) and a WSD of antral follicles ≥1 mm was increased by WSD as a function of T exposure (Diet*Steroid; P<0.05). Compared to C, circulating LH (but not FSH) levels were elevated by T (C vs T; P<0.04), with a similar trend for WSD+T (P=0.09). Estradiol (E2) levels produced during the early follicular phase, as judged by area under the curve (AUC) were reduced by WSD as a function of T exposure (Diet*Steroid; P<0.016). There were no differences in the AUC of the E2 peak, or all E2 produced during the follicular phase (P=0.1). Nine to ten monkeys/group displayed elevated progesterone (P4) levels during week 3 of the menstrual cycle. However, luteal production of P4 (AUC) was reduced by exposure to the WSD (Diet; P<0.002), with the WSD+T group producing the least P4 (P<0.05). Blood volume was reduced in the CL by exposure to WSD (Diet; P<0.012), and CL vascular flow was reduced by WSD as a function of T exposure (Diet*Steroid; P=0.03), with the WSD alone group displaying the slowest luteal vascular flow (P<0.05).

Conclusions: After 3 years of treatment beginning at menarche, WSD in the presence and absence of mildly elevated T did not prevent ovarian cyclicity. However, changes in structure and steroidogenic function of the antral follicle cohort and the CL were observed in WSD and WSD+T groups. On-going studies utilizing this cohort will reveal if continued treatment exacerbates these effects, including selection and the steroidogenic or gametogenic function of the dominant follicle.

References:
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**IMMUNOLOGICAL, STRUCTURAL, AND STEM CELL CHARACTERISTICS OF SUBCUTANEOUS (SC) ABDOMINAL ADIPOSE IN LEAN POLYCYSTIC OVARY SYNDROME (PCOS) WOMEN VERSUS NORMOANDROGENIC OVULATORY (NL) WOMEN.** J. Phan, a V. K. Madrigal, a A. Guedikian, a X. Li, b D. A. Dumesc, a G. D. Chazenbalk, a OB/GYN, UCLA, Los Angeles, CA; aUCAL, Los Angeles, CA.

**OBJECTIVE:** To determine immunological (i.e., infiltrating adipose tissue macrophages [ATMs]), structural (i.e., extracellular matrix [ECM]) and stem cell (i.e. adipose stem cell [ASC] gene expression) characteristics of SC abdominal adipose in lean PCOS versus NL women.

**DESIGN:** Prospective Cohort Study

**MATERIALS AND METHODS:** Four lean (BMI, 19-25 kg/m²) Non-Hispanic, Caucasian women with PCOS by 1990 NIH criteria ages 21-32 years, and 4 BMI- and age-matched NL women were studied. Fixed histological sections of SC abdominal adipose were stained with markers of ATMs (CD68), ECM (COL1A1, TGFβ), and fibrosis (Masson-Trichrome [M-T], Sirius Red [SR]), digitally imaged using Aperio ScanScope and quantified by Definiens analysis. ASCs collected after SC adipose collagenase treatment and differential centrifugation were characterized as CD105(+) cells. Following RNA extraction, microarray analysis was performed using Affymetrix Human Genome U133 2.0 and data were analyzed using Ingenuity Pathway Analysis. Microarray data was confirmed by qRT-PCR.

**RESULTS:** There were no significant changes between PCOS and NL SC abdominal adipose in (i) ATMs (PCOS: 31.9 ± 20.0; NL: 60.3 ± 5.16 immunofluorescence [IF] units/area, mean ± SD, P = 0.3); (ii) ECM protein COL1A1 (PCOS: 38.1 ± 33.6; NL: 52.6 ± 39.5 IF units/area, P = 0.6); (iii) ECM TGFβ1 (PCOS: 34.0 ± 22.2; NL: 26.8 ± 13.1 IF units/area, P = 0.6); (iv) fibrotic marker M-T (PCOS: 48.1 ± 19.9; NL: 91.3 ± 46.0 M-T/area, P = 0.14); or (v) fibrotic marker SR (PCOS: 9.85 ± 4.3; NL: 13.2 ± 2.56 SR/area, P = 0.2). Microarray analysis of PCOS versus NL ASCs identified 9 up- and 17 down-regulated genes involving ECM organization, structure and development. Differential gene expression in lean PCOS versus NL ASCs showed a positive correlation with genes involving cardiovascular (CV) system and development, specifically angiogenesis (P = 1.7E-06) and vasculogenesis (P = 8.5E-04), with a trend of activation (z-scores, 1.35 and 1.30, respectively). qRT-PCR validated differential expression of 6 genes involved with CV system and development (ANKRD1 P = 0.03, CHISLI P = 0.009, F11R P = 0.03, TNC P = 0.0006, MYOCID P = 0.0002, NTN4 P = 0.01). Differential gene expression in lean PCOS versus NL ASCs showed a positive correlation with genes involved in CV disease (p = 1.89E-05).

**CONCLUSIONS:** Despite similarities between SC abdominal adipose of PCOS vs NL women in infiltrating ATMs, ECM proteins and fibrosis levels, abnormal gene expression in PCOS SC abdominal ASCs is associated with CV system development, specifically angiogenesis and vasculogenesis.

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**P-384** Wednesday, October 19, 2016

**ANTI-MULLERIAN HORMONE (AMH) AS A PREDICTOR OF POLYCYSTIC OVARY SYNDROME (PCOS): AGE AND BODY MASS INDEX (BMI)-STRATIFIED THRESHOLDS FOR DISTINGUISHING PCOS FROM CONTROLS USING AN IDENTICAL ASSAY.** M. Quinn, a C. Kao, a A. K. Ahmad, a M. Cedars, b N. Santoro, b E. Eisenberg, b D. J. Haisenleder, a R. S. Legro, a,d Department of Obstetrics, Gynecology and Reproductive Sciences, University of California, San Francisco, San Francisco, CA; bObstetrics and Gynecology, University of Colorado School of Medicine, Aurora, CO; bNICHD, Bethesda, MD; bUniversity of Virginia, Charlottesville, VA; bPenna State University College of Medicine, Hershey, PA; bFor the Reproductive Medicine Network, Bethesda, MD.

**OBJECTIVE:** Due to its consistent elevation in PCOS and correlation with polycystic ovarian morphology, AMH has been proposed as a marker of the disease. Prior studies reporting thresholds of AMH for a diagnosis of PCOS have been limited by small sample size, inappropriate control populations, and heterogeneous AMH assays. We sought to evaluate the accuracy of a standardized AMH assay as a predictor of PCOS diagnosis in an age and BMI-stratified analysis.

**DESIGN:** Cross-sectional cohort study.

**MATERIALS AND METHODS:** One hundred and nine patients with PCOS by Rotterdam Criteria, recruited between 2010-2015 from a tertiary academic center’s multidisciplinary PCOS clinic, and 286 subjects with PCOS, enrolled between 2009-2012 in the multi-site PPCOS II trial, had AMH levels determined by a central laboratory (ELISA immunossay, ANSH Labs). Controls included 245 participants in the Ovarian Aging (OVA) study, a community-based cohort of healthy, ovulatory women not seeking treatment for fertility who were enrolled between 2006-2010 and had AMH levels determined by the same laboratory with the same assay. Receiver operating characteristic analyses investigated the accuracy of using thresholds of AMH for prediction of PCOS diagnosis for the population at large and with stratification by age and BMI category. Youden’s J statistic was calculated to capture the performance of each threshold. Thresholds of AMH for distinction of PCOS from controls were selected by maximizing the youden statistic assuming a minimum sensitivity of 0.80.

**RESULTS:** The optimal threshold of AMH to distinguish Rotterdam PCOS from controls for the entire population was 7.75 ng/mL (sensitivity:0.82, specificity:0.78, youden:0.60). Thresholds of AMH trended downwards with increasing age and BMI.

**CONCLUSIONS:** To our knowledge, this is the largest analysis of AMH in patients with PCOS and appropriate controls. AMH level is an effective predictor of PCOS diagnosis. We demonstrate that thresholds of AMH for prediction of PCOS decreased among older age groups and among obese populations. Age and BMI-adjusted thresholds were more accurate predictors than an overall population-based threshold and may serve as an important tool in making appropriate PCOS diagnoses in women of varying age and BMI categories.

<table>
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<th>Age Category</th>
<th>BMI≤30</th>
<th>AMH Threshold (ng/mL)</th>
<th>Sensitivity, Specificity</th>
<th>Youden</th>
<th>AMH Threshold (ng/mL)</th>
<th>Sensitivity, Specificity</th>
<th>Youden</th>
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<td>(n=269)</td>
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<td>≥7.75</td>
<td>0.95, 0.57</td>
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<td>0.64, 0.84</td>
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PLATELET FACTOR 4 – AN ANTIANGIOGENIC CHEMOKINE THAT IS FIRST IDENTIFIED TO BE POSSIBLY ASSOCIATED WITH THE ABERRANT FOLLICULOCYGENESIS IN POLYCYSTIC OVARIAN SYNDROME. C. Huang, a C. Chou, b M. Chen, c S. Chen, d H. Ho, e Y. Yang. a Obstetrics and Gynecology Department, National Taiwan University Hospital, Taipei, Taiwan; a Obstetrics and Gynecology, National Taiwan University Hospital, Taipei, Taiwan; a National Taiwan University, Taipei, Taiwan; a National Taiwan University Hospital, Taipei, Taiwan; a Obstetrics and Gynecology, National Taiwan University Hospital, Taipei, Taiwan.

OBJECTIVE: In order to elucidate the underlying mechanism related to the abnormal follicular formation in polycystic ovarian syndrome (PCOS), a comprehensive analysis of the possible angiogenetic aberration and endothelial cell permeability was performed.

DESIGN: A case-control study.

MATERIALS AND METHODS: From 2014 to 2016, patients of PCOS who underwent in vitro fertilization-embryo transfer (IVF-ET) treatment at our hospital were enrolled. Patients who underwent IVF-ET treatment due to male factor infertility were selected as control group. After a period of controlled ovarian stimulation, follicular fluid (FF) was collected during oocyte retrieval. The influence of FF on endothelial cell permeability was evaluated by the monolayer human umbilical vein endothelial cells (HUVECs) permeability assay. The intrafollicular expression profiles of angiogenesis-related proteins were analyzed by Human Angiogenesis Protein Array Kit (R&D Systems, Inc. USA). Recombinant human PF4 (rhPF4) and anti-PF4 antibody were used to confirm the biological effect of intrafollicular PF4. The Mann-Whitney U test was performed for nonparametric analysis. The intrafollicular expression profiles of angiogenesis-related proteins and intrafollicular PF4 antibody were used to confirm the biological effect of intrafollicular PF4. The Mann-Whitney U test was performed for nonparametric analysis. The intrafollicular expression profiles of angiogenesis-related proteins and intrafollicular PF4 antibody were used to confirm the biological effect of intrafollicular PF4. The Mann-Whitney U test was performed for nonparametric analysis. The intrafollicular expression profiles of angiogenesis-related proteins and intrafollicular PF4 antibody were used to confirm the biological effect of intrafollicular PF4. The Mann-Whitney U test was performed for nonparametric analysis.

RESULTS: Pregnancy occurred in 80 subjects (50.5%), clinical pregnancies in 71 subjects (44.7%) and live births in 55 subjects (34.6%). Significant predictors of pregnancy included if 19 or more oocytes collected (OR: 0.46, CI 0.30-0.70), and grade of the embryos at transfer (OR: 0.44, CI 0.28-0.72). Subjects with better grade embryos and 19 or more oocytes collected were more likely to conceive. Significant predictors of clinical pregnancy included only maternal age (OR: 0.58, CI 0.40-0.84), with younger women more likely to conceive a clinical pregnancy. Significant predictors of live birth included 19 or more oocytes collected (OR: 0.64, CI 0.31-0.99), transferring embryos with 4 or more cells as compared to 3 or less (OR: 0.60, CI 0.38-0.82) and the grade of embryo at transfer (OR:0.57, CI 0.39-0.86), with higher grade embryos doing better.

CONCLUSIONS: In a relatively young cohort of PCOS women undergoing IVF, embryo quality and number of cells in the best predictor of pregnancy outcomes. Having a large number of oocytes is also an excellent predictor of success. This is likely due to the fact that the age of the cohort was young and devoid of many older women.

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IS ABERRANT HIPPO SIGNALING THE UNDERLYING ETOLOGY OF POLYCYSTIC OVARIAN SYNDROME? K. Maas, a,b S. Mirabai, a,b C. Chua, a,b A. Penzias, a,b P. M. Sweetnam, a,b K. C. Eggan, a,b D. Sakkas, a OB/GYN, REI Division, Beth Israel Deaconess Medical Center / Harvard Medical School, Boston, MA; a Boston IVF, Waltham, MA; a CellBridge LLC, Salem, MA; a Nano Terra Inc, Cambridge, MA; a CellBridge LLC, Bio-Medical Research, Salem, MA; a HSCRB, Harvard University, Cambridge, MA.

OBJECTIVE: To evaluate variances in the Hippo signaling pathway in patients with polycystic ovarian syndrome (PCOS) undergoing infertility treatment compared to baseline control patients without PCOS and without a diagnosis of infertility.

DESIGN: Gene expression analysis between study population and control population.

MATERIALS AND METHODS: Two study populations were identified: 1) patients with PCOS [Rotterdam Criteria] who were undergoing fertility treatment and 2) control oocyte donor and cryopreservation patients without a diagnosis of PCOS. Granulosa cells adherent to retrieved oocytes were trimmed, collected, and analyzed. Gene expression was measured using RT-qPCR and expression levels were normalized using standard housekeeping genes. Variations in the Hippo signaling pathway genes between two study populations were assessed using t-tests. ROC curve analysis was used to determine the predictive power of individual genes, all genes, and genes with statistically significant differences for the diagnosis of PCOS.

RESULTS: A total of 27 PCOS patients and 28 controls were analyzed. Gene expression variance with a p<0.05 was considered statistically significant. We identified multiple genes including, YAP1 and WWTR1, whose expression level in isolation and in combination in patients with PCOS was significantly different [range p<0.0001 to p=0.019] from control patient expression. PCOS patients exhibited a spectrum of phenotypic and clinical variations in 71 subjects (44.7%) and live births in 55 subjects (34.6%). Significant predictors of pregnancy included if 19 or more oocytes collected (OR: 0.46, CI 0.30-0.70), and grade of the embryos at transfer (OR: 0.44, CI 0.28-0.72). Subjects with better grade embryos and 19 or more oocytes collected were more likely to conceive. Significant predictors of clinical pregnancy included only maternal age (OR: 0.58, CI 0.40-0.84), with younger women more likely to conceive a clinical pregnancy. Significant predictors of live birth included 19 or more oocytes collected (OR: 0.64, CI 0.31-0.99), transferring embryos with 4 or more cells as compared to 3 or less (OR: 0.60, CI 0.38-0.82) and the grade of embryo at transfer (OR:0.57, CI 0.39-0.86), with higher grade embryos doing better.

CONCLUSIONS: In a relatively young cohort of PCOS women undergoing IVF, embryo quality and number of cells in the best predictor of pregnancy outcomes. Having a large number of oocytes is also an excellent predictor of success. This is likely due to the fact that the age of the cohort was young and devoid of many older women.

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PREDICTORS OF PREGNANCY OUTCOMES IN WOMEN WITH POLYCYSTIC OVARY SYNDROME WHO PERFORMED IN-VITRO MATURATION (IVM) OF OOCYTES. M. Dahan, a E. Hatirmaz, a S. Tan, a B. Ata, a A. Ozey, a M. Kanat-Pektas, a S. Hatirnaz. a Obstetrics and Gynecology Department, National Taiwan University Hospital, Taipei, Taiwan; a Obstetrics and Gynecology, National Taiwan University Hospital, Taipei, Taiwan; a National Taiwan University, Taipei, Taiwan; a National Taiwan University Hospital, Taipei, Taiwan; a Obstetrics and Gynecology, National Taiwan University Hospital, Taipei, Taiwan.

OBJECTIVE: Although much is known about predictors of pregnancy in IVF cycles, this analysis has yet to be performed in IVM cycles. Therefore, this study was done to determine factors which predict pregnancy clinical pregnancy and live birth after performing IVM of human oocytes.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: A retrospective analysis of 159 women with PCOS per the Rotterdam criteria, who underwent IVM between September 2007 and May 2014 was performed. Couples with severe male factor infertility were excluded from analysis. Logistic regression analysis was used to determine predictors of pregnancy outcomes. Subjects underwent IVM after 3 days of recombinant-FSH administration, 75 IU daily for 3 days, and hCG trigger 36-hours before oocyte retrieval, when the lead follicle was 10mm in diameter. Embryos were transferred fresh, day two after fertilization. Oocyte collection was performed per the McGill IVM protocol. Factors analyzed for significance include female age, duration of infertility, number of oocytes collected, number of cells in the transferred embryos and grade of the embryos transferred. Data is presented as odds ratio (OR) and confidence intervals (CI).

RESULTS: Pregnancy occurred in 80 subjects (50.5%), clinical pregnancies in 71 subjects (44.7%) and live births in 55 subjects (34.6%). Significant predictors of pregnancy included if 19 or more oocytes collected (OR: 0.46, CI 0.30-0.70), and grade of the embryos at transfer (OR: 0.44, CI 0.28-0.72). Subjects with better grade embryos and 19 or more oocytes collected were more likely to conceive. Significant predictors of clinical pregnancy included only maternal age (OR: 0.58, CI 0.40-0.84), with younger women more likely to conceive a clinical pregnancy. Significant predictors of live birth included 19 or more oocytes collected (OR: 0.64, CI 0.31-0.99), transferring embryos with 4 or more cells as compared to 3 or less (OR: 0.60, CI 0.38-0.82) and the grade of embryo at transfer (OR:0.57, CI 0.39-0.86), with higher grade embryos doing better.

CONCLUSIONS: In a relatively young cohort of PCOS women undergoing IVM, embryo quality and number of cells in the best predictor of pregnancy outcomes. Having a large number of oocytes is also an excellent predictor of success. Surprisingly, maternal age was not a consistent predictor of success. This is likely due to the fact that the age of the cohort was young and devoid of many older women.
of oligo-ovulation in some patients, especially those with normal body mass indices, and the need for careful stimulation and customized stimulation protocols for PCOS patients who have an increased risk of over-response and higher percentage of immature oocyte yield it is important to identify these patients prior to treatment. It may be possible to create a test using Hippo gene expression to identify patients with PCOS. Additionally, targeting this pathway with pharmacologic agents could potentially lead to non-surgical therapeutic options for PCOS.

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COMPARISON OF PREGNANCY OUTCOMES BETWEEN OBESE AND NON-OBESE POLYCYSTIC OVARY SYNDROME (PCOS) PATIENTS UNDERGOING IN VITRO FERTILIZATION (IVF) CYCLES. M. A. Clapp, H. E. Feil, E. Buyuk. Albert Einstein College of Medicine/Montefiore, M, Bronx, NY.

OBJECTIVE: PCOS is commonly associated with metabolic abnormalities and obesity. Obesity has been shown to have adverse effects on both assisted reproductive technology (ART) cycles and pregnancy outcomes. The primary objective of this study was to determine whether there was a difference in reproductive outcomes between obese and non-obese PCOS patients undergoing IVF. A secondary objective was to determine demographic and clinical factors that may predict clinical pregnancy among women with PCOS.

MATERIALS AND METHODS: Women (n = 79) meeting the Rotterdam PCOS criteria and undergoing IVF from 2007 to 2016 were included in the study. Data collected included baseline demographics, clinical parameters, and treatment outcomes. Obesity was defined as BMI ≥30 kg/m². Clinical pregnancy was defined as the presence of fetal heart beat on ultrasound. Bivariate analysis was done using Student’s t, Pearson’s chi-squared, and Wilcoxon rank sum tests as appropriate. Logistic regression and generalized estimating equations (GEE) were performed to control for confounding variables and to account for multiple cycles from the same patients.

RESULTS: A total of 108 IVF cycles (obese group n = 63 and non-obese group n = 45) were included in the analysis. Baseline demographics and clinical parameters were similar when examining pregnant versus non-pregnant women except for age (32.3 ± 35 years old, p = 0.007), baseline antral follicle count (AFC) (24.1 ± 17.7, p = 0.003), and progesterone level on day of trigger (0.6 ± 0.8 ng/mL, p = 0.06). The obese group had lower serum peak estradiol level (1898 vs. 2623 pg/mL, p = 0.001), required more total gonadotropins (2907 vs. 2187 units, p < 0.001), and needed a longer stimulation course (11.7 vs. 10.6 days, p = 0.02) compared to the non-obese group. After adjusting for confounding variables, the pregnancy rates were similar in the obese (37.5%) compared to the non-obese group (41.7%) (p = 0.7). After adjusting for age and serum progesterone level on day of trigger, AFC was the only significant predictor of clinical pregnancy (OR 2.1, 95% CI 1.1-4.1; p = 0.02).

CONCLUSIONS: Obesity does not affect clinical pregnancy rates in PCOS patients undergoing IVF. On the other hand, AFC seems to be associated with clinical pregnancy in PCOS patients. Further investigation is needed to determine if AFC is an accurate predictor of clinical pregnancy in women with PCOS.

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VITAMIN D DECREASES SERUM VEGF LEVELS CORRELATING WITH CLINICAL IMPROVEMENT IN VITAMIN D-DEFICIENT WOMEN WITH PCOS: A RANDOMIZED PLACEBO-CONTROLLED TRIAL. M. Irani,1 R. Seifer,2 R. V. Grazi,2 S. Irani,2 R. Tal.4 Weill Cornell Medicine, New York, NY; 2Dartmouth-Hitchcock Medical Center, Lebanon, NH; 3Maimonides Medical Center, Brooklyn, NY; 4SUNY Downstate Medical Center, Brooklyn, NY; 5Yale University School of Medicine, New Haven, CT.

OBJECTIVE: Polycystic ovary syndrome (PCOS) affects ~10% of reproductive-aged women. There is an abnormal increase in serum vascular endothelial growth factor (VEGF) levels in PCOS, which has been suggested to play a role in the pathophysiology of this syndrome and its closely related ovarian hyperstimulation syndrome. Women with PCOS have higher incidence of vitamin D (VD) deficiency, and VD supplementation has been shown to improve multiple clinical parameters of PCOS. VD decreases VEGF levels in several diseases such as preeclampsia, endometriosis, and diabetic retinopathy. Thus, we aimed to explore the possible effect of VD supplementation on VEGF levels in women with PCOS and assess whether changes in VEGF levels correlate with an improvement in their clinical manifestations. This is an extension of our previous study showing in the same patient cohort that transforming growth factor-β1 bioavailability decreases following VD treatment (Irani et al. JCEM 2015).

DESIGN: Prospective randomized placebo-controlled trial (RCT).

MATERIALS AND METHODS: The study was conducted from October 2013 to January 2015 involving 93 VD-deficient (25-hydroxyvitamin D < 20 ng/mL) women with PCOS who were not pregnant or taking any exogenous hormone. 54 participants completed the study: 36 women received 50,000 IU of oral vitamin D3 and 18 women received oral placebo once weekly for 8 weeks. The clinical parameters were evaluated before and four months after treatment. Serum VEGF levels were measured before and after treatment by ELISA. The changes in VEGF levels were correlated with changes in the clinical parameters following VD supplementation. Values were expressed as mean ± SEM. Paired t-test and Pearson correlation were used as appropriate.

RESULTS: There was a significant decrease in serum VEGF levels (1106.4 ± 65.4 to 965.3 ± 42.7 pg/mL, p < 0.001) in the VD group, but not in the control group (893.1 ± 90.2 to 866 ± 70.8 pg/mL, p = 0.83). The findings of this RCT previously reported a significant decrease in the interval between menstrual periods, Ferriman-Gallwey hirsutism score (FGS), and serum triglyceride levels after VD supplementation but not other parameters measured (androgens, fasting glucose, insulin, total cholesterol). Interestingly, 1,25(VD)2 was positively correlated with VEGF (r = 0.17, p = 0.02) following VD supplementation. There was no significant correlation between 1,25(VD)2 and FGS (p = 0.25) or menstrual interval (p = 0.7).

CONCLUSIONS: VD supplementation significantly decreases serum VEGF levels in VD-deficient women with PCOS, which correlates with an improvement in some abnormal clinical parameters associated with PCOS. This is a novel molecular explanation for the beneficial role of vitamin D replacement. These data may support new therapeutic approaches for PCOS such as anti-VEGF drugs or VD supplementation.

Reference:

Supported by: Internal fund.

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OBJECTIVE: Despite the known association between PCOS and both mood disorders and metabolic risk factors, there is limited information on the additional benefits of treatment of depression/anxiety on weight and metabolic outcomes. Our objective was to compare the effects of cognitive behavioral therapy (CBT) and lifestyle management (LS) vs. LS alone in women with PCOS with depressive symptoms.

DESIGN: 16 week randomized clinical trial of CBT+LS vs LS.

MATERIALS AND METHODS: Overweight/obese women with PCOS 18-45 years who screened positive for depressive symptoms were randomized to receive CBT+LS (n = 36) or LS (n = 54) treatment. Both groups received weekly LS x16 weeks. Subjects completed weekly LS x16 weeks. The clinical parameters were evaluated before and four months after treatment. Serum VEGF levels were measured before and after treatment by ELISA. The clinical parameters were evaluated before and four months after treatment.

RESULTS: A total of 108 IVF cycles (obese group n = 63 and non-obese group n = 45) were included in the analysis. Baseline demographics and clinical parameters were similar when examining pregnant versus non-pregnant women except for age (32.3 ± 35 years old, p = 0.007), baseline antral follicle count (AFC) (24.1 ± 17.7, p = 0.003), and progesterone level on day of trigger (0.6 ± 0.8 ng/mL, p = 0.06). The obese group had lower serum peak estradiol level (1898 vs. 2623 pg/mL, p = 0.001), required more total gonadotropins (2907 vs. 2187 units, p < 0.001), and needed a longer stimulation course (11.7 vs. 10.6 days, p = 0.02) compared to the non-obese group. After adjusting for confounding variables, the pregnancy rates were similar in the obese (37.5%) compared to the non-obese group (41.7%) (p = 0.7). After adjusting for age and serum progesterone level on day of trigger, AFC was the only significant predictor of clinical pregnancy (OR 2.1, 95% CI 1.1-4.1; p = 0.02).

CONCLUSIONS: Obesity does not affect clinical pregnancy rates in PCOS patients undergoing IVF. On the other hand, AFC seems to be associated with clinical pregnancy in PCOS patients. Further investigation is needed to determine if AFC is an accurate predictor of clinical pregnancy in women with PCOS.
Gender and ethnic differences in overall DNA methylation at CpG sites have been observed, suggesting the existence of sex-specific methylation profiles. This study aimed to identify sex-specific DNA methylation signatures in ovarian tissues of women with polycystic ovary syndrome (PCOS) and women without PCOS.

**MATERIALS AND METHODS:** Fresh ovarian tissue was obtained from women undergoing laparoscopic wedge resection (n=17), and samples were analyzed using the Human Genome U133 Plus 2.0 Array. DNA methylation profiling was performed using the Infinium HumanMethylation450 BeadChip and Affymetrix GeneChip Operating Software. Differential methylation analysis was conducted using the LIMMA package in R software.

**RESULTS:** A total of 54 genes were identified with methylated levels that were correlated with transcriptional expression in PCOS ovaries. These genes were further verified by pyrosequencing. Notably, PCOS ovarian tissues exhibited a significant difference in DNA methylation status of DDB2, KCNMA1, CCL2, fibrillin 1 gene (unpublished data), and TNIK gene (published data). In addition, our previous study suggested that several significant pathways, including the type I diabetes mellitus pathway, p53 signaling pathway, and NOD-like receptor signaling pathway, may be involved in PCOS development. However, recent studies further indicated that the functional significance of type I diabetes mellitus pathway, p53 signaling pathway, and NOD-like receptor signaling pathway may play an essential and nonredundant role in PCOS.

**CONCLUSIONS:** Our preliminary results show that differences in genome-wide DNA methylation and expression patterns exist between PCOS ovaries and normal ovaries. The results indicate that epigenetic mechanisms may play a significant role in the pathogenesis of PCOS.
volume (OV) > 10 cm³. The data to support either of these specific cutoffs is limited and neither account for age, which is known to impact ovarian features over time. These thresholds were recently re-evaluated in 2014 by Androgen Excess and PCOS (AE-PCOS) Society, leading to a proposal for FNPO ≥ 6.5 cm³ and OV > 10 as new thresholds. Using a large population of women with National Institutes of Health (NIH) PCOS and community controls, we examined the diagnostic performance of FNPO and OV in predicting PCOS overall and across age groups.

**DESIGN:** Cross-sectional.

**MATERIALS AND METHODS:** Women seen in a multidisciplinary PCOS clinic from 2006-2015 who were diagnosed with PCOS by NIH criteria were consented and considered for inclusion. Comparison controls were from the Ovarian Aging (OVA) study, a longitudinal study with a cohort of healthy women without PCOS. FNPO and OV measurements were conducted by transvaginal ultrasound, by the same physicians and equipment. Receiver operating characteristic (ROC) curves were created for both maximum (max) FNPO and OV based on age groups. Age groups were divided into 5-year increments (25 to 40 years old (y)0). Youden’s distance was used for each curve to find the optimal max FNPO and OV threshold.

**RESULTS:** 245 PCOS patients were included in the FNPO analysis and had mean max FNPO 22.6 ± (12.4). 756 OVA patients with mean max FNPO 10 ± (5.3) were also included. The overall threshold was FNPO > 13. There was a decreasing trend seen with the age groups (>15, >14 and >12, respectively).

297 PCOS patients were included in the OV analysis and had mean max OV of 10 cm³ ± (5). 756 OVA patients with mean max OV of 6.5 cm³ ± (5) were also included. The overall threshold was OV > 6.75 cm³. There was a decreasing trend seen with the age groups (>10, >7, and >6.25 cm³, respectively).

**CONCLUSIONS:** Our findings reflect that the appropriate diagnostic cutoff for PCO changes over time, as max FNPO and OV thresholds trend downwards with increasing age. We propose age-specific thresholds for FNPO and OV that would allow for better diagnostic performance of PCOS compared to the uniform thresholds currently being used with Rotterdam criteria and AE-PCOS.

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**WESTERN-STYLE DIET (WSD) IN THE PRESENCE AND ABSENCE OF ELEVATED CIRCULATING ANDROGEN ALTERS HORMONE RESPONSIVENESS IN THE RHESUS MACAQUE ENDOMETRIUM.** O. D. Slayden, C. V. Bishop, E. Thompson, R. L. Stouffer. Division of Reprod. & Develop. Sciences, Oregon National Primate Research Center (ONPRC), Oregon Health & Science University (OHSU), Beaverton, OR.

**OBJECTIVE:** To evaluate the effects of a WSD in the absence and presence of mildly elevated testosterone (T) on endometrium structure and hormone responsiveness.

**DESIGN:** 2 by 2 factorial in a nonhuman primate model.

**MATERIALS AND METHODS:** 40 female rhesus macaques were either fed a normal monkey diet or a WSD [1] from time of menarche (2.5 y) through 5.5 y of age (3 years on study). They also received SC capsules of cholesterol or T, which elevated serum T 3-4 fold [2]. This resulted in 4 treatment groups, controls (C), C and WSD (n=10/group). Menstrual cyclicity was monitored daily by vaginal swab. At ~5 y of age, endometrial volume was assessed by 3D/4D ultrasound in the late follicular and mid luteal phase of the cycle (n=6/group). TruCut needle biopsies of endometrium (C, n=4; T, n=7; WSD, n=4 WSD +T, n=8) were collected from animals in the mid luteal phase (6-8 d after ovulation). Biopsies were analyzed by immunohistochemistry for estrogen receptor 1 (ESR1) progesterone receptor (PGR), androgen receptor (AR) and cell proliferation (Ki-67). Numeric data were analyzed by Linear Models function of SAS (v9.4).

**RESULTS:** There was no significant effect of treatment on menstrual cyclicity and uterine size was within the normal range for all animals. Endometrial volume was greater in the luteal phase than follicular phase for all groups (P<0.01). This increase in endometrial volume from follicular to luteal phase was slightly greater in the WSD+T group (P=0.13). All groups displayed strong nuclear staining ESR1, and PGR, and abundant Ki-67 positive cells in the glands of the basalis zone. As expected for the luteal phase, C and WSD groups displayed secretory glands with decreased glandular staining for ESR1 and PGR in the functionalis and retained PGR in the stroma. In contrast, treatment with T and WSD+T resulted functionalis zone glands with a less secretory morphology, ESR1 retained in the glandular epithelium, and PGR absent from the functionalis zone. Treatment with WSD+T resulted in the presence of more Ki-67 positive cells in the glands of functionalis zone (P=0.15). AR staining was observed in the endometrial stromal only from all groups, but AR staining was notably stronger in animals treated with T and WSD+T.

**CONCLUSIONS:** Pregesterone in the luteal phase downregulates ESR1 and PGR in the glands of the endometrial functionalis zone. Failure of progesterone to suppress and PGR indicates a mild dysregulation of normal hormone action in animals exposed to mildly elevated levels of T or WSD+T. The absence of suppression of cell proliferation in the basalis zone supports the observation that endometrial volume was not different between groups. On-going studies will determine if hormonal dysregulation of functionalis zone will alter fertility of these animals.

**References:**

Supported by: SUPPORT: P50HD071836 (RLS; ODS), P51OD011092 (ONPRC).
HYPERANDROGENIC ENVIRONMENT CAUSES IMPAIRED GLUT EXPRESSION AND GLUCOSE METABOLISM IN HUMAN ENDOMERIUM. J. Yoon, M. Lee, K. Choi, E. Kim, H. Song, D. Choi. "Fertility Center of CHA Gangnam Medical Center, Seoul, Korea, Republic of; Obstetrics and Gynecology, CHA Bundang Medical Center, Seongnam-si, Gyeonggi-do, Korea, Republic of; Fertility Center, CHA Bundang Medical Center, CHA University, Seongnam-si, Gyeonggi-do, Korea, Republic of; CHA Seoul Fertility Center, CHA University, Seoul, Korea, Republic of.

OBJECTIVE: Polycystic ovary syndrome (PCOS) is a common endocrine and metabolic disorder characterized by chronic anovulation, hyperandrogenism, and frequently accompanying insulin resistance and hyperinsulinemia. However, a comprehensive investigation of the consequence of PCOS on endometrial homeostasis and pathophysiology has not been undertaken. In this study, we investigated whether hyperandrogenic condition impairs the expression patterns of facilitated glucose transporters (GLUTs) as well as factors associated with insulin signaling pathway in human endometrial stromal cells (hESCs) during in vitro decidualization and endometriosis of patients with PCOS.

DESIGN: Experimental study using human endometrial tissues and a human endometrial cell line.

MATERIALS AND METHODS: In vitro decidualization was induced in hESCs purchased from ATCC (CRL-4003) when cultured with 0.5 mM and 1 mM medroxyprogesterone-17-acetate for 3-9 days. In order to mimic the condition of hyperandrogenism in patients with PCOS in vitro, hESCs were treated with 1, 10, or 100 μM dihydrotestosterone (DHT) for 4 weeks. mRNA and protein experiments were performed for hESCs treated with 10 μM DHT and data were analyzed by GSEA. Seven healthy women and 18 patients with PCOS were recruited for this study. The control endometrium was biopsied in the proliferative phase due to morphologic and physiologic similarities to that of patients with PCOS. RT-PCR, realtime RT-PCR and/or western blotting were performed.

RESULTS: DHT significantly disturbed mRNA expression of PRL and IGFBP1, well-known decidualization markers, and morphological changes during in vitro decidualization. Among GLUTs, expression levels of GLUT1 and two insulin-dependent GLUTs, GLUT8 and GLUT12, were gradually increased during in vitro decidualization. However, protein and mRNA levels of GLUT1 and GLUT12 were significantly decreased in decidualizing cells treated with DHT. Impaired GLUT expression and in vitro decidualization by DHT were partially restored by flutamide, an androgen receptor antagonist. mRNA microarray data reinforced that hyperandrogenic condition interferes with glucose metabolism. Furthermore, cell cycle regulators are systemically decreased in this condition. In endometria of patients with PCOS, GLUT1, GLUT12, and IRS1 were significantly increased. Interestingly, there is any difference with respect to their expression between endometria of obese and lean patients with PCOS.

CONCLUSIONS: Hyperandrogenic environments by PCOS could impair decidualization and dysregulate expression profiles of GLUTs as well as glucose metabolism in the endometrium.

References:
3. Youla D, Bhide P, W. Huang. Department of Obstetrics & Gynecology, West China Second University Hospital of Sichuan U, Chengdu, China.

OBJECTIVE: To compare the therapeutic efficacy of clomiphene citrate (CC) and Letrozole (LE) on ovulation, pregnancy, and live birth in women with polycystic ovary syndrome (POCS) and to ensure if LE can replace CC as the first line therapy for ovulation induction in women with PCOS.

DESIGN: A prospectively, randomized, controlled trial (Chinese Clinical Trial Registry Center Registration Number ChiCTR-TRC-11001821) in the tertiary hospital.

MATERIALS AND METHODS: Two-hundred and sixty-eight anovulatory PCOS patients were treated by CC or CC plus Metformin and LE or LE plus Metformin for three continuous cycles or conception; their ovulation rate, pregnancy rate, and live birth rate were calculated and compared.

RESULTS: No significant difference was noted among the four groups regarding the baseline data of clinical manifestations, serum sex hormone levels, and serum insulin levels. A total of 240 patients completed therapies. The ovulation rate was significantly higher in group LE than in group CC; however, no significant difference was noted between the groups CC and LE, CC and CC + MET, or LE and LE + MET with respect to the pregnancy rate, abortion rate, and live birth rate. No birth defect was found in a total of 63 newborns.

CONCLUSIONS: Though LE might increase the ovulation rate, no significant difference was found with the CC treatment regarding the pregnancy rate, abortion rate, or live birth rate. Therefore, CC regimen might be the first-line induction for PCOS.

Key words: Polycystic ovary syndrome, induced ovulation; clomiphene citrate, letrozole, metformin.
P-398 Wednesday, October 19, 2016

SEXUAL FUNCTION IN POLYCYSTIC OVARY SYNDROME: A SYSTEMATIC REVIEW AND META-ANALYSIS. W. J. Walker, D. L. Lizenne, L. Gavrilova-Jordan, L. E. Blake, S. Brakta, I. Atabayev, L. V. Suturina, M. P. Diamond, R. Aziz. Obstetrics and Gynecology, Augusta University, Augusta, GA; OB&GYN, Georgia Regents University, Augusta, GA; Libraries, Augusta University, Augusta, GA; Augusta University, Augusta, GA; General Surgery, Maykop, Russian Federation; Laboratory of Gynecological Endocrinology, Scientific Center of Family Health and Human Reproduction, Irkutsk, Russian Federation; OB/GYN, and Medicine, Augusta University, Augusta, GA.

OBJECTIVE: Changes in self-image related to obesity, hirsutism, acne (1) as well as depression and anxiety (2,3) associated with PCOS appear to have negative effects on sexual health. Alternatively, higher androgen levels found in PCOS women may actually improve libido (4). Currently published data are based on under-powered studies and results are often inconclusive; therefore, pooled data is needed. The purpose of our study is to determine differences in sexual function between women with and without PCOS.

DESIGN: Systematic review and meta-analysis.

MATERIALS AND METHODS: Electronic databases (MEDLINE through PubMed, EMBASE, Web of Science, LILACS, Cochrane Library, CINAHL, and PsycINFO) were searched through October 2015. Search terms included: polycystic ovarian syndrome, PCOD, PCOS, quality of life, sexual dysfunction, sexual function, and other relevant subject or thesaurus terms. Observational studies reporting sexual function of PCOS vs unaffected subjects were considered. Data was extracted using a web-based, piloted form. The inverse variance method, based on a random or fixed effects model (Review Manager, Version 5) was used to analyze the data. Data from eligible studies was independently extracted by two reviewers.

RESULTS: The original search yielded 880 publications. Hand searching of titles and abstracts was conducted to exclude articles which did not focus on PCOS and quality of life or sexual function. Duplicates were removed, yielding a total of 431 articles. These articles were reviewed, and eight comparative studies were identified (428 PCOS women and 423 controls) in the systematic review. The pooled analysis revealed no significant differences between PCOS and controls in sexual desire (SMD -0.01; 95% CI: -0.43, 0.42; Z=0.02, p=0.98); lubrication during intercourse (SMD -0.20; 95% CI -0.43, 0.03; Z=1.73, p=0.08); orgasm (SMD -0.11; 95% CI -0.34, 0.12; Z=0.95, p=0.34); satisfaction (SMD -0.40; 95% CI -0.94, 0.14; Z=1.45, p=0.15); pain during intercourse (SMD -0.12, 95% CI -0.25, 0.48; Z=0.62, p=0.53); and total sexual function score (SMD -0.20; 95% CI -0.43, 0.03; Z=1.73, p=0.08). PCOS patients had less arousal scores then controls (SMD -0.26; -0.49, -0.04; Z=2.27, p=0.02).

CONCLUSIONS: Our systematic review, though based on the limited comparative data, suggests that women with PCOS, compared to controls, have some degree of impairment in the domain of sexual arousal, but little evidence of any other sexual dysfunction. Additional well designed studies are needed.


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PHENOTYPIC MARKERS OF POLYCYSTIC OVARY SYNDROME AND FECUNDITY. A. J. Gaskins, J. Rich-Edwards, S. Mahalingiah, S. A. Missmer, J. E. Chavarro. Department of Nutrition, Harvard T.H. Chan School of Public Health, Boston, MA; Brigham and Women’s Hospital, Boston, MA; Obstetrics and Gynecology, Harvard T.H. Chan School of Public Health, Boston, MA; Obstetrics, Gynecology and Reproductive Biology, Brigham and Women’s Hospital and Harvard Medical School, Boston, MA.

OBJECTIVE: To examine the relationship between phenotypic markers of polycystic ovary syndrome (PCOS) and fecundity.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: Our study included 2,213 women currently attempting pregnancy in the Nurses’ Health Study 3 (2010-2016). Self-reported information on physician diagnosed PCOS, body hair severity (scored from 0-4) at 6 locations (chin, upper abdomen, lower abdomen, thigh, chest, and lip), menstrual cycle regularity and length, and acne severity was assessed on the second questionnaire. Every 3-6 months thereafter, women reported the current duration of their pregnancy attempt. A total body hair score was calculated by summing across the 6 body hair locations (range 0-24). Multivariable-accelerated failure time models were used to estimate the time ratios and 95% confidence intervals (CIs) adjusting for age, smoking, marital status, race, and BMI.

RESULTS: Women in this cohort were, on average, 35 years old (range: 24-48 years), 94% Caucasian, 77% never smokers, with a mean BMI of 25.9 kg/m² (range: 15.8-64.5 kg/m²). Women self-reporting a diagnosis of PCOS (9.2%) had a 73% (95% CI 49, 101%) longer current duration of pregnancy attempt. In regards to phenotypic characteristics of PCOS, body hair, acne, and menstrual cycle function were all associated with fecundity. A 3-unit increase in severity of body hair across all locations was association with a 6% (95% CI 2, 10%) longer current duration of pregnancy attempt. Out of the 6 locations, severe body hair on the chin was associated with the largest fecundity impairment (TR= 1.34 95% CI 1.03, 1.72). Women with 1-4 pimples (60%) or ≥5 pimples (15%) had 13% (95% CI 2, 25%) and 36% (95% CI 18, 58%) longer current durations of pregnancy attempt respectively compared to women with no current acne. Finally women with always irregular cycles (69%) had 37% (95% CI 8, 74%) longer current duration of pregnancy attempt compared to women with very regular cycles.

CONCLUSIONS: Phenotypic characteristics of PCOS including body hair, acne, and irregular menstrual cycle function are all associated with reduced fecundity.

Supported by: Supported by a grant from the Breast Cancer Research Foundation and NIH grant L50-HD08539.

P-400 Wednesday, October 19, 2016

COMPARISON OF FRESH VERSUS PREVIOUSLY FROZEN EMBRYO TRANSFER IN WOMEN WITH POLYCYSTIC OVARY SYNDROME. O. S. Abdalmageed, T. A. Farghaly, I. Elbashir, A. M. Ismail. Assiut University IVF Center, Assiut, Egypt; Obstetrics and Gynecology, Assiut University IVF Unit, Assiut, Egypt; Assiut University, Assiut, Egypt; Obstetrics and Gynecology, Women’s Health Hospital, Assiut, Egypt.

OBJECTIVE: The objective of our study was to examine the difference in the clinical pregnancy and live birth rates in fresh in vitro fertilization (IVF) cycles compared to previously frozen embryo cycles in women with polycystic ovary syndrome (PCOS).

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Clinical records were examined for all women with PCOS aged 40 years of age who underwent IVF cycles in a private university center during the years 2010 through 2014. The study population was restricted to the women with cleavage stage ET (day 2 or 3 embryos). Cycles complicated by ovarian hyperstimulation syndrome (OHSS) were excluded. Cycles were divided into two groups: fresh embryo transfer and previously frozen embryo transfer. Primary outcome measures were clinical pregnancy and life birth rates. Secondary outcomes were miscarriage and multiple pregnancy rates. Statistical analysis was performed using chi-square analysis and student t-tests.

RESULTS: A total of 121 cycles were included in the study: 62 fresh and 59 previously frozen cycles. Both groups were comparable regarding age, body mass index (BMI), basal follicular stimulating hormone (FSH), Anti-mullerian hormone (AMH), and antral follicle count (AFC) (Table 1). Estradiol levels were higher in the fresh group than in the previously frozen group (Table 2). Fresh embryos had a higher pregnancy rate compared to previously frozen embryos. The miscarriage rate and the multiple pregnancy rate were similar in both groups. (Table2)

CONCLUSIONS: In women with polycystic ovary syndrome (PCOS) undergoing in vitro fertilization (IVF), fresh embryo transfer of cleavage stage embryos is associated with higher clinical pregnancy and live birth rates than previously frozen embryo transfer.
Comparative Study of the Therapeutic Effects of Drosiporen (DRSP, 3 mg) with Ethinyl Estradiol (EE, 20 mcg) Pill with or without Metformin 500 mg in Polycystic Ovary Syndrome (PCOS).

OBJECTIVE: To compare the therapeutic effects of Drosiporen (DRSP 3 mg) with Ethinyl Estradiol (EE, 20 mcg) pill with or without Metformin (500 mg) in polycystic ovary syndrome (PCOS) patients at 6 and 12 months of treatment.

DESIGN: Single blind randomized controlled study.

MATERIALS AND METHODS: 129 patients with PCOS were enrolled in a randomized control trial in Kolkata between May 2013 and September 2014. Cases were selected based on Rotterdam Criteria (2003). Eligible patients were randomly assigned (1:1) using a computer-generated randomization table to receive daily DRSP pill (DRSP 3mg with EE 20 mcg, cyclically 24+4 regimen) with 500 mg Metformin (Group A) or only DRSP pill (Group B). Informed written consent was obtained from all participants. The interventions were sequenced in a randomized order. Interventions included changes in metabolic and select clinical variables like Body Mass Index (BMI), abdominal circumference, Ferriman Galwey score, presence (%) of acne and acanthosis nigricans, blood pressure, serum T, SHBG, serum post prandial glucose (PPG) and insulin (PII). PPG: PPI ratio less than 1.0 was considered as indicative of insulin resistance.

RESULTS: After 6 months of treatment, there were comparable results between the two groups except significantly greater reduction of BMI in Group A (p=0.031) and increase in SHBG in Group B (p=0.001). After 12 months of treatment, despite the lower BMI in Group A, SHBG level demonstrated significant increase in Group B only. No differences in changes in other parameters were found.

CONCLUSIONS: There were no differences in therapeutic effects between the two groups of PCOS cases except in BMI and SHBG at 6 months of treatment. It may be of interest to explore therapeutic options with higher doses of metformin and study the clinical/metabolic effects.

Reference:

Table 2: IVF Cycle Outcomes

<table>
<thead>
<tr>
<th></th>
<th>Fresh ET, n=62</th>
<th>Frozen-Thawed ET, n=59</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak E2 before ET</td>
<td>3040 ±1468</td>
<td>709±312</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>(Mean ±SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Embryo transferred</td>
<td>2±0</td>
<td>1.95±0.40</td>
<td>0.42</td>
</tr>
<tr>
<td>(Mean ±SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CPR (per transferred cycle) %</td>
<td>63</td>
<td>35.6</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Multiple pregnancy rate (per transferred cycle) %</td>
<td>14.5</td>
<td>6.8</td>
<td>0.17</td>
</tr>
<tr>
<td>Miscarriage rate (per clinical pregnancy) %</td>
<td>23</td>
<td>40</td>
<td>0.21</td>
</tr>
<tr>
<td>LBR (per transferred cycle) %</td>
<td>46.8</td>
<td>25.4</td>
<td>0.01</td>
</tr>
</tbody>
</table>

References:

P-402 Wednesday, October 19, 2016

THE DISTINCTIVE ROLE OF A DISINTTEGRIN AND METALLOPROTEINASE WITH THROMBOSPONDIN MOTIFS 19 (ADAMTS19) IN POLYCYSTIC OVARY SYNDROME. E. Ersoy, S. Ozler, E. Oztas, A. Ersoy, M. Ergin, N. Yilmaz. Obstetrics and Gynecology, Zekai Tahir Burak Women’s Healthcare Training and Research Hospital, Ankara, Turkey; 25th December State Hospital, Gaziantep, Turkey; Reproductive Endocrinology Department, ZTB, Ankara, Turkey.

OBJECTIVE: A Disintegrin and Metalloproteinase with Thrombospondin motifs (ADAMTS) enzymes take part in extracellular matrix (ECM) remodeling which has been shown to contribute to the ovulation and follicular functions. Here we aimed to investigate the diagnostic value of the venous levels of ADAMTS19 in patients with different fertility situations.

DESIGN: Prospective case-control study.

MATERIALS AND METHODS: 86 patients who were recruited voluntarily, 21 consecutive women were diagnosed with premature ovarian failure (POF), 21 consecutive women were diagnosed as natural post-menopause, 22 consecutive women were diagnosed with polycystic ovary syndrome (PCOS), and 22 women were recruited as a fertile control group. The diagnosis of POF was made when the patient was below the age of 40, had a follicle stimulating hormone (FSH) level above 40 units per liter (U/L), and amenorrhea for at least 6 months. The diagnosis of PCOS was made according to the Rotterdam criteria (1). Fertile group included patients who had regular menstrual periods.
and had a live birth in the last two years. Serum ADAMTS19 levels and individual characteristics were compared among groups.

RESULTS: The age and BMI values were comparable between the POF and fertile group. ADAMTS19 levels were significantly different among groups. Specifically, ADAMTS19 levels in the PCOS group were significantly higher than the POF group, as found in dual comparisons. Regression analyses revealed that ADAMTS19 was a risk factor and a predictor for PCOS.

CONCLUSIONS: ADAMTS19 was found as a risk factor for PCOS in this preliminary analysis. This work provides a novel vantage point for function of ECM within the ovary. Further tissular based research with larger sample size should focus on the clinical and pathogenetic role of the ADAMTS19 in different fertility situations and metabolic settings.

Footnotes of the table:

a The significant difference between POF and Fertile groups
b The significant difference between POF and Post-menopause groups
c The significant difference between POF and PCOS groups
d The significant difference between Fertile and Post-menopause groups

References:

P-403 Wednesday, October 19, 2016

ABSTRACT WITHDRAWN

P-404 Wednesday, October 19, 2016

PROTEIN PATHWAYS IN FOLLICULAR FLUID FROM POLYCYSTIC OVARIAN SYNDROME (PCOS) PATIENTS AND OVOX DONORS UNDERGOING IVF CYCLES. T. S. Domingues,a,b
T. C. Bonetti,a,c,d C. Gomes,a J. R. Alegretti,a B. Barros,a E. Motta,a,c,d Clinical, Huntington Medicina Reprodutiva, Sao Paulo, Brazil; bGynecology, Universidade Federal de Sao Paulo, Sao Paulo, Brazil; cGynecology, Federal University of Sao Paulo, Sao Paulo, Brazil; dScientific, Huntington Medicina Reprodutiva, Sao Paulo, Brazil; eEmbyrology, Huntington Medicina Reprodutiva, Sao Paulo, Brazil.

OJECTIVE: PCOS is the most common anovulatory dysfunction and prevalent cause of infertility. Although patients with PCOS have an enhanced response during ovarian stimulation, the clinical outcomes are poor. Previous studies have shown relevant molecules, which are speculated to be linked in the pathogenesis of PCOS. The exact mechanism affecting ovulatory process is still unclear. The aim of this study was to analyze the proteomic profile of follicular fluid in PCOS patients undergoing IVF cycles and compared to ovum-donors.

DESIGN: This is an experimental study including FF from PCOS patients (n=8) and oocyte donors (OD: n=9) undergoing IVF cycles. Patients were submitted to pituitary down-regulation with GnRH agonist, ovarian stimulation using rFSH and follicular maturation triggered by rHCG. The FF from leading follicle was recovered and samples were combined in two pools for each group, PCOS and OD.

MATERIALS AND METHODS: Sample pools were submitted to albumin-IgG depletion, digestion and desalting, and tryptic peptides were analyzed by nanoliquid chromatography (nLC) on-line by positive-ion micro-electro spray with a linear Ion Trap (LTQ- XL). Data was searched against human Uniprot database with Mascot and validated with Scaffold 2.6 with a 2% false positive rate. Pathway analysis was performed by the Metacore.

RESULTS: Gene ontology processes were highlighted based on 107 proteins identified using a threshold of 10 for spectrum counts. Immune responses by classical and alternative complement pathways and blood coagulation pathway were the most highlighted based on proteins expressed. The inflammatory process through the cell-matrix interaction network was up-regulated in PCOS patients, while OD proteins emphasized the angiogenesis signaling due to interleucin-6 pathway.

CONCLUSIONS: The inflammatory process through the cell-matrix interaction network up-regulated in PCOS patients could be linked to a folliculogenesis impairment. In patients with PCOS, the expression of proteins associated with inappropriate follicular development and may be related to an increased ovarian extra-cellular matrix remodeling and multiple cyst formation. On the other hand, OD are supposed to be fertile supporting a normal folliculogenesis and proteins emphasized the angiogenesis signaling due to interleucin-6. The IL-6 may represent a potent angiogenesis factor, which allow the satisfactory follicle vascularization and development.

References:

P-405 Wednesday, October 19, 2016

THE ASSOCIATION OF -429T>C AND -374T>A POLYMORPHISMS IN THE RAGE GENE WITH POLYCYSTIC OVARY SYNDROME. S. Song,a J. Park,b L. Li,c M. Jeon,c B. Choi,a K. Baek,a Laboratory of Reproductive Medicine, Creation & Love Women’s Hospital, Gwangju, Korea, Republic of; bDepartment of Biomedical Science, CHA University, Pocheon, Korea, Republic of; cDepartment of Obstetrics and Gynecology, Center for Recurrent Miscarriage and Infertility, Creation & Love Women’s Hospital, Gwangju, Korea, Republic of.

OBJECTIVE: Polycystic ovary syndrome (PCOS) is a complex disorder characterized by hyperandrogenism and insulin resistance. In addition, a number of females with PCOS have ovaries with multiple cysts, an irregular or no menstrual cycle and an imbalance of female hormones compared to those of normal controls. A variety of genetic factors have been involved in the pathogenesis of PCOS. Among these genetic factors, the receptor for advanced glycation end products (RAGE) that is associated with diabetes and involved in the complications of PCOS, was selected. We aimed to assess the relationship between -429T>C and -374T>A single nucleotide polymorphisms (SNPs) of RAGE gene with the susceptibility to PCOS.

DESIGN: Laboratory research environment.

MATERIALS AND METHODS: 128 controls and 265 PCOS patients were used for -429T>C polymorphism and 141 controls and 290 PCOS patients were used for -429T>C polymorphism, respectively. Genotyping of two polymorphisms were analyzed by polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) assay and statistical analysis was performed.

RESULTS: P values for both alleles were higher than 0.05. Frequencies of genotype and allele of two polymorphisms in RAGE gene showed no significant differences between controls and PCOS patients.

CONCLUSIONS: The initial study on the correlation between RAGE gene and PCOS indicates that the two polymorphisms of RAGE are not associated with the pathogenesis of PCOS. However, further studies regarding the association between RAGE gene and PCOS patients in different ethnic groups are required.

P-406 Wednesday, October 19, 2016

OUTCOMES OF SINGLE VS DOUBLE EMBRYO TRANSFER IN IN-VITRO MATURATION CYCLES DONE IN WOMEN WITH POLYCYSTIC OVARY SYNDROME. S. hatimaz,a E. S. Hatimaz,a S. L. Tan,b A. Ata,a M. kanat pektas,a A. ozer,a M. Dahan,a 1ivf center, Ozel Konak Hastanesi, Kocaeli, Turkey; bobstetrics and gynecology, McGill University School of Medicine, Montreal, QC, Canada; cKoc University School of Medicine, Istanbul, Turkey; dOb & gyn, kocatepe university, afyonkarahisar, Turkey; eetu imam university, kahramannar, Turkey; Mgill University, Montreal, QC, Canada.

OBJECTIVE: This study was performed to compare the clinical outcome of single with double embryo transfer in in-vitro maturation (IVM) cycles.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: A retrospective analysis of 159 women with PCOS per the Rotterdam criteria, who underwent IVM between September 2007 and May 2014 was performed. Twenty women whose partners were diagnosed with azoospermia, cryptozoospermia and severe oligoasthenoteratozoospermia were excluded from the analysis. Continuous variables are presented as mean±standard deviation while categorical variables are expressed as percentages. Continuous variables were compared by t-tests or Mann Whitney U test depending on distribution characteristics. Categorical variables were compared by chi-square tests. Logistic regression was used to compare pregnancy outcomes while controlling for confounding effects.
RESULTS: Single embryo transfer was performed in 83 patients (52.2%) whereas double embryo transfer was performed in 76 patients (47.7%). The patients who had single vs. double embryo transfer had significantly younger ages (24.1±2.4 vs. 32.4±3.5 years; p=0.001), shorter infertility durations (4.4±2.3 vs. 9.2±2.2 years; p=0.001), less previous attempts for in vitro fertilization (p=0.001), less collected oocytes (12.6±3.8 vs. 15.1±4.6; p=0.001), less metaphase II oocytes (5.7±2.9 vs. 9.0±4.1 vs.; p=0.004), and less embryos (3.6±2.3 vs. 8.2±3.7; p=0.002), respectively. The single and double embryo transfer groups were statistically similar with respect to embryo quality (p=0.11). When controlling for confounding effects, miscarriage rates (7.2 vs. 7.8%; p=0.84) and live birth rates (34.9 vs 34.2%; p=0.92) were similar. Twin clinical pregnancy rates were statistically higher in the double as compared to the single embryo transfer groups (9.2 vs. 2.4%; p=0.03), while twin live birth rates trended higher (2.4 vs 0%. P=0.07).

CONCLUSIONS: Although much is known about the effect of multiple embryo transfer in IVF cycles, little data is available in IVM cycles. Most centers transfer 3-4 embryos in IVM, with multiple pregnancy rates that are much lower than when transferring 2 oocytes at IVF [1-3]. This is likely due to abnormalities in IVM embryos which prevent continued development. In the current study it has been shown that single embryo transfer in IVM can result in excellent pregnancy rates comparable to double embryo transfer, while reducing the risk of twin gestation. For the first time this has been demonstrated in IVM cycles.

References:

P-407 Wednesday, October 19, 2016
NON INVASIVE PREDICTION OF OVARIAN HYPER STIMULATION SYNDROME RISK IN POLYCYSTIC OVARY SYNDROME (PCOS) PATIENTS BY FOLLICULAR FLUID METABOLICS. Madhu Gandhi,a B. Kang,b aObstetrics and Gynecology, College of Medicine, University of Toledo, Toledo, Ohio; bObstetrics and Gynecology, College of Medicine, University of Toledo, Toledo, Ohio.

OBJECTIVE: To identify biomarkers of ovarian hyper stimulation syndrome (OHSS) risk in PCOS and hyper-responders patients undergoing In vitro fertilization (IVF).

DESIGN: Case control study.

MATERIALS AND METHODS: Follicular fluid (FF) samples from 88 patients undergoing IVF were split into three groups, according to their response to controlled ovarian stimulation (COS): Control Group (n=22), including normal responders patients with <15 retrieved oocytes; PCOS group (n=15), including clinically diagnosed patients with ≥15 retrieved oocytes; and Hyper responder Group (n=44), including patients with ≥15 retrieved oocytes, presenting PCOS secondary characteristics, but not clinically diagnosed. Metabolite extraction was performed by the Bruker Diode-400 protocol and mass spectra were obtained by liquid chromatography coupled to a mass spectrometer (LC-MS). Data were analyzed by principal component analysis (PCA) and partial least square analysis (PLS-DA).

RESULTS: A trend towards group separation was observed by PCA, and PLS-DA showed a model with an accuracy of 95%. Diacylglycerols were of high abundance in the Control Group, while the PCOS presented an increased abundance of fatty acids and sphingolipids. The Hyper-responders Group presented triacylglycerol as the most abundant biomarker.

CONCLUSIONS: The present study identified potential biomarkers of PCOS related to hyper response to COS and OHSS risk, the dreadful complication of the IVF treatment. Since FF is derived from plasma, these biomarkers may be further investigated in plasma, which would be useful for identifying patients at risk of developing OHSS. This may contribute to develop individualized treatment for these patients, avoiding cycles’ cancelation and increasing the pregnancy success.
continued to the day of oocyte pick-up (OPU). In the placebo group, placebo of 1 tablet twice a day was given during the same period.

RESULTS: There were no significant differences in patient’s characteristics between the metformin and control groups. In the metformin group, two patients suffered from nausea and diarrhea and were withdrawn from the study. In the control group, a patient asked withdrawal and was withdrawn from the study. Total dose of recombinant human FSH (rhFSH) used for COS was lower in the treatment group of 1403.8 ± 577.8 IU compared with 1896.1 ± 1132.1 IU in the placebo group, but the difference did not achieve the statistical significance. The numbers of oocytes retrieved, mature oocytes and fertilized oocytes were comparable between the two groups. However, the number of grade 1 or II embryos was significantly higher in the metformin group than in the control group (p = 0.002). FF adiponectin levels were significantly higher in the metformin group (p = 0.002) and FF TNF-α and FF IL-6 concentrations were significantly lower in the metformin group (p < 0.001, p = 0.006, respectively). Clinical pregnancy rate was significantly higher in the metformin group of 80.0% (8/10) compared with 18.2% (2/11) in the control group (p = 0.009). Embryo implantation rate was also significantly higher in the metformin group (p = 0.018).

CONCLUSIONS: Metformin supplementation during the COS period increases FF adiponectin concentrations and reduces FF TNF-α and IL-6 concentrations, and also improves the embryo quality and increase the clinical pregnancy and embryo implantation rates in infertile patients with PCOS undergoing IVF.

Supported by: Funding by Merck-Serono.

P-410 Wednesday, October 19, 2016

PROGESTERONE SUPPLEMENTATION IN PCOS WOMEN UNDERGOING CLOMIPHENE CITRATE STIMULATED IUI MAY IMPROVE PREGNANCY BY INCREASING UTERINE BLOOD. G. Mukherjee, a H. Konar, b P. Mandve, c S. Sharma, d S. Ghosh, e P. Chakraborty, f B. Chakravarty, g

OBJECTIVE: PCOS patients have irregular menstrual cycles, abnormal follicular development and chronic anovulation or oligoovulation, which may result in insufficiency of corpus luteum, hence this group makes an attractive model to study the beneficial effects of progesterone supplementation in luteal phase. The objective of this study is to evaluate the efficacy of progesterone supplementation in clomiphene citrate (CC) stimulated PCOS women undergoing intrauterine insemination (IUI).

DESIGN: This was a prospective observational study.

MATERIALS AND METHODS: This study was conducted on 1010 PCOS women undergoing IUI in their first cycle from January 2013 to March 2015. Ovarian stimulation was done with 100mg CC from day 3 to day 7. In 860 women, CC was performed successfully. They were divided into two groups, the study group (n=442) received 600 mg intravaginal progesterone for LPS daily for 14 days and the control group (n=418) did not receive progesterone for LPS. Uterine blood flow was assessed on the day of IUI and 14 days after insemination. Cycle characteristic of patients in terms of number of follicles, size of follicle on day of hCG, day of hCG, endometrial thickness (ET) were compared. Pregnancy rate per completed cycle, miscarriage rate and live birth rate were compared between the groups.

RESULTS: Data from 860 women were analyzed. IUI was cancelled in 150 women due to inadequate response, luteinized unruptured follicle, failed semen collection and on demand cancellation. The pregnancy rate per cycle was significantly higher in the progesterone supplemented group than unsupported group (19% vs 12.4%, respectively p=0.11). However, miscarriage rate was insignificantly higher in the study group compared with the control group (10% vs 8.7%, respectively p=0.05).Live birth rate was significantly higher in supported group compared with control subjects (16.2% vs 8.61%, p=0.02).The progesterone supported group demonstrated significant reduction in resistance index, pulsatility index and systolic/diastolic ratio of uterine artery on day14.

CONCLUSIONS: In conclusion, the present prospective study suggests use of progesterone supplementation for luteal phase in PCOS woman in CC stimulated IUI cycles is beneficial.

P-411 Wednesday, October 19, 2016

THE EFFECT OF METFORMIN ON PREGNANCY OUTCOME, ENDOMETRIAL RECEPIVITY & miRNAs IN ENDOMETRIUM

OF PATIENTS WITH PCOS UNDERGOING IVF/ICSI. D. Sun, G. Yao, L. Wu, J. Wang, Z. Zhao, J. Zhai. Reproductive Medicine, Zhengzhou, China.

OBJECTIVE: The exact mechanism of metformin improve endometrial receptivity in patients with polycystic ovary syndrome (PCOS) is unclear. miRNAs play a key role in the process of endometrial receptivity. Our aim was to study the effect of metformin on pregnancy outcome, endometrial receptivity and miRNAs expression in endometrium of patients with PCOS undergoing in vitro fertilization and intracytoplasmic sperm injection (IVF/ICSI).

DESIGN: Perspective study.

MATERIALS AND METHODS: A total of 120 enrolled PCOS patients scheduled for first IVF/ICSI treatment between October 2015 and March 2016 were randomly divided into two groups: metformin group (A group) and control group (B group). Patients in A group received metformin at a dose of 500mg three time one day on the third day of menstrual period or withdrawal bleeding until the sixth day of ovum pick-up (OPU). Embryo transfer was conducted for those patient with a good condition. Luteal support would be stopped and endometrial samples were collected on the sixth day of OPU if one had the risk of ovarian hyperstimulation syndrome (OHSS). Samples were for western blot to assess the protein levels of endometrial homeobox gene 10 (HOXA10), integrin 3 (ITGB3) and microRNA array to analyze differential expression of miRNAs. miRDB and TargetScan databases were searched to predict their potential target genes. Gene ontology (GO) and pathway enrichment to analyze these miRNAs. Real-time quantitative RT-PCR was performed to confirm the microRNA array result. Primary outcomes were clinical pregnancy rate (CPR), OHSS rate, differential expression of HOXA10, ITGB3 and miRNAs.

RESULTS: Significantly higher CPR were observed in the A group versus B group (58.9% versus 37.5%, P<0.05). OHSS rate significantly lower with the use of metformin (8.3% versus 21.7%, P<0.05). Other reproductive parameters associated with IVF/ICSI were no significant differences between two groups. Treatment with metformin induced a significant increase in HOXA10 (30.95±0.03 vs. 58.0±0.08, P<0.05) and ITGB3 (0.97±0.02 vs. 0.42±0.19,P<0.05) protein expression compared with the B group. Array showed that the expression of a total of 40 miRNA (19 upregulated and 21 downregulated) was found to be significantly altered in the two groups. Then we selected respectively 5 miRNAs from above-mentioned results to confirm the array results through quantitative RT-PCR technology and the result showed that it was consistent with alteration of array. These miRNAs mainly revealed events such as WNT signaling pathway, FoxO signaling pathway, adhesion pathway by GO and Pathway analysis. Among these significantly differential miRNAs, miRDB and TargetScan databases showed that downstream target genes of the miRNA-194-5p and miRNA-491-3p were HOXA10 and ITGB3.

CONCLUSIONS: Metformin for patients with PCOS before IVF/ICSI can improve their pregnancy outcome and endometrial receptivity possibly by altering the expression of miRNAs of endometrium, but the exact effect of these miRNAs need further study.

Supported by: This study was supported by found from the Key Project Department (No. 2014042013) Henan Province.

P-412 Wednesday, October 19, 2016

INCREASED RISK OF EATING DISORDERS IN WOMEN WITH POLYCYSTIC OVARY SYNDROME. 1. Lee, a L. Cooney, b S. Saini, a M. E. Smith, a K. C. Allison, a A. Dokras. a Obstetrics and Gynecology, University of Pennsylvania, Philadelphia, PA; bPsychiatry, University of Pennsylvania, Philadelphia, PA.

OBJECTIVE: Women with PCOS are at increased risk of anxiety and depression, but the is limited data on the prevalence of eating disorders (ED) in this population. The objective of the study was to determine the prevalence of ED in women with PCOS and associated risk factors.

DESIGN: Cross-sectional study.

MATERIALS AND METHODS: Women with PCOS (Rotterdam Criteria; n=121) were recruited from an academic PCOS Center. Control subjects (n=57) had regular menses and no hirsutism and were receiving routine gynecologic care in the same time period. Both groups completed the Eating Disorder Examination Questionnaire (EDEQ), Night Eating Questionnaire (NEQ), and Hospital Anxiety and Depression Scale (HADS), ≥ 4 was clinically significant on the EDEQ, ≥ 25 on NEQ, and ≥ 11 on HADS. The PCOS group also completed the PCOS Health-Related Quality of Life Questionnaire (PCOSQ). Fisher exact and two-tailed t tests were used for descriptive statistics. Multivariate logistic regression was used for prediction for confounders.
RESULTS: PCOS subjects were younger with a higher mean BMI compared to controls (Table). Global and all individual EDEQ scores were significantly higher in PCOS subjects compared to controls. EDEQ Global Score inversely correlated with overall PCOSQ score (r = -0.57, p = 0.001) and with all PCOSQ domains, particularly emotion (r = -0.51, p = 0.001) and weight (r = -0.79, p < 0.0001). Women with PCOS had an increased odds of abnormal EDEQ Global Score ≥ 4 (OR = 6.87, 95% CI 0.88-53.86, p = 0.04) however, the age and BMI-adjusted OR was 5.78 (CI 0.60-55.4, p = 0.13). As expected, more women with PCOS had abnormal anxiety (41.7 vs 14%, p = 0.001) and depressive scores (13.2 v. 3.5%, p = 0.06) compared to controls. Among PCOS patients with anxiety, the odds ratio of EDEQ ≥ 4 was 9.70, 95%CI: 2.0, 46.1, p = 0.004 compared to those without anxiety. This association increased after controlling for age and BMI (AOR 19.6, 95%CI: 1.0-14.6, p = 0.048; age and BMI AOR: 3.96, 95%CI: 1.0-15.6, p = 0.049). The prevalences of bulimia, binge eating disorder, and night eating disorder in PCOS subjects were higher than in controls, but the differences were not statistically significant (Table).

CONCLUSIONS: Our study demonstrates a significant increase in disordered eating attitudes and behaviors associated with decreased quality of life in women with PCOS. Further, it highlights the need to screen for eating disorders especially in women with PCOS and co-existing anxiety or depressive symptoms.

<table>
<thead>
<tr>
<th>Eating disorders in women with PCOS and controls</th>
<th>PCOS PATIENTS (n=121)</th>
<th>CONTROLS (n=57)</th>
<th>p-VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (SD)</td>
<td>28.08 (5.42)</td>
<td>33.26 (8.63)</td>
<td>0.0002</td>
</tr>
<tr>
<td>BMI (SD)</td>
<td>33.56 (8.78)</td>
<td>25.40 (5.70)</td>
<td>&lt;0.0001</td>
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<tr>
<td>EDEQ Global Score</td>
<td>2.33 (0.12)</td>
<td>1.24 (0.14)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>EDEQ Restraint Score</td>
<td>2.07 (0.12)</td>
<td>1.34 (0.19)</td>
<td>0.0009</td>
</tr>
<tr>
<td>EDEQ Shape Concern</td>
<td>3.22 (0.16)</td>
<td>1.87 (0.21)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>EDEQ Weight Concern</td>
<td>2.91 (0.15)</td>
<td>1.47 (0.19)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>EDEQ Eating Concern</td>
<td>1.11 (0.15)</td>
<td>0.25 (0.08)</td>
<td>0.0002</td>
</tr>
<tr>
<td>EDEQ Global Score, Number ≥ 4 (%)</td>
<td>13 (10.92)</td>
<td>1 (1.75)</td>
<td>0.038</td>
</tr>
<tr>
<td>Bulimia</td>
<td>9 (7.44)</td>
<td>1 (1.75)</td>
<td>0.172</td>
</tr>
<tr>
<td>Binge Eating Disorder</td>
<td>21 (17.4)</td>
<td>5 (8.8)</td>
<td>0.173</td>
</tr>
<tr>
<td>Night Eating Disorder</td>
<td>16 (13.3)</td>
<td>4 (7.02)</td>
<td>0.310</td>
</tr>
</tbody>
</table>

**P-414** Wednesday, October 19, 2016


OBJECTIVE: Changes in self-image related to obesity, hirsutism, acne, as well as depression and anxiety associated with PCOS appear to have negative effects on sexual health. Alternatively, higher androgen levels found in PCOS women may actually improve libido. Unfortunately, currently published data are based on under-powered studies and results are often inconclusive; therefore, pooled data is needed. The purpose of our study is to determine differences in sexual function between women with and without PCOS.

DESIGN: Systematic review and meta-analysis

MATERIALS AND METHODS: Electronic databases (MEDLINE through PubMed, EMBASE, Web of Science, LILACS, Cochrane Library, CINAHL, and PsycINFO) were searched through October 2015. Search terms included: polycystic ovarian syndrome, PCOD, PCOS, quality of life, sexual dysfunction, sexual function, sexual dissatisfaction, sexual comfort, sexual intercourse, libido, arousal, orgasm, dyspareunia, satiation, craving, lubrication, coitus, desire, excitement, and sexarche. Observational studies (cross-sectional, case-control, cohort) reporting sexual function of PCOS vs unaffected subjects were considered. Data was extracted using a web-based, piloted form. The inverse variance method, based on a random- or fixed-effects model (Review Manager, Version 5) was used to analyze the data. Data from eligible studies was independently extracted by two reviewers.

RESULTS: The original search yielded 880 publications. Hand searching of titles and abstracts was conducted to exclude articles which did not focus on PCOS and quality of life or sexual function, and duplicates were removed, yielding a total of 431 articles. These articles were reviewed, and eight comparative studies were included (428 PCOS women and 423 controls) in the systematic review. The pooled analysis revealed no significant differences between PCOS and controls in sexual desire (SMD = 0.09; 95% CI: -0.32, 0.49; Z = 0.42, p = 0.67); sexual desire (SMD = 0.34; 95% CI: -0.03, 0.71; Z = 1.73, p = 0.08); orgasm (SMD = 0.34; 95% CI: 0.12, 0.56; Z = 0.03, p = 0.98); satisfaction (SMD = 0.41; 95% CI: -0.33, 0.14; Z = 1.65, p = 0.10); sexual activity (SMD = 0.4; 95% CI: -0.27, 0.25; Z = 0.83, p = 0.41); and total sexual function score (SMD = 0.34; 95% CI: -0.27, 0.28; Z = 0.83, p = 0.41); pregnancy (SMD = 0.34; 95% CI: -0.27, 0.25; Z = 0.83, p = 0.41). The pregnancy rate in the PCOS group was 31% compared to 29% in controls.

CONCLUSIONS: Our study is one of the largest and most comprehensive meta-analyses of the literature to date. The authors concluded that PCOS is associated with a reduction in sexual satisfaction, but little evidence of any other sexual dysfunction. Additional well designed studies are needed.

Supported by: Partial funding from MD Medical Group, MDMD00001, “The Epidemiology and Phenotype of PCOS in Women”.

P-413 Wednesday, October 19, 2016

**EFFECTIVENESS OF A LETROZOLE ESCALATION PROTOCOL IN ACHIEVING OVULATION IN PATIENTS WITH POLYCYSTIC OVARY SYNDROME.** T. L. Jones, C. C. Shenoy, J. Jensen, E. A. Stewart, G. S. Daftary, C. Coddington. Reproductive Endocrinology and Infertility, Mayo Clinic, Rochester, MN.

OBJECTIVE: In the absence of follicular recruitment, immediate dose escalation is effective to achieve ovulation in oligo- or anovulatory women using clomiphene citrate. Limited data exist for using letrozole in a similar manner. We sought to determine if immediately increasing the letrozole dose during the same cycle is efficacious to achieve ovulation in oligo- or anovulatory women with polycystic ovary syndrome (PCOS). We also evaluated endometrial thickness and pregnancy rates in women undergoing the escalation protocol versus standard treatment.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Oligo- or anovulatory women with PCOS based on Rotterdam criteria undergoing their first cycle of ovulation induction with letrozole at Mayo Clinic in Rochester, MN, from January 1, 2014 to March 31, 2016 were selected. The escalation protocol was performed by administering letrozole at a starting dose of 2.5 mg for 5 days starting cycle day 3. A transvaginal ultrasound was performed on cycle day 10-12 to assess follicular recruitment. If no follicle(s) ≥ 10 mm were observed, the dose was immediately increased by 2.5 mg of letrozole for an additional 5 days. This was repeated until a follicle was recruited or a maximum dose of 7.5 mg of letrozole was reached. Treatment consisted of administering 10 days of oral progesterin to induce a withdrawal bleed if there was no follicular recruitment on CD 10-12 ultrasound, followed by an increased dose of letrozole in the subsequent cycle. Ovulation was determined by detection of urinary luteinizing hormone surge or by administering human chorionic gonadotropin (hCG) at a dosage reaching 20 mIU/mL. Clinical pregnancy was defined by a positive HCG and by fetal cardiac activity on ultrasound. Statistical analysis was performed using the Wilcoxon Rank Sum and Fisher Exact tests where appropriate.

RESULTS: Forty-six PCOS patients with ovarioly dysfunction were identified; 11 utilized the escalation protocol. There were no differences in baseline age, body mass index, and ovarian reserve between the two groups. Of the 35 patients using the standard protocol, 72% ovulated versus 100% of the 11 using the escalation protocol (p = 0.042). There were no differences in mean follicular recruitment (2.1 ± 1.6 vs 2.4 ± 1.6, p = 0.62) or endometrial thickness (5.8 ± 2.1 vs 5.7 ± 2.4 mm, p = 0.90) between standard and escalation protocol, respectively. There were no statistical difference in clinical pregnancies (3 (11%) in the standard and 1 (9%) in the escalation group.

CONCLUSIONS: The escalation protocol increases ovulation rates in patients with PCOS by effectively identifying the letrozole dose necessary to achieve follicular recruitment during the initial ovulation induction cycle. Immediately increasing the dose of letrozole in a single cycle does not exhibit detrimental effects on the number of follicles recruited, endometrial development or pregnancy rates.
IMPACT OF METFORMIN ON IN VITRO FERTILIZATION OUTCOMES IN OVERWEIGHT AND OBSEPOLYCYSTIC OVARY SYNDROME WOMEN: A PROSPECTIVE COHORT STUDY. O. S. Abdalmageed,a T. A. Farghaly,a A. M. Ismail,a W. W. Hurd,b* Assist University IVF Center, Assiut, Egypt; *Obstetrics and Gynecology, Assiut University IVF Unit, Assiut, Egypt; *Obstetrics and Gynecology, Women’s Health Hospital, Assiut, Egypt; bObstetrics and Gynecology, Duke University, Durham, NC.

OBJECTIVE: To determine the impact of short-term metformin therapy on in vitro fertilization-embryo transfer (IVF-ET) outcomes in overweight and obese women with polycystic ovary syndrome (PCOS).

RESULTS: A total of 120 overweight and obese women (BMI 30 kg/m2) with PCOS who were undergoing their first autologous IVF-ET cycle with intracytoplasmic sperm injection (ICSI) were included. The study population was composed of two groups according to whether or not they received metformin during the IVF cycle treatment (51 patients in each group). The metformin-treated group received metformin (1000 mg per day orally) starting from onset of ovarian stimulation therapy and continued until the day of the pregnancy test. Women with a positive pregnancy test, the patients continued metformin until the end of the 12th week of gestation. The primary outcome measures were the number of retrieved oocytes, the number of the fertilized oocytes (two pronuclei), fertilization rate, implantation rate, clinical pregnancy rate and miscarriage rate.

RESULTS: Both the metformin-treated group and the control group were comparable in terms of age, BMI, duration of infertility, basal FSH, and AFC. The metformin-treated group demonstrated a decreased number of the retrieved oocytes and 2pn oocytes (p < 0.01). There was no difference between the two groups regarding the fertilization rate, implantation rate, multiple pregnancy rates, miscarriage rate or birth rate (Table 2). There were no cases of ovarian hyperstimulation syndrome in either group.

CONCLUSIONS: Short-term administration of Metformin to overweight and obese women with PCOS women decreases the number of oocytes retrieved, but otherwise does not affect IVF outcomes.


OBESITY AND METABOLISM

ASSOCIATION OF INSULIN SENSITIVITY (IS) WITH AGE AT MENARCHE (AAM) IN GIRLS WITH TYPE 1 DIABETES (T1D): SEARCH FOR DIABETES IN YOUTH STUDY. H. Borg,a W. Lang,b R. D’Agostino,b S. L. Young,a J. Lawrence,a C. Pihoker,a G. Kim,a P. Wadwa,a W. Tamborlane,f E. Mayer-Davis.a aUniversity of North Carolina, Chapel Hill, NC; bWake Forest School of Medicine, Winston-Salem, NC; cKaiser Permanente, Pasadena, CA; dUniversity of Washington, Seattle, WA; eUniversity of Colorado, Aurora, CO; fYale University, New Haven, CT.

OBJECTIVE: Abnormal timing of menarche is a predictor of many pathological conditions. Those pathologies include reproductive dysfunctions, metabolic disorders and cardiovascular diseases. It has been reported that early AAM is associated with lower IS and increased risk of type 2 diabetes. However, the association of IS with AAM in girls with T1D has not been studied. We have previously demonstrated that in girls with T1D, poor glycemic control correlates with delayed AAM, while obesity - reflected by Body Mass Index (BMI) correlates with earlier AAM. In this study, we examine the association of IS with the AAM.

DESIGN: The SEARCH for Diabetes in Youth study comprises the largest contemporary cohort of youth with diabetes in the US, inclusive of youth diagnosed with diabetes younger than age 20 years whose diabetes was prevalent in 2001, or incident in the years thereafter.

MATERIALS AND METHODS: Participants included in our analyses were girls (n = 379) diagnosed with T1D from 2002-2005. Their mean age at diagnosis was 9.6 ± 2.7 years and T1D duration 9.8 ± 6.1 months. All subjects had a baseline visit prior to menarche and ≥ 1 follow-up visits. Their A1c was 7.8 ± 1.4 % and BMI 18.5 ± 3.4 kg/m². This cohort included 71% of non-Hispanic Whites, 12% African-Americans, 8% Hispanics, and 9% others. IS was determined using the IS score validated by euglycemic-hyperinsulenic clamp studies [1]. A series of multiple linear regression (MLR) models with AAM as the outcome variable was fitted to examine the confounder-adjusted impact of IS (measured at each visit) on AAM, including linear and non-linear terms.

RESULTS: Unadjusted MLR models demonstrated neither linear nor quadratic effects of IS as significant predictors for AAM (p > NS). However, when adjusted for the potential confounders, including duration of T1D, BMI, race, and socioeconomic status - IS had a significant negative linear effect (β = -0.09; p < 0.01), and a significant quadratic effect (p < 0.01) on AAM. This pattern was opposite to the one seen in girls without T1D.

CONCLUSIONS: In our cohort of girls with T1D, lower IS is associated with later AAM after the adjustment for potential confounders. This pattern is the opposite of that seen in girls without T1D. The reversal of pattern may be secondary to pathological processes underlying T1D such as autoimmunity. Further studies are needed to better understand the impact of IS on reproductive system, including functionality of hypothalamic-pituitary-gonadal axis of women with T1D.

Supported by: SEARCH is funded by the Centers for Disease and Prevention and the National Institute of Diabetes and Digestive and Kidney Diseases.

References:

DOSE OF HUMAN CHORIONIC GONADOTROPIN TO TRIGGER FINAL OOCYTE MATURATION. M. Irani,a R. Setton,a V. Gunnala,a T. Kligman,a D. E. Goldschlag,a Z. Rosenwaks.a Reproductive Endocrinology and Infertility, Weill Cornell Medical College, New York, NY; aDepartment of Obstetrics and Gynecology, Weill Cornell Medical College, New York, NY; bOB/GYN, REI Fellow, New York, NY; cWeill Cornell Medical College, New York, NY; eObstetrics, Gynecology and Reproductive Medicine, Weill Cornell Medical Center, Manhattan, NY; eWeill Cornell Medicine - Center for Reproductive Medicine, 1305 York Avenue, New York, NY.
OBJECTIVE: One of the methods to reduce the risk of ovarian hyperstimulation syndrome (OHSS) in high responders is to modify the trigger medication by decreasing HCG dosing or administering GnRH-agonist trigger alone or combined with low dose HCG. However, patients with hypothalamic amenorrhea or those undergoing stimulation with GnRH-agonist protocol are not candidates for GnRH-agonist trigger. Therefore, such patients have to be triggered with HCG. In this study, we aim to determine the dose of HCG needed to achieve final oocyte maturation during IVF.

DESIGN: A retrospective cohort study.

MATERIALS AND METHODS: Patients undergoing IVF between January 2004 and May 2013 and receiving HCG trigger were included. Patients were divided into two groups based on level on the day after HCG trigger (DAHT), which was then correlated with patient’s body mass index (BMI) and dose of HCG trigger. Patients who received a combination of GnRH-agonist and HCG triggers were excluded. Values were expressed as mean ± SEM, x² test, t-test, and Fisher’s exact test were used as appropriate. Odds ratio (OR) with 95% confidence intervals (CI) were calculated and adjusted when indicated.

RESULTS: 18666 patients with β-hCG ≥ 50 mIU/mL and 418 patients with low β-hCG levels (< 50 mIU/mL) on the day after HCG trigger (DAHT) were included. Patients with BMI ≥ 30 kg/m² who received HCG 5000 IU had more than 21-fold increased risk of having low β-hCG levels on DAHT (22.6% vs 1.3%, p < 0.001; OR=21.4, 95% CI=15.0-30.4) compared to patients with BMI < 30 kg/m². Please find attached a table illustrating the proportion of patients who had low β-hCG levels on DAHT, which was correlated with BMI and dose of HCG trigger. Patients with low β-hCG levels on DAHT had a significantly lower percentage of mature oocytes (76.9% vs 80.5%; p < 0.001), lower fertilization rate of mature oocytes (62.8% vs 72%; p < 0.001), and lower live birth rate after adjusting for patient’s age, number and stage of transferred embryos (aOR=0.67; 95%CI=0.5-0.8).

CONCLUSIONS: Patient’s BMI should be taken into consideration when determining the dose of HCG trigger. Obese patients (BMI ≥ 30 kg/m²) should receive more than 5000 IU of HCG to trigger final oocyte maturation.

<table>
<thead>
<tr>
<th>BMI (Kg/m2)</th>
<th>Trigger dose (IU)</th>
<th>β-hCG &lt; 50 mIU/mL (proportion of patients)</th>
<th>β-hCG &lt; 50 mIU/mL (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;40</td>
<td>5000</td>
<td>23/44</td>
<td>52.2</td>
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<td>&gt;40</td>
<td>10000</td>
<td>17/170</td>
<td>10</td>
</tr>
<tr>
<td>30-40</td>
<td>5000</td>
<td>61/327</td>
<td>18.6</td>
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<tr>
<td>30-40</td>
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<td>2</td>
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<td>25-30</td>
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<tr>
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<tr>
<td>&lt; 25</td>
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<td>6/7407</td>
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</table>

P-420 Wednesday, October 19, 2016

ARTIFICIAL SWEETENERS - DO THEY BEAR AN INFERTILITY RISK? G. Halpern, D. P. Braga, S. S. Setti, R. C. Figueira, A. Iaconelli Jr, E. Borges Jr, Fertility Medical Group, Sao Paulo, Brazil; Instituto Sapientiae - Centro de Estudos e Pesquisa em Reprodução Assistida, Sao Paulo, Brazil; Disciplina de Urologia, Departamento de Cirurgia – UNIFESP, Sao Paulo, Brazil.

OBJECTIVE: To investigate if the oocyte quality and intracytoplasmic sperm injection (ICSI) outcomes are influenced by the consumption of soft drinks and coffee, sweetened with sugar or artificial sweeteners.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: This study included 5,548 oocytes retrieved from 524 patients undergoing ICSI cycles from Jan/2012 to Dec/2014, in which embryo transfer was performed on day 5. All patients were interviewed face-to-face by the same nutrition professional before the beginning of the treatment. Women were asked about the frequency of consumption of any food items, regular coffee, regular diet soft drink, unsweetened coffee and coffee sweetened with sugar or any kind of artificial sweetener. Oocytes were evaluated before ICSI and the presence or absence of at least one morphological defect was recorded. All embryos were evaluated on days 2, 3, and 5 of development. The effects of dietary habits on oocyte quality, embryo quality on days 2 and 3, and blastocyst formation were evaluated. The influence of dietary habits on implantation, clinical pregnancy and miscarriage rates was also investigated.

RESULTS: The oocyte quality was negatively influenced by the consumption of regular (OR = 0.61, p = 0.032) and diet (OR= 0.47, p = 0.026) soft drinks. The consumption of diet soft drinks also negatively influenced embryo quality on days 2 (OR = 0.67, p = 0.035) and 3 (OR= 0.69, p = 0.039), and tended to decrease the implantation rate (RC= -0.891, r² = 3.5%, p = 0.063) and pregnancy chance (OR= 0.91, p = 0.068). The consumption of unsweetened coffee did not influence any evaluated parameter; however when sugar was added, a negative influence was observed on oocyte quality (OR= 0.89, p = 0.049). The consumption of artificial sweetened coffee negatively influenced oocyte quality (OR= 0.51, p = 0.028), embryo quality on days 2 (OR = 0.68, p= 0.035) and 3 (OR = 0.68, p = 0.035), and also tended to decrease the implantation rate (RC= -0.911, r² = 4.8%, p = 0.058) and pregnancy chance (OR= 0.93, p = 0.067).

CONCLUSIONS: The consumption of soft drinks and artificial sweeteners, but not coffee, negatively affects oocyte quality and ICSI outcomes. The general population believes that artificial sweeteners are healthier than regular sugar, and is not aware of the dangers hidden behind the promise of reduced calorie food and beverages. Patients should be advised about the adverse effect of sugar and mainly artificial sweeteners on the success of assisted reproduction.
HIGH FAT DIET DOES NOT INCREASE ENDOMETRIAL MACROPHAGE INFILTRATION IN SUPEROVULATED MICE. S. Chang, a M. Charron, a E. Buyuk, a Albert Einstein College of Medicine / Montefiore M, Bronx, NY; bBiochemistry, Albert Einstein College of Medicine, Bronx, NY.

OBJECTIVE: Maternal obesity is associated with reduced fertility and lower live birth rate after in vitro fertilization (IVF), but the mechanism remains unclear. Although infertility associated with obesity may be partly attributed to changes in the endometrial gene expression at the time of implantation, studies suggest that oocyte quantity and quality—rather than endometrial receptivity—may be more important factors in obese women trying to conceive via IVF. Obesity is a state of chronic low-grade inflammation; previously, we showed that it is associated with increased macrophage infiltration in the ovaries. It is unknown whether macrophage infiltration is also increased in the endometrium in obese individuals. We aimed to determine whether obesity and high fat diet would lead to increased macrophage infiltration within the endometrium of superovulated mice, which could be a potential explanation for decreased fertility.

DESIGN: Prospective controlled study

MATERIALS AND METHODS: C57BL/6 mice were allocated to (a) control group (N=6), which received a normal chow diet, or (b) high fat diet group (N=4), which received a high fat diet for 12 weeks. Animals were weighed weekly. Body fat composition was determined using Echo MRI. Animals were sacrificed at 20 weeks of age following superovulation with pregnant mare serum gonadotropin followed by chorionic gonadotropin. Uteri were removed, embedded in paraffin, and subjected to immunofluorescence staining using IBA1 antibody to identify macrophages. Images were analyzed using Velocity software to determine the number of macrophages per square millimeter and percentage area of macrophages in each tissue. Data are presented as mean±SEM. Student’s t-test was performed. IACUC approval was obtained.

RESULTS: High fat diet mice gained more weight than normal chow mice (28.2±2.5 g vs. 21.5±0.5 g; respectively, p=0.01) and accumulated more body fat (11.5±2.4 g vs. 2.5±0.3 g; respectively, p=0.002). The number of macrophages per endometrial mm² area was similar between obese (886±69 mm²) and non-obese mice (1034±94 mm²) (p=0.3). Similarly, there was no difference in the percentage of area occupied by the macrophages between obese (8.4±0.8%) and non obese mice (9.1±0.8). (p=0.6).

CONCLUSIONS: High fat diet does not increase macrophage infiltration in the endometrium of obese mice compared to non-obese mice following superovulation. Since the same diet increases macrophage infiltration in the ovaries, these results support the notion that obesity and high fat diet may be associated with impaired ovarian rather than endometrial function.

References:

Supported by: SIG #150000019961-01.

P-422 Wednesday, October 19, 2016

OBESITY AND ART: DOES BMI AFFECT EUPLOIDY RATES AND/OR PREGNANCY OUTCOMES IN COUPLES UNDERGOING IVF WITH CCS? A. L. Ganza, a,a M. C. Whitehouse, a J. A. Lee, a OBSTETRICS, GYNECOLOGY AND REPRODUCTIVE SCIENCE, Icahn School of Medicine at Mount Sinai, New York, NY; bOBSTETRICS, GYNECOLOGY AND REPRODUCTIVE SCIENCE, Icahn School of Medicine at Mount Sinai, New York, NY.

OBJECTIVE: Maternal obesity is associated with reduced fertility and lower live birth rate after in vitro fertilization (IVF), but the mechanism remains unclear. Although infertility associated with obesity may be partly attributed to changes in the endometrial gene expression at the time of implantation, studies suggest that oocyte quantity and quality—rather than endometrial receptivity—may be more important factors in obese women trying to conceive via IVF. Obesity is a state of chronic low-grade inflammation; previously, we showed that it is associated with increased macrophage infiltration in the ovaries. It is unknown whether macrophage infiltration is also increased in the endometrium in obese individuals. We aimed to determine whether obesity and high fat diet would lead to increased macrophage infiltration within the endometrium of superovulated mice, which could be a potential explanation for decreased fertility.

DESIGN: Prospective controlled study

MATERIALS AND METHODS: C57BL/6 mice were allocated to (a) control group (N=6), which received a normal chow diet, or (b) high fat diet group (N=4), which received a high fat diet for 12 weeks. Animals were weighed weekly. Body fat composition was determined using Echo MRI. Animals were sacrificed at 20 weeks of age following superovulation with pregnant mare serum gonadotropin followed by chorionic gonadotropin. Uteri were removed, embedded in paraffin, and subjected to immunofluorescence staining using IBA1 antibody to identify macrophages. Images were analyzed using Velocity software to determine the number of macrophages per square millimeter and percentage area of macrophages in each tissue. Data are presented as mean±SEM. Student’s t-test was performed. IACUC approval was obtained.

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CONCLUSIONS: High fat diet does not increase macrophage infiltration in the endometrium of obese mice compared to non-obese mice following superovulation. Since the same diet increases macrophage infiltration in the ovaries, these results support the notion that obesity and high fat diet may be associated with impaired ovarian rather than endometrial function.

References:

P-423 Wednesday, October 19, 2016

EFFECT OF BODY MASS INDEX (BMI) IN OOCYTE DONOR, RECIPIENT AND MALE PARTNER ON LABORATORY AND REPRODUCTIVE OUTCOMES IN CYCLES WITH DONOR OOCYTES. T. Fecreur, a,p Massart, a,b F. Bateh-Poisot, a,p Garcia, a,b P. Barriere, a,b V. Vernaeve, a,b "University Hospital of Nantes, Nantes, France; University Hospital of Nantes, Nantes, France; Clinic Eugin, Barcelona, Spain; Fundacio Privada EUGIN, Barcelona, Spain.

OBJECTIVE: The primary objective of this study was to evaluate if body mass index (BMI) in donors, recipients and male partners was associated with live birth in oocyte donation cycles. The secondary objectives were to evaluate the association of BMI in donors, recipients and male partner BMI at the time of treatment with ovarian response to stimulation, laboratory outcome and early pregnancy events.

DESIGN: This retrospective cohort study encompassed all oocyte donation cycles with partner sperm performed between 2010 and 2014 in a large fertility center. A total of 3,323 donors and 9,238 couples undergoing 11,806 oocyte reception cycles were included.

MATERIALS AND METHODS: BMI was categorized for each party as follows: underweight (BMI<18.5 kg/m²), normalweight (18.5-24.9 kg/m²), overweight (25-29.9 kg/m²), obese (30-34.9 kg/m²), and very obese (BMI>35 kg/m²).

Supported by: SIG #150000019961-01.
overweight (25.29-29.9 kg/m²), obese (30.34-39.9 kg/m²), and severely obese (≥ 35 kg/m²). The main outcome of the study was live birth, which was analyzed by univariate and multivariate analysis, adjusted for recipients’ race, status of sperm, day of ET, number of transferred embryos and embryo quality. Secondary outcomes were ovarian response to stimulation, biochemical, clinical, and ongoing pregnancy.

RESULTS: Mean age was 26.1 years (4.8), 41.7 (4.7), 42.4 (6.9) in donors, recipients and male partners respectively. Mean (SD) BMI was 22.7 kg/m² (3.2), 23.7 (4.3), 25.6 (3.5) in donors, recipients and male partners respectively. Live birth rate was 37.9%, 33.7%, 32.3%, 23.9% and 21.7% for underweight, normoweight, overweight, and obese recipients, respectively. Live birth rate in recipients was slightly but significantly affected by BMI in donors (OR 0.98 [0.96-0.99]), recipients (OR 0.98 [0.97-0.99]) and male partners (OR 0.98 [0.97-1]). Biochemical, clinical, and ongoing pregnancy rates were similarly slightly affected by BMI. We obtained 14.8 (SD 7.3), 15.0 (SD 7.5), 14.3 (SD 6.9), 12.7 mature oocytes (SD 6.1) for underweight, normoweight and overweight donors respectively. Ovarian response to stimulation was significantly reduced in underweight compared to normoweight donors after adjustment (B=-1.5.2, 95% CI -2.83, -0.21; P<0.001), but not in overweight or obese ones.

CONCLUSIONS: We found a weak but statistically significant negative association between BMI and live birth rate in oocyte donation cycles. However, the clinical relevance of this association remains to be defined.

P-424 Wednesday, October 19, 2016
NATURAL ANTI-OXIDANT SUPPLEMENTATION PRIOR TO INFERTILITY TREATMENT RESULTS IN EXCELLENT CLINICAL OUTCOMES FOR INFERTILITY PATIENTS WITH PRIOR IVF FAILURES. L. A. Munkwitz, W. B. Schoorsch, M. Katz-Jaffe. Colorado Center for Reproductive Medicine, Lone Tree, CO.

OBJECTIVE: Oxidative stress is known to be a significant contributor to ovarian dysfunction and subsequent poor oocyte quality. The aim of this study was to examine the clinical benefit of supplementation with a natural anti-oxidant prior to ovarian stimulation and in vitro fertilization (IVF) for women with prior IVF failures.

DESIGN: Prospective study.

MATERIALS AND METHODS: Infertility patients presenting with ≥ 1 prior failed IVF cycle, maternal age <45 years and no severe male factor infertility were consented into the study (n=124). Female patients (mean age = 37.8 ± 5.8 years) were instructed to take 600mg of natural Euterpe oleracea three times a day for 8-12 weeks prior to routine ovarian stimulation. The Euterpe oleracea administered in this study was biochemically tested to confirm high anti-oxidant activity. IVF cycle and FET outcomes were analyzed for each patient comparing their most recent IVF cycle without as a control to their IVF cycle with anti-oxidant supplementation using the Student’s paired t-test and Fisher’s exact test, with significance at P<0.05.

RESULTS: The vast majority of the women presented with normal ovarian reserve (AMH= 3.9 ±3.3 ng/ml; FSH=7.5 ±2.7 IU/L) and they all experienced ≥ 1 failed IVF cycle prior to the study. Following anti-oxidant supplementation only one patient had her cycle cancelled (0.8%), four patients had no embryos develop to the blastocyst stage (3.2%) and 25 patients had all aneuploid blastocysts (20.2%). Of the remaining 93 patients with euploid blastocysts (54% overall euploidy) there were significant improvements in comparison to the control cycle in oocyte yield (19.6 ±9.7 vs. 14.5 ±7.6; P=0.0001) and in number of fertilized zygotes (11.1 ±6.0 vs. 7.9 ±5.1; P=0.0003). Outcomes after transfer of euploid blastocyst (mean 1.6) for these 93 patients all with prior IVF failure were excellent: 84.9% clinical pregnancy with fetal heart tone, 6.3% miscarriage rate and 79.6% live birth rate.

CONCLUSIONS: Preliminary results indicate improvements in clinical IVF outcomes following the supplementation of a highly active anti-oxidant prior to ovarian stimulation. The restoration of the balance between oxidants and anti-oxidants in the ovary during the early stages of oocyte development may account for the clinical improvements observed. Ongoing investigations into the factors associated with oocyte quality will contribute to improved success for women with a history of IVF failures.

P-425 Wednesday, October 19, 2016

OBJECTIVE: To determine the effect of body mass index (BMI) on outcomes after euploid frozen embryo transfers (FET).

DESIGN: Retrospective chart review.

MATERIALS AND METHODS: All FET cycles between 2013 and 2015 at a single academic infertility center were included. Only cycles involving the transfer of a single euploid blastocyst after 24-chromosome analysis of a trophectoderm biopsy were included. Cycles were excluded if the blastocyst did not survive thaw. The primary outcome was live birth/ongoing pregnancy rate. Secondary outcomes included implantation, clinical pregnancy, and miscarriage rates. Patient age at oocyte retrieval, age at embryo transfer, day of PGS (5 versus 6), type of FET (hormone replacement, supplemented natural cycle, natural supplemented converted to hormone replacement, and augmented), endometrial thickness prior to transfer, blastocyst quality (expansion, ICM and trophectoderm grades) and infertility diagnosis were controlled for with a multivariate log regression model. Chi-squared analysis was used to compare FET outcomes stratified by BMI.

RESULTS: 190 FET cycles during the study period met inclusion criteria. The average age of the patients at time of retrieval and transfer was 36.6 and 37.1 years respectively. Twenty percent of patients had primary infertility and 25.9% had ≥2 previous pregnancy losses. Average BMI was 23.5 with a range from 16 to 41. The majority (56.3%) of FETs occurred within a supplemented natural cycle. There were similar FET outcomes between overweight patients and those with a normal BMI, while there was a trend for obese patients having a lower live birth rate than overweight patients (Table). Within the multivariate log regression model, BMI did not correlate with live birth/ ongoing pregnancy (r=0.19, 95% CI [-0.19 to 0.57]), implantation (r=0.018, 95% CI [-0.242 to 0.278]), intrauterine pregnancy (r=0.16, 95% CI [-0.164 to 0.478], or miscarriage (r=0.07, 95% CI [-0.150 to 0.282]) after controlling for age, type of FET, day of PGS, endometrial thickness, blastocyst quality and infertility diagnosis.

CONCLUSIONS: For patients with a BMI <30 with a euploid blastocyst available to transfer, BMI does not significantly affect implantation or live birth/ongoing pregnancy rates in FET cycles; however obese patients may have lower live birth rates than normal or overweight patients, although this may be confounded by the higher incidence of RPL among our obese cohort. Given our limited sample of obese patients, more studies are needed to understand the effect of increasing BMI on euploid FET outcomes in an obese population.

P-426 Wednesday, October 19, 2016
THE效应 OF TELOMERES ON IN VITRO FERTILIZATION RESULTS. N. Weeg, E. Haikin Herzberger, T. Biron-Shental, A. Wiser. Obstetrics and Gynecology, Meir Medical Center, Israel, Kfar Saba, Israel; IVF Unit, Department of Obstetrics and Gynecology, Sackler Faculty of Medicine, Tel Aviv University, Tzur Yigal, Israel; Obstetrics an Gynecology, Consultant of Maternal Fetal Medicine, Kfar Saba, Israel; IVF Unit, Meir Medical Center, Kfar Sava, Israel.

OBJECTIVE: Telomeres are a specific base sequence of DNA, responsible for chromosome stability and DNA protection. The presence of telomeres at the end of chromosomes means that bases lost at replication are those of telomeres and not those of genetic material. Telomere sequence is added to the chromosome by telomerase and thus chromosomes lengthen. Other ways of preventing telomere shortening include telomere capture, senescence and telomere aggregate formation. It is well established that telomere length is shortened in the obese and in the older populations but information is lacking regarding the association between the telomere array and IVF results.

We aimed to investigate whether the telomere system affects IVF results in patients with raised BMI and patients with normal BMI.

DESIGN: Prospective, observational, cohort study, of 20 IVF patients aged 18-40, over the course of three months.

MATERIALS AND METHODS: The patients’ leucocytes were analysed for telomere characteristics after undergoing Fluorescent in situ Hybridization (FISH) and Quantitative Fluorescent in situ Hybridization (Q-FISH) with the use of probes for lTERC, 15q, 13q and FNA. Characteristics analysed included:

<table>
<thead>
<tr>
<th>Single euploid FET outcomes stratified by patient BMI</th>
<th>BMI&lt;25</th>
<th>BMI 25 to 30</th>
<th>BMI &gt;30</th>
<th>p-value</th>
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</thead>
<tbody>
<tr>
<td>(+) HCG</td>
<td>66.4%</td>
<td>70.5%</td>
<td>66.7%</td>
<td>0.82</td>
</tr>
<tr>
<td>Intrauterine pregnancy</td>
<td>56.2%</td>
<td>61.4%</td>
<td>33.3%</td>
<td>0.12</td>
</tr>
<tr>
<td>Live birth</td>
<td>50.3%</td>
<td>47.8%</td>
<td>33.3%</td>
<td>0.43</td>
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</table>
and follicular fluid of obese and normal body mass index (BMI) women un-
GYN, Washington University in St. Louis, St. Louis, MO.
explain the association between obesity and sub-optimal IVF results.
the telomere array.
Board of Vivere Health, and the American Diabetes Association.
analyzing CoQ10 levels in our samples. We received support from the Na-
of oocytes retrieved, or fertilization rates between the obese and normal-BMI
P < 0.04) and were significantly, positively correlated with
< 0.04) as compared to non-obese patients (BMI < 30 kg/m²). These odds remained
unchanged after adjusting for patient's age. The number of transferred blasto-
cell(s) (grade 3BB) were included. Patients who had transfer of
of embryos and quality of embryos were not affected by the
CONCLUSIONS: We found an association between telomere features and IVF results as depicted above.
While there is paucity of data in the literature concerning the association between telomere characteristics and infertility, telomeres might be able to explain the association between obesity and sub-optimal IVF results.

P-427 Wednesday, October 19, 2016
OBESITY INCREASES COENZYME Q10. C. Boots K. Moley. OB/GYN, Washington University in St. Louis, St. Louis, MO.
OBJECTIVE: To compare levels of coenzyme Q10 (CoQ10) in the serum and follicular fluid of obese and normal body mass index (BMI) women under-
going assisted reproductive technology (ART).
DESIGN: Retrospective cohort study.
MATERIALS AND METHODS: Ten obese (BMI ≥ 30 kg/m²) and ten normal weight (BMI 18.9-24.9) women 30-35 years old who underwent ART treatment of infertility were selected. Only women stimulated with a long gonadotropin releasing hormone agonist protocol were included. Women with a diagnosis of endometriosis, primary ovarian insufficiency, polycystic ovarian syndrome, recurrent pregnancy loss, or oocyte donors were excluded. Fasting serum was collected in the morning of the oocyte retrieval, and follicular fluid was collected from aspiration of the first mature follicle. Analysis of CoQ10 was performed using a liquid chromatography-tandem mass spectrometry method. For parametric analysis of continuous variables, students t-test and Pearson correlation were utilized. Mann-Whitney U test and Spearman correlation were used for non-parametric variables. Results are expressed as median and \( P \) values of < 0.05 were considered significant.
RESULTS: There were no differences in age, antral follicle count, total dose of gonadotropins, duration of stimulation, peak estradiol levels, number of oocytes retrieved, or fertilization rates between the obese and normal-BMI women. Five women in each group ended in miscarriage, and four women did not conceive. Serum CoQ10 levels were significantly higher in obese women (133.5 ng/mL vs. 102.7 ng/mL, \( P = 0.04 \)) and were significantly, positively correlated with BMI (R = 0.54, \( P = 0.13 \)). In addition, both BMI and serum CoQ10 significantly, inversely correlated with the number of oocytes retrieved (R = -0.47, \( P < 0.05 \); R = -0.51, \( P = 0.02 \)). When compared to women who achieved a live birth, women who did not get pregnant had higher levels of CoQ10, although this did not reach statistical significance (122.5 ng/mL vs. 115 ng/mL, \( P = 0.86 \)). Follicular fluid concentrations of CoQ10 were not different between obese and normal-BMI women and did not correlate with any ART stimulation characteristics. The correlation between CoQ10 concentrations in serum and follicular fluid did not reach statistical significance (R = 0.442, \( P = 0.51 \)).
CONCLUSIONS: Obesity induces oxidative stress and has been shown to impair oocyte mitochondrial function (1,2). Levels of CoQ10, a key antioxidant in mitochondrial energetics, are elevated in the serum but not in the follicular fluid of subfertile, obese women. Further research is needed to investigate whether additional supplementation could improve reproductive outcomes.

References:

Supported by: We would like to acknowledge the Women and Infants Health Science Consortium for providing serum and follicular samples and the Diabetic Cardiovascular Disease Center- Metabolomics Facility for analyzing CoQ10 levels in our samples. We received support from the National Research Training Program in Reproductive Medicine sponsored by the National Institute of Health (T32 HD040135-13), the Scientific Advisory Board of Vivere Health, and the American Diabetes Association.

P-428 Wednesday, October 19, 2016
THE ROLE OF TAC1 NEURONS IN THE METABOLIC AND REPRODUCTIVE ACTION OF LEPTIN. E. I. Lewis,*, C. A. Maguire,*, R. S. Carroll,*, U. B. Kaiser,*, V. M. Navarro,*, Department of OB/GYN, Brigham and Women’s, Boston, MA; *Harvard Medical School, Boston, MA; †Department of Medicine, Division of Endocrinology, Brigham and Women’s, Boston, MA.
OBJECTIVE: Central deficiency of leptin signaling is well known to be associated with metabolic and reproductive dysregulation, but the identification of leptin responsive 1st order neurons remains elusive. The Tac1 gene (encoding substance P and neurokinin A) has recently been implicated in the timing of puberty onset and control of body weight. Importantly, Tac1 neurons have been described to express leptin receptor (Lepr) in lateral hypothalamic nuclei and the ventral premamillary nuclei. We aimed to deter-
mine whether Tac1 neurons mediate the reproductive and/or metabolic actions of leptin.
DESIGN: Cohort study.
MATERIALS AND METHODS: To evaluate the interaction between lep-
tin and Tac1 neurons, we selectively ablated the leptin receptor from Tac1 neu-ons of male and female mice (Tac1-Cre:Leprfl/fl), Tac1-Cre:Leprfl/fl mice were compared to wild type (WT) littermate controls . Body weight, puberty onset and response to high fat diet (HFD) were monitored in female mice.
RESULTS: Leprfl/fl and littermate control mice displayed similar body weight when fed a standard chow diet over 20 weeks. However, our prelimi-
ary data indicate that adult Tac1-Cre:Leprfl/fl females subjected to a 60% HFD gained more weight than controls over a 7 day period. In terms of their
reproductive function, our preliminary studies have not revealed any disrup-
tion in the timing of puberty onset, as determined by timing of vaginal opening or first estrus in females.
CONCLUSIONS: Our results suggest that lepr-expressing Tac1 neurons may participate in the metabolic actions of leptin. These data increase our un-
derstanding of the neuroendocrine mechanisms that govern energy balance and their possible link with fertility and may offer new avenues of research to treat reproductive disorders derived from metabolic alterations, e.g. obesity, diabetes or PCOS. Further studies are underway to fully characterize the metabolic and reproductive phenotype of these mice with Lepr deletion from Tac1 neurons.

P-429 Wednesday, October 19, 2016
OBESITY IS ASSOCIATED WITH AN INCREASE IN SPONTANEOUS ABORTION RATE IN YOUNG WOMEN UNDERGOING IVF WITHOUT AFFECTING THE ANEUPLOIDY RATE. M. Irani,*, V. Gunalda,*, Z. Rosenwaks,* S. D. Spandorfer,* Re-
productive Endocrinology and Infertility, Weill Cornell Medicine, New York, NY; *OB/GYN, REI Fellow, New York, NY; *Weill Cornell Medicine - Center for Reproductive Medicine, New York, NY; *Cornell University Medical Center, New York City, NY.
OBJECTIVE: To determine the effect of obesity on pregnancy outcomes in young patients undergoing IVF.
DESIGN: Retrospective cohort study.
MATERIALS AND METHODS: Young patients (age ≤ 35 years) who underwent autologous fresh or frozen IVF cycles between January 2004 and May 2013 were screened for inclusion. Patients who had transfer of good quality blastocyst(s) (grade ≥ 3BB) were included. Patients with his-
tory of recurrent pregnancy loss were excluded. Values were expressed as mean ± SD. \( \chi^2 \) test, t-test, and Fisher’s exact test were used as appropriate. Odds ratio (OR) with 95% confidence intervals (CI) were calculated and adjusted when indicated.
RESULTS: 970 pregnant women (60.1%) of 1613 young patients undergo-
ing IVF were included. Among patients who achieved clinical pregnancy, obese patients (BMI ≥ 30 kg/m²) had more than twice the risk of having spontaneous abortion (OR = 2.2; 95% CI = 1.1 - 4.1) and less than half the chance of achieving live birth (OR = 0.45; 95% CR = 0.24 - 0.85) as compared to non-obese patients (BMI < 30 kg/m²). These odds remained un-
changed after adjusting for patient’s age. The number of transferred blasto-
cysts was compared between the two groups (1.8 ± 0.5 vs 1.7 ± 0.5; \( P < 0.05 \)), as was the rate of spontaneous abortion that occurred in obese patients and 52% of those that occurred in non-obese patients (p = 0.2) had normal karyo-
type on cytogenetic analysis of the products of conception.
CONCLUSIONS: Obesity is associated with a significant increase in spontaneous abortion rate and a significantly lower live birth rates in young patients undergoing IVF. It is associated with a decline in pregnancy out-
comes without affecting the aneuploidy rate.

OBJECTIVE: To develop a non-invasive diagnostic test for endometriosis based on a comparison of miRNA expression in plasma from patients with and without endometriosis.

DESIGN: Whole genome miRNA expression profiling by small RNA next generation sequencing (NGS) in 120 patients. All patients had laparoscopically proven presence (n=82; stage I-II n=41, stage III-IV n=41) or absence (n=38) of endometriosis.

MATERIALS AND METHODS: Plasma samples of all patients were available in the biobank of the Leuven Endometriosis Center of Excellence. RNA was extracted with the miRNeasy Plasma Kit (Qiagen) according to the manufacturers protocol and library prep was done with the NEBBNext small RNA library prep kit (New England Biolabs). Small RNA NGS was performed with the NextSeq 500 System (Illumina) at a read length of 75 base pairs and 15 million reads per sample. The miRBase 21 was used for read mapping and annotation. Multivariate logistic regression with stepwise feature selection was used to build the diagnostic models for endometriosis. Only miRNAs that were expressed in 80% of samples of either one of both analyzed patients subgroups were included.

RESULTS: We built 2 diagnostic models consisting of 6 miRNAs. Model 1 (Let-7b-3p, Let-7d-5p, miR-106a-5p, miR-98-5p, miR29b-3p, miR-92a-3p) could discriminate between controls and patients with stage I-II endometriosis with an area under the curve (AUC) of 92%, a sensitivity of 86% and specificity of 92%. Model 2 (miR-29b-3p, miR-101-3p, miR-92a-3p, miR-107, miR-148a-3p, miR-23a-3p) could discriminate between controls and patients with stage III-IV endometriosis with an AUC of 89%, a sensitivity of 79% and specificity of 88%.

CONCLUSIONS: We are the first group to use NGS for miRNA expression analysis in plasma from patients with and without endometriosis. This state-of-the art technology is ideal for unbiased genome wide miRNA expression profiling. Two panels of 6 miRNAs could discriminate between controls and stage I-II or stage III-IV endometriosis with high sensitivity and specificity. When validated, these models would allow non-invasive diagnosis of endometriosis. This would be a major improvement in care of patients with endometriosis by reducing the diagnostic delay of 4-7 years and obviate the need for a diagnostic laparoscopy.

CONCLUSIONS: Women taking NA reported more breakthrough bleeding than those who received LD treatment. Bleeding remained constant throughout treatment for those in the NA only group. Breakthrough bleeding in those who initially received LD worsened when transitioned to NA.

Supported by: NIH Grant R01-HD043281, SUNY Downstate Medical Center.

INCIDENTIAL COSTS OF HEALTHCARE AND WORK LOSS ATTRIBUTED TO ENDOMETRIOSIS IN A COHORT OF COMMERCIALY INSURED WOMEN. A. M. Soliman, E. Surrey, M. Bonafe, J. K. Nelson, J. Castelli-Haley, C. A. Winkel. AbbVie Inc, North Chicago, IL; Colorado Center for Reproductive Medicine, Lone Tree, CO; Truven Health Analytics, An IBM Company, Ann Arbor, MI; AbbVie, North Chicago, IL; Obstetrics and Gynecology, Georgetown University, Shepherdstown, WV.

OBJECTIVE: To quantify incremental direct healthcare costs and indirect costs among newly-diagnosed endometriosis patients compared to patients without an endometriosis diagnosis.

DESIGN: Retrospective cohort study using a deidentified administrative claims database.

MATERIALS AND METHODS: Truven Health MarketScan Commercial and Medicare supplemental claims databases were used to identify women aged 18-49 newly diagnosed with endometriosis (ICD-9-CM 617.xx) between January 2010 and June 2014 (index date). Age- and gender-matched controls selected from the database and were assigned index dates matching the distribution of endometriosis patients index dates. Women with 12 months continuous enrollment pre- and post-index and no evidence of endometriosis pre-index were included in the analysis. Study outcomes were annual direct healthcare costs (medical and pharmacy costs) and indirect costs (absenteeism, short-term and long-term disability) for 12-months post-index in 2014 US$. Indirect costs were assessed on a subset of patients with available data. Multivariable gamma regression models were used to estimate incremental costs associated with endometriosis while controlling for baseline demographic and clinical characteristics.

RESULTS: The final study sample included 113,506 endometriosis patients and 927,599 controls. Among endometriosis patients, unadjusted and multivariable-adjusted annual direct costs and indirect costs were significantly higher for endometriosis patients (table). Pharmacy costs were 11% of healthcare costs among endometriosis patients, and 26% among controls. The majority (62%) of annual costs for endometriosis patients were incurred within 3 months post-index.

CONCLUSIONS: Endometriosis was associated with substantial incremental direct and indirect costs among commercially insured patients in the United States. Given its prevalence, this suggests substantial disease burden associated with endometriosis to the individual, health care system, and society.

Multivariable-adjusted 12-month costs per patient (2014 $)

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<thead>
<tr>
<th>Cost Category</th>
<th>Endometriosis Patients</th>
<th>Controls</th>
<th>Adjusted difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Healthcare Costs (N = 1,041,105)</td>
<td>$14,648</td>
<td>$4,646</td>
<td>$10,002</td>
</tr>
<tr>
<td>Indirect costs: Absence (N = 11,416)</td>
<td>$5,157</td>
<td>$4,254</td>
<td>$903</td>
</tr>
<tr>
<td>Indirect costs: Short-term disability (N = 87,967)</td>
<td>$1,632</td>
<td>$404</td>
<td>$1,228</td>
</tr>
<tr>
<td>Total Indirect Costs</td>
<td>$6,819</td>
<td>$4,687</td>
<td>$2,132</td>
</tr>
</tbody>
</table>

All cohort differences are statistically significant, P<.001, endometriosis cohort > control cohort

Supported by: The design and financial support for the study were provided by AbbVie. AbbVie participated in data analysis, interpretation of data, review, and approval of the abstract. Medical writing services were provided by Isabelle Winer, an employee of Truven Health Analytics. Medical writing services were funded by AbbVie.
**OBJECTIVE:** Endometriosis is a chronic disease characterized by the growth of endometrial glands and stroma outside the uterus. We have previously shown that bone marrow-derived cells (BMDCs) can migrate to ectopic sites and contribute to the development of endometriosis. In this study we determined the effect of the three well-known endometriosis treatments on stem cell recruitment to the endometriotic lesions.

**DESIGN:** Randomized trial treating murine experimental endometriosis. MATERIALS AND METHODS: C57BL/6 mice (age 8 weeks, n=20) underwent bone marrow transplant following myeloablation with 5-Fluorouracil using 20x10^6 bone marrow stem cells from green fluorescent protein (GFP) mice. After two weeks, experiment endometriosis was established by implanting 4 mm² uterine tissue fragments into the peritoneal cavity. After 10 days the mice were divided into 4 groups and treated with either vehicle (DMSO control), medroxyprogesterone acetate (MPA) (50 μg/day s.c.), leuprolide acetate (10 mg/kg/week s.c.) or letrozole (0.5 mg/kg/day s.c.). Three weeks after treatment, mice were euthanized and endometriosis lesions were harvested. Lesion weights were calculated. Immunofluorescence staining was done with GFP and CD45 antibodies. The number of GFP positive CD45 negative cells were counted in multiple high power fields to determine the number of engrafted bone marrow derived stromal stem cells (BMDSCs). Differences were compared using the student’s T test.

**RESULTS:** As expected, lesion size was improved by treatment. The vehicle group had the greatest lesion weight, MPA had little effect while letrozole and leuprolide acetate treatment resulted in significantly lower lesion weights to approximately 1/3 of the original size (p<0.01). There was no significant difference in the number of BMDSCs recruited to endometriosis between the MPA and vehicle treated groups. Significantly fewer BMDSCs were identified in the letrozole and leuprolide acetate treatment groups. Lesions treated with either of the latter medications showed an approximately 50% reduction in density of BMDSC engraftment (p<0.001).

**CONCLUSIONS:** Letrozole and leuprolide acetate prevent the stem cell recruitment to endometriosis and limit the growth of lesions. Diminished stem cell recruitment is a novel mechanism of action in the treatment of endometriosis and limit the growth of lesions. Diminished stem cell recruitment is a novel mechanism of action in the treatment of endometriosis and limit the growth of lesions. Diminished stem cell recruitment is a novel mechanism of action in the treatment of endometriosis and limit the growth of lesions. Diminished stem cell recruitment is a novel mechanism of action in the treatment of endometriosis and limit the growth of lesions.

**Secondary Endpoints:** NRS, PGIC, and DYSP

<table>
<thead>
<tr>
<th>Secondary Pain Parameters</th>
<th>STUDY1, Placebo N=374</th>
<th>STUDY1, Elagolix 150 mg QD N=249</th>
<th>STUDY1, Elagolix 200 mg BID N=248</th>
<th>STUDY2, Placebo N=360</th>
<th>STUDY2, Elagolix 150 QD N=226</th>
<th>STUDY2, Elagolix 200 mg BID N=229</th>
</tr>
</thead>
<tbody>
<tr>
<td>NRS, mean (SD) score at BL</td>
<td>5.58 (1.57)</td>
<td>5.72 (1.73)</td>
<td>5.48 (1.59)</td>
<td>5.56 (1.76)</td>
<td>5.69 (1.78)</td>
<td>5.33 (1.78)</td>
</tr>
<tr>
<td>NRS, mean (SD) score at M6</td>
<td>4.48 (2.24)</td>
<td>3.98 (2.60)</td>
<td>2.96 (2.55)</td>
<td>4.03 (2.35)</td>
<td>4.32 (2.51)</td>
<td>2.59 (2.39)</td>
</tr>
<tr>
<td>NRS, LS mean (SE) change from BL to M6</td>
<td>-1.15 (0.11)</td>
<td>-1.80 (0.14)***</td>
<td>-2.75 (0.14)***</td>
<td>-1.60 (0.11)</td>
<td>-2.28 (0.14)***</td>
<td>-2.87 (0.14)***</td>
</tr>
<tr>
<td>PGIC Response at M6, n/n [%]</td>
<td>95/308 [31]</td>
<td>115/207 [56]***</td>
<td>149/200 [75]***</td>
<td>116/326 [36]</td>
<td>123/213 [58]***</td>
<td>159/210 [76]***</td>
</tr>
<tr>
<td>DYSP, mean (SD) score at BL</td>
<td>1.51 (0.83)</td>
<td>1.52 (0.82)</td>
<td>1.55 (0.86)</td>
<td>1.45 (0.83)</td>
<td>1.48 (0.88)</td>
<td>1.43 (0.85)</td>
</tr>
<tr>
<td>DYSP, LS mean (SE) change from BL to M6</td>
<td>-0.29 (0.05)</td>
<td>-0.41 (0.06)</td>
<td>-0.60 (0.06)***</td>
<td>-0.36 (0.05)</td>
<td>-0.42 (0.06)</td>
<td>-0.69 (0.06)***</td>
</tr>
<tr>
<td>DYSP, responders at M6, n [%]</td>
<td>90 [33]</td>
<td>74 [40]</td>
<td>81 [50]*</td>
<td>100 [39]</td>
<td>65 [40]</td>
<td>92 [56]**</td>
</tr>
</tbody>
</table>

NRS = numeric rating scale; PGIC = Patient Global Impression of Change; DYSP = dyspareunia; LS = least squares. Statistical significance vs. placebo is indicated for P<0.05 (*), P<0.01 (**), P<0.001 (***). Ns vary for each time point and will be reported in the presentation. NRS and DYSP change from baseline p-values derived from a mixed-model with repeated measures analysis with treatment as a main effect and baseline value as a covariate. DYSP responder p-values derived from a logistic regression with treatment as a main effect and baseline value as a covariate. PGIC p-values derived from a chi-square test. a. Proportion of participants whose response was “very much improved” or “much improved” on the PGIC.
CONCLUSIONS: In women with endometriosis, 6 months of elagolix treatment led to a dose-dependent improvement in EAP, when self-assessed using NRS and PGIC scales, and DYSF, which was statistically signifi cantly improved for elagolix 200 mg BID compared to placebo.

Supported by: AbbVie Inc. funded these studies and participated in the study design, research, analysis, data collection, interpretation of data, reviewing, and approval of the publication.

**P-435 Wednesday, October 19, 2016**

**PROLONGED ADMINISTRATION OF GnRH AGONIST (GnRHa) PRIOR TO EMBRYO TRANSFER (ET) IN ENDOMETRIOSIS (ENDO) AND INTEGRIN (INT)NEGATIVE PATIENTS: THE IMPACT OF FREEZE-ALL CYCLES.** E. Surrey, M. Katz-Jaffe, L. A. Kondapalli, R. L. Gustafson, W. B. Schoolcraft. Colorado Center for Reproductive Medicine, Lone Tree, CO.

OBJECTIVE: The benefit of prolonged GnRHa administration prior to initiation of IVF with fresh ET in patients with endo or aberrant endometrial αvβ3 Int expression has been previously demonstrated (1, 2). However, this approach may suppress ovarian response to gonadotropin stimulation. This study evaluates the impact of freeze-all cycles with subsequent prolonged GnRHa therapy prior to frozen embryo transfer (FET) in these patient populations.

DESIGN: Retrospective cohort.

MATERIALS AND METHODS: All consecutive patients from 2010-15 who underwent IVF with autologous oocytes, vitrification of all embryos at the blastocyst or cleavage stage and subsequent FET cycles after prolonged GnRHa were evaluated (42 patients and 45 transfers). All patients had a prior surgical diagnosis of endo and/or aberrant endometrial Int expression (Pathology Consultants, Greenville, SC). A subset of cycles included comprehensive chromosomal screening (CCS) subsequent to trophotrope biopsy after which only embryos predicted to be euploid were transferred. Lupon Depot 3.75 mg (Abbvie, N. Chicago, IL) was administered every 28 days x 2 to all patients prior to FET. 3 patient groups were identified. Group 1: + CCS, + Endo (20 patients, 20 transfers). Group 2: + CCS, -Int (12 patients, 13 transfers). Group 3: No CCS, + Endo and/or -Int (10 patients, 12 transfers). Data analysis: Student’s paired t-tests, chi square tests where appropriate. P<0.05 was considered to be statistically significant.

RESULTS: Expressed as mean ± standard deviation unless otherwise indicated.

CONCLUSIONS: Administration of prolonged GnRHa after vitriﬁ cation of all embryos in IVF patients with endo and/or aberrant Int expression led to higher IR and OPR in all treatment groups despite a high incidence of prior cycle failure. A trend towards higher IR and OPR which did not reach statistical signiﬁ cance was noted in Gr. 1 patients with a history of endo who also underwent CCS. This approach avoids excessive ovarian suppression which can result from prolonged GnRHa administration prior to fresh IVF/ET and also allows for performance of CCS when indicated.

References:

**P-436 Wednesday, October 19, 2016**

**LOW PREVALENCE OF ENDOMETRIAL BIOPSIES CONTAINING NERVE FIBERS IN WOMEN WITH AND WITHOUT ENDOMETRIOSIS.** D. O. A. F. Manconi, R. Markham, A. Fassbender, D. P. Peterse, A. Vanhie, C. Meuleman, I. S. Fraser, T. D’Hooge. Department of Development & Regeneration, KU Leuven, Leuven, Belgium; *University of Sydney, Sydney, Australia; †Women’s and Children’s Health, University of New South Wales, Sydney, Australia.

OBJECTIVE: To test the hypothesis that nerve fiber density is higher in eutopic endometrium of women with endometriosis compared to controls without endometriosis in samples collected in a university fertility center.

DESIGN: A retrospective biobank-based cohort study was conducted. Biopsies of secretory endometrium (n=66) were selected for immunohistochemistry. Biopsies had been obtained using a Novak curette prior to laparoscopy for pelvic pain and/or infertility.

MATERIALS AND METHODS: 4 μm sections of endometrial biopsies from women (n=37) and without (n=29) endometriosis were immunohistochemically stained using the pan-neuronal marker PGP9.5 (1:400; Dako) with 3,3'-Diaminobenzidinetetrahydrochloride (DAB) as chromogen. Identification of nerve fibers was undertaken blindly and was independent of the surgical assessment of endometriosis. The prevalence of endometrial biopsies containing nerve fibers was compared between endometriosis cases and controls by using the χ² test.

RESULTS: The overall prevalence of samples containing nerve fibers was low (5/66 = 7.6%) and no significant difference was found between women with (3/37 = 8.1%) and without (2/29 = 6.9%) endometriosis (p = 0.8535).

CONCLUSIONS: We were not able to confirm previous reports of endometrial nerve fiber density as a promising semi-invasive diagnosis for endometriosis. More research is needed to explain the large variability of published results in this research area before nerve fiber presence in endometrium can be used as a diagnostic test for endometriosis or pelvic pain. Technical issues appeared to be at the root of the low detection rate of nerve fibers, e.g. several aspects of biopsy quality, perhaps patient selection and assessment, or the implemented staining protocols. This study with negative outcome underlines the importance of rigorous protocols for patient selection, sample collection and sample processing in order to maximize biopsy quality allowing detection of the fine, narrow and limited axon lengths within endometrial tissue.

Supported by: Funding of this research was obtained from the Research Foundation-Flanders (FWO, application number 11X5515N) and the Clinical Research Foundation of Leuven University Hospitals.

**P-437 Wednesday, October 19, 2016**

**FERTILITY IN PATIENTS WITH UNTREATED COLORECTAL ENDOMETRIOSIS.** S. Ferrero, U. Leone Roberti Maggiore, C. Scala, E. Tah, P. Venturellini, A. Racca. Unit of Obstetrics and Gynaecology, IRCCS AOU San Martino – IST, DiNOGMI, University of Genova, Genova, Italy; Unit of Obstetrics and Gynaecology, IRCCS AOU San Martino – IST, DiNOGMI, University of Genova, Genova, Italy.

OBJECTIVE: Reproductive outcomes after surgical treatment of colorectal endometriosis are well documented both in infertile women and in those with unknown fertility status. However, the pregnancy rate of patients with untreated bowel endometriosis is unknown. The aim of this study is to evaluate the pregnancy rate in patients with colorectal endometriosis who did not undergo surgery.

<table>
<thead>
<tr>
<th>Group (Gr.)</th>
<th>Transfer Cycles (n)</th>
<th>Age (years)</th>
<th>AMH (ng/mL)</th>
<th>Prior Failed Transfers (Range)</th>
<th>Embryos Transferred</th>
<th>Implantation Rate (IR) (+FHT)</th>
<th>Ongoing Pregnancy Rate (OPR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>20</td>
<td>35±3.7</td>
<td>3.01±2.59</td>
<td>1.7±1.76 (0-6)</td>
<td>1.4±0.49</td>
<td>79%</td>
<td>75%</td>
</tr>
<tr>
<td>2</td>
<td>13</td>
<td>34.2±5.2</td>
<td>3.15±1.92</td>
<td>2.62±1.64 (0-3)</td>
<td>1.69±0.46</td>
<td>68%</td>
<td>54%</td>
</tr>
<tr>
<td>3</td>
<td>12</td>
<td>32±4.1</td>
<td>2.83±2.9</td>
<td>1.17±1.54 (0-4)</td>
<td>1.36±0.48</td>
<td>71%</td>
<td>50%</td>
</tr>
<tr>
<td>P</td>
<td>NS*</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

*NS = Not significant for all between group comparisons, p>0.05
CONCLUSIONS: We show here that females are predisposed to progressive fibrosis and this is likely mediated by sex steroid mediated dysregulation of the disease relevant transcription factor KLF11. These findings also explain the reproductive age predilection of fibrotic scarring in females. We use a unique peritoneal scarring model to evaluate fibrotic progression in response to oophorectomy. Our findings corroborate those in the endometriosis model that precludes evaluation after ovariectomy. We further characterized individual sex hormones using in vitro to show that estradiol/Klf11 signaling is critical for progression of scarring in association with endometriosis and other chronic diseases.

References:

Supported by: Supported by a Fellowship Research Funds from the Division of Reproductive Endocrinology at the Mayo Clinic.

P-439 Wednesday, October 19, 2016

THE REGULATORY ROLE OF ENDOMETRIOSIS DERIVED CIRCULATING MICRO-RNAS 125B-5P AND LET-7B-5P IN MACROPHAGE CYTOKINE PRODUCTION. T. S. Kadakia,a,b,c S. E. Nematian,a R. Mamillapalli,a H. S. Taylor,a OB/GYN, Mount Sinai Beth Israel Medical Center, New York, NY; OC Obstetrics, Gynecology and Reproductive Medicine, Yale University, New Haven, CT; OB/GYN, Mount Sinai Beth Israel Medical Center, New York, NY; OB/GYN, Mount Sinai Beth Israel Medical Center, New York, NY; aOB/GYN, Mount Sinai Beth Israel Medical Center, New York, NY; bObstetrics, Gynecology and Reproductive Medicine, Yale University, New Haven, CT; cObstetrics, Gynecology and Reproductive Sciences, Research, New haven, CT; dYale School of Medicine, New Haven, CT.

OBJECTIVE: To determine the role of microRNAs (miRNAs) 125b-5p and let-7b-5p in the regulation of pro-inflammatory cytokine expression by macrophages. We have previously reported that the miRNA 125b-5p is increased in serum of patients with endometriosis, while miRNA let-7b-5p is decreased. Here we postulate that these miRNAs may have direct regulatory effects on circulating macrophages and thereby contribute to inflammation associated with endometriosis.

DESIGN: Differentiated macrophages from a human monocyte cell line were transfected with miRNA mimics of 125b-5p and let-7b-5p. The total RNA collected and reverse transcribed were analyzed for relative expression of cytokines, tumor necrosis factor- alpha (TNF-a), Interleukin-6 (IL-6), Interleukin-8 (IL-8), and Interleukin-1B (IL1B) using Real-time PCR.

MATERIALS AND METHODS: The human myelomonocytic U937 cells were cultured in RPMI 1640 growth medium. The cell differentiation was carried out by treating the cell suspension (1 x 10^6 cells/ml) with Phorbol-12-myristate-13-acetate (PMA, 100 ng/ml) for 48 hours. PMA-treated cells were washed twice with ice-cold PBS to remove PMA and non-adherent cells and fresh growth medium was added to the adherent cells to grow for 48 hr. The differentiated macrophages from myelomonocytic cells were transfected with either hsa-miR-125b-5p or hsa-let-7b-5p miRNA mimics in a 6-well plate containing 2.0 x10^5 cells/well. Total RNA was isolated from the post-transfected (48 hr) cells with TRIzol method. The relative expression of cytokines was quantified by qRT-PCR. The statistical significance of the results was analyzed by Mann-Whitney U test.

RESULTS: qRT-PCR results showed a statistically significant increase in expression of cytokines TNF-a (2.66 fold, p<0.001), IL-1B (1.86 fold, p=0.002), IL-6 (1.51 fold, p<0.001), and a trend toward upregulation for IL6 (1.51 fold) in macrophages transfected with miRNA 125b-5p. The use of a unique peritoneal scarring model to evaluate fibrotic progression in response to oophorectomy demonstrated a statistically significant decrease in expression of cytokines TNF-a (0.58 fold difference, p<0.001), IL-1B (0.56 fold difference, p=0.001), and a trend toward downregulation for IL-1B (0.88 fold difference) and IL-6 (0.74 fold difference) in macrophages transfected with miRNA let-7b-5p.
CONCLUSIONS: This is the first study to identify a direct mechanism by which endometriosis leads to inflammation. Circulating microRNA from endometriosis may directly regulate immune cell function. miRNA 125-5p and let-7b-5p regulate macrophage cytokine production leading to a pro-inflammatory state. Modulating circulating microRNAs are a novel potential treatment for endometriosis associated inflammation.

Supported by: OvaScience Inc., Boston, MA, USA.

P-440 Wednesday, October 19, 2016
ELAGOLIX, AN ORAL GONADOTROPIN-RELEASING HORMONE ANTAGONIST, FOR THE MANAGEMENT OF ENDOMETRIOSIS-ASSOCIATED PAIN: SAFETY AND EFFICACY RESULTS FROM TWO DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED STUDIES. H. S. Taylor, L. C. Giudice, B. A. Lessey, M. Abrao, I. Kotarski, L. A. Williams, J. P. Rowan, K. Chwalisz, W. R. Duan, B. Schwefel, J. W. Thomas, R. I. Jain, Yale School of Medicine, New Haven, CT; Obstetrics, Gynecology and Reproductive Sciences, University of California San Francisco, San Francisco, CA; Obstetrics and Gynecology, Reproductive Endocrinology and Infertility, Greenville Health System, Greenville, SC; Sao Paulo University, Sao Paulo, Brazil; Gynecological Oncology and Gynecology, Medical University, Lublin, Poland; AbbVie Inc., North Chicago, IL.

OBJECTIVE: To evaluate the safety and efficacy of elagolix, an oral, non-peptide gonadotropin-releasing hormone antagonist, as compared to placebo in the management of moderate/severe endometriosis-associated pain (EAP).

DESIGN: These were two similar, double-blind, randomized, placebo-controlled, multicenter, 6-month, phase 3 studies (Studies 1 [North America] and 2 [global]) evaluating two doses of elagolix (150mg once daily [QD] and 200mg twice daily [BID]). Each study has an ongoing 6-month extension study.

MATERIALS AND METHODS: Participants were 18-49 year-old women with surgically diagnosed endometriosis within prior 10 years and moderate/severe EAP. The co-primary efficacy endpoints were the proportion of responders (controlled for rescue analgesic use) at month 3 based on daily dysmenorrhea (DYS) and non-menstrual pelvic pain (NMPP) scores recorded in an electronic diary. The clinically meaningful response for DYS and NMPP responders at month 6 was a secondary endpoint. Safety assessments included adverse events (AE), clinical laboratory tests, and changes in bone mineral density and endometrium.

RESULTS: In Studies 1 and 2 respectively, 871 and 815 participants were randomized and treated; 653 (75%) and 631 (77%) completed. Compared to placebo, each dose of elagolix resulted in a significantly greater proportion of responders for DYS and NMPP, at months 3 (Table) and 6. Hot flush (mostly placebo, each dose of elagolix) was also a secondary endpoint. Safety assessments included adverse events (AE), clinical laboratory tests, and changes in bone mineral density and endometrium.

Primary Efficacy and Safety of Elogalix vs. Placebo in Studies 1 and 2

<table>
<thead>
<tr>
<th>Efficacy at Month 3</th>
<th>STUDY1, Placebo, N=373</th>
<th>STUDY1, Elagolix, 150mg QD, N=248</th>
<th>STUDY2, Placebo, N=358</th>
<th>STUDY2, Elagolix, 150mg QD, N=225</th>
</tr>
</thead>
<tbody>
<tr>
<td>DYS responders, n (%)</td>
<td>73 (20)</td>
<td>115 (46)***</td>
<td>185 (76)***</td>
<td>96 (43)***</td>
</tr>
<tr>
<td>NMPP responders, n (%)</td>
<td>136 (36)</td>
<td>125 (50)***</td>
<td>133 (55)**</td>
<td>110 (50)**</td>
</tr>
<tr>
<td>Safety during treatment period, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any adverse event (AE)</td>
<td>277 (74)</td>
<td>201 (81)</td>
<td>205 (83)</td>
<td>177 (78)</td>
</tr>
<tr>
<td>Any serious AE</td>
<td>12 (3.2)</td>
<td>2 (0.8)</td>
<td>7 (2.8)</td>
<td>12 (5.3)</td>
</tr>
<tr>
<td>Any AE leading to discontinuation</td>
<td>22 (5.9)</td>
<td>16 (6.4)</td>
<td>23 (9.3)</td>
<td>22 (6.1)</td>
</tr>
<tr>
<td>Frequently reported AEs, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hot flush</td>
<td>26 (7.0)</td>
<td>59 (24)***</td>
<td>105 (42)***</td>
<td>49 (22)***</td>
</tr>
<tr>
<td>Headache</td>
<td>37 (9.9)</td>
<td>38 (15)</td>
<td>43 (17)**</td>
<td>51 (14)</td>
</tr>
<tr>
<td>Nausea</td>
<td>51 (14)</td>
<td>25 (10)</td>
<td>40 (16)</td>
<td>41 (11)</td>
</tr>
</tbody>
</table>

DYS = dysmenorrhea; NMPP = non-menstrual pelvic pain. Statistical significance vs. placebo is indicated for P<0.01 (**), P≤0.001 (**).
of epithelial and stromal cells in the implants. Par treatment attenuated these LPS-induced stimulatory effects.

CONCLUSIONS: LPS-induced pelvic inflammation status enhanced the development of murine endometriosis-like lesions via NF-κB pathway.

Supported by: KAKENHI (Japan Society for the Promotion of Science Grant-in-Aid).

P-442 Wednesday, October 19, 2016

HISTONE DEACETYLASES IN EUTOPIC AND ECTOPIC ENDOMETRIAL TISSUE OF PATIENTS WITH ENDOMETRIOSIS. C. Kim, J. Park, Y. Jeung, J. Moon. Obstetrics and Gynecology, College of Medicine, University of Ulsan, Asan Medical Center, Seoul, Korea, Republic of.

OBJECTIVE: We performed this study to investigate the expression of class 1, 2, 3, 4 and 5 histone deacetylase (HDAC-1, 2, 3, 4, and 5) mRNA and proteins in eutopic and ectopic endometrial tissues of patients with endometriosis and in eutopic endometrial tissues of women without endometriosis, and to evaluate the relationship between HDAC and the development of endometriosis.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: For this prospective cohort study, twenty patients who underwent surgery for stage III or IV endometriosis for the study group and 20 patients who underwent surgery for other benign gynecologic disease for controls between Jul 2010 to Mar 2013. All subjects were not pregnant and had normal regular menstruation. No one received hormonal therapy for at least 6 months before surgical treatment. During surgical treatment, eutopic endometrial tissues were collected from study and control groups and ectopic endometrial tissues were collected from study group. To quantify the expression of HDAC mRNA, real time reverse transcriptase polymerase chain reaction (RT-PCR) was employed. To measure the expression of HDAC protein, Western blotting was employed. Mean values were expressed as mean±standard deviation (SD). Kruskal-Wallis test was used to compare the mean value. Statistical significance was defined as P<0.05. All analyses were performed by using SPSS statistical package for Windows, version 11.0 (SPSS Inc, Chicago, IL).

RESULTS: The amounts of HDAC-1, 2, 3, 4, and 5 mRNAs were significantly higher in eutopic and ectopic endometrial tissue of patients with endometriosis compared to eutopic endometrial tissue of normal women (p<0.05). The expression of HDAC 1 protein was significantly higher in eutopic and ectopic endometrial tissue of patients with endometriosis.

CONCLUSIONS: Our results suggest the possible relationship between the development of endometriosis and HDAC. Especially high level of HDAC 1 in endometrial tissue may be associated with the development of endometriosis.

References:
1. Eleftherios P. Samartzis, MD1, Aurelia Noske, et al. The Expression of histone deacetylase 1, but not other class I histone deacetylases, is significantly increased in endometriosis. Reprod Sci 2013;20(12):1416-22.

P-444 Wednesday, October 19, 2016

DOES MEDICAL THERAPY EFFECT CIRCULATING MiRNAS? E. Cosar,1 R. Mamilapalli,2 L. Moridi,2 A. Duleba,3 H. S. Taylor,1 2Yale School of Medicine, New Haven, CT; 3Obstetrics, Gynecology and Reproductive Sciences, Research, New Haven, CT; 4Obstetrics and Gynecology, Infertility, New Haven, CT; 5Reproductive Medicine, University of California, San Diego, La Jolla, CA.

OBJECTIVE: We have previously identified circulating microRNAs (miRs) that can serve as biomarkers of endometriosis. Altered levels of several miRs are highly correlated with the presence of endometriosis in women. Here we determined prospectively that endometriosis leads to alterations in these biomarkers and that levels of circulating miRs are altered by medical therapy in a controlled non-human primate model.

DESIGN: Statins have been previously shown to decrease endometriosis in animals and humans. Experimental endometriosis was induced in sixteen baboons and half were randomized to treatment with Simvastatin. At 0 and 6 weeks all underwent serum miR analysis and laparoscopy.

MATERIALS AND METHODS: Before each surgery serum was obtained and total RNA was extracted and Poly(A) Reverse Transcription-Ploymerase Chain reaction was conducted with Invitrogen NCode miRNA First-Strand cDNA profile Synthesis MIRC-50 kit (Invitrogen). Conventional RT-qPCR was performed to detect differences between the groups. The relative expression of each miRNA was normalized by U6. Mann-Whitney U test was used to compare differences between groups.

RESULTS: Before induction of endometriosis there were no statistically significant difference in serum miR levels between groups. At 6 weeks miR-125b-5p, miR-150-5p were significantly increased in the untreated endometriosis group (p=0.02, p=0.03 respectively). miR-3613-5p was significantly increased in the untreated endometriosis group (p=0.04). Each of these alterations was decreased in animals treated with Simvastatin as shown in Table 1.

CONCLUSIONS: We demonstrate differential expression of miRNAs in the serum of baboons after creation of experimental endometriosis.

<table>
<thead>
<tr>
<th>miRNA</th>
<th>Endometriosis</th>
<th>Simvastatin</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>miR-125b-5p</td>
<td>0.029±0.018</td>
<td>0.116±0.055</td>
<td>0.02</td>
</tr>
<tr>
<td>miR-150-5p</td>
<td>0.033±0.021</td>
<td>0.189±0.062</td>
<td>0.03</td>
</tr>
<tr>
<td>miR-3613-5p</td>
<td>0.551±0.108</td>
<td>0.386±0.087</td>
<td>0.04</td>
</tr>
</tbody>
</table>

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OBJECTIVE: As the price of genetic sequencing has plummeted over the last decade, the evidence base for genetic drivers of reproductive disorders has grown. One area of focus in particular for genetic studies has been endometriosis, which impacts 10% of all women. Here we undertook a systematic literature review and meta-analysis of human genetic studies in women with endometriosis in order to better understand the biological pathways that are commonly impacted.

DESIGN: Systematic literature review and meta-analysis.

MATERIALS AND METHODS: From the ~25 million citations within the NCBI Pubmed repository, our natural language processing algorithms identified 4,516 reports on the molecular and genetic drivers of endometriosis. 868 of these articles (which included 893 distinct case-control experiments) reported a statistical or functional association between one or more genetic region(s) and endometriosis. We assessed these associations using the clinical validity classification system, defined by the American College of Medical Genetics (ACMG), to rank these genes according to the strength of their association with endometriosis. We then utilized a custom, fertility-centric genome annotation database to categorize the biological functions associated with these genetic regions.

RESULTS: We found that 91% of the endometriosis cases included in our review were confirmed surgically, 65% of these by laparotomy. Of the papers reviewed, 40 genes showed adequate evidence to be categorized as having “strong” evidence of a causal role in endometriosis according to ACMG ranking guidelines. Furthermore, we observed that these genes have well established roles in 1) the immune response, 2) tissue remodeling, 3) cell proliferation and differentiation, and 4) DNA replication and repair.

CONCLUSIONS: It is thought that the number of confirmed endometriosis cases is significantly lower than the true incidence of the disease, owing in part to lack of non-invasive diagnostic tools. Our study shows that the evidence base for genetic markers of endometriosis has finally reached the same level as for many markers that are now commonly used in other fields of medicine, such as oncology, for identifying people at significantly elevated risk for developing the disease. As with cancer, early intervention with endometriosis is key to minimizing long term impacts, including infertility. Leveraging these biomarkers to help identify women who could benefit from early intervention could help minimize the long-term impacts of allowing endometriosis to go undiagnosed and untreated.

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</tbody>
</table>

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MicroRNA levels in treated and untreated animals.
Additionally medical therapy decreased the serum levels of these miRNAs in endometriosis. Differential miR levels serve as biomarkers of the disease and response to treatment.

Supported by: OvaScience Inc. Boston, MA.

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EFFECTS OF SINGLE ORAL ADMINISTRATION OF SKI2670, GONADOTROPIN-RELEASING HORMONE(GNRH) ANTAGONIST, IN HEALTHY PRE-MENOPAUSAL WOMEN. S. Han,* K. Lim,* S. Cho,* J. Kim,* S. Choe,* J. Jung,* J. Ghim,* H. Jeong,* T. Yoo,* S. Kim,* H. Lim,* J. Shim,* K. Bae,* Department of Clinical Pharmacology and Therapeutics, Asan Medical Center, University of Ulsan, Seoul, Korea, Republic of; †Department of Clinical Pharmacology and Therapeutics, CHA University School of Medicine and CHA Bundang Medical Center, Seongnam, Korea, Republic of; ‡Department of Clinical Pharmacology, Inha University Hospital, Inha University School of Medicine, Incheon, Korea, Republic of; §Department of Clinical Pharmacology and Therapeutics, Pusan National University Hospital, Busan, Korea, Republic of; ¶Department of Clinical Pharmacology and Therapeutics, Inje University Busan Paik Hospital, Busan, Korea, Republic of; ‡Department of Clinical Pharmacology and Toxicology, Anam Hospital, Korea University College of Medicine, Seoul, Korea, Republic of; §SK Chemicals, Seongnam, Korea, Republic of; ¶Department of Obstetrics and Gynecology, Asan Medical Center, University of Ulsan, Seoul, Korea, Republic of.

OBJECTIVE: SKI2670 is a novel orally active, non-peptide GnRH antagonist. We investigated the safety, tolerability, pharmacokinetics and pharmacodynamics of SKI2670 after oral administration in healthy female subjects.

DESIGN: Phase I, double-blind, randomized, placebo-controlled, single-dose first-in-human clinical trial. 12 premenopausal women aged 23 to 45 (n=4 each group) received SKI2670 (20, 40 or 80 mg) or placebo (SKI2670:placebo=3:1).

MATERIALS AND METHODS: Blood samples were collected frequently before and after dose to assay luteinizing hormone (LH), follicle stimulating hormone (FSH), estradiol and SKI2670. We monitored vital signs, ECG and adverse events and also performed ovulation test and ultrasonography. We did non-compartmental analysis of SKI2670, and calculated Cmin, tmin and AUC of each hormone.

RESULTS: There were no significant differences among treatments with respect to vital signs, ECG, adverse events, ovulation test and ultrasonography. SKI2670 was rapidly absorbed on dosing and plasma exposure was increased related to dose. On pharmacodynamics analysis, after single administration of SKI2670, there were dose-dependent suppressions on LH, FSH and estradiol. Maximal suppression were 58-82% at 6-8hr for LH, 25-37% at 6-12hr for FSH, and 23-64% at 12-24hr for estradiol.

CONCLUSIONS: Single administration of SKI2670 in healthy premenopausal women was well tolerated and resulted in the dose-dependent suppression of LH, FSH and estradiol. These findings suggest that SKI2670 would be an effective therapeutic option for reproductive disorders, such as endometriosis.

Supported by: SK Chemicals.

Table 1 Mean PD parameters after the single dose

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Placebo (n=3)</th>
<th>20 mg (n=3)</th>
<th>40 mg (n=3)</th>
<th>80 mg (n=3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LH</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline (IU/L)</td>
<td>4.88</td>
<td>4.94</td>
<td>6.33</td>
<td>7.46</td>
</tr>
<tr>
<td>Cmin (IU/L)</td>
<td>4.31 (-12%)</td>
<td>2.08 (-58%)</td>
<td>1.41 (-78%)</td>
<td>1.33 (-82%)</td>
</tr>
<tr>
<td>Tmin (h)</td>
<td>3</td>
<td>6</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>FSH</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline (IU/L)</td>
<td>8.39</td>
<td>5.72</td>
<td>6.18</td>
<td>7.52</td>
</tr>
<tr>
<td>Cmin (IU/L)</td>
<td>6.19 (-26%)</td>
<td>4.31 (-25%)</td>
<td>4.51 (-27%)</td>
<td>4.72 (-37%)</td>
</tr>
<tr>
<td>Tmin (h)</td>
<td>24</td>
<td>6</td>
<td>8</td>
<td>12</td>
</tr>
<tr>
<td>Estradiol</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline (IU/L)</td>
<td>65.73</td>
<td>67.56</td>
<td>47.45</td>
<td>25.48</td>
</tr>
<tr>
<td>Cmin (IU/L)</td>
<td>64.22 (-2%)</td>
<td>51.92 (-23%)</td>
<td>31.79 (-33%)</td>
<td>9.12 (-64%)</td>
</tr>
<tr>
<td>Tmin (h)</td>
<td>6</td>
<td>12</td>
<td>12</td>
<td>24</td>
</tr>
</tbody>
</table>

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DMARD USAGE DECREASES OPIOID USAGE IN ENDOMETRIOSIS PATIENTS. A. Kotlyar,* X. Liu,* T. Falcone.* Ob/Gyn and Women’s Health Institute, The Cleveland Clinic Foundation, Cleveland, OH; †Quantitative Health Sciences, The Cleveland Clinic Foundation, Cleveland, OH; ‡Ob Gyn, Cleveland Clinic, Cleveland, OH.

OBJECTIVE: It has yet to be extensively studied how the inhibitory effects of disease modifying anti-rheumatic drugs (DMARDs) affect the course of endometriosis, we therefore sought to determine if DMARDs can lead to decreased use of hormonal treatments, ablative surgery, and adjunct therapies.

DESIGN: Single institution retrospective cohort study.

MATERIALS AND METHODS: Retrospective review was performed of 259 patients with surgically-confirmed endometriosis, those exposed to DMARDs for at least six weeks (n=25) and those unexposed (n=234). For our primary outcomes, we compared the total post-operative use of hormonal treatments, and number of subsequent ablative surgeries in patients exposed and unexposed to DMARDS. Secondary outcomes included the use of adjunct therapies such as antidepressants, steroids, and opioid use following surgery. Statistical analyses were performed using two sample T-test for continuous measures. The Pearson’s chi-square test or Fisher’s exact test was used to assess the association between categorical measures. Logistic regressions were performed for the multivariate analysis. All tests were performed at a significance level of 0.05 using SAS 9.4 software.

RESULTS: The DMARD-exposed and DMARD-unexposed patients showed significant differences in age and follow-up time (p=0.007 and <0.001, respectively). The most common DMARD used in our exposed patient was hydroxychloroquine (40%) with a small minority using biologic DMARDs such as etanercept (6%). Our univariate analysis showed increased use of depo-provera (p =0.045), no difference in number of ablative surgeries, and increased antidepressant use (p=0.006) in DMARDs-users. This analysis also showed significantly decreased post-diagnostic laparoscopy opioid usage in patients exposed to DMARDs (p=0.001). Multivariate analysis (controlling for age, BMI, time of follow-up, ethnicity and type of surgery at diagnosis) confirmed the significantly decreased use of opioids in the DMARDs exposed group compared to controls (p=0.003).

CONCLUSIONS: These findings suggest that opioid usage in patient with endometriosis may be attenuated following prolonged treatment with DMARDs. Furthermore, these results support the notion that immune-modulation via DMARDs could potentially be a tool in treating endometriosis by aiding in pain control.

References:
ELEVATED ANTIMULLERIAN HORMONE (AMH) DOES NOT FALSELY PREDICT OVARIAN RESPONSE IN PATIENTS WITH ADVANCED STAGE ENDOMETRIOSIS. C. R. Juneau, J. M. Franasiak, S. J. Morin, T. A. Molinaro, R. T. Scott, M. Maguire, RMANJ, Basking Ridge, NJ.

OBJECTIVE: AMH has been recognized as a useful diagnostic and prognostic tool as a reliable marker of ovarian reserve and predictor of ovarian response to controlled ovarian hyperstimulation. AMH is a member of the transforming growth factor β (TGF-β) superfamily and may be more elevated in endometriosis patients (1) as these growth factors are involved in the inflammatory cascade incited by endometriotic lesions. We sought to determine whether AMH levels overestimate actual ovarian response in patients with endometriosis given that AMH is more likely to be elevated in these patients.

DESIGN: Retrospective cohort.

MATERIALS AND METHODS: Patients participating in their first IVF cycle at a single infertility clinic from 2010-2016 were included. Patients with endometriosis were identified by surgical diagnosis or ultrasound findings consistent with persistent space-occupying disease whose sonographic appearance was consistent with endometriosis. Patients were stratified by SART age group and the number of metaphase II (M2) oocytes retrieved was compared between endometriosis patients and the general IVF population as a function of AMH. Statistical analysis was performed using a student-t test.

RESULTS: 639 endometriosis patients and 5619 patients from the general IVF population were analyzed. AMH levels were lower in the endometriosis group overall, 2.8 ng/mL v. 3.4 ng/mL (p = 0.0004). Likewise the number of M2 oocytes was lower in the endometriosis group overall, 8.0 ± 5.2 v. 8.7 ± 5.5 oocytes (p = 0.0121). When the groups were stratified by SART age group as a function of AMH, there was no difference in number of M2 oocytes retrieved between endometriosis patients and the general IVF population (table 1, *p=NS for all comparisons). Even when AMH was >10 ng/mL or ≥15 ng/mL, where a difference might be expected, there was no difference in M2 oocytes retrieved.

<table>
<thead>
<tr>
<th># Metaphase II (M2) oocytes</th>
<th>SART Age</th>
<th>AMH&gt;3 ng/mL*</th>
<th>AMH&gt;5 ng/mL*</th>
<th>AMH&gt;10 ng/mL*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group</td>
<td>No Endo</td>
<td>No Endo</td>
<td>No Endo</td>
<td>No Endo</td>
</tr>
<tr>
<td>&lt;35</td>
<td>17.2±1.9</td>
<td>17.9±9.4</td>
<td>19.1±1.0</td>
<td>20.0±0.4</td>
</tr>
<tr>
<td>35-37</td>
<td>15.7±7.9</td>
<td>17.9±9.7</td>
<td>17.9±7.5</td>
<td>18.1±9.4</td>
</tr>
<tr>
<td>38-40</td>
<td>15.2±7.8</td>
<td>15.2±8.3</td>
<td>17.3±9.7</td>
<td>18.1±9.4</td>
</tr>
<tr>
<td>41-42</td>
<td>12.7±7.1</td>
<td>11.5±5.4</td>
<td>17.2±9.5</td>
<td>10.5±4.9</td>
</tr>
</tbody>
</table>

CONCLUSIONS: In patients with moderate to severe endometriosis, the predictive value of a high AMH level is not diminished compared to patients from the general IVF population.

References:

DIFFERENTIAL EXPRESSION OF KISSPEPTIN IN PATIENTS WITH AND WITHOUT ENDOMETRIOSIS. A. O. Abdelkareem, A. S. Ait-Allah, S. M. Rasheed, Y. A. Helmy, P. Yong, M. A. Bedawi, Obstetrics and Gynecology, Faculty of Medicine, Sohag University, Sohag, Egypt; 2Obstetrics and Gynecology, REI Division, University of British Columbia, Vancouver, BC, Canada; 3Obstetrics and Gynecology, Faculty of Medicine-Sohag University, Sohag, Egypt; 4Obstetrics & Gynecology, Assistant Professor, Vancouver, BC, Canada; 5Department of Obstetrics and Gynecology, BC Women’s Hospital, Vancouver, BC, Canada.

OBJECTIVE: Kisspeptin is a neuropeptide that belongs to the Rfamide family. It is known for its crucial role in regulating the onset of puberty. In addition it also regulates sex hormone mediated secretion of gonadotrophins. Recently, expression of Kisspeptin in endometrium was reported. Kisspeptin has also been shown to have antimitastatic properties in different types of cancer. Endometriosis shares many of the biological features of cancer particularly migration and invasion. Our objective was to evaluate the abundance and localization of Kisspeptin in the endometrium of women with and without endometriosis. In addition, kisspeptin was evaluated in deep infiltrating endometriosis (DIE) and Endometrioma (OMA).

DESIGN: This is a case control study.

MATERIALS AND METHODS: We evaluated tissues obtained from a total of 21 patients (13 with endometriosis and 8 controls). In the controls, only eutopic endometrium “EUO-C” was obtained. In the endometriosis group, representative samples from eutopic endometrium “EUO-E” (n=8), as well as DIE (n=5) and OMA (n=5) were obtained. All tissues were immunostained for Kisspeptin using (sc-15400, Santacruz Biotechnology Inc.). Slides were scored according to the intensity and abundance of signal using histo-score. Data were analyzed using student-t and ANOVA one way with post hoc tests where appropriate.

RESULTS: In eutopic endometrium, Kisspeptin expression was significantly lower in the glandular epithelium but not the stroma of EUO-C compared to EUO-E (p<0.01). Kisspeptin expression was significantly lower in the endometrial stroma of both OMA and DIE compared to EUO-E (p<0.01). On the other hand, Kisspeptin expression was significantly lower only in the endometriotic glandular epithelium of DIE compared to EUO-E (p<0.01).

CONCLUSIONS: We have shown that Kisspeptin has a differential expression in patients with endometriosis with a tendency towards lower expression in ectopic locations. Given its antimitastatic properties, lower Kisspeptin expression may play a role in endometriosis invasiveness.

THE ENDOMETRIAL EXPRESSION AND PARACRINE REGULATION OF COMPLEMENT REGULATORY PROTEIN DECAY ACCELERATING FACTOR IN RESPONSE TO EMBRYO SIGNAL. HUMAN CHORIONIC GONADOTROPIN IS IMPAIRED IN ENDOMETRIA FROM WOMEN WITH ENDOMETRIOSIS. W. A. Palomino, F. Argandía, C. Aguirre, P. Kohen, L. Devoto. Obstetrics&Gynecology Institute for Maternal and Child Research, University of Chile, Santiago, Chile; Institute for Maternal and Child Research, University of Chile, Santiago, Chile.

OBJECTIVE: To assess the expression and paracrine regulation of complement regulatory protein Decay accelerating factor (DAF) in response to Human chorionic gonadotropin (hCG) in endometria from women with and without endometriosis.

DESIGN: University affiliated hospital.

MATERIALS AND METHODS: Endometrial biopsies were obtained from women with endometriosis during gynecologic laparoscopy (n=10) or fertile controls during laparoscopic surgical sterilization (n=12). The protocol of this study was approved the Institutional Ethics Committee for Human Research (University of Chile). Endometrial explants from women with endometriosis and disease free fertile controls were cultured with Estradiol 10^-7M or Progesterone 10^-7M or Human chorionic gonadotropin (hCG) 4 IU/mL or culture media alone (control) for 24 hrs. To investigate the paracrine regulation of DAF, the endometrial epithelial immortalized cell line Ishikawa, were incubated with conditioned media from endometrial stromal cells (isolated from women with and without endometriosis) cultured with Progesterone (ESC+P 4) or hCG (ESC+hCG) or culture media alone (control). The protein and mRNA levels of DAF were determined by western blot and by quantitative real time PCR (qRT-PCR). The Kruskal-Wallis test was employed for multiple comparisons statistics.

RESULTS: The incubation with hCG increases protein and mRNA levels of DAF in endometrial explants from fertile controls compared to samples from endometriosis patients (p=0.001 and P=0.02). The ESC+P 4 or ESC+hCG conditioned media from fertile controls but not from endometriosis patients significantly increases the quantity of DAF in Ishikawa cells (p=0.012 and p=0.02).

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THE ENDOMETRIAL EXPRESSION AND PARACRINE REGULATION OF COMPLEMENT REGULATORY PROTEIN DECAY ACCELERATING FACTOR IN RESPONSE TO EMBRYO SIGNAL. HUMAN CHORIONIC GONADOTROPIN IS IMPAIRED IN ENDOMETRIA FROM WOMEN WITH ENDOMETRIOSIS. W. A. Palomino, F. Argandía, C. Aguirre, P. Kohen, L. Devoto. Obstetrics&Gynecology Institute for Maternal and Child Research, University of Chile, Santiago, Chile; Institute for Maternal and Child Research, University of Chile, Santiago, Chile.

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CONCLUSIONS: The control of complement activation within embryo-maternal environment is essential for embryo survival. Impaired endometrial regulation of DAF in response to early embryo signal hCG may create hostile immune environment disrupting implantation process in women with endometriosis.

Supported by: Fondecyt grant 1140688.

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DYSGREGULATED INFERTILITY-RELATED GENES IN WOMEN WITH ENDOMETRIOSIS. K. D. Nayak, M. Saxena, G. Kant, R. Ahuja, S. Chulet, A. Mohan. IVF, Akanksha IVF Centre, New Delhi, India.

OBJECTIVE: A number of mechanisms may be responsible for endometriosis-related infertility, such as inflammatory microenvironment, altered immune response, reduced/absent adhesion molecules and oxidative stress. Many genes play important roles in these processes and their expression levels may be altered in women with endometriosis.

DESIGN: A prospective case-control study was conducted to assess expression of dysregulated genes in the eutopic endometrium of women with endometriosis compared to that of women without endometriosis.

MATERIALS AND METHODS: Eutopic endometrial biopsies from 29 women (N=16 with endometriosis; N=13 without endometriosis) were obtained by Pipelle curette between 1 January 2015 and 31 December 2015 in Akanksha IVF centre. Paralleled gene expression profiling using high density oligonucleotide microarrays was applied to investigate dysregulated genes in eutopic endometrium of women with endometriosis compared to women without endometriosis. Data analysis was conducted by GeneSpring version 4.0.4. T-test using P-value >0.05 and a fold-change expression >1.5 was applied to assess statistical significance. Selected dysregulated genes were randomly chosen and validated by RT-PCR.

RESULTS: This study has shown that in the eutopic endometrium from women with endometriosis infertility-related genes were significantly dysregulated. Particularly, genes involved in inflammation, immune response and oxidative stress were upregulated whereas genes involved in the expression of adhesion molecules were downregulated.

CONCLUSIONS: Dysregulation of genes involved in infertility likely contributes to decreased pregnancy rates in women with endometriosis. Increased inflammation in the eutopic endometrium may contribute to increased cytokine production and altered immune environment leading to oxidative stress thereby impairing embryo implantation. Moreover, downregulation of adhesion molecules in the eutopic endometrium may affect the endometrial receptivity in women with endometriosis. An improved understanding of the underlying molecular infertility mechanisms may aid in identifying candidate genes for managing endometriosis-associated infertility.

References:

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OBJECTIVE: A non-invasive diagnostic test for endometriosis is needed to shorten the current diagnostic delay of 8-11 years. The goal of this study was to discover new plasma biomarkers for endometriosis using a proteomics approach.

DESIGN: A total of 21 plasma samples collected during menstruation from patients with laparoscopically confirmed presence (n=11) or absence (n=10) of endometriosis was selected from our biobank. The disease samples were randomly divided into two pools (n=6 and n=5), as were the control samples (n=5 and n=5).

MATERIALS AND METHODS: Pools were enriched for low-abundant proteins using ProteoMiner (Bio-Rad), applied onto the Thermo Scientific Orbitrap Q Exactive MS and analyzed with Progenesis LC-MS (Nonlinear Dynamics). For identification of peptides, Mascot was used to search against the SwissProt database (April 2014). A 1.5-fold increase or decrease in protein abundance between both sets of endometriosis and controls pools was considered a measurable and significant difference. Protein-protein interactions were examined using the STRING database.

RESULTS: 30 proteins were identified with at least a 1.5-fold change in expression in the endometriosis pools, including 5 upregulated proteins and 25 downregulated proteins. The upregulated proteins were: Gelsolin (4.8-fold), Lumican (2.5-fold), Inter-alpha-trypsin inhibitor heavy chain H3 (2.4-fold), Apolipoprotein A-IV (2.2-fold) and Alpha-2-HS-glycoprotein (1.7-fold). The five most promising downregulated proteins were: Thrombospordin-1 (6.6-fold), C4b-binding protein alpha chain (3.3-fold), Alpha-2-macroglobulin (1.7-fold), Hemopexin (2.4-fold) and Complement factor B (10.1-fold). The network of differentially expressed proteins was enriched in interactions. Enriched pathways included regulation of proteolysis, acute phase response and wound healing.

CONCLUSIONS: Differentially expressed proteins were part of molecular networks known to be involved in endometriosis. After validation, these proteins could be integrated into existing menstrual plasma biomarker platforms (1) to improve their accuracy for the diagnosis of endometriosis.

References:

Supported by: This study was supported by grants from the Leuven University Hospital Fund and by the Flemish Foundation for Scientific Research (FWO).
INCREASED EXPRESSION AND CHEMOATTRACTANT ACTIVITY OF CXCR4 AND CXCL12 IN ENDOMETRIOTIC LESIONS. I. Moridi,‡ R. Mamillapalli,‡ E. Cosar,‡ G. Sahin Ersoy,‡ H. S. Taylor,‡ Obstetrics and Gynecology, infertility, New Haven, CT; ‡Canakkale 18 March University Medical Faculty, Canakkale, Turkey; †Obstetrics and Gynecology, Dr. Luth Kirdar Education and Research Hospital, Istanbul, Turkey; †Yale School of Medicine, New Haven, CT.

OBJECTIVE: The chemokine CXCL12 attracts bone marrow derived cells, which express the CXCL12 receptor, CXCR4. Here we determined the expression and role of CXCL12-CXCR4 in endometriosis.

DESIGN: case-control study.

MATERIALS AND METHODS: Biopsies of endometriosis were obtained from 11 patients undergoing laparoscopy. Control endometrium was obtained from 11 patients without endometriosis. Endometriosis was confirmed histologically. The cellular localization of CXCR4 and CXCL12 protein were determined by immunohistochemistry (IHC). The H score was used to compare expression levels. Stromal cell cultures were prepared from 5 biopsies of endometriosis as well as 5 biopsies of eutopic endometrium. Total RNA was isolated from these primary cells and the expression of CXCR4 and CXCL12 genes was analyzed by qRT-PCR. CXCL12 was assayed in the stromal cell conditioned using ELISA. The chemo attractant activity of CXCL12 was determined by the transwell chamber migration assay. ELISA and qRT-PCR results were compared using the students T test. The Mann-Whitney rank test was used to compare H scores.

RESULTS: qRT-PCR analysis showed increased expression of CXCR4 (3.9 fold, p < 0.01) and CXCL12 (2.7 fold, p < 0.04) in women with endometriosis compared with eutopic endometrium. IHC revealed that CXCR4 was expressed in stroma, glands, and epithelium in both endometriosis as well as in control tissues; however, the intensity was significantly higher in all cellular compartments of the endometriotic lesions when compared to control endometrium (H score: 243 versus 142, p < 0.01). CXCL12 expression was also higher in endometriotic lesions and was greatest in the epithelial compartment (H score: 250 versus 160, p < 0.02). Secreted CXCL12 protein concentration was higher in the endometriosis conditioned media than in controls (1146 ± 60 versus 439±: 172 pg/ml, p < 0.01). The migration assay demonstrated increased chemo attraction of mouse bone marrow cells (mBMc) towards endometriotic conditioned medium than conditioned medium of controls.

CONCLUSIONS: The CXCR4-CXCL12 signaling pathway attracts BM-derived stem cells into endometriotic lesions. Higher level of CXCL12 production by endometriosis compared to normal endometrium results in preferential recruitment of stem cells to endometriosis. These data explain prior research showing that endometriosis outcompetes eutopic endometrium, preferentially recruiting the limited supply of circulating stem cells. This pathway presents a potential therapeutic target for the treatment of endometriosis and associated endometrial disorders.

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THE EFFECT OF ELAGOLIX ON BONE MINERAL DENSITY: SAFETY RESULTS FROM TWO RANDOMIZED, PLACEBO-CONTROLLED STUDIES IN WOMEN WITH ENDOMETRIOSIS-ASSOCIATED PAIN. D. F. Archer,† N. Watts,‡ C. Gallagher,‡ J. Simon,§ W. R. Duan,∥ J. P. Rowan,∥ K. Chwlisz,∥ B. Schwefel,∥ J. W. Thomas,∥ R. L. Jain,∥ L. A. Williams,∥ Department of Obstetrics & Gynecology, Eastern Virginia Medical School, Norfolk, VA; ‡Mercy Health Osteoporosis and Bone Health Services, Cincinnati, OH; †Cleveland Univer- sity School of Medicine, Omaha, NE;∥Women’s Health and Research Consultants and George Washington University, Washington, DC; †AbbVie Inc., North Chicago, IL.

OBJECTIVE: To evaluate the effect of elagolix, an oral, non-peptide gonadotropin-releasing hormone antagonist, on bone mineral density (BMD) in women with endometriosis-associated pain (EAP).

DESIGN: These were two similar, double-blind, randomized, placebo-controlled, multicenter, 6-month, phase 3 studies (Studies 1 [North America] and 2 [global]) evaluating two doses of elagolix (150 mg once daily [QD] or 200 mg twice daily [BID]). Each study has an ongoing 6-month extension study.

MATERIALS AND METHODS: Participants included in either study were premenopausal, 18-49 years old, surgically diagnosed with endometriosis, with a baseline BMD Z-score higher than -1.5. BMD of the lumbar spine, total hip and femoral neck was measured by dual energy X-ray absorptiometry (DXA) at baseline and month 6 with GE Lunar or Hologic equipment. Images were reviewed and evaluated by a central reader (different for each study), blinded to treatment groups. The mean percentage change from baseline to month 6 was analyzed using a one-way ANOVA. Treatment-emergent adverse events (AEs) were recorded.

RESULTS: Compared with baseline, there was a dose-dependent decrease in lumbar spine BMD following 6 months of treatment with elagolix. The mean percentage change from baseline to month 6 was significantly different from placebo for each elagolix dose in both studies (Table). The proportion of participants with lumbar spine BMD decrease from baseline greater than 3% was also dose-dependent (Table). There were also dose-dependent decreases in BMD of the total hip and femoral neck.

CONCLUSIONS: In women with EAP, there was a dose-dependent decrease in BMD after 6 months of elagolix treatment.

Supported by: AbbVie Inc. funded these studies and participated in the study design, research, analysis, data collection, interpretation of data, reviewing, and approval of the publication.
An IGF1R inhibitor in vivo reduced IGF-I-induced endometriosis graft. In ESCs, growth and ERβ expression occurred, enhancing binding to the ESR2 and CYP19A1 promoters. Following IGF-I treatment, a marked increase in c-Jun and CREB phosphorylation (15.26 mm³ vs. 22.59 mm³). A trend towards a reduced endometriotic group, the endometriotic lesions volume increased in the IGF-I treatment group (22.59 mm³ vs. 14.73 mm³). Real-time qPCR analysis of the tissue respectively. Similar inhibitory patterns could also be observed for ERα. AG reduced the levels of ESR2 and CYP19A1 mRNA by 70% and 78%, and 9.56-fold respectively. By contrast, treatment with the IGF1R inhibitor grafts showed that the ESR2 and CYP19A1 mRNA expression levels were measured by real-time PCR and western, respectively. The binding of c-Jun and CREB to the ESR2 and CYP19A1 promoters were assessed by chromatin immunoprecipitation assay. Animal experiments were performed in a xenograft mouse model. Levels of IGF-I mRNA in ESCs were markedly higher (55-89-fold) than those in EMs. IGF-1 stimulated ESR2 and CYP19A1 mRNA expression, with a maximal effect (3.36-fold and 4.58-fold, respectively), compared to controls. MENSTRUAL ABNORMALITIES and aromatase expression regulated by IGF-I

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UP-REGULATED HYALURONAN SYNTHASE 2 MEDIATES EPIDERMAL GROWTH FACTOR-INDUCED CELL MIGRATION AND INVASION IN HUMAN ENDOMETRIOTIC Stromal CELLS. B. Peng, M. A. Bedaiwy, M. A. Bedaiwy. Department of Obstetrics & Gynecology, Child & Family Research Institute, University of British Columbia, Vancouver, BC, Canada; Department of Gynecology and Obstetrics, Women’s Hospital, Zhejiang University Medical College, Hangzhou, China.

OBJECTIVE: Endometriosis is characterized by the outgrowth of endometrial cells outside the uterus. Progression of endometriosis is often associated with endometriotic cell migration and invasion. Epidermal growth factor (EGF) and hyaluronic syntheses 2 (HAS2) have been reported to regulate cancer cell migration and invasion. The aims of our study were to examine the expression of HAS2 in endometriotic tissues and to investigate the role of HAS2 in EGF-induced endometriotic stromal cell (ESC) migration and invasion.

DESIGN: Eutopic and/or ectopic endometrial tissues were collected from women with/without endometriosis. Primary ESCs isolated from ectopic endometrial tissues and immortalized ESCs (CRL-7566) were used in our in vitro study.

MATERIALS AND METHODS: The expression of HAS2 in eutopic and ectopic endometrium was examined by immunohistochemistry and Histo-score method. Primary and immortalized ESCs were treated with EGF alone or in combination with EGF receptor inhibitor AG1478, mitogen-activated protein kinase kinase inhibitor U0126, phosphoinositide 3-kinases inhibitor LY294002, or small-interfering RNA against HAS2. The mRNA levels of HAS2 were measured by RT-qPCR. The protein levels of extracellular signal-regulated kinase (ERK) and phospho-ERK, AKT and phospho-AKT, were measured by Western blot analysis. The protein levels of secreted hyaluronic were measured by enzyme-linked immunosorbent assay. Cell migratory and invasive capability was evaluated by transwell migration and invasion assays, respectively.

RESULTS: HAS2 expression levels were detected in glandular epithelial cells and endometriotic stromal endometriotic endometrium (n=10) compared to eutopic endometrium from women with (n=10) or without (n=10) endometriosis. Treatment with EGF resulted in increased HAS2 mRNA and protein levels and elevated hyaluronan secretion in ESCs. Additionally, EGF increased ERK and AKT phosphorylation, and pretreatment of U0126 and LY294002 attenuated EGF-induced HAS2 expression. Moreover, EGF treatment significantly increased cell migration and invasion of ESCs, and knockdown of HAS2 attenuated EGF-induced cell migration and invasion.

CONCLUSIONS: HAS2 expression is elevated in ectopic endometrium from women with endometriosis. EGF induces HAS2 expression in ESCs, which may result in increased cell migration and invasion in these cells.

Supported by: This work is supported by a BC Women’s Hospital fund to MAB and a grant from National Natural Science Foundation of China (No. 81170546) to JL. BP and HZ contribute equally to this work.
Multivariable logistic regression was performed to calculate the odds ratio (OR) and 95% confidence interval (CI) for letrozole addition.

RESULTS: Following laparoscopy, 21 women declined a LNG-IUD, primarily for fertility plans. Laparoscopy and LNG-IUD placement occurred in 29 women. Among the 29 women, within 6 months, 11 women required addition of letrozole for persistent pain. In this case series, all 11 women had previously attempted management with hormones and/or IUD, and 64% had a prior laparoscopy. Women who required letrozole tended to be younger at laparoscopy (mean age 28 vs. 33 years; OR=0.89, CI=0.78-1.01), white (100 vs. 72%), and nulliparous (100 vs. 78%), as shown in the table. The data also suggested that the women requiring letrozole were more likely to be overweight or obese compared to those who did not require additional therapy, an observation that did not reach statistical significance due to the small sample size.

CONCLUSIONS: In our study population, the addition of letrozole for persistent pain post-laparoscopy and LNG-IUD placement was more common in younger, white, nulliparous women who had previously undergone laparoscopy and attempted medical management. Notably, these results warrant further investigation in order to help physicians develop an individualized post-operative plan to effectively manage endometriosis pain.

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RISK FACTOR SCORE OF SYMPTOMS IN PATIENT WITH ENDOMETRIOSIS. Y. Chen. Center for Reproductive Medicine and Science, Taipei Medical University, Taipei, Taiwan.

OBJECTIVE: To perform a validation of estimating score for the patients who may suffer with endometriosis, and to identify risk factors for endometriosis.

DESIGN: We analyzed the questionnaire of the patients with/without endometriosis in TMUH.

MATERIALS AND METHODS: A sample of 543 women, aged 20-45 years was selected. Using the questionnaire to validate the risk factors of patient with endometriosis. The sociodemographic and gynecological characteristics of comparison groups were analyzed with student t-test and Chi-test. The statistical difference was defined as p < 0.05.

RESULTS: The risk factors we integrated in our study included dysmenorrhea, diarrrhea, low BMI, inter-menstrual spotting etc. The most representative risk factor of the score is dysmenorrhea. Moreover, the factors turned into the estimated score based on the statistical difference value (p < 0.0001 equal to 3 score, p < 0.001 equal to 2 score and p < 0.05 equal to 1 score).

CONCLUSIONS: The risk factors we integrated in our study included dysmenorrhea, inter-menstrual spotting etc. The score was internally validated with endometriosis patients’ questionnaires in TMUH.

References:

Supported by: Acknowledge the project financial support of Academic Sinica.

P-463 Wednesday, October 19, 2016

DISCOVERY OF NOVEL CHEMOKINE AS A CLINICAL MARKER OF ENDOMETRIOSIS. Y. Chou, C. Tzeng. Department of Obstetrics & Gynecology, Taipei Medical University, Center for Reproductive Medicine, Taipei Medical University Hospital, Taipei, Taiwan.

OBJECTIVE: To systematically analyze the chemokine expression and evaluate novel clinical marker of endometriosis.

DESIGN: We have enrolled 9 control and 32 endometriosis cases to compare the chemokine and cytokine expression levels.

MATERIALS AND METHODS: In this study, we systematically defined the endometriosis-associated genes using Bio-plex assay of 40 chemokines and cytokines. Receiver-operating characteristic (ROC) curve was analyzed in control and endometriosis groups. Statistical significance was analyze by paired Student’s t-test. P<0.05 is considered significant.

RESULTS: Among 40 chemokines and cytokines, five genes are increased in serum of endometriosis patients, including, CXCL10 (IP-10) [3.28-fold], IL-1β [2.15-fold], CXCL9 (MIG) [1.63-fold], CCL17 (TARC) [1.78-fold], and CCL25 (TECK) [2.08-fold]. Moreover, we analyzed the ROC curve and found that the Area Under Curve of these chemokines and cytokine expression was ranging from 0.722 to 0.809. CXCL10 is an effector of lymphocyte recruitment. IL-1β promotes inflammatory process and tissue remodeling. CXCL9 promotes Th1-type inflammation. CCL17 regulates T-reg cell

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activity. CCL25 promotes invasion of endometrial stromal cells. These upregulated-chemokines and -cytokine are novelty detected in human serum with endometriosis and it may be involved in the endometriosis pathogenesis.

CONCLUSIONS: These results suggested that chemokines and cytokine may serve as biomarkers and help us to understand the etiology of endometriosis and offer the possibility to develop a diagnostic system for non-invasive detection.

LEIOMYOMA

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SILIBININ INHIBITS PROGESTERONE INDUCED RANKL EXPRESSION IN HUMAN UTERINE LEIOMYOMA CELLS. D. E. Ilieva, S. Liu, A. Kujawa, S. Bulan, P. Yin, Obstetrics and Gynecology, Prentice Women’s Hospital, Northwestern University Feinberg School of Medicine, Chicago, IL.

OBJECTIVE: Silibinin is a natural compound that was reported to inhibit the effects of RANKL; the underlying mechanism however is unclear. We previously demonstrated that progesterone stimulates receptor activator of nuclear factor kappa-B ligand (RANKL) expression in leiomyoma. Here we investigate whether silibinin inhibits progesterone induced RANKL expression, cell cycle proteins and extracellular matrix deposition.

DESIGN: Molecular analysis in freshly isolated leiomyoma tissue and cells.

MATERIALS AND METHODS: Fresh leiomyoma tissue explants (n = 3 patients) were treated with vehicle or silibinin alone, as well as in the presence or absence of synthetic progesterone agonist R5020. Total RNA was extracted and quantitative real-time reverse transcriptase polymerase chain reaction (RT-PCR) was performed to assess fold change of RANKL mRNA levels. Next, we isolated leiomyoma smooth muscle cells from fresh fibroid tissues and maintained them in primary culture (n = 3). The cells were treated with vehicle or varying doses of silibinin (30, 60, or 90 mM) for 24, 48, or 72 hours (h). RANKL mRNA levels in primary cells were measured by RT-PCR. Total RNA was extracted and RT-PCR was used to measure mRNA levels of RANKL, Cyclin D1 (a downstream target of RANKL and a cell cycle protein increased with cell proliferation) and Col1A2 and Col3A1 (markers of extracellular matrix deposition).

RESULTS: Treatment of tissue explants with R5020 lead to a significant increase in RANKL expression (p < 0.001), which was significantly decreased by treatment with silibinin (p < 0.01). In primary cells, silibinin reduced RANKL expression in a dose-dependent manner with the most significant change observed at 60 mM (up to 60% decrease, p < 0.05). Silibinin significantly decreased Cyclin D1, Col1A2 and Col3A1 mRNA levels in a dose-dependent manner by up to 80% change (p < 0.05). Inhibition of RANKL, Cyclin D1, Col1A2 and Col3A1 expression by silibinin was observed as early as 24 h, peaked at 48 h and persisted till 72 h of treatment.

CONCLUSIONS: Silibinin is an effective inhibitor of RANKL expression. Silibinin also decreased proliferative activity and extracellular matrix deposition in leiomyoma smooth muscle cells. Thus, silibinin may serve as a novel medical treatment option with no known side effects for uterine leiomyoma.

Supported by: National Institutes of Health Grant P01-057877.

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A-KINASE ANCHORING PROTEIN-13 (AKAP13) BINDS AND ACTIVATES PROGESTERONE RECEPTOR. F. S. Chuong, C. Washington, K. C. Cayton, P. Driggers, M. Malik, J. Segars, Johns Hopkins University School of Medicine, Baltimore, MD, OBG, Uniformed Services University of the Health Scienc, Bethesda, MD.

OBJECTIVE: Fibroid growth is progesterone-dependent (P4), in part, but the underlying mechanism(s) remain unclear. Previously, we reported that fibroids have elevated levels of AKAP13, an A kinase anchoring protein that augmented ligand-dependent progesterone receptor B (PR-B) activity. Additionally, we showed a direct and specific interaction between AKAP13 and PR in vitro. Here we further assessed the interaction between AKAP13 and PR as well as functional activation of PR isoforms.

DESIGN: Laboratory Research.

MATERIALS AND METHODS: Lysates prepared from immortalized fibroid cells containing progesterone receptors were incubated with anti-PR antibody. Magnetic Protein A particles were added to lysates, washed, and eluted. Samples were resolved by electrophoresis and bound proteins were detected by western blot. Blots were probed anti-PR or anti-AKAP13 antibodies. HEK293T cells were transfected with constructs encoding a progesterone responsive element luciferase (PRE-Luc) reporter, AKAP13 expression plasmid, and PR isoforms and treated with ligand or vehicle control. Cells were assayed for luciferase activity at 24 hours.

RESULTS: As expected, progesterone receptor was precipitated and detected by anti-PR antibody in western analysis. AKAP13 was also detected in co-immunoprecipitated complexes from lysates of fibroid cells. Transfection of HEK293T cells with an AKAP13 expression construct in the presence of PR-B and P4 resulted in an 18-fold, ligand-dependent increase in reporter activity compared to controls (p < 0.05). In contrast, activity of PR-A was low and not greatly affected by AKAP13.

CONCLUSIONS: We observed a significant augmentation in gene activation through PR-B, but not PR-A, in the presence of AKAP13 and ligand in HEK293T cells. The co-immunoprecipitation results support a direct interaction between AKAP13 and PR. These findings suggest that AKAP13 may complex with PR to promote PR-mediated gene activation.

Supported by: This research was supported by the Howard W. and Geor-geanna Seegar Jones Endowment.

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CYTOKINE REGULATION CENTRAL TO ULIPRISTAL-MEDIATED LEIOMYOMA TREATMENT. M. Malik, J. L. Britten, X. Zhang, D. Wilkerson, L. K. Nieman, W. H. Catherino. Obstetrics and Gynecology, Uniformed Services University of the Health Sciences, Bethesda, MD; Fort Belvoir Community Hospi-tal, Fort Belvoir, VA; Collaborative Health Initiative Research Program, USUHS, Bethesda, MD; NIDDK, Bethesda, MD.

OBJECTIVE: Human fibroids are highly prevalent and symptomatic uterine tumors. Treatment with selective progesterone receptor modulators such as ulipristal acetate (UA) both decrease fibroid size and symptoms. However, the mechanism of action for UA remains elusive. Our objective was to understand which signaling pathways, involved in fibroid pathogenesis are affected by UA.

DESIGN: Surgical samples from a prospective, randomized, placebo-controlled trial of UA to analyze the fibroid and patient-matched myometrium by next generation sequencing to obtain genome-wide quantitative expression.

MATERIALS AND METHODS: RNA-Seq analysis followed by differential gene expression calculation using DESeq2. Pathway and gene ontology enrichment was used to identify differentially expressed pathways using DAVID. Immunohistochemistry was used for confirmatory analysis.

RESULTS: RNA-Seq analysis of uterine fibroids from patients treated with UA to patient matched myometrium demonstrated a major reduction in expression of cytokine-cytokine and cell-cytokine interaction pathways. Most cytokines including the chemokines that are increased by progesterone treatment have been implicated in the development and growth of fibroids. Nearly 600 genes were differentially expressed by UA treatment in fibroids compared to myometrium. Over 2-fold reduction (P < 0.05) was observed in qPCR for two receptors to tumor necrosis factor (TNF) receptors, and fibroblast growth factor (FGF) receptors, and bone morphogenetic proteins (BMPs). This pathway acts as a fibrosis promoting pathway supporting angiogenesis, cell proliferation and extracellular matrix production. Reduction in receptors was supported by IHC of treated fibroids. Higher than 2-fold reduced expression was also observed in pro-inflammatory cytokine, tumor necrosis factor (TNF) and Interleukin (IL1A, IL2 and IL10) receptors. TNF pathway is known to regulate the MAPK pathways that are also known to be affected by UA treatment. Over 2-fold reduction is observed in the MAPK pathway supporting angiogenesis, cell proliferation and extracellular matrix deposition. Inhibition of RANKL, a cell cycle protein increased with cell proliferation and cell signaling pathways. These cytokine pathways included regulation of Leukemia inhibitory factor (LIF) as well as the LIF receptors by over 2-fold.

CONCLUSIONS: Genome-wide analysis of leiomyoma surgical specimens of women treated with uteripristal compared with placebo demonstrated broad decreased sensitivity to cytokine exposure via decreases in receptor expression of platelet-derived growth factors has been observed in fibroids. UA significantly affected the expression of various receptors involved in this pathway. Similar to mifepristone, UA reduced expression of Leukemia inhibitory factor (LIF) as well as the LIF receptors by over 2-fold.

Supported by: This research was supported by Intramural grant from Uniformed Services University of the Health Sciences, OGPSGF13 and NICHD, NIH R21, HD070152-01-A1. The research was also supported, in part, by the intramural research Program in Reproductive and Adult Endocrinology, NIH.
CINE MRI CAN BE AN EFFECTIVE TOOL TO DETERMINE SURGICAL INDICATION FOR UTERINE FIBROIDS IN INFERTILE WOMEN. C. Tabata, T. Fujisawa, O. Tsutsumi. Center for Human Reproduction and Gynecologic Endoscopy, Sanno Hospital, Tokyo, Japan.

OBJECTIVE: Intramural fibroids seem to cause an adverse effect for infertile women, but it is controversial whether myomectomy should be performed or not, especially for intramural fibroids without distortion of the uterine cavity. It is reported that uterine peristalsis during implantation phase might be associated with infertility and myomectomy may improve pregnancy outcome. Our aim is to evaluate the effectiveness of cine MRI about uterine peristalsis for choosing a treatment approach to uterine fibroids for infertile women.

DESIGN: Non-randomized Controlled study. Informed consents were obtained from all patients in every procedure such as MRI and operations.

MATERIALS AND METHODS: Sixty-two infertile patients with uterine fibroids were examined using cine MRI between October 2010 and August 2015. Eligibility criteria were intramural fibroid without distortion or elongation to the endometrial cavity. Cine MRI was performed at mid-luteal phase. Women who had 2 or more of functional zone movement within 3 minutes (uterine peristalsis, P+ group) were referred for myomectomy and infertility treatments were undergone after surgery. Women with 0 or 1 time of uterine peristalsis (P- group) were managed expectantly about fibroids and received infertility treatments at first. Serum estrogen and progesterone levels were measured on the day of cine MRI and pregnancy rate was evaluated prospectively. Student's t-test and chi-squared test were used for statistical analysis of hormone levels and pregnancy rate.

RESULTS: Among 62 patients, 35(56.5%) and 27(43.5%) were assigned to the P+ or P- group, respectively. No significant differences were observed in serum estrogen and progesterone levels between the two groups (235.4±114.4 pg/ml and 12.6±5.2 ng/ml vs. 198.2±68.6 pg/ml and 15.4±4.1 ng/ml). Fifteen out of 26 patients (57.7%) in the P- group without myomectomy achieved pregnancy. In the P+ group, 16 out of 23 patients with myomectomy (69.6%) conceived, compared with 2 out of 8 patients. Myomectomy tented to increase pregnancy rates of P+ group. In the P- group, 16 out of 23 patients with myomectomy achieved pregnancy. In the P+ group, 16 out of 23 patients with myomectomy conceived, compared with 2 out of 8 patients with myomectomy (69.6%) conceived, compared with 2 out of 8 patients. Myomectomy tented to increase pregnancy rates of P+ group. In the P- group, 16 out of 23 patients with myomectomy achieved pregnancy. In the P+ group, 16 out of 23 patients with myomectomy conceived, compared with 2 out of 8 patients with myomectomy (69.6%) conceived, compared with 2 out of 8 patients with myomectomy (69.6%) conceived, compared with 2 out of 8 patients with myomectomy (69.6%) conceived, compared with 2 out of 8 patients with myomectomy (69.6%) conceived, compared with 2 out of 8 patients with myomectomy (69.6%) conceived, compared with 2 out of 8 patients with myomectomy (69.6%).

CONCLUSIONS: Our study showed cine MRI could identify surgical indication and improve pregnancy rate in patients who had uterine peristalsis caused by intramural fibroids. Thus, establishment of treatment strategy for fibroids could be expected as part of infertility treatment and cine MRI may be a useful tool to evaluate the pathology of fibroid and the effect of myomectomy.

References:

The analysis of cine MRI and pregnancy rate

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CINE MRI ANALYSIS FOR UTERINE FIBROIDS IN INFERTILE WOMEN.
end of the 3-month treatment (n = 20), 12 patients had PBAC 28-day score < 2 and 8 patients had PBAC 28-days score < 75; 35.0% of these patients reported a worsening of pain symptoms. The mean (±SD) maximal junctional zone thickness (JZmax) significantly increased at the completion of treatment (17.4±2.9 mm) compared to baseline (15.3±2.4 mm; p < 0.01). UPA treatment increased the number of subendometrial linear striations (p < 0.01), the number of myometrial cysts (p < 0.005), the size of anechoic areas (p < 0.01) and in the size of myometrial cysts (p < 0.001). The treatment significantly decreased the largest diameter of the uterine fibroids (p < 0.005) and the volume of fibroids (p < 0.05; percentage reduction, mean ±SD: 36.76±11.4%).

CONCLUSIONS: In patients with adenomyosis and uterine fibroids, UPA causes a significant improvement in bleeding but it may worsen pain symptoms in more than half of the patients. This observation is justified by the worsening of several ultrasonographic characteristics of adenomyosis. Patients treated with UPA should be assessed for the presence of uterine adenomyosis.

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EVALY-EIGHT EXPOSURE TO ENDOCRINE-DISRUPTING CHEMICALS (EDCS) LEADS TO THE DEVELOPMENT OF UTERINE FIBROIDS BY IMPAIRING DNA REPAIR CAPACITY IN MYOMETRIAL STEM CELLS. L. Prusinski, 1 Q. Yang, 1 A. Mas, 1 M. P. Diamond, 2 C. Walker, 1 A. Al-Hendy, 2 Obstetrics and Gynecology, Augusta University, Augusta, GA; 1OB/GYN, Augusta University, Augusta, GA; 2PhD, Pernera (Valencia), Spain; 3Augusta University, Augusta, GA; 4Texas A&M Institute of Biosciences and Technology, Houston, TX; 5Obstetrics & Gynecology, Augusta University, Augusta, GA.

OBJECTIVE: Uterine fibroids (UFs), benign myometrial tumors, negatively impact female reproductive health. The accepted model for their origin implicates somatic fibroid-causing mutations in gene MED12 (detected in ~85% of all sporadic human UFs) in myometrial stem cells (MSCs) converting them into UF-forming MSCs. While the origin of these mutations remains unknown, defective DNA repair systems increase the risk of emergence of somatic tumor-forming mutations. We have shown earlier that Tsc2-mutant Eker (Tsc2/knockout) rats exposed to diethylstilbestrol (DES, a tool compound of environmental EDCs) during early-life uterus development form fibroids at high frequency later in adult life versus unexposed counterparts. We aimed to analyze the DNA repair system in the Stro1+/CD44+ MSC population of an early-life EDC-exposed versus unexposed authentic rat fibroid model.

DESIGN: Laboratory research studies using MSCs isolated from Eker Tsc2−/− fibroid model rats exposed to DES during sensitive period of uterus development.

MATERIALS AND METHODS: Female newborn rats were treated S.C. with vehicle (VEH) or 1 μg/kg of diethylstilbestrol (DES) on postnatal days 10-12, a sensitive period of uterus development. Stro1+/CD44+ MSCs were isolated from 5-month old adult endometrium-free myometrium (N=5/group) using Stro-1 and CD44 surface markers and selective sorting. Whole-genome RNA-sequencing was performed on Stro1+/CD44+ myometrial Eker versus VEH rat MSCs. Expression of DNA repair genes with ≤ 0.5 fold-change was validated by quantitative PCR.

RESULTS: By RNA-sequencing, 122 DNA repair genes were downregulated in DES versus VEH rat MSCs. Among 20 genes selected (fold-change <0.5) for further analysis, the expression of 14 genes was significantly downregulated (P <0.05) as validated by quantitative PCR. These deregulated genes have implications in multiple DNA repair mechanisms, including double-strand break (DSB) homologous recombination: Bard1, Brc2a, Cdk1, Fanca2, Rad51ap1, Rad52, and Xrcc2; DSB non-homologous end-joining: Gstk1 and Polq; regulation of cell cycle progression and environmental stress responses: Cenbl, Cdk1, Gadd45b; and other genes with pivotal roles in DNA repair mechanisms: Hap1, Recq4. Further characterization of these genes in human Stro1+/CD44+ MSCs isolated from normal (MoY) and at-risk (MoYo) myometrium is currently underway in our laboratory.

CONCLUSIONS: Our data suggest early-life exposure to DES can permanently impair DNA repair capacity in rat MSCs, leading to the eventual emergence of fibroid-causing DNA mutations and the development of UFs. Further studies are needed in human MSCs, as well, to meticulously understand the early cellular events leading to the origination of UFs in different ethnic groups.

Supported by: Augusta University Startup package, National Institutes of Health grant HD04611811

ENVIRONMENT AND TOXICOLOGY

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AUTOGRAPHY AND FIBROIDS: AUTOGRAPHY RELATED PROTEINS ATG4 AND ATG10 ARE DEFFECT IN HUMAN UTERINE FIBROIDS WITH HIGH FREQUENCY. A. El Andaloussi, 2 S. Habib, 3 G. Soylemez, 2 N. Ismail, 2 A. Al-Hendy. 2 Obstetrics & Gynecology, Augusta Univ, Augusta, GA; 3Pathology Clinical Microbiology Division, University of Pittsburgh, Pittsburgh, PA.

OBJECTIVE: Uterine fibroids (UFs) are the most common pelvic tumors in reproductive age women, they usually cause heavy menstrual bleeding, bulk symptoms and subfertility. Autophagy is a collection of processes that enable the cells to digest and recycle their cytoplasmic contents such as toxic protein aggregates, defunct or disused organelles and invading microorganisms. Disturbances in autophagy process have been recently described in many diseases. The role of autophagy in UFs is still unknown.

DESIGN: Our hypothesis was tested in UFs collected from 20 cases of endometriomyomatosus women (n=10) from consented premenopausal women undergoing hysterectomy (F) and adjacent normal myometrial tissue (MoY). All patients were matched for menstrual phase, age, ethnicity and body mass index.

MATERIALS AND METHODS: We analyzed autophagy markers involved in the initiation and the elongation phase of autophagy by western-blot, Q-PCR and flow cytometry. Electron microscopy was used to analyze the autophagic structure in F vs MoY. For the in vitro studies of autophagy flux with Rapamycin/Bafilomycin A1, we used human immortalized fibroid (HuLM) vs normal myometrial (UTSM) cell lines. The statistical evaluation will be done on more significant number of patients. Appropriate approvals were secured for this project from Augusta University institutional review board.

RESULTS: Ultrastructural comparison by transmission electron microscopy between F versus MoY revealed significant accumulation of autophagosomes in F and total absence of autophagosomes present in MoY. The quantification by Q-PCR of the major ATGs governing the autophagy process showed that ATG4 (70%) and ATG10 (60%) are the most defective targets in F versus MoY. Molecular analysis, by western-blot and real-time PCR, revealed mTOR activation and Beclin-1 induction in F vs MoY. The in vitro treatment of UTSM and HuLM with Rapamycin was able to upregulate autophagy flux in UTSM only. The addition of Bafilomycin A1 resulted in a significant increase in LC3-II levels for UTSM versus non treated control (Mean Fluorescence intensity = 2402), quantified by flow cytometry, and no change for HuLM (Mean Fluorescence intensity = 217). These data are reflecting myometrium autophagic flux under basal conditions and that the accumulation of LC3-II is due to inhibition of LC3-II turnover, involving block in autophagic flux. This finding, align with the electron microscopy data that autophagy is dysregulated at the autophagosome stage in fibroid tissue.

CONCLUSIONS: The present study suggests, for first time, a link between impairment of autophagy and pathogenesis of uterine fibroids. Further understanding of its regulation and significance will provide novel therapeutic targets and might present a utility for autophagy enhancing compounds as potential effective anti-fibroid agents.

Supported by: Augusta University startup package and the National Institute of Health grant HD0422811.
they knew ways to reduce their exposure to environmental chemicals. There were no differences between cases and controls in their knowledge and concern about environmental chemicals (all p > 0.05). Women who reported knowing how to reduce exposures were significantly older than women who did not (p = 0.01). Although awareness of lead, mercury, and pesticides was ubiquitous among participants, awareness of endocrine disrupting chemicals such as Bisphenol A (BPA) and phthalates was less common (Table). Of the specific chemicals queried, concern was greatest about pesticides and least about phthalates. When asked about whether they took action to avoid or reduce chemical exposures, there were no differences between cases and controls (p > 0.05).

**Conclusions:** Although the scientific and clinical community recognizes the adverse effects of environmental chemicals on fertility and fetal development, there is a lag in the dissemination of this information to reproductive aged women seeking fertility care. This is particularly true of endocrine disrupting chemicals. While women were able to articulate specific strategies to avoid mercury, pesticides, and lead, they were less aware and had more difficulty identifying specific, appropriate measures to reduce exposure to BPA and phthalates. There is a need for targeted physician counseling to increase environmental health literacy in the context of reproductive health and to help guide women towards appropriate behaviors to reduce exposures.

**RESULTS:** In vitro acrylamide exposure did not affect in vitro oocyte maturation and meiotic spindle. In vivo acrylamide treatment caused an accumulation of oocytes at prometaphase-I (10.3% vs 2.3% in controls, p = 0.039). Majority of the M-II stage oocytes from in vivo acrylamide treated group showed a decrease in the meiotic spindle mass and a misalignment of the chromosomes. This finding indicated that acrylamide might show its action via its metabolite glycidamide. Therefore, isolated GV-stage oocytes treated with 25 or 250 μM of glycidamide in vitro. All oocytes were degen-

**EFFECT OF IN VITRO AND IN VIVO ACRYLAMIDE EXPOSURE ON MOUSE OOCYTES.** O. Cinar, D. Aras, Z. Cakar, S. Ozkavukcu, A. Can. *Department of Histology and Embryology, Ankara University School of Medicine, Ankara, Turkey;* "Ankara University, Biotechnology Institute, Ankara, Turkey;* "Center for Assisted Reproduction, Dep. of Obstetrics and Gynecology, Ankara University School of Medicine, Ankara, Turkey.

**OBJECTIVE:** Acrylamide is a chemical that widely used in the treatment of wastewater, paper/pulp manufacturing, mining and scientific research. Processed foods such as roasted almonds, coated peanuts, dips, fried potato, biscuits, coffee, contain high levels of acrylamide. The consultation of the United Nations Food and Agricultural Organization and the World Health Organization on “Health Implications of Acrylamide in Food”, indicated several important points such as: dietary habits in particular countries may lead to severe carcinogenic implications, as well as genotoxicity. Acrylamide effects on the oocyte maturation and meiotic spindle still need to be evaluated.

**DESIGN:** BALB/c mice were used. In vitro and in vivo maturation kinetics of acrylamide treated oocytes (n = 182 and n = 133, respectively) were compared to control group (n = 77 and n = 102). In vitro maturation dynamics of glycidamide, one of the metabolites of acrylamide, treated oocytes (n = 61) were compared to control oocytes (n = 24). Meiotic spindles were evaluated under a confocal microscope following fluorescently labeling the meiotic chromosomes and spindle microtubules.

**MATERIALS AND METHODS:** In vitro maturation kinetics of control oocytes were compared to 100, 500 or 1000 μM of acrylamide treated ones. In vivo maturation analyses were performed following oocyte isolation from the animals that were intraperitoneally treated with either vehicle or 25 mg/kg/day of acrylamide for 7 days. To test whether in vivo effects of acrylamide resulted from its metabolite glycidamide or not, isolated oocytes were treated with 25 or 250 μM of glycidamide.

**RESULTS:** In vitro acrylamide exposure did not affect in vitro oocyte maturation and meiotic spindle. In vivo acrylamide treatment caused an accumulation of oocytes at prometaphase-I (10.3% vs 2.3% in controls, p = 0.039). Majority of the M-II stage oocytes from in vivo acrylamide treated group showed a decrease in the meiotic spindle mass and a misalignment of the chromosomes. This finding indicated that acrylamide might show its action via its metabolite glycidamide. Therefore, isolated GV-stage oocytes treated with 25 or 250 μM of glycidamide in vitro. All oocytes were degenerated after the culture period.

**CONCLUSIONS:** Dietary habits have been changing in parallel with the modern life. The finding, which acrylamide negatively affects oocyte maturation, suggests that it may reduce fertilization and implantation rates and could cause aneuploidy in higher doses, and thus implies that changing dietary habits must be reconsidered regarding female fertility.

**Supported by:** This study was supported by Ankara University Scientific Research Council (#13B330012).
the testis, and agglomerates of AgNPs in the testis. However, the testis index and concentrations of fertility-associated hormones were not changed markedly among the different groups. A microarray analysis showed that 383 genes were significantly altered in the testis of mice after 125 mg/kg AgNP treatment, and these altered genes were associated with apoptosis, oxidative stress and other signaling pathways. Furthermore, the increased expression of apoptosis-related molecules (caspase 3, Myc and Mdm2) may explain the high levels of apoptosis in the testis after 125 mg/kg AgNPs treatment.

CONCLUSIONS: These results demonstrate that AgNPs evoke detrimental changes in the male reproductive system was involved in apoptosis.

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ASSESSMENT OF THE EMBRYO TRANSFER CATHETER MICROBIOME AFTER EUPLOID BLASTOCYST TRANSFER IS NOT PREDICTIVE OF SUSTAINED IMPLANTATION. J. M. Fransasiak,a C. R. Juneau,a S. J. Morin,a X. Tao,a J. Rajchel,b J. N. Landis,b Y. Zhan,b N. Treif,b R. T. Scott.c "Reproductive Medicine Associates of New Jersey, Basking Ridge, NJ; bFAEEC, Basking Ridge, NJ.

OBJECTIVE: Feasibility of embryo transfer (ET) catheter tip microbiome assessment has been demonstrated utilizing the unique 16S ribosomal RNA hypervariable regions to determine genus level classification. The microbiome of the lower genital tract can prognosticate obstetrical outcome while the outcomes data for upper reproductive tract remain poorly characterized. To date, the ET data has been cultivation-dependent, a technique known to lack the ability to assess many of the dominant and major genera in the environment. Indeed, the microbiome at the time of ET has only been evaluated utilizing culture-based technology which is known to capture only a fraction of dominant and major organisms. This study analyzes the microbiome at the time of single euploid blastocyst ET and characterizes the microbiome by reproductive outcome.

DESIGN: Prospective cohort.

MATERIALS AND METHODS: Consecutive patients undergoing euploid, single ET were included in the analysis. The ET was performed per routine. After transfer, the most distal 5 mm portion of the ET catheter was sterilized placed in a DNA free PCR tubes. Cell lysis and DNA purification were performed and DNA sequencing was performed using Next Generation Sequencing of the bacteria specific 16S ribosomal RNA gene. Positive E. coli controls and negative controls were run. The sequences were assigned to operational taxonomic units (OTUs) using the RDP classifier with confidence cutoffs of 0.8 in the QIIME package. This allowed for identification and relative quantification of bacteria present in the sample. Sustained implantation was defined as positive fetal cardiac activity at the time of discharge from infertility care at 8 weeks. All other outcomes were considered failed. The Shannon Diversity Index (SDI), total OTU counts, and fraction of reads were compared utilizing generalized linear models.

RESULTS: There were 497 samples collected. 410 passed initial amplification and were included in the analysis. OTUs were assigned to OTUs with greater than 10,000 read counts, 250 (63%) with sustained implantation and 145 (37%) with failed transfers. There were a total of 248 genera detected amongst all specimens. As expected, Lactobacillus genera were detected in the samples. When analyzing fraction of reads there were highly significant differences, but these did not survive multiple comparison testing (p<0.053).

CONCLUSIONS: The data presented here show the microbiome at the time of ET may differ by pregnancy outcome but highlights the challenge of low bacterial load and read counts when analyzing ET catheter tips alone. In order to more fully investigate the microbiome’s affect utilizing this robust analytic technique, specimens with a more reliable and higher bacterial load would be required. To accomplish this, the catheter tip analysis would be required. To accomplish this, the catheter tip analysis would be required.

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TRIMESTER-SPECIFIC URINARY PARABEN CONCENTRATIONS AND PREGNANCY GLUCOSE LEVELS AMONG WOMEN FROM A FERTILITY CLINIC. Y. Chiu,a L. Minguez-Alarcon,b C. Messerlian,b J. B. Ford,b M. Keller,b J. C. Petrozza,a P. L. Williams,b R. Hauser,b T. James-Todd.b "Nutrition, Harvard T.H. Chan School of Public Health, Boston, MA; Environmental Health, Harvard T.H. Chan School of Public Health, Boston, MA; Obstetrics and Gynecology, Massachusetts General Hospital, Boston, MA; Biostatistics, Harvard T.H. Chan School of Public Health, Boston, MA; Harvard Chan School of Public Health, Boston, MA.

OBJECTIVE: Parabens, widely used as preservatives in medication, food and personal care products, have a weak estrogenic effect, which could alter pancreatic beta cell function. This study evaluated the association between trimester-specific urinary paraben concentrations and 2nd trimester glucose levels among women who conceived after treatment at a fertility center.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: A total of 242 pregnant women contributed at least one spot urine sample during the 1st or 2nd trimesters. Urinary paraben concentrations, including methylparaben (MP), propylparaben (PP), and butylparaben (BP), were quantified by isotope dilution tandem mass spectrometry at the Centers for Disease Control and Prevention. Blood glucose levels were measured after a 50-gm glucose challenge test performed at 24-28 weeks gestation. Linear regression models were used to evaluate associations between quartiles of trimester-specific specific gravity (SG)-adjusted paraben concentrations and blood glucose levels adjusting for age, race/ethnicity, pre-pregnancy body mass index, smoking, education, fetus number, and infertility diagnosis. A metabolic risk index (MB) was estimated at each time point during 1st and 2nd trimester, respectively, were 117 and 113 µg/L for MP, 22.0 and 23.8 µg/L for PP, and 0.87 and 0.97 µg/L for BP. Concentrations of BP were similar, but slightly higher for MB and PP compared to general US female population. Neither 1st or 2nd trimester urinary MP, PP, and BP concentrations were associated with blood glucose levels. For example, adjusted...
glucose levels [mean (95% CI) mg/dL] for women in increasing quartile of the 2nd trimester BP were 109 (103, 114), 119 (112, 127), 113 (106, 120), and 115 (108, 122). For MP and PP, the adjusted glucose levels also appeared similar across quartiles.

CONCLUSIONS: Urinary paraben concentrations were not associated with 2nd trimester glucose levels among women from a fertility clinic.

References:

Supported by: NIH grants R01ES026166, R01ES022955, R01ES009718, and R01ES000002 from the NIEHS and grant T32DK00770316 from the NICHD.
The decrease of birth rate in the last century in all industrialized countries is related to exponential increase of Earth temperature. Very little is known about the relationship between global temperature and oocyte development. Several studies in animals showed that IVF achieves better outcomes in cold temperature mainly because hot climates promote oxidative stress which is directly involved in energetic changes and in cellular metabolism.

DESIGN: The aim of the study is to determine whether seasonal changes of temperature affect follicular recruitment, number of oocytes retrieved and pregnancies achieved in assisted reproduction technology (ART).

MATERIALS AND METHODS: IVF cycles performed in Our Centre from 2010 to 2015 were analyzed and divided in two groups according to the month of execution: cold month from December to February (with a mean temperature of 4°C - 39, 2°F) and hot months from June to July (with a mean temperature of 24,4°C - 75, 9°F). All patients underwent ovulation induction with recombinant FSH.

RESULTS: 1645 cycles were studied, of which 841 in cold months and 804 in hot months. The two groups showed no differences in women age (36 years in cold months vs 36,3 in hot months), ovarian reserve (average FSH and AMH respectively: 8,5 U/IL in cold months vs 8,7 U/IL in hot months and 2,2 ng/ml in cold months and 2,3 ng/ml in hot months) and average number of oocytes retrieved (6 in cold months vs 5,9 in hot months). The study showed no differences also in fertilization rate (75,7% in cold months vs 75,1% in hot months) and pregnancy rate per transfer (29,3% in cold months vs 30,2% in hot months). The abortion rate was respectively 21,7% and 25% in cold and hot months.

CONCLUSIONS: Our study showed no significant differences in number of oocytes retrieved and pregnancies achieved. Literature suggests that temperature changes can affect natural fertility, but until now no clinical data confirm this influence in IVF treatment.

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CAN GLOBAL TEMPERATURE AFFECT IN VITRO FERTILIZATION CYCLES?. L. Cipriani, A. Bianchi, A. Bazzocchi, F. Fabbri, G. Damiano, P. Ciotti, L. Notarangelo, N. Calza, L. Orazi, E. Porcu. S. Orsola Hospital, Infertility and IVF Center, Bologna, Italy; Sant'Orsola Hospital, Infertility and IVF Center, Bologna, Italy; In- fidelity and IVF Center, University of Bologna, Bologna, Italy; Orsola Hospital, Infertility and IVF Center, University of Bologna, Bologna, Italy; Carlo Poma Hospital, Gynaecologic Unit, Mantova, Italy.

OBJECTIVE: Changes in global temperature are believed to influence fertility. Sperm counts are lowest in summer months and highest in winter. The decrease of birth rate in the last century in all industrialized countries

Table 1. Fully loaded Micro with different Labels (ppb)

<table>
<thead>
<tr>
<th>Label Type</th>
<th>VOC Level (ppb)</th>
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</thead>
<tbody>
<tr>
<td>Sharpie extrafine point permanent markers</td>
<td>65</td>
</tr>
<tr>
<td>Sharpie fine point permanent markers</td>
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</tr>
<tr>
<td>Wax pencil</td>
<td>58</td>
</tr>
<tr>
<td>Brady LabXPert label</td>
<td>46</td>
</tr>
<tr>
<td>Brady harsh Environment labels</td>
<td>67</td>
</tr>
</tbody>
</table>
VAGINAL LUBRICANT USE AMONG WOMEN TRYING TO CONCEIVE: INSIGHTS FROM A SURVEY OF OVER 1000 PARTICIPANTS. S. Johnson, L. Marriott, M. Reay, P. Parsons. SPD Development Company Ltd, Bedford, United Kingdom.

OBJECTIVE: Personal lubricants are frequently used by women to relieve vaginal dryness and enhance sexual experience. However, not all personal lubricants are suitable for women who are trying to conceive, as some have been reported to interfere with sperm motility and viability, thereby decreasing the chances of natural conception. The aim of this study was to assess the prevalence of lubricant use in women of reproductive age who are actively trying to conceive and to understand whether there is a demand for ‘fertility-friendly’ personal lubricants in this specific subgroup of users.

MATERIALS AND METHODS: A survey was conducted in 1540 women aged 18 years and older who were actively trying to conceive. Participants were asked to answer eight questions relating to the presence of vaginal discomfort during sex and the use of vaginal lubricants at varying points in their lifetime.

RESULTS: Approximately 10% of participants reported using a vaginal lubricant at the time of the survey (9.2%; 142/1540). However, just under 3% of participants (2.7%; 42/1521) reported suffering from vaginal dryness or discomfort during sex at this time. Approximately one in ten participants (10.3%; 158/1540) reported that they had suffered from vaginal dryness or discomfort during sex at some point in their lifetime. Almost 3% of participants (2.5%; 39/1540) stated that they had suffered from vaginal dryness when trying to conceive in the past, and 1.6% of participants (24/1540) reported using a lubricant during that period.

CONCLUSIONS: This study found that some women who are actively trying to conceive use personal lubricants, and the proportion of those using vaginal lubricants exceeds the proportion of women suffering from vaginal discomfort/dryness. This observation could suggest that personal lubricant use in this group of women serves additional purposes rather than simply alleviating vaginal discomfort. The availability of ‘fertility-friendly’ lubricants would allow women who are actively trying to conceive to enhance their sexual experience without reducing the chances of pregnancy.

SUPPORTED BY: Study was funded by SPD Development Company Ltd., a fully owned subsidiary of SPD Swiss Precision Diagnostics GmbH, the manufacturer of Clearblue Pregnancy and Fertility Tests.

OXIDATIVE STRESS

GASTRIC BYPASS SURGERY IS ASSOCIATED WITH REDUCTION IN OVARIAN ENDOPLASMIC RETICULUM STRESS. J. P. Alvarez, a,b A. Frank, b D. Clegg, b Obstetrics and Gynecology, UCLA, Los Angeles, CA; Cedars Sinai, Los Angeles, CA.

OBJECTIVE: Obesity is characterized by accumulation of lipids in non-adipose tissue leading to high levels of free fatty acids that are subject to oxidative damage and formation of cytotoxic and highly reactive lipid peroxides, which are detrimental to the endoplasmic reticulum (ER) function (1). As a result, unfolded proteins accumulate leading to ER stress. This aggregation of unfolded proteins activates a compensatory reaction termed the unfolded protein reaction (UPR) and failure of these proteins to re-establish homeostasis can lead to apoptosis (2). Previous data showed that Roux-en-Y gastric bypass (RYGB) surgery reduces lipid accumulation in the liver by upregulating hepatic autophagy in the liver (3). By postoperative week six, body weight significantly decreased for both SO (42.0 g ± 1.3 vs 27.9 g ± 1.2 P < 0.01) and RYGB groups (42.5 g ± 3.3 vs 28.5 g ± 2.6 P < 0.01), however bodyweight was equivalent between the two groups (27.9 g ± 1.2 for SO vs 28.5 g ± 2.6 for RYGB, P = 0.66). In RYGB there was a significant reduction in relative gene expression of Hspa6 (-1.7 fold change vs SO, P < 0.05) and Hsp90b1 (-1.7 fold change vs SO, P = 0.02). Other UPR genes showed a comparable, but less relative expression: Pparalpha (-1.4 fold change vs SO, P = 0.18), Ddit3 (-1.3 fold change vs SO, P = 0.37) and Edem1 (-1.3 fold change vs SO, P = 0.52).

CONCLUSIONS: Weight reduction in mice after RYGB surgery, but not caloric restriction led to reduced expression of Hspa6 and Hsp90b1, genes associated with oxidative stress in the ovary. Further studies are needed to assess whether this reduction in oxidative stress could lead to better ovarian function.

References:

OOCYTES ARE MORE RESISTENT TO OXIDATIVE STRESS THAN EMBRYOS. L. Wang, a,b F. Wang, a L. G. Robinson, a Y. G. Kramer, c M. L. Seth-Smith, c N. M. Sachdev, c D. L. Keefe. a Department of Obstetrics and Gynecology, NYU Langone Medical College, Laboratory of Reproductive Medicine, New York, NY; b Reproductive Medicine Center, Tongji Hospital, Tongji Medical College of Huazhong University of Science and Technology, Wuhan, China; c OBS-GYN, NYU Fertility Center, New York, NY.

OBJECTIVE: Reactive oxygen species (ROS) are a major cause of aging in all tissues studied, including reproductive tissues. Recent studies demonstrate extensive DNA damage repair capacity in oocytes (1), and genetic variation in DNA damage repair pathways is associated with reproductive lifespan in women (2). We hypothesized that MII oocytes are more resistant to oxidative stress than other stages of development.

DESIGN: Prospective, randomized study of a biologic intervention on mouse oocytes and embryos.

MATERIALS AND METHODS: 80 MII oocytes and 40 cleavage embryos from B6C3F1 mice (Embyrtech Laboratories, Inc, USA) were thawed and exposed to oxidative stress induced by Carbonyl cyanide-4-(trifluoromethoxy) phenylhydrazone (FFCP, 750mM), which generates ROS by uncoupling mitochondrial electron transport and disrupting mitochondrial function. Oocytes and embryos were randomized into untreated controls, or 5, 10 or 20 hour exposure to FFCP. DNA damage was determined by immuno-fluorescent staining for γ-H2AX, or by mean telomere length, measured by single-cell qPCR. Data were analyzed by chi-square test and one-way ANOVA.

RESULTS: 20 hours of exposure to FFCP is lethal for all embryos. Embryos exposed to FFCP for 5 and 10 hours of FFCP show increased γ-H2AX staining (5 hours: 87.5% vs 25% positive cells P < 0.05; 10 hours 100% vs 25%, P < 0.05). However, these same doses and durations of FFCP do not increase DNA damage in oocytes - there is no significant increase of γ-H2AX positive MII oocytes compared to controls (30% in the control group, 40% in the 5-hour group and 30% in the 10-hour group, P > 0.05). Significantly higher numbers of γ-H2AX positive MII oocytes

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CONCLUSIONS: Incubator chamber spaces, as well as dish loads are associated with higher VOC count. Among the 3 tested incubators, the Hera-cell showed the lowest VOC count. However, all three incubators are at an accepted VOC level. To minimize the VOC levels within the incubator, attempts should be made to minimize dish load and labeling with a Sharpie.

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are found only in the 20-hour group (100%, P<0.05), a dose which is uniformly lethal to embryos. As previously demonstrated, 45 minutes of 750nM FCCP treatment shortens telomeres in cleavage stage mouse embryos (3). However, MII oocytes exposed to 750nM FCCP for 5, 10, or 20 hours show no statistically significant telomere shortening compared to controls (P>0.05).

CONCLUSIONS: MII oocytes are more resistant to oxidative stress than cleavage embryos.

References:

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THE ACTIONS OF SILDENAFIL ON TROPHOBLAST SURVIVAL IS DEPENDENT ON HBEGF SIGNALING. A. Bolnick, a C. Jain, a B. Kilburn, a P. Singhal, a S. Svytka, a J. Bolnick, a C. Barnak, a R. Greige, a D. Arman. a Obstetrics and Gynecology, Wayne State University, Detroit, MI; bObstetrics and Gynecology/Oncology, Good Samaritan Medical Center, West Islip, NY.

OBJECTIVE: Sildenafil (Viagra) has proved useful for alleviating fetal growth restriction, but we have found that it has direct effects on trophoblast invasion and survival during oxidative stress. However, the mechanism is not completely understood. Heparin-binding EGF-like growth factor (HBEGF) has similar effects on human trophoblast cells. Therefore, we examined whether there is a link between sildenafil and HBEGF signaling.

DESIGN: In vitro study of a first trimester trophoblast cell line, HTR-8/SVneo cells.

MATERIALS AND METHODS: HTR-8/SVneo cells were cultured at 20% O2, or in a hypoxia/reoxygenation (H/R) model, defined as 2 h at 2% O2, 20% O2, or in a hypoxia/reoxygenation (H/R) model, defined as 2 h at 2% O2, 20% O2, or in a hypoxia/reoxygenation (H/R) model, defined as 2 h at 2% O2, 20% O2, or in a hypoxia/reoxygenation (H/R) model, defined as 2 h at 2% O2, 20% O2, or in a hypoxia/reoxygenation (H/R) model, defined as 2 h at 2% O2, 20% O2. Cell death was evaluated using terminal deoxynucleotidyl transferase-mediated dUTP nick end-labeling (TUNEL). HBEGF mRNA. The HBEGF protein was measured by ELISA. Cell death was evaluated using terminal deoxynucleotidyl transferase-mediated dUTP nick end-labeling (TUNEL).

RESULTS: The expression of HBEGF increased 8-fold (0.35 ± 0.04 to 2.81 ± 0.14 ng/µg, P<0.05) after culture with sildenafil, without a change in HBEGF mRNA. Sildenafil rescue of trophoblast cell death due to H/R injury (H/R, TUNEL = 0.13 ± 0.01; sildenafil, TUNEL = 0.06 ± 0.01, P<0.05) was attenuated (CRM197, TUNEL = 0.15 ± 0.03, P<0.05 compared to sildenafil) by treatment with CRM197.

CONCLUSIONS: Our findings suggest that sildenafil increases HBEGF biosynthesis and secretion, which contributes to trophoblast survival and could have a beneficial effect in treating placental insufficiency.

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EPIDIDYMAL SPERM ANALYSIS FOLLOWING TIME AND DOSE DEPENDENT ADMINISTRATION OF MONOSODIUM GLUMATE IN PREADOLESCENT RATS. D. Kianifard. Department of Basic Sciences, Faculty of Veterinary Medicine, University of Tabriz, Tabriz, Iran, Islamic Republic of.

OBJECTIVE: Monosodium glutamate (MSG) is a food additive. Extreme use of MSG may induce multiple complications in body systems. Monosodium glutamate can induce the production of reactive oxygen species (ROS), oxidative stress and cellular death. Testicular tissue and spermatogenic cells are susceptible to environmental and exogenous ROS producing risk factors. According to cytotoxic effects of MSG on testicular tissue, the various time and dose dependent effects of MSG on spermatogenesis producing activity of testicular tissue was evaluated in preadolescence period.

DESIGN: Forty two, 21 days old rats were divided into six groups: 1) control (1); 2) control (2); 3) short-term low dose MSG; 4) short-term high dose MSG; 5) long-term low dose MSG and 6) long-term high dose MSG. The animals in short-term groups were euthanized at 36 days of age and the animals in long-term groups were euthanized at 50 days of age.

MATERIALS AND METHODS: Low and high doses of MSG (6 and 60 mg/kg i.p.) were administrated to preadolescent rats for 14 (short-term) and 28 (long-term) days. Epididymal sperm analysis (sperm count, sperm motility and viability percentage) was performed.

RESULTS: The administration of MSG with low dose for 14 days was not altered sperm analysis indices. Short-term administration of MSG with high dose was led to non-significant reduction of sperm count and sperm motility. Long-term administration of MSG with low dose was led to non-significant decrement of sperm count and motility and significant reduction of sperm viability. High dose administration of MSG for long time was led to significant reduction of all sperm analysis parameters.

CONCLUSIONS: The results of this study showed that, dose dependent continuous long-term administration of monosodium glutamate may affect the normal spermatogenesis in preadolescence period and could induce some spermatogenetic alterations and fertility complications in adolescents.

References:

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STANDARDIZATION OF THE TUNEL PROTOCOL FOR SPERM DNA FRAGMENTATION BETWEEN TWO LABORATORIES. R. Sharma, a S. Forte, b S. Gupta, a Z. Cakar, a C. DeGeyter, 1 A. Agarwal, 1 American Center for Reproductive Medicine, Department of Urology, Cleveland Clinic, Cleveland, OH; 2Gyn. Endokrinologie und Reproduktionsmedizin, Universitatsspital Basel Frauenklinik, Basel, Switzerland; 3Division of Gynecological Endocrinology and Reproductive Medicine, University Women’s Hospital of Basel, Basel, Switzerland.

OBJECTIVE: The TUNEL assay measures both single- and double-stranded DNA fragmentation in spermatozoa. There is a lack of consensus on a reference value, however, due to the absence of a standard protocol in the literature. Moreover, the results of this test differ greatly between laboratories, making it difficult to use the assay for clinical management. Therefore, the standardization of the TUNEL assay by flow cytometer is essential for accurate assessment of DNA fragmentation to categorize men as infertile. Our objective was to: 1) standardize the protocol for sperm DNA fragmentation by the TUNEL assay utilizing a bench top flow cytometer, and 2) assess the reproducibility of this assay between two laboratories.

DESIGN: In vitro study.

**Table 1: Sperm analysis indices**

<table>
<thead>
<tr>
<th>Group Number</th>
<th>Sperm Count (10⁹/ml)</th>
<th>Sperm Motility (%)</th>
<th>Sperm Viability (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Control (1)</td>
<td>16.57±1.98</td>
<td>68.71±9.74</td>
</tr>
<tr>
<td>2</td>
<td>Control (2)</td>
<td>20.14±1.95</td>
<td>75.86±6.46</td>
</tr>
<tr>
<td>3</td>
<td>Short-term Low dose</td>
<td>16.86±1.57</td>
<td>69.29±6.23</td>
</tr>
<tr>
<td>4</td>
<td>Short-term High dose</td>
<td>15.57±1.71</td>
<td>66.29±9.03</td>
</tr>
<tr>
<td>5</td>
<td>Long-term High dose</td>
<td>18.86±2.41</td>
<td>73.00±7.43</td>
</tr>
<tr>
<td>6</td>
<td>Long-term High dose</td>
<td>15.29±1.11</td>
<td>61.71±8.26</td>
</tr>
</tbody>
</table>
Materials and Methods: Both laboratories analyzed the same set of semen samples from 31 patients using the same assay kit (Aptoptosis detection kit, BD Pharmingen), with an identical lot number, test protocol and bench flow cytomter (BD Accuri C6). Two experienced operators from independent laboratories using centralizing services for patient in two countries performed the tests. The analysis was done in duplicate at two times with 3 cohorts of patient samples; n=10 first run, n=11 second run and n=10 third run. Each sample was split into 2 sets consisting of a negative control, positive control and test sample. Analysis was done using identical acquisition settings. Results were analyzed using a Spearman correlation measure, and a P value of <0.001 was considered significant.

Results: The correlation of TUNEL results between the labs was significant in cohort 1: r=0.891; p<0.001; cohort 2: r=0.745; p<0.012, and cohort 3: r=0.709; p=0.028. The average TUNEL values (for run 1 and run 2) in the test and positive controls across the two labs were highly correlated in cohort 2 and 3 combined (r=0.773; p<0.001 and r=0.839; p<0.001, respectively).

Conclusions: We found that the results of the TUNEL assay are highly reproducible within and across laboratories. The use of a standardized test protocol by independent laboratories is critical for establishing the TUNEL assay as an advanced, reproducible and accurate diagnostic test. Use of a standardized test protocol for the TUNEL assay by laboratories across the world will prove to be of immense benefit in the evaluation of male infertility.

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In Human Germinal Vesicle Oocytes Mitochondrial Stress Disrupts Meiotic Spindles Without Affecting Mean Telomere Length

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Objective: The architecture and structure of the meiotic spindle influence embryo development(1) and risk of aneuploidy in women(2). The factors that disrupt the meiotic spindle remain incompletely understood. Dysfunctional mitochondria produce reactive oxygen species (ROS), which may directly perturb spindles(3). ROS also can disrupt spindles by inducing telomere attrition, since telomeres are essential for spindle formation and are especially susceptible to ROS(4). We studied the impact of ROS, produced by uncoupling mitochondria, on the area and retardance (measure of molecular order) of meiotic spindles and on mean telomere length of individual human oocytes.

Design: Prospective, randomized, paired research laboratory intervention.

Materials and Methods: 44 germinal vesicle (GV) stage oocytes were accessioned from 16 patients undergoing IVF/ICSI. GV's from each patient were randomly assigned to control or treatment group. Oocytes in the treatment group were cultured in media containing Carboxyl cyanide-4-(tri-fluoromethoxy) phenylhydrazzone (FCCP; 750mM) for one hour to induce mitochondrial stress. Control oocytes were cultured in media without FCCP. GV oocytes from both groups were further cultured to permit meiotic maturation itself is relatively resistant to ROS, consistent with prior studies showing limited cell cycle check point control during oogenesis. However, ROS produced by acute mitochondrial stress disrupts spindle retardance and size. Reactive oxygen, at least acutely, does not induce telomere attrition in human oocytes.

References:

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Efficacy of Ascorbic Acid in Alleviating Oxidative Stress Using In-Vitro Human Sperm Model

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Objective: The aim of the study was to simulate condition of heat stress by exposing sperm to testicular temperature (34.5°C), normal human body temperature (37°C) and pathological temperature (39.5°C) encountered during fever. The goal was to address two questions: i) does the mild increase in sperm temperature in the presence of oxidant over a period of time result in a decrease in motility and increased oxidative stress and ii) is ascorbic acid (AA) helpful in reducing oxidative stress in this in-vitro model?

Design: In-vitro model using heat and hydrogen peroxide (H2O2) exposure for 2h and 4h in the presence of AA on sperm motility and oxidative stress.

Materials and Methods: Highly motile sperm (10x10⁶/mL) (n = 11) were prepared by density gradient separation and exposed at 34.5°C, 37°C and 39.5°C for 2 and 4h. Oxidative stress was created by incubating with 200 μM of hydrogen peroxide (H2O2). Samples were incubated in the presence of Heat alone or Heat + H2O2. Ascorbic acid was tested at 400 μM/L or 600 μM/L. Oxidative stress was measured by examining the decrease in static oxidation reduction potential (sORP; millivolts/10⁶ sperm/mL) utilizing the MIOXSYS System. Repeated measures models were used to assess the effect of ascorbic acid with respect to motility and sORP. Interactions among factors (heat, H2O2 and incubation time) in the model were also investigated.

Results: A statistically significant dose-dependent association between ascorbic acid concentration and sORP was seen when accounting for H2O2, time, and temperature. Compared to control (no ascorbic acid), sORP decreased by 6.70 mV/10⁶ sperm/mL at 400 μM/L and 7.31 mV/10⁶ sperm/mL at 600 μM/L AA (p < 0.001). No statistically significant association was seen between ascorbic acid concentration and sperm motility when accounting for Heat, H2O2, and time. H2O2 was associated with reduced motility, but an identified interaction between H2O2 and temperature (p=0.002) suggested that the degree of change in mean motility with the inclusion of H2O2 was dependent on temperature.

Conclusions: Our repeated measures models show that in the presence of increased temperature, ascorbic acid is effective in reducing oxidative stress. Ascorbic acid may be beneficial in men exposed to both heat and oxidative stress environment such as experienced during occupational exposure.

Male Reproduction and Urology - Clinical

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OBJECTIVE: The growing interest in evaluating the reproductive competence of the male gamete requires the assessment of the karyotype to gain information on the health and the ability of the germinal epithelium to properly complete meiosis. This is currently carried out by FISH, with its limitations in chromosomes number and accuracy. We aim to confirm, by copy number variants (CNVs) through Next Generation Sequencing, the actual karyotype and provide information on the fertility potential of the male gamete.

DESIGN: Aneuploidy assessment on spermatozoa was carried out by FISH in 79 consenting men that according to their ART outcome, were subdivided in fertile and infertile. Four anonymous donors with proven fertility served as control. In some of these men, a whole chromosome analysis was carried out by NGS to identify the accuracy of the procedure and the ability to estimate the reproductive competence of the male gamete.

MATERIALS AND METHODS: A total of 79 ejaculated specimens were obtained from consenting male partners of couples who underwent at least one ICSI cycle. FISH was performed on at least 1000 spermatozoa for each of these patients as well as 2 anonymous donor controls, with a threshold of >1.6% (euploid) while maintaining a 2.3% FISH error. DNA was extracted and amplified from as few as 500 spermatozoa per sample for some of the men, as well as the 2 fertile donors, by using a commercially available kit followed by PCR-based random hexamer amplification. After achieving a DNA concentration of 447.8±198ng/ul and quality of 1.7±0.1nm, aneuploidy was calculated using CNVs obtained by CASAVA and VarScan2 software.

RESULTS: In total, 79 men with an average age of 38.0±7yrs and normal semen analysis underwent ICSI treatment with their female partners aged 35.2±4.3yrs. A total of 22 couples in 69 cycles achieved a fertilization of 71.9% and a clinical pregnancy rate of 40.6%, defining the fertile group. The remaining 57 couples with a maternal age of 35.6±4yrs were treated in 153 cycles achieving a fertilization rate of 59.3%. This cohort had a clinical pregnancy rate of 6.5% that resulted in pregnancy losses, defining the infertile group. The average aneuploidy assessed by FISH did not significantly differ among donor (1.4±0.1%), the fertile (2.7±2.1%) and infertile cohorts (3.9±4.3%). Whole chromosome analysis by NGS evidenced an overall aneuploidy of 2.9±2.3% for the donors, 5.4±2.1% for the fertile and 8.3±0.8% for the infertile cohort (P<0.01). When we compared the two procedures, NGS confirmed for all chromosomes a higher sperm aneuploidy than FISH in the fertile (P<0.05) and infertile cohorts (P<0.01).

CONCLUSIONS: In couples with normal semen parameters treated by ART, sperm aneuploidy assessment may be beneficial. While most spermatozoa undergo DNA repair, reactive oxygen species (ROS) are the main cause for DNA injury. We question whether sperm chromatin integrity differs among spermatozoa isolated at different stages of the male genital tract and how it may affect reproductive outcome.

DESIGN: Over 30 months, men with high SCF in their ejaculates (n=74) underwent surgical sampling, often bilateral, from vas deferens, epididymis, and testis. SCF was assessed by terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL) and clinical outcome was recorded for each sperm source for men undergoing ICSI treatment.

RESULTS: Of the original 74 patients, 33 were treated by ART with an average SCF of 27.4±17% (range 26.0-96.0) in their ejaculate. In 10 men aspiration of the vas deferens resulted in 18.6±8% SCF (range 5.8-34.8) and in 74 the SCF on testicular spermatozoa was 11.7±6% (range 2.0-27.0). The SCF progressively decreased as TUNEL was measured proximally from the ejaculate toward the vas deferens (P<0.03), the epididymis (P=0.001), and testis (P=0.001). A fertilization of 63.4% (281/443), 65.2% (58/89) and 59.9% (217/362) was achieved by ICSI using ejaculated, epididymal, and testicular spermatozoa, respectively. ART outcome with ICSI utilizing these surgical sources yielded a clinical pregnancy of 26.4%, while with the ejaculated counterpart only 14.6%. Based on these preliminary findings a subgroup of patients (n=19), with SCF of 40.1±18 bypassed the prerequisite cycle with ejaculated spermatozoa and opted to undergo TESE with ICSI. The clinical pregnancy rate achieved was 29.0% per cycle that translated to 55.6% per couple treated.

CONCLUSIONS: DNA integrity assessment on the spermatozoa isolated at different levels of the male genital tract evidenced that oxidative stressors progressively compromise DNA integrity toward the ejaculate, this may be obviated by utilizing testicular spermatozoa. Couples unable to achieve a pregnancy using ejaculated spermatozoa with compromised DNA may benefit from undergoing testicular retrieval for diagnostic and therapeutic purposes.

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DNA FRAGMENTATION IN RELATION TO SPERM SOURCE AND REPRODUCTIVE OUTCOME. T. Paniza,1 T. Cozzubbo,5 S. Cheung,5 A. Parello,2 M. Goldstein,7 Z. Rosenwalks,5 G. D. Palermo.1 Reproductive Medicine, Weill Cornell Medicine, New York, NY, 1Urology, Weill Cornell Medicine, New York, NY.

OBJECTIVE: During the later stages of spermiogenesis DNA breakage is physiologically required to allow tight chromatin compaction. While most spermatozoa undergo DNA repair, reactive oxygen species (ROS) are the main cause for DNA injury. We question whether sperm chromatin integrity differs among spermatozoa isolated at different stages of the male genital tract and how it may affect reproductive outcome.

DESIGN: Over 30 months, men with high SCF in their ejaculates (n=74) underwent surgical sampling, often bilateral, from vas deferens, epididymis, and testis to process spermatozoa by terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL) and clinical outcome was recorded for each sperm source for men undergoing ICSI treatment.

MATERIALS AND METHODS: Ejaculates processed in the standard fashion were assessed for SCF by TUNEL. Surgical samples were minced and prepared for SCF evaluation and were cryopreserved for later use with ICSI. DNA fragmentation was measured by TUNEL on specimens isolated from vas deferens, epididymis and testis by using a commercial kit (In Situ Cell Death Detection Kit, Roche). At least 500 spermatozoa were counted per site under fluorescent microscopy with an adopted threshold of 15%.

RESULTS: Of the original 74 patients, 33 were treated by ART with an average SCF of 27.4±17% (range 26.0-96.0) in their ejaculate. In 10 men aspiration of the vas deferens resulted in 18.6±8% SCF (range 5.8-34.8) while in 40 men epididymal sampling yielded 17.1±8% SCF (range 5.3-34.8) and in 74 the SCF on testicular spermatozoa was 11.7±6% (range 2.0-27.0). The SCF progressively decreased as TUNEL was measured proximally from the ejaculate toward the vas deferens (P<0.03), the epididymis (P<0.001), and testis (P<0.001). A fertilization of 63.4% (281/443), 65.2% (58/89) and 59.9% (217/362) was achieved by ICSI using ejaculated, epididymal, and testicular spermatozoa, respectively. ART outcome with ICSI utilizing these surgical sources yielded a clinical pregnancy of 26.4%, while with the ejaculated counterpart only 14.6%. Based on these preliminary findings a subgroup of patients (n=19), with SCF of 40.1±18 bypassed the prerequisite cycle with ejaculated spermatozoa and opted to undergo TESE with ICSI. The clinical pregnancy rate achieved was 29.0% per cycle that translated to 55.6% per couple treated.

CONCLUSIONS: DNA integrity assessment on the spermatozoa isolated at different levels of the male genital tract evidenced that oxidative stressors progressively compromise DNA integrity toward the ejaculate, this may be obviated by utilizing testicular spermatozoa. Couples unable to achieve a pregnancy using ejaculated spermatozoa with compromised DNA may benefit from undergoing testicular retrieval for diagnostic and therapeutic purposes.

Table 1: Comparison of the evaluated parameters among the groups: DGC; MACS-DGC; MACS-MACS; MACS.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>DGC</th>
<th>DGC-MACS</th>
<th>MACS-DGC</th>
<th>MACS</th>
</tr>
</thead>
<tbody>
<tr>
<td>DNA Fragmentation TUNEL (%)</td>
<td>10(5.0-16.0)</td>
<td>6(3.0-11.0)</td>
<td>4.0(2.0-7.0)</td>
<td>8.0(6.0-16.0)</td>
</tr>
<tr>
<td>Concentration (%)</td>
<td>12(6.5-15.5)</td>
<td>5(2.5-9.0)</td>
<td>4.0(3.0-7.0)</td>
<td>15(12.5-23.5)</td>
</tr>
<tr>
<td>Progressive motility (%)</td>
<td>61(39.70.6)</td>
<td>61(39.70.6)</td>
<td>68(44.70.8)</td>
<td>11(2.0-27.0)</td>
</tr>
<tr>
<td>Normal morphology (%)</td>
<td>6(5.0-7.0)</td>
<td>5(4.0-6.0)</td>
<td>7(6.0-9.0)</td>
<td>5(4.0-8.0)</td>
</tr>
</tbody>
</table>
similar to DGC-MACS. Sperm concentration recovered in DGC and MACS groups were similar and significantly higher than MACS-DGC and DGC-MACS, which were similar to each other. Progressive motility of spermatozoa recovered was similar in MACS-DGC and DGC groups and significantly higher than DGC-MACS and MACS. Normal morphology percentage was significantly higher in MACS-DGC group when compared to DGC-MACS and MACS groups, and similar when compared to DGC.

CONCLUSIONS: According to the data, performing MACS before DGC allows the recovery of samples with a greater percentage of spermatozoa with progressive motility, normal morphology and lower percentage of fragmented DNA. It suggests the potential clinical value of using MACS-DGC to improve the sperm quality in seminal preparation.

References:
OBJECTIVE: Vasopostidymostomy (VE) is a cost-effective option for the treatment of epididymal obstruction. Microsurgical VE is the most technically challenging procedure performed for obstructive azoospermia due to the small diameters of the vas lumen (0.3 mm) and tissue paper thin tiny epididymal tubule (0.2 mm). There are few procedures where the outcomes are so dependent on technical perfection. We report the learning curve for microsurgical VE using the longitudinal intussusception (LIVE) technique performed by an experienced microsurgeon.

DESIGN: We reviewed a database of 754 microsurgical reconstructive procedures of the male reproductive tract done by a single surgeon (MG).

MATERIALS AND METHODS: Since adopting the LIVE technique, 37 men have undergone the procedure and had post-operative semen analysis data available. We divided the cases into tertiles by date. Patency was assessed as outcome and defined as the presence of motile sperm in the ejaculate at six months post-operatively. Men who did not meet this criteria, but had unassisted clinical pregnancies were also considered patent. Men with a sperm concentration <100,000/mL and/or <6 month follow-up were considered not patent.

RESULTS: The median follow-up for this cohort was 8 months (IQR 11), and there was no difference in follow-up between the three groups (p=0.267). There were no significant differences in the baseline characteristics of the three groups (Table 1). There was a trend toward the most recent cohort presenting with infertility and primary epididymal obstruction rather than vasectomy reversal (p=0.079). The overall patency rate was 73%, and there was a significant relationship between surgeon experience with LIVE and patency (Figure). The overall pregnancy rate was 35% and there were no differences between the groups.

CONCLUSIONS: Reconstruction of epididymal obstruction is amongst the most challenging procedures in all of surgery. Patency outcomes with the LIVE technique improve with experience, with a 92% patency in our population.

RESULTS: Of all, 46 (14.8%) men were diagnosed with CFTR polymorphisms. Men with CFTR polymorphisms did not differ from the remaining idiopathic ones except from having lower sperm PT motility (19% vs. 32%; p=0.02). At multivariable logistic regression analysis, the presence of any CFTR gene polymorphism (OR: 1.34; p=0.02) was the only independent predictor of PT motility <32% after accounting for patient age, BMI, FSH, and inhibin B values.

CONCLUSIONS: Current findings suggested an association between CFTR polymorphisms and lower sperm PT motility. Such alteration might contribute to explain a discreet share of idiopathic male infertility.

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CFTR GENE POLYMORPHISM ARE ASSOCIATED WITH REDUCED SPERM PROGRESSIVE MOTILITY IN IDIOPATHIC INFERTILE MEN. E. Ventimiglia,1 P. Capogrosso,4 P. Filippo,1 F. Montorsi,1 A. Salonia,1 1Division of Experimental Oncology/Unit of Urology, Milan, Italy; 4IRCCS Ospedale San Raffaele, Milan, Italy.

OBJECTIVE: We aimed to investigate clinical implication of CFTR gene polymorphisms in idiopathic infertile Caucasian-European men.

DESIGN: Cross-sectional study.

MATERIALS AND METHODS: Complete socio-demographic, clinical and hormonal data from 311 consecutive idiopathic infertile men were analysed. Patients with endocrine disorders, varicocele, and known genetic abnormalities were excluded from the study. The Charlson Comorbidity Index (CCI; categorized 0 vs 1 vs ≥2) was used to score health-significant comorbidity. Testicular volume was recorded using a Prader orchidometer. Serum hormones were always measured in the morning (8-10 am). Analysis of the CFTR gene was performed for every patient through direct gene sequencing from peripheral blood samples. Patients with F508, R117H, and W1282X mutations were excluded from the study. Semen parameters were assessed based on 2010 World Health Organization reference criteria. Descriptive statistics and logistic regression models tested the association between CFTR gene polymorphisms and clinical, seminal, hormonal characteristics in our population.

RESULTS: Of all, 46 (14.8%) men were diagnosed with CFTR polymorphisms. Men with CFTR polymorphisms did not differ from the remaining idiopathic ones except from having lower sperm PT motility (19% vs. 32%; p=0.02). At multivariable logistic regression analysis, the presence of any CFTR gene polymorphism (OR: 1.34; p=0.02) was the only independent predictor of PT motility <32% after accounting for patient age, BMI, FSH, and inhibin B values.

CONCLUSIONS: Current findings suggested an association between CFTR polymorphisms and lower sperm PT motility. Such alteration might contribute to explain a discreet share of idiopathic male infertility.

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EPIGENETIC DYSREGULATION OF MAEL GENE CONTRIBUTES TO ONE OF THE CAUSES OF NON-OBSTRUCTIVE AZOOSPERMIA WITH HYPOSPERMATOGENESIS. Y. Lin, Y. Cheng, C. Lu. Urology, National Cheng Kung University, College of Medicine, Tainan, Taiwan.

OBJECTIVE: Hypospermatogenesis (HS) is highly prevalent in non-obstructive azoospermia; however, our previous study showed that 55.6% of HS patients were thought to be idiopathic. To date, an in-depth molecular analysis of the causes of HS has not yet been reported. With the high throughput Methylated-DNA IP-on-chip (mDIP) assay, we identified that epigenetic regulation of MAEL may be associated with the phenotype of HS. This study was conducted to explore the methylation status of the promoter region of MAEL gene and the association of MAEL methylation pattern with MAEL transcript levels in men with normal spermatogenesis and HS.

DESIGN: High throughput mDIP assay, pyrosequencing analysis and quantitative real-time RT-PCR in the testes of azoospermic men with normal spermatogenesis and HS. Targeted DNA methylation with two-component reporter system was used to methylate MAEL promoter in vitro.

MATERIALS AND METHODS: The CpG enriched area in the promoter region of MAEL gene was determined by the comparison of mDIP assay between the testicular tissues of normal spermatogenesis and HS. The methylation status of each CpG was determined by pyrosequencing analysis after bisulfate treatment and PCR. The degree of each methylation at each CpG position was determined by the ratio of C to T incorporated during pyrosequencing (percentage of DNA methylation). The mRNA transcript levels were determined by qRT-PCR. Targeted methylation of specific site of MAEL promoter was performed in NCI-H358 cells.

RESULTS: The mRNA transcript levels of MAEL were significantly lower in the testes with hypospermatogenesis (P = 0.004). The amplified...
fragment in the promoter region (-453 to +36) of the MAEL gene was sequenced by using five pairs of primers to analyze a total of 33 CpG positions. Of the 33 CpG position, 30 showed significantly higher % methylation in hypospermatogenesis group, and significantly reverse correlations was found between each CpG % methylation and MAEL transcript levels. For individual sequencing segment (S1-S5), only S1 and S2 showed significantly higher methylation index (MI, mean of % methylation at all CpG positions) in HS, and both segments reversely correlated with MAEL transcript levels. Targeted methylation of S2 in H358 cells resulted in decreased expression of MAEL.

CONCLUSIONS: Our study provides evidence that MAEL gene participates in the epigenetic regulation of human spermatogenesis. Specific CpG sites in the promoter region are associated with the low expression levels of MAEL. Because MAEL has been shown to play an important role in the piRNA-mediated defense mechanism of the mammalian germline from retrotransposons, epigenetic dysregulation of MAEL should contribute to one of the causes of male infertility.

Supported by: This work was supported by the Ministry of Science and Technology of Taiwan (100-2314-B-006-017).

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REPEAT MICROSURGICAL RECONSTRUCTION AFTER FAILED INITIAL VASECTOMY REVERSAL. P. V. Bach, a B. B. Najarib, a F. Neto, a A. Ayangbesana, a A. V. Gottesdiener,b M. Goldstein,b aUrology, Weill Cornell Medical College, New York, NY; bMale Reproductive Medicine, and Urology, Weill Cornell Medical College, New York Presbyterian, New York, NY.

OBJECTIVE: Repeat vasectomy reversals are common, accounting for up to 15% of vasectomy reversals performed. While patency rates of up to 99% have been described by our group for unselected vasovasostomies, repeat reversals represent a more difficult cohort to manage surgically and may have lower patency rates. We aim to characterize the patency rates in men with history of one or more failed vasectomy reversals undergoing repeat microsurgical reconstruction.

DESIGN: Retrospective case series.

MATERIALS AND METHODS: We reviewed a database of 754 vasectomy reversals done by a single surgeon (M.G.) and identified 116 cases (15%) with a history of one or more failed vasectomy reversals. We included all cases in which unilateral and bilateral vasovasostomies or vasoepididymostomies were performed and post-operative semen analyses were available. Patency was defined as the presence of motile sperm in the ejaculate at six months post-operatively. Statistical analyses were done using chi-squared test and t-test.

RESULTS: Mean patient age was 43.8 ± 6.5 years old with a median obstructive interval of 11.0 years (IQR 5.0 years). 99 patients (85%) had undergone a single failed vasectomy reversal and 17 patients (15%) had undergone two or more failed vasectomy reversals. 61 men (53%) underwent unilateral vasoepididymostomy, 28 men (24%) underwent bilateral vasoepididymostomy, and 27 men (23%) underwent unilateral vasovasostomy with contralateral vasoepididymostomy. Overall patency rate was 82%, but was significantly higher for those undergoing unilateral/bilateral vasoepididymostomy compared to unilateral/bilateral vasoepididymostomy or unilateral vasovasostomy and contralateral vasoepididymostomy (Table 1). The type of repair required was significantly associated with obstructive interval, with those requiring at least one vasoepididymostomy presenting after longer obstructive intervals (Table 1).

CONCLUSIONS: Microsurgical vasal reconstruction in men with history of failed vasectomy reversal is a technically challenging situation that results in lower patency rates than those reported for unselected vasovasostomies and requires vasoepididymostomy in nearly 50% of cases. Taken together, to maximize the potential for patency in these men, only urologists adept at vasoepididymostomy should attempt repeat microsurgical reconstruction.

Supported by: The project was supported by The Frederick J. and Theresa Dow Wallace Fund of the New York Community Trust. This project was also supported by grant number T32HS000066 from the Agency for Healthcare Research and Quality. The content is solely the responsibility of the authors and does not necessarily represent the official views of the Agency for Healthcare Research and Quality.

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VARIABILITY OF MALE FERTILITY NUTRICEUTICALS: SUPPLEMENT ANALYSIS, COST AND QUALITY CONTROL. S. Pan a S. C. Honig,a b Urology, Yale New Haven Hospital, New Haven, CT; bUrology, Yale University, New Haven, CT.

OBJECTIVE: A large percentage of male infertility patients take supplements for improvement of semen quality. Formulation of supplements, costs, and third-party quality assurance vary considerably. The purpose of this study is to evaluate the composition of each supplement in various commercial products as compared to published data of known efficacy. Secondary endpoints in evaluation include cost and independent testing agency of quality control.

DESIGN: Review of “pro” fertility products available on the market and analysis of active ingredients in accordance to the most up to date meta-analysis of efficacy.

MATERIALS AND METHODS: 9 supplements were selected that target male factor infertility. Supplements were selected from products that had exhibit booths at the 2015 American Society of Reproductive Medicine meeting, as well as others listed on a Google search of “Male Infertility supplements”. Each product was reviewed based on information provided in package insert or listed proprietary info. Criteria used for reasonable supplementation were based on review article summaries of published evidence deemed to be of the highest quality (Cochrane review 2014, review articles Ko et al 2012, Zini et al 2011). RESULTS: Table attached shows supplements identified to have some published efficacy. Due to the paucity of well conducted randomized controlled studies, the antioxidants included were also based on the authors’ review of data.

(Please see uploaded excel file for table)

CONCLUSIONS: Use of nutritional supplements in male factor infertility is certainly perplexing. It is difficult to ascertain dosages of supplements that may improve male infertility. Percentage of individual supplements vary widely between available products, and some products may have more of one antioxidant and none of another. There are no recommended daily allowances of individual antioxidants optimized for male factor infertility. As such, amounts of vitamin C, E, Carnitine, zinc, selenium, and coenzyme Q10 vary greatly between different available supplements. Costs and testing agency quality assurance differed as well. Physicians should be aware of these variability before they endorse the use of specific commercial regimens.

FERTILITY & STERILITY® e293
OUTCOMES OF VARICOCELECTOMY IN MEN WITH HISTORY OF ORCHIOPEXY FOR UNDESCENDED TESTES. J. L. Chiang, a P. V. Bach, b B. B. Najari, b A. Gottdesdiener, b A. Ayangbesan, b P. S. Li, b M. Goldstein. b Urology, Weill Cornell Medical College, New York, NY; b Weill Cornell Medical College, New York, NY; b Male Reproductive Medicine, and Urology, Weill Cornell Medical College, New York Presbyterian, New York, NY.

OBJECTIVE: Undescended testis (UDT) is the most common male genitourinary abnormality and is present in 5% of all newborns [1]. The condition can impact fertility, especially when left uncorrected for a long time. Varicocele is the most common treatable cause of male infertility, found in 50% of men with primary infertility, and in 80% with secondary infertility [2]. Varicocelectomy can halt further damage to the testes, and may improve both spermatogenesis and Leydig cell function. Varicocele repair can be difficult in men with prior orchioxyphraphy, and outcomes in this population have not been reported. We present outcomes of microsurgical varicocelectomy in men with prior history of orchioxyphraphy for UDT.

DESIGN: Retrospective chart review.

MATERIALS AND METHODS: We reviewed a database of 564 men undergoing microsurgical varicocelectomy by a single surgeon. We identified 31 infertile men who had previous orchioxyphraphy for UDT, 22 of whom had semen analysis follow-up. Semen analysis parameters, hormonal evaluation, and pregnancy outcomes were assessed.

RESULTS: The mean patient age was 36.2 ± 7.6 years, and the couple reported being infertile for a mean of 18 ± 15.6 months. Mean age at UDT treatment was 9.3 ± 4.0 years. Five men (22%) had bilateral UDT, and 9 (40%) had unilateral varicoceles. Nine men (42%) had grade 3 left varicocele, while right varicoceles were grade 3 in only 1 case (22%). Intraoperative findings included an average number of arteries isolated of 3.1 ± 1.2 on the left side and 3.0 ± 0.8 on the right side. Post-operatively, there was one complication (3%), a hematoma managed conservatively. Although post-operative semen parameters were not statistically different postoperatively (Table 1), 19 (86%) had improvement in their parameters. Post-operative serum total testosterone did not differ preoperatively (p = 0.586).

OBJECTIVE: To evaluate the effect of moderate (4 hours) or intense (1 hour) exercise sessions on LH level, variation, and pulsatility in healthy males.

DESIGN: In this crossover design study, participants engaged in three different regimens in randomized order, with 2 weeks between each regimen: (i) resting for 4 hours, (ii) 4-hour treadmill jogging at 50% VO2max, (iii) 1-hour exercise biking at 75% VO2max followed by 3 hours of rest. Serum samples were stored at -20°C prior to batch measurement of LH levels by radioimmunoassay. LH pulses were identified using a cut-off of >9% or 3 mIU/mL from preceding nadir to peak, as described by Veldhuis et al. [1].

RESULTS: Six male subjects aged 22-34 years enrolled in the study. There was no effect of regimen, time, or time by regimen interaction (p-values of 0.35, 0.45 and 0.46 respectively) on LH levels. During the first hour, there was no significant difference in pulse count among the three regimens. During hours 2-4, mean (SD) LH pulse count at rest [2.67 (1.03)] was significantly higher than after biking [1.00 (0.89), p = 0.026] or when running [0.67 (0.82), p = 0.009]. Mean LH pulse count for the overall 4-hour session was higher for the resting group compared to the running group [3.17 versus 1.33 pulses (p = 0.015)], but not for the resting group compared to the biking group [3.17 versus 1.83 pulses (p = 0.13)].

CONCLUSIONS: Exercise had no significant effect on mean LH levels during the 4-hour study. However, both intense exercise and moderate running regimens were associated with significant decreases in LH pulse count during hours 2-4. Moderate running for 4 hours was associated with a significantly decreased pulse count overall compared to rest. Further work is needed to investigate the implications of these findings for male fertility.

References:

OXIDATION REDUCTION POTENTIAL: A NOVEL MARKER OF VARICOCELE PATHOPHYSIOLOGY. A. Agarwal, a A. Majzoub, a O. F. Neto, a Obstetrics and Gynecology, Maine Medical Center, Portland, ME; a Reproductive Endocrinology and Infertility, Reproductive Medicine Associates of Connecticut, Norwalk, CT; b Maine Medical Center Research Institute, Scarborough, ME; b Reproductive Endocrinology and Infertility, Maine Medical Center, Portland, ME.

OBJECTIVE: To evaluate the effect of moderate (4 hours) or intense (1 hour) exercise sessions on LH level, variation, and pulsatility in healthy males.

DESIGN: In this crossover design study, participants engaged in three different regimens in randomized order, with 2 weeks between each regimen: (i) resting for 4 hours, (ii) 4-hour treadmill jogging at 50% VO2max, (iii) 1-hour exercise biking at 75% VO2max followed by 3 hours of rest. Serum samples were stored at -20°C prior to batch measurement of LH levels by radioimmunoassay. LH pulses were identified using a cut-off of >9% or 3 mIU/mL from preceding nadir to peak, as described by Veldhuis et al. (Am J Physiol Endocrinol Metab 2009), and then counted over all 4 hours, and within two time periods (1st hour and 2nd-4th hour) for each regimen. The effect of time and condition on LH were evaluated by mixed model analysis. Differences in pulse count between time periods were compared among the three regimens by Kruskal-Wallis test. Post hoc analysis by Mann-Whitney U test was used to compare differences between specific regimen pairs.

RESULTS: Six male subjects aged 22-34 years enrolled in the study. There was no effect of regimen, time, or time by regimen interaction (p-values of 0.35, 0.45 and 0.46 respectively) on LH levels. During the first hour, there was no significant difference in pulse count among the three regimens. During hours 2-4, mean (SD) LH pulse count at rest [2.67 (1.03)] was significantly higher than after biking [1.00 (0.89), p = 0.026] or when running [0.67 (0.82), p = 0.009]. Mean LH pulse count for the overall 4-hour session was higher for the resting group compared to the running group [3.17 versus 1.33 pulses (p = 0.015)], but not for the resting group compared to the biking group [3.17 versus 1.83 pulses (p = 0.13)].

CONCLUSIONS: Exercise had no significant effect on mean LH levels during the 4-hour study. However, both intense exercise and moderate running regimens were associated with significant decreases in LH pulse count during hours 2-4. Moderate running for 4 hours was associated with a significantly decreased pulse count overall compared to rest. Further work is needed to investigate the implications of these findings for male fertility.

References:
normal morphology (Table 1). Grade 2 varicocele patients had a significantly lower sperm concentration and % normal morphology while grade 1 varicocele patients had a significantly lower % normal morphology than the control group (table 1). sORP levels were higher in all the infertile groups than in the fertile controls. However, these results were statistically significant only among patients with grade 3 varicocele. A direct linear relationship was seen between the sORP level and varicocele grade (p<0.05). * Statistically significant compared to control (p<0.05). - 1 Significant between varicocele groups M: Million - mIVF: Millivolts.

CONCLUSIONS: Patients with clinical varicocele have elevated ORP values that are highest in men with Grade 3 varicocele. The ORP levels could serve as an index of sperm dysfunction in men with varicocele. We speculate that ORP measurement may be utilized before and after varicocele surgery to assess surgical success.

P-500 Wednesday, October 19, 2016


OBJECTIVE: AZF microdeletions are the leading genetic cause of male infertility and useful to obtain reliable genetic information for assisted reproductive techniques. Thus, the detection is clinically relevant for appropriate genetic counseling. However, there are only a few reports evaluating clinical course of the patients with AZF microdeletions. The aim of this study was to investigate the prevalence and the results of microdissection testicular extraction (micro TESE) outcome in Japanese azospermic patients with AZF microdeletions.

DESIGN: A retrospective study in a reproductive center.

MATERIALS AND METHODS: A total of 573 azospermic patients and 15 relatives whose son and brother affect AZF microdeletion were examined genetic testing for AZF deletions by Promega Y Chromosome AZF Analysis System (version 2.0) in a Japanese medical center from September 2013 to March 2016. We analyzed sperm retrieval rate (SRR) of the patients with AZF microdeletion. In addition, we analyzed fertilization and clinical pregnancy rates of those in whom the sperm retrieval was successful.

RESULTS: AZF microdeletions were found in 75 cases (13.1%) of men with azoospermia: 6 AZFa, 4 AZFb, 28 AZFc, 1 AZFa+b, 24 AZFb+c, and 12 AZFa+b+c. All of 12 fathers of affected son with AZF microdeletion were not observed AZF microdeletion. One of 3 brothers showed AZFb+c microdeletion (same pattern as sibling). No spermatozoa were found with micro TESE of the patients with AZFa, AZFb, AZFa+b, AZFb+c and AZFb+bc deletions. Spermatozoa was only obtained from patients with AZFc microdeletions. Of men with isolated AZFc deletion, spermatozoa were found in 85.7% (24/28) by micro TESE. Patient age was 35.9 ± 5.4 years old. Testicular atrophy was seen in almost all men (mean testicular volume: 13.7 ± 4.0ml). Follicular stimulating hormone (FSH), luteinizing hormone (LH), and testosterone (T) levels before surgery was 18.6 ± 9.3 mIU/ml, 5.7 ± 2.1 mIU/ml, and 383.1 ± 143.7 ng/dl, respectively. No correlation was found between serum FSH, LH, and T level with the success of sperm retrieval. Patients’ age and testicular volume and also did not affect the SRR for micro-TESE. Fertilization rate was 49.6% and clinical pregnancy rate per embryo transfer (ET) was 23.5%. Three children were safely delivered and 7 pregnancies were ongoing. Two of them had miscarriages.

CONCLUSIONS: The frequency of AZF deletions in Japan is similar to in other countries. AZFc deletions are associated with severe dysregulations of spermatogenesis, however, sperm retrieval is possible in more than half by micro TESE. It is useful to obtain reliable genetic information from azoospermic patients and to avoid unnecessary micro TESE. Patients with those Y microdeletions does not seem to have ICSI outcomes comparable (lower 2PN rates and clinical pregnancy rates).

P-501 Wednesday, October 19, 2016

FEMALE PARTNER DEMOGRAPHICS OF MEN SEEKING VASECTOMY REVERSAL. J. M. Rehmer, H. Sayles, A. Perkins, S. L. Gustin, S. H. Marks, C. M. Deibert, Department of Obstetrics and Gynecology, University of Nebraska Medical Center, Omaha, NE; Department of Biostatistics, University of Nebraska Medical Center, Omaha, NE; International Center for Vasectomy Reversal, Tucson, AZ; Division of Urologic Surgery, University of Nebraska Medical Center, Omaha, NE.

OBJECTIVE: To analyze the demographics of the female partners of males seeking vasectomy reversal and compare the data over time assessing for trends.

DESIGN: Retrospective analysis of vasectomy reversal patient and partner data collected from December 1989 through December 2015.

MATERIALS AND METHODS: The original dataset contained 4,259 couples. Reasons for vasectomy reversal included: fertility (n=3,789), pain (n=126), pain/fertility (n=3), pain/personal (n=1), personal (n=6), religious (n=6), or unspecified (n=327). The following analyses are limited to the 3,789 observations that reported fertility as the lone reason for reversal. Final analysis included 3,484 patients, after 87 without surgical dates, 4 with female age >50, and 214 missing female partner age, were removed. For comparison of data over time, the cohort was divided into 5-year intervals from 1990-1995, 1996-2000, 2000-2005, 2006-2010, and 2011-2015.

RESULTS: During the last 25 years, among 3,484 couples seeking vasectomy reversal, mean female partner age has remained nearly constant at 32 years (18-50). Though female partners were asked about their own fertility status, the vast majority left this blank. Additionally we analyzed the number of children (live births) the couple had after vasectomy reversal. There was a small decline in the mean number of live births per couple over time from 1996-2000 to 2011-2015 of 0.54 +/- 1.08 to 0.31 +/- 0.89, respectively (p<0.001).

CONCLUSIONS: Comparison of female partner demographics of men seeking vasectomy reversal shows that there has not been a significant change in the mean age of female partners over the last 25 years. There has been a small but significant decline in the number of live births following vasectomy reversal.

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DIETARY ZINC INTAKE AND REPRODUCTIVE FUNCTION IN YOUNG MEN. J. Gabrielsen, G. J. Wood, A. J. Gaskins, S. L. Gustin, S. H. Marks, C. M. Deibert. Department of Urology, Massachusetts General Hospital, Boston, MA; Division of Urology, Universidade de Sao Paulo, Sao Paulo, Brazil; Department of Nutrition, Harvard School of Public Health, Boston, MA; Preventive Medicine, Icahn School of Medicine at Mount Sinai, New York, NY; Preventive Medicine and Public Health, University of Murcia, Murcia, Spain; University Department of Growth and Reproduction, Rigshospitalet, Copenhagen, Denmark.

OBJECTIVE: To determine whether zinc intake is associated with reproductive hormones and semen parameters in young men.

DESIGN: Cross-sectional analysis.

Table 1: Comparison of semen analysis and sORP levels between study groups.

<table>
<thead>
<tr>
<th>Variococele (n=38)</th>
<th>Control (n=15)</th>
<th>Grade 1 (n=13)</th>
<th>Grade 2 (n=10)</th>
<th>Grade 3 (15)</th>
<th>Idiopathic Infertility (n=15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume (ml)</td>
<td>2.82 ± 0.4</td>
<td>3.25 ± 0.41</td>
<td>3.15 ± 0.44</td>
<td>3.22 ± 0.33</td>
<td>4.01 ± 0.88</td>
</tr>
<tr>
<td>Concentration (M/ml)</td>
<td>55 ± 9.9</td>
<td>32.06 ± 8.1</td>
<td>14.37 ± 5.12*</td>
<td>19.76 ± 8.45*</td>
<td>29.58 ± 11.32*</td>
</tr>
<tr>
<td>Total Motility (%)</td>
<td>55.8 ± 2.0</td>
<td>49.53 ± 6.19</td>
<td>45.4 ± 5.22</td>
<td>40.93 ± 3.02*</td>
<td>32 ± 4.079*</td>
</tr>
<tr>
<td>Morphology (%)</td>
<td>7.8 ± 0.71</td>
<td>3.15 ± 0.64*</td>
<td>2.5 ± 0.56*</td>
<td>3.73 ± 0.77*</td>
<td>3.69 ± 0.84*</td>
</tr>
<tr>
<td>sORP (mV/10^5 sperm)</td>
<td>2.52 ± 0.47</td>
<td>3.16 ± 1.33†</td>
<td>5.59 ± 2.31</td>
<td>11.25 ± 3.92†</td>
<td>7.53 ± 2.7</td>
</tr>
</tbody>
</table>
MATERIALS AND METHODS: Healthy men aged 18-22 years (n = 189) completed a validated 131-item food frequency questionnaire and provided serum and semen samples. Nutrient intakes were estimated by summing the nutrient contribution of all food and supplement items. Reproductive hormones were measured by standard assays. Sperm analyses were performed according to WHO guidelines. Linear regression was used to analyze the relation between zinc intake and reproductive hormones and semen parameters adjusting for total calorie intake, body mass index, smoking status, physical activity, meat/dairy intake, dietary patterns, abstinence time (semen parameters only), and time of blood sample collection (hormones only).

RESULTS: Zinc intake ranged from 4.2 to 122.3 mg/day. Zinc intake was inversely associated with lower serum concentrations of sex hormone binding globulin (SHBG). Specifically, men in the highest quintile of zinc intake (> 25.3 mg/d) had SHBG levels that were 22% lower than men in the lowest quintile of intake (< 13.0 mg/d) (p for trend = 0.02). Higher zinc intake was associated with lower semen concentrations of inhibitor B, total testosterone (T) and estradiol (E2) in calorie-adjusted analyses, but after multivariate adjustment these associations did not reach statistical significance (p for trend = 0.15, 0.05, and 0.07, respectively). Zinc intake was not associated with other reproductive hormones or semen parameters.

CONCLUSIONS: Higher dietary zinc intake was associated with lower serum concentrations of SHBG and possibly lower levels of T and E2 in healthy, young men, although we did not observe any association between zinc intake and calculated free T or any of the examined semen quality parameters.

Supported by: European Union Seventh Framework Programme DEER grant 212844, NIH grants P30 DK046200 and T32 DK007703-16.

P-505 Tuesday, October 19, 2016
OXIDATION REDUCTION POTENTIAL - A NOVEL TEST FOR EVALUATING MALE INFERTILITY.  A. Agarwal, a S. Roychoudhury, b R. Sharma, a S. Gupta, a Z. Cakar, a M. M. Arafat, a E. S. Sabanegh. a aAmerican Center for Reproductive Medicine, Department of Urology, Cleveland Clinic, Cleveland, OH; bUrology, Hamad Medical Corporation, Doha, Qatar.

OBJECTIVE: Oxidative stress (OS) is associated with male infertility. The oxidation-reduction potential (ORP) represents the balance of all known and unknown contributors of OS. It is not limited to a specific constituent such as reactive oxygen species, toxicants, or lipid peroxidation. The MiOXSYS System is a novel tool for measuring ORP. It provides an alternative for measuring seminal OS in male infertility patients by facilitating rapid measurement in small sample volumes in real-time. The objective was to establish a reference value for ORP in semen to distinguish between normal men and abnormal semen quality (at least one of the sperm parameters abnormal: volume, concentration, total count, motility, morphology) that may be used in the qualitative diagnostic testing of male infertility.

DESIGN: Measurement of ORP in fertile and infertile men.

MATERIALS AND METHODS: Semen samples were collected from 51 normal healthy fertile men and 106 infertile men. Controls were recruited based on normal semen analyses according to 2010 WHO guidelines. Static ORP (sORP) was measured using the MiOXSYS System. A receiver operating characteristic curve was plotted to predict a preferred cutoff value of sORP in semen to distinguish controls from infertile males.

RESULTS: sORP was higher in the semen of the infertile patients (6.22±1.10 mV/10^6 sperm/mL) than in the controls (1.59±0.29 mV/10^6 sperm/mL; p<0.05). An sORP cutoff value of 1.36 mV/10^6 sperm/mL was able to identify normal and abnormal semen quality with a sensitivity of 69.6%, a specificity of 83.1%, a positive predictive value of 85.3% and a negative predictive value of 65.9%. The accuracy of the test was 75.2% (AUC = 0.770). In the control group, the median sORP level was below the sORP cutoff of 1.36 whereas it was above this cutoff in the infertile patients.

CONCLUSIONS: We have standardized the ORP test in semen using the new MiOXSYS System as a novel method for OS testing. Results distinguish between healthy normal men and male factor infertility patients. These findings suggest that a semen sORP level of 1.36 mV/10^6/mL can serve as a preferred cutoff value to distinguish between normal and abnormal semen quality in men with OS-induced male infertility.

P-504 Tuesday, October 19, 2016
ROLE OF SPERM CELL SPECIFIC RNA TO SCREEN FOR UNEXPLAINED MALE INFERTILITY.  T. Cozzubbo, N. Pereira, S. Cheung, A. P. Clement, Z. Rosenwaks, G. D. Palermo. Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: Idiopathic male infertility is a puzzling indication because it often is characterized by normal semen parameters, but inevitably by a poor reproductive outcome. We aim at assessing the proteins localized within the human sperm cell compartments that may provide insight on the specific function of these reproductive cells and gauge information on its developmental competence.

DESIGN: In a 15 month period we queried gene transcripts that ordain fundamental sperm function and we assessed their eventual impact on ICSI outcome. Following RNA extraction from semen specimens of 25 consenting men undergoing infertility screening, specific proteins were identified by a function annotation software related to structural components of the spermatozoon, such as the acrosomal vesicle, nucleus, and flagellum. Three men of proven fertility with natural conception served as a control.

MATERIALS AND METHODS: A range of 7 to 25x10^6/mL human spermatozoa was used to isolate total RNA using a spin column commercial kit. Their spermatozoal nucleic acid quality and concentration were measured. Expression values were calculated in fragments per kilobase of transcript per million mapped reads (FPKM). Genes were analyzed via the Database for Annotation, Visualization and Integrated Discovery (DAVID) for functional determination and classified accordingly.

RESULTS: A total of 25 consenting men provided semen samples and we were able to get adequate nucleic acid that was processed for RNA-Seq. Participants had an average age of 26 ± 5 years and presented with a sperm concentration of 27.3 ± 27x10^6/mL, a motility of 46.6 ± 24%, and normal morphology. Sperm localization analysis evidenced ATP6V1E2 localized to the acrosomal vesicle, HIF1A to the nucleus, AGPAT2 to the centrosome, AGRAP2 to the endoplasmic reticulum, and AKAP4 & CATS- PER1 to the flagellum. After plotting the expression in FPKM of all above mention genes against the sperm function parameters, AKAP4 had a strong correlation with motility (P = 0.01). In men with ICSI reproductive outcome (n = 8), ATP6V1E2 involved in the development and function of the acrosome had a strong correlation with fertilization rates (P = 0.03). All these men had a compromised expression of the genes responsible for nuclear compaction and centrosome development and although they were able to achieve fertilization, all failed to sustain embryo implantation. The fertile control (n = 3), on the other hand, had expression of all the studied genes in check that invariably were able to establish a viable pregnancy (P = 0.01).

CONCLUSIONS: Evaluation of the gene function whose protein is localized in various components of the sperm cell may provide a novel approach to genome annotation on male germ cell competence. Deep sequencing of sperm RNA is a robust screening tool that can corroborate a standard semen analysis of the male partner. Querying the RNA of specific gene function may actually elucidate specific sperm cell compartment function and embryo developmental competence.

P-505 Wednesday, October 19, 2016
TRIPÉPTIDYL PEPTIDASE I (TPP1) IS A POSITIVE OUTCOME MARKER FOR VARIICOCELECTOMY IN ADULTS.  M. Camargo, a P. Intasqui, a L. Berloffo Belardin, a M. P. Antoniassi, a K. Cardozo, b V. Melechco Carvalho, b A. Cedenho, a R. Bertolla. a Sao Paulo Federal University, Sao Paulo, Brazil; bFleury Group, Sao Paulo, Brazil; cDepartment of Surgery, Division of Urology, Human R, Sao Paulo Federal University, Sao Paulo, Brazil.

OBJECTIVE: Although varicocele is the main treatable cause of male infertility, not all infertile men treated for varicocele will present improved semen quality and/or fertility potential. Moreover, we currently do not have mechanisms to assess if varicocelectomy will lead to a positive outcome. In this context, we wished to compare the pre-treatment seminal plasma proteome of men submitted to varicocelectomy with improved semen quality (positive outcome) after a one year follow-up.

DESIGN: Prospective case-control study.

MATERIALS AND METHODS: Fifteen men with varicocele provided one semen sample before and another one year after bilateral subinguinal microsurgical varicocelectomy. An aliquot was used for semen analysis (WHO, 2010), and at least a 10% improvement in semen quality (sperm concentration, motility or morphology) was considered an improvement. Seven men were included in the Positive outcome group (POG) and 8 were included in the Negative outcome group (NOG). Because we wished to identify a semen marker which could predict positive outcome, individual pre-varicocelectomy samples were submitted to mass spectrometry-based quantitative proteomics analysis. Quantity of each protein was normalized to semen volume (total ejaculated protein), and a Mann-Whitney test was
used to compare groups. Significant proteins were submitted to logistic regression. For semen analysis, groups (POG versus NOG) were compared using a Mann-Whitney test (α = 5%).

RESULTS: No differences were observed in semen quality between pre-varicocelectomy samples in the POG and NOG groups. In total, 53 proteins were differentially expressed, of which 17 were over-represented and 4 exclusive in POG (mostly involved in peptide regulation, calcium transport, energy production, and antioxidant protection), and 27 were under-represented or absent in the POG (mostly involved in immune function, cell-matrix adhesion, lipid degradation, and inflammatory response). A logistic regression model demonstrated that Tripeptidyl-peptidase 1 protein (TPP1), overexpressed in POG, is a positive predictor of outcome, with an area under a ROC curve of 85.2% (p = 0.025) and a predictive power of 86.7%. In other tissues, decreased TPP1 levels are associated to oxidative stress, which likely indicates an oxidative pathway in determining a negative outcome for varicocelectomy in adults.

CONCLUSIONS: TPP1 is a marker of improvement in semen quality following treatment of varicoceles (one-year follow-up). The use of proteins may assist in establishing prognosis and treatment indications in the surgical management of the adult varicocele.

Supported by: Sao Paulo Research Foundation (FAPESP) (Scholarship #2012/15039-7).

P-506 Wednesday, October 19, 2016

EXPERT PERSPECTIVES ON SEMEN ANALYSIS PARAMETERS THAT ARE IMPORTANT TO PATIENT COUNSELING. K. Ostrowski,1 J. Gore,2 M. Rogers,3 T. J. Walsh,4 University of Washington, Department of Urology, Seattle, WA; 5University of Pittsburgh, Department of Urology, Pittsburgh, PA.

OBJECTIVE: The semen analysis is the cornerstone of the male fertility evaluation. Semen parameters of concentration, motility, morphology, and total motile count (TMC) are important for patient counseling and treatment decision-making. Patients frequently have difficulty interpreting semen analysis results and clinic-based test result counseling can be time-consuming. In an effort to develop a patient-centered semen analysis report, we surveyed male fertility experts and obtained consensus on semen parameters that are foundational to clinical decision making.

DESIGN: MATERIALS AND METHODS: A web-based questionnaire was developed with intent to complete a modified Delphi process. All registered Society for the Study of Male Reproduction (SSMR) members were invited to complete the questionnaire. Survey queries were submitted using the University of Washington Catalyst platform.

RESULTS: The survey was completed by 16 SSMR members. When asked to rank the most important elements of a semen analysis, 28% of respondents listed TMC as the most or 2nd most important element. Motility and concentration were next in ranked importance with 22% of respondents listing these parameters among their two highest ranked. 69% stated that patients were most confused by morphology. Agglutination or fructose was not clinically useful to 81% of respondents.

CONCLUSIONS: There was considerable variability among providers regarding the relative importance of specific semen parameters. The majority of specialists agreed that patients are confused by morphology and other commonly reported parameters are not clinically useful. A patient-centered semen analysis report could help patients to better understand this important aspect of their fertility evaluation.

P-507 Wednesday, October 19, 2016

DOES THE DEGREE OF SPERM DNA FRAGMENTATION AFFECT EMBRYO ANEUPLOIDY RATE. J. Gai, K. Tang, V. Kuznetsov, R. Abramov, R. Antes, S. Mukovtsev, C. L. Librach. Create Fertility Centre, Toronto, ON, Canada; 3CreAte Fertility Centre, Toronto, ON, Canada.

OBJECTIVE: The rate of human embryo aneuploidy increases dramatically with advancing maternal age. However, existing literature pertaining to the role of a male factor contribution to embryo aneuploidy has yielded conflicting results. The objective of this study was to determine if there is an association between sperm DNA fragmentation index (DFI) and embryo aneuploidy.

DESIGN: Retrospective data from CreAte patients (N = 82) who underwent sperm analysis with assessment of DFI as well as IVF with PGS between May 2010 and July 2015.

MATERIALS AND METHODS: Couples were categorized into two groups: DFI ≥ 30% for high degree of DNA damage and DFI < 30% (control group). Maternal factors of both groups were matched for age, BMI, ovarian reserve (AMH, AFC) and Day 3 FSH to isolate the effects of male factor. Embryo ploidy status was assessed using array comparative genomic hybridization (aCGH) (Bluegnome 24sure).

RESULTS: In the high DFI group, 78 embryos from 14 couples undergoing PGS were evaluated; 40.0% of the embryos were euploid. In the control lower DFI group, 315 embryos from 68 couples undergoing PGS were evaluated; 40.0% of the embryos were euploid as well without statistically significant difference in the embryo aneuploidy rate between the two DFI groups.

CONCLUSIONS: Embryo aneuploidy rate, as determined by PGS-aCGH, reveals that sperm with high DFI (≥ 30%) is not associated with higher aneuploidy rates compared to sperm with moderate to low DFI (< 30%). Further work by our group, currently underway, will aim to investigate the effect of other sperm parameters on embryo aneuploidy.

Supported by: This project was funded by CreAte Program Inc.

P-508 Wednesday, October 19, 2016

CORRELATION BETWEEN TWO SPERM DNA FRAGMENTATION TESTS (TUNEL AND SCSA) AND EVALUATION OF TUNEL ASSAY INTER-LAB VARIABILITY. C. LeSaint, L. Vingataramin, S. Alix, S. Phillips, A. Zini, J. I. Kadoch. Clinique OVO, Montreal, QC, Canada; OVO Fertility, Montreal, QC, Canada; McGill University, Cote St-Luc, QC, Canada.

OBJECTIVE: Numerous studies have shown the presence of DNA strand breaks in human ejaculated spermatozoa using a number of different assays. The two commonly used tests to measure sperm DNA damage are the sperm chromatin structure assay (SCSA) and the TUNEL assay. However, little is known about the correlation between assays and the inter-lab variability of these assays. We thought to validate the TUNEL assay, examine the correlation between sperm chromatin structure assay (SCSA) and the TUNEL assay and the inter-lab variability of the TUNEL assay.

DESIGN: Semen samples from 38 men referred to a male infertility clinic (ovo clinic) were tested for sperm DNA fragmentation.

MATERIALS AND METHODS: These samples were freshly fixed before the TUNEL assay analysis using the Apo-Direct Kit with a bench top flow cytometer Accuri C6 (BD Pharmingen, CA, USA). We determined the percentage of positive cells for the TUNEL assay. We also observed a good correlation between assays and the inter-lab variability of the sperm chromatin structure assay (SCSA) and the TUNEL assay. More- over, our data indicate that the TUNEL assay exhibits a low inter-laboratory variability.

Supported by: ovo labo.

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OBJECTIVE: The link between male fertility and general health status has been suggested. Previous studies reported higher rate of medical comorbidities in patients with male factor infertility (MFI). However, most studies were based on aggregate administrative and registry data, comorbidity indices with limited application to young infertile men, and suboptimal control groups. The goal of this retrospective case-controlled study was to compare major medical comorbidities in the cohort of infertile and fertile men utilizing granular data from individual medical records.
We did not undergo preoperative hormonal therapy for KS patients. In our study, KS patients didn’t have microlines of Y chromosomes. Statistical analysis was performed using unpaired t-tests and chi-squared tests.

RESULTS: SRR of first attempt micro TESE in KS (25/49=51.0%) was significantly higher than unexplained NOA (35/428=8.2%) (p<0.05). However, spermatozoa were successfully retrieved in 5 of 20 (15.0%) KS and 19 of 125 (15.2%) unexplained NOA who had previously undergone micro TESE with no sperm found. No correlation was found between serum FSH, LH, and T level with the success of sperm retrieval. Testicular volume and patient age also did not affect the SRR for micro TESE. 2PN oocytes, blastocysts development, and good-quality blastocysts rates were 57.8%, 44.6%, and 29.3% in KS, 61.4%, 47.6%, and 40.7% in unexplained NOA, and 66.9%, 51.9%, and 43.1% in OA, respectively. Clinical pregnancy rates per ET were 22.2% in KS, 27.3% in unexplained NOA, and 35.9% in OA. Significant difference was only observed in 2PN oocytes and clinical pregnancy per patient between KS and OA (p<0.05). With respect to motility of retrieved sperm, the blastocyst rate using motile sperm (65.7%) was significantly higher than that of using immotile sperm even after pentoxifyllin administration (15.0%) (p<0.005) from KS couples.

CONCLUSIONS: Micro TESE is particularly helpful for successful sperm retrieval in KS cases, however, in men with KS who have undergone previous attempts with negative results, a salvage micro TESE offers a less chance of finding sperm. In KS, the motile sperm retrieval from testicular tissue in micro-TESE is a critical key to succeed and rationale for good embryonic development and clinical pregnancy.

Table 1. Chi-square analysis

<table>
<thead>
<tr>
<th>COMORBITIES</th>
<th>INFERTILE MEN</th>
<th>VASECTOMY GROUP</th>
<th>Y/N %</th>
<th>P-VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>10.6/89.2</td>
<td>12.4/87.6</td>
<td>0.47</td>
<td>0.49</td>
</tr>
<tr>
<td>Diabetes</td>
<td>4.9/95.1</td>
<td>2.8/97.2</td>
<td>2.11</td>
<td>0.12</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>8.2/91.8</td>
<td>10.6/89.4</td>
<td>0.12</td>
<td>0.25</td>
</tr>
<tr>
<td>CAD</td>
<td>1.5/98.5</td>
<td>1.0/99.0</td>
<td>0.45</td>
<td>0.50</td>
</tr>
<tr>
<td>Hyperthyroidism</td>
<td>0.5/99.5</td>
<td>0/100</td>
<td>2.82</td>
<td>0.09</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>2.8/97.2</td>
<td>2.8/97.2</td>
<td>0.03</td>
<td>0.96</td>
</tr>
<tr>
<td>Autoimmune disease</td>
<td>3.6/96.4</td>
<td>2.5/97.5</td>
<td>0.79</td>
<td>0.37</td>
</tr>
<tr>
<td>Cancer</td>
<td>2.1/97.9</td>
<td>1.5/98.5</td>
<td>0.33</td>
<td>0.57</td>
</tr>
<tr>
<td>Asthma</td>
<td>5.9/94.1</td>
<td>6.8/93.2</td>
<td>0.24</td>
<td>0.62</td>
</tr>
</tbody>
</table>

P-510 Wednesday, October 19, 2016


Reproduction Clinic Osaka, Osaka, Japan.

OBJECTIVE: Microdissection (Micro) TESE, in combination with intracytoplasmic sperm injection (ICSI), is presently used to treat infertility in cases of NOA including Klinefelter syndrome (KS). KS is the most common sex-chromosome disorder among fertile males, with a prevalence of 1 in 1000 men and is a frequent cause of hypogonadism and infertility. The aim of this study was to assess the prevalence and the significance including sperm retrieval rate (SRR) by micro-TESE and ICSI outcomes with embryonic development in KS couples.

DESIGN: A retrospective study in a reproductive center.

MATERIALS AND METHODS: We evaluated SRR of micro TESE, two pronuclei (2PN) oocyte rates, blastocyst development rates, good-quality blastocyst (Grade 3BB and above on day 5 by the Gardner scoring) rates, and clinical pregnancy rates per embryo transfer (ET) in 68 cases with non-mosaic KS patients, 364 cases without past history (unexplained NOA; not including after orchidopexy, Klinefelter syndrome, cryptozoospermia, mumps orchitis, etc), and 69 cases of obstructive azoospermia (OA) between September 2013 and February 2016. Chromosomal analysis was performed on all patients on cultured lymphocytes from peripheral blood.

We did not undergo preoperative hormonal therapy for KS patients. In our study, KS patients didn’t have microlines of Y chromosomes. Statistical analysis was performed using unpaired t-tests and chi-squared tests.

RESULTS: SRR of first attempt micro TESE in KS (25/49=51.0%) was significantly higher than unexplained NOA (35/428=8.2%) (p<0.05). However, spermatozoa were successfully retrieved in 5 of 20 (15.0%) KS and 19 of 125 (15.2%) unexplained NOA who had previously undergone micro TESE with no sperm found. No correlation was found between serum FSH, LH, and T level with the success of sperm retrieval. Testicular volume and patient age also did not affect the SRR for micro TESE. 2PN oocytes, blastocysts development, and good-quality blastocysts rates were 57.8%, 44.6%, and 29.3% in KS, 61.4%, 47.6%, and 40.7% in unexplained NOA, and 66.9%, 51.9%, and 43.1% in OA, respectively. Clinical pregnancy rates per ET were 22.2% in KS, 27.3% in unexplained NOA, and 35.9% in OA. Significant difference was only observed in 2PN oocytes and clinical pregnancy per patient between KS and OA (p<0.05). With respect to motility of retrieved sperm, the blastocyst rate using motile sperm (65.7%) was significantly higher than that of using immotile sperm even after pentoxifyllin administration (15.0%) (p<0.005) from KS couples.

CONCLUSIONS: Micro TESE is particularly helpful for successful sperm retrieval in KS cases, however, in men with KS who have undergone previous attempts with negative results, a salvage micro TESE offers a less chance of finding sperm. In KS, the motile sperm retrieval from testicular tissue in micro-TESE is a critical key to succeed and rationale for good embryonic development and clinical pregnancy.

Table 1. Chi-square analysis

<table>
<thead>
<tr>
<th>COMORBITIES</th>
<th>INFERTILE MEN</th>
<th>VASECTOMY GROUP</th>
<th>Y/N %</th>
<th>P-VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>10.6/89.2</td>
<td>12.4/87.6</td>
<td>0.47</td>
<td>0.49</td>
</tr>
<tr>
<td>Diabetes</td>
<td>4.9/95.1</td>
<td>2.8/97.2</td>
<td>2.11</td>
<td>0.12</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>8.2/91.8</td>
<td>10.6/89.4</td>
<td>0.12</td>
<td>0.25</td>
</tr>
<tr>
<td>CAD</td>
<td>1.5/98.5</td>
<td>1.0/99.0</td>
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<td>0.62</td>
</tr>
</tbody>
</table>
and medical costs comparing the use of the Cap-Score
of this study was to estimate the differences in clinical pregnancy rates
pregnancy rates and reduced medical costs.
ysis places the range of this cost reduction from $2,700 to $6,500 per
mean medical costs by $4,621 ($19,319 vs. $23,941). Sensitivity anal-
crease rate of IVF. Compared to SOC, CS-TI is projected to reduce
mean IVF-ICSI costs by $3,906 ($17,207 vs. $13,301) compared to
of therapy and also underlines the importance of duration of therapy (3 and 6
months). The study demonstrated that an increase of seminal carboxyli
and glucosidase positively impacted upon the patient progressive sperm motility.
Supported by: Sigma-tau HealthScience provided Proxeed Plus product for the study.

P-512 Wednesday, October 19, 2016

POSSIBLE IMPACT OF THE CAP-SCORE TEST™ ON CLINICAL PREGNANCY AND MEDICAL COSTS IN COUPLES WITH UNEX-
plained Infertility. J. B. Babigumira, a F. Sharara, b L. P. Garrison. a Global Health, University of Washington, Seattle, WA; b Virginia Center for Reproductive Medicine, Reston, VA; c Pharmacy, University of Washington, Seattle, WA.

OBJECTIVE: Sperm capacitation is a necessary precursor to fertilization. The Cap-Score™ was developed to assess the capacitation status of men. This enables personalized management of infertility for some couples by selecting among timed intra-uterine insemination (IUI), versus moving immediately to in vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI) in those with a low Cap-Score™. The objective

Table of Parameter Estimates used in the Model

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Baseline Estimate</th>
<th>Sensitivity Range</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Costs (all 2016 $US)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IUI</td>
<td>$2,550</td>
<td>$1,275 — $3,825</td>
<td>Expert (+/- 50% SR)</td>
</tr>
<tr>
<td>IVF-ICSI</td>
<td>$15,000</td>
<td>$7,500 — $22,500</td>
<td>Expert (+/- 50% SR)</td>
</tr>
<tr>
<td>Pregnancy Probabilities</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IUI in SOC</td>
<td>0.125</td>
<td>0.100 — 0.150</td>
<td>Expert (+/- 20% SR)</td>
</tr>
<tr>
<td>IUI after Cap-Score</td>
<td>0.400</td>
<td>0.320 — 0.480</td>
<td>Expert (+/- 20% SR)</td>
</tr>
<tr>
<td>IVF-ICSI</td>
<td>0.519</td>
<td>0.415 — 0.632</td>
<td>SART weighted mean for 35 — 37 (+/- 20% SR)</td>
</tr>
<tr>
<td>Low Cap Score</td>
<td>0.385</td>
<td>0.308 — 0.462</td>
<td>Travis et al. poster (+/- 20% SR)</td>
</tr>
</tbody>
</table>

with timed IUI (CS-TI) and the current standard of care (SOC), namely 3 IUI cycles followed by 3 IVF-ICSI cycles.

DESIGN: Decision-analytic modeling.

MATERIALS AND METHODS: We developed and parameterized a decision-analytic model of management of unexplained infertility for a hypothetical woman 35 to 37 years of age, using her own eggs, based on data from published and unpublished sources. Model parameters are shown in the table. We calculated the clinical pregnancy rates and medical costs comparing CS-TI and SOC. We conducted univariate sensitivity analyses. The test has not yet been launched, and no price has been established, so the medical costs include no price.

RESULTS: Compared to SOC, CS-TI is projected to increase the cumulative pregnancy rate by 1.7% (94.2% vs. 92.5%). This increase varies from 0.8% to 3.2% depending on the assumed pregnancy success rate of IVF. Compared to SOC, CS-TI is projected to reduce mean medical costs by $4,621 ($19,319 vs. $23,941). Sensitivity analysis places the range of this cost reduction from $2,700 to $6,500 per individual patient depending on the costs of IVF-ICSI. CS-TI is projected to reduce mean IUI costs by $715 ($6,734 vs. $6,019) and mean IVF-ICSI costs by $3,906 ($17,207 vs. $13,301) compared to SOC.

CONCLUSIONS: Use of the Cap-Score™ to personalize management of couples with unexplained infertility is projected to result in higher clinical pregnancy rates and reduced medical costs.

References:

Supported by: Androvia Life Sciences.

P-513 Wednesday, October 19, 2016

SOURCES OF KNOWLEDGE AND EFFECT OF EDUCATION ON UROLOGISTS’ ATTITUDES TOWARDS PENILE TRANSPLANTATION. B. B. Najari, a P. V. Bach, b A. Bolyakov, c R. Lischer, d D. Paduch. a Urology, Weill Cornell Medical College, New York, NY; b Weill Cornell Medical College, New York, NY; c Dept of Urology, Weill Cornell Medical College, New York, NY.

OBJECTIVE: While penile transplantation (PT) has long been surgically feasible, only two such procedures have been performed worldwide. Despite the potential for improved quality of life in men who have experienced genitourinary trauma, there is a dearth of information regarding barriers to implementation of PT programs. Our objective was to evaluate the source of knowledge and effect of education on urologists’ attitudes towards PT.

DESIGN: Online Survey.

MATERIALS AND METHODS: An online survey was sent to members of the American Urological Association (AUA) using the SurveyMonkey platform. Respondents were asked from what sources they had learned about PT. Respondents were also asked if they are in favor of (1) organ transplantation in general, (2) transplantation of visceral organs that prolong life (i.e. kidney), (3) transplantation of organs that improve quality of life (i.e. face), and (4) PT. The responses ranged from “Extremely in favor (1)” to “Not at all in favor (5)”. The PT question was repeated after reading a book excerpt about soldiers’ concerns about genitourinary trauma.

RESULTS: Two hundred twenty eight urologists responded to the survey. Only 75 people (32.9%) had learned about PT from a professional health source (scientific journal, professional colleague, or formal lecture). One hundred twenty six (55.3%) of respondents had learned about PT from the mass media and 45 (19.7%) had no knowledge of PT. At baseline, the participants were significantly less if favor of PT (mean (SD) 2.4 (1.2)), than other forms of organ transplant (Table). After reading the book excerpt, attitudes toward PT significantly improved to 2.2 (1.1), p<0.001. White respondents had a more favorable opinion of PT after reading the book excerpt compared to non-whites [2.1 (1.1) vs. 2.9 (1.4), p=0.009]. Respondents older than 54 also had a more favorable opinion after reading the book excerpt [2.0 (1.0) vs. 2.3 (1.2), p=0.027] compared to younger respondents. Older respondents were also more likely to be in favor of PT being covered by veteran’s health care plan [2.0 (1.1) vs. 2.3 (1.3), p=0.047]. Older respondents were more agreeable to the potential for improved quality of life in men who have experienced genitourinary trauma, there is a dearth of information regarding barriers to implementation of PT programs. Our objective was to evaluate the source of knowledge and effect of education on urologists’ attitudes towards PT.

Attitudes Toward Penile Transplantation Before and After Excerpt

<table>
<thead>
<tr>
<th>Overall Mean (SD)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>In favor of penile transplantation? (Baseline)</td>
<td>2.4 (1.2)</td>
</tr>
<tr>
<td>In favor of organ transplantation?</td>
<td>1.6 (0.9)</td>
</tr>
<tr>
<td>In favor of organ transplantation to prolong life?</td>
<td>1.2 (0.5)</td>
</tr>
<tr>
<td>In favor of organ transplantation for QOL?</td>
<td>1.9 (0.9)</td>
</tr>
<tr>
<td>In favor of penile transplantation insurance coverage?</td>
<td>2.2 (1.2)</td>
</tr>
<tr>
<td>In favor of penile transplantation? (After reading)</td>
<td>2.2 (1.1)</td>
</tr>
</tbody>
</table>
likely to have ever been employed by the armed forces (32.7% vs 11.7%, p<0.001).

CONCLUSIONS: Most urologists learn on PT from the mass media. Education by framing PT as a means of improving the lives of injured veterans appears to improve urologists’ attitudes. Various demographic differences exist in race and age that can inform educational efforts.

Supported by: This project was supported by grant number T32HS00066 from the Agency for Healthcare Research and Quality. The content is solely the responsibility of the authors and does not necessarily represent the official views of the Agency for Healthcare Research and Quality. The project was also supported by The Frederick J. and Theresa Dow Wallace Fund of the New York Community Trust.

P-514 Wednesday, October 19, 2016

PREGNANCY TRIALS USING THE DEVICE FOR IMPROVED SEMEN IMPROVED SEMEN COLLECTION. S. Prien, C. A. Dehn, K. K. Evenson, L. Penrose. ObGyn, Texas Tech University Health Sciences Center, Lubbock, TX; Umbrella Corporation, San Antonio, TX; Animal Science, Texas Tech University Health Sciences Center, Lubbock, TX; Department of Obstetrics and Gynecology, Texas Tech University Health Sciences Center, Lubbock, TX.

OBJECTIVE: It is well documented that sperm undergo significant physiological and biochemical processes, many of them brought on by changes in the environment at ejaculation. While the preponderance of the individual changes can be seen as positive and necessary for fertilization, collectively they set the cell on course for its eventual death. Previous research from this laboratory has demonstrated that modification of the collection environment using the Device for Improved Semen Collection (DISC), can lead to a delay in certain activation pathways and help provide a better quality sample for treatment procedures. A small human trial demonstrated superior semen parameters and equivalent pregnancy rates. The present study presents pregnancy data in two controlled trials in domestic animal species.

DESIGN: Controlled prospective trial.

MATERIALS AND METHODS: Two large scale pregnancy trials were conducted with the DISC in the equine and bovine. In both trials, semen was collected from the males in a real-time split collection where approximately half of the ejaculate was collected into the DISC or an appropriate control. Parameters measured manually at the time of collection and time of insemination. In the equine trial mares were inseminated at ovulation with semen 24, 48, or 72 hrs old to mimic industry practice (49 total inseminations). In the bovine, 43 females were divided for insemination with semen from either control or DISC collections. Inseminations were timed to occur 12 hrs after semen collection using industry standard techniques. Pregnancy was determined by ultrasound.

RESULTS: Semen parameters were similar between controls and DISC samples at collection (P = 0.832). Further, as expected all parameters decrease with time (P < 0.01). However, semen collected in the DISC retained more motility at all other time points (Buil P < 0.002 and Stallion P < 0.001). Pregnancy rates in the mares were similar between treatments at 24 hrs, but higher at both 48 and 72 hrs (P < 0.001). Pregnancy rates in cattle trended higher in animals inseminated with DISC semen (P = 0.06).

CONCLUSIONS: Data continue to indicate semen collected in the DISC provides higher quality cells for reproductive purposes. Further, pregnancy rates appear higher in animals bred with semen from the DISC. Additional research is warranted to confirm these findings.

Supported by: Texas Tech University Office of Research Commercialization.

P-515 Wednesday, October 19, 2016

THE PREDICT VALUE OF SEMINIFEROUS TUBULE HYALINIZATION FOR THE SPERM RETRIEVAL RATE OF MICRO-DISSECTION TESTICULAR SPERM EXTRACTION IN THE NON-OBSTRUCTIVE AZOOSPERMIA PATIENTS. G. Liu, J. Zhang, Z. Wang, X. Liang. Andrology, Reproductive Center, Sixth Affiliated Hospital of Sun Yan-Sen University, Guangzhou, China; Urology, Sixth Affiliated Hospital of Sun Yan-Sen University, Guangzhou, China; Obstetrics & Gynecology, Reproductive Center, The Sixth Affiliated Hospital of Sun Yat-Sen University, Guangzhou, China.

OBJECTIVE: A retrospective study was designed to evaluate the predict value of seminiferous tubule hyalinization for sperm retrieval rate (SRR) of micro-TESE in non-obstructive azoospermia (NOA) patients who diagnosed as Sertoli cell-only syndrome (SCO).

DESIGN: The azoospermia patients who suffered micro-TESE from Jan. to Dec. 2015 were picked up from our database. Then the patients who diagnosed as SCO were enrolled in the study. All the semen samples at collection were divided into two groups (with or without seminiferous tubule hyalinization) according to the pathology and the SRR was calculated.

MATERIALS AND METHODS: The age, testicular volumes, level of FSH, LH, inhibin B and testosterone, SRR and microscopic findings of testicular tubules during operation of patients were compared in these two groups. Comparisons between groups were analyzed using the spot16.0 software. P<0.05 was considered statistically significant. Micro-TESE was performed at x20 magnification under the operating microscope. Seminiferous tubules were removed and immediately placed within a sperm culture buffer. Then the tubules were dissected and examined immediately by three embryologists under a phase microscope at x20 magnification.

RESULTS: Totally, 50 NOA patients who diagnosed as SCO were enrolled in this study. Seminiferous tubule hyalinization was found in the testis of 34 patients (68%), while other 16 patients (32%) without that pathological feature. No significant differences were observed in age (35.2±6.7 years vs. 33.3±5.1 years), FSH (32.6±12.8 IU/L vs. 27.8±9.3 IU/L), LH (14.7±6.1 IU/L vs. 12.1±5.8 IU/L), testosterone (3.1±0.9 ng/ml vs. 3.5±1.2 ng/ml) and inhibin B(15.7±10.4 pg/ml vs. 28.3±8.3 pg/ml) levels between these two groups(p>0.05). Interestingly, 15 patients (15/50(30%)) showed heterogeneous thickness of seminiferous tubule and 12 of them have found the testicular sperms (12/15(80%)). Patients in hyalinization group had more incidence of heterogeneous tubule than non-hyalinization group (12/34(35.3%) vs. 3/16(18.8%), p=0.05). Spermatozoa were successfully retrieved from 16 patients (16/50(32%), SRR of hyalinization group was higher than non-hyalinization group (14/34(41.2%) vs. 2/18(12.5%),p<0.05). Patients in hyalinization group had more incidence of heterogeneous tubule than non-hyalinization group (12/34(35.3%) vs. 3/16(18.8%), p=0.05).

CONCLUSIONS: Based on our results, micro-TESE should be recommended to NOA patients who diagnosed as SCO with seminiferous tubule hyalinization. Importantly, considering micro-TESE wouldn’t provide an advantage if seminiferous tubules show homogeneous thickness, needle biopsy should be performed prior to micro-TESE to minimize testicular damage.

Supported by: The study was supported by the Natural Science Foundation of China (No.81471449, 81270696, 81401197). Natural Science Foundation of Guangdong Province, China (No. 2015A030313013, 2016A020214004).

P-516 Wednesday, October 19, 2016

EVALUATION OF INTRA- AND INTER-OBSERVER RELIABILITY OF THE ORP (OXIDATION-REDUCTION POTENTIAL) TEST FOR OS (OXIDATIVE STRESS) IN MALE FACTOR INFERTILITY. A. Agarwal, S. Roychoudhury, R. Sharma, S. Gupta, A. Majzoub, K. Bjugstad, E. S. Sabanegh.a American Center for Reproductive Medicine, Department of Urology, Cleveland Clinic, Cleveland, OH; bAytu BioScience, Englewood, CO.

OBJECTIVE: Oxidative stress (OS) plays a role in male infertility. Because OS is a state in which oxidant activity exceeds antioxidant protection, a measure of both would be the best indicator of OS in male infertility. Static ORP (sORP) is a measure of the relationship between oxidants and antioxidants. Measuring sORP is a novel approach in the workup of male infertility and as such, both the repeatability and reproducibility of an ORP test is crucial to its clinical application. The objective of this study was to evaluate the intra-observer and inter-observer reliability of the ORP test.

DESIGN: Test-retest design measuring sORP in normozoospermic men.

MATERIALS AND METHODS: Semen sORP was measured using the MOXSYS System. For intra-observer reliability, 3 samples were measured 3 times by 3 observers using the same analyzer. The reliability was determined using the average coefficient of variation (%CV) across samples within an individual observer. For inter-observer reliability, 10 samples were measured 4 times by 3 observers. The extent to which there was agreement between observers was determined by the difference between observer measurement correlation, and accuracy.

RESULTS: Results of the intra- and inter-observer reliability experiments are summarized in Table 1. The overall %CV was 8.39% suggesting a strong level of intra-observer reliability. The %CV across observers was 3.61%. Similar sORP values across observers, high correlations between them, and a low %CV supports a strong level of inter-observer reliability.
CONCLUSIONS: Our results of the intra- and inter-observer reliability experiments confirm the repeatability and reproducibility of the sORP test. Based on these results, we can recommend the use of MiOXYS System for the quantitative measurement of sORP in human semen.

P-517 Wednesday, October 19, 2016

THE IMPACT OF EMBRYO MORPHOKINETICS ON ICSI OUTCOME: UNEXPLAINED INFERTILITY VS. MALE FACTOR INFERTILITY.

N. Adel, M. Elmahdy, A. A. Aboali, S. A. Hebisha, A. Elmasdy, M. Galal

Madina Fertility Center, Alexandria, Egypt; Obs. Gyn., Alexandria University - Faculty of Medicine, Alexandria, Egypt.

OBJECTIVE: To evaluate morphokinetics of embryos using Embryoscope (unisense Fertilite-tech. Denmark) on ICSI outcome in patients with male factor infertility vs. patients with unexplained infertility.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: 445 oocytes were retrieved from 48 patients with unexplained infertility and 247 oocytes were retrieved from 24 patients with male factor infertility. Fertilization of oocytes was performed by conventional ICSI between April 2014 and January 2016 at Madina Fertility Center, Alexandria, Egypt. Embryos were cultured and loaded into Embryoscope immediately after injection and annotated for pattern time of cleavage (tPNa: time of pronuclei appearance, t2: time of 2-cell, t3: time of 3-cell, t4: time of 4-cell, t5: time of 5-cell, CC2: second cell cycle t3-t2, S2: the time period of the synchrony of the first cell cycle (t4-t3), fertilization rate, blastulation rate, pregnancy rate and implantation rate were compared between the two studied groups. Statistical analysis was conducted using Whitney test for comparing between the two groups. P values ≤ 0.05 considered significant.

RESULTS: No significant difference was observed between groups regarding fertilization rate and blastulation rate. The pregnancy and implantation rates in patients with unexplained infertility were significantly higher than those with male factor infertility 52.08% (25/48) vs. 37.5% (9/24) and 26.02% (38/146) vs. 16.66% (13/78), respectively (p < 0.05). The mean time-points for patients with unexplained infertility were significantly higher at t2, t3, and t4 (31.13, 40.10, and 42.87, respectively) compared to t2, t3, t4 of patients with male factor infertility (29.72, 38.07, 41.37, respectively, p < 0.05) as shown in the following table:

<table>
<thead>
<tr>
<th>Unexplained infertility</th>
<th>Male factor infertility</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>tPNa</td>
<td>14.53 ± 7.70</td>
<td>13.86 ± 7.37</td>
</tr>
<tr>
<td>t2</td>
<td>31.13 ± 9.62</td>
<td>29.72 ± 8.19</td>
</tr>
<tr>
<td>t3</td>
<td>40.10 ± 10.16</td>
<td>38.07 ± 8.95</td>
</tr>
<tr>
<td>t4</td>
<td>42.87 ± 10.41</td>
<td>41.37 ± 9.02</td>
</tr>
<tr>
<td>t5</td>
<td>52.41 ± 10.90</td>
<td>50.63 ± 9.38</td>
</tr>
<tr>
<td>CC2</td>
<td>10.17 ± 4.84</td>
<td>9.49 ± 4.16</td>
</tr>
<tr>
<td>S2</td>
<td>4.13 ± 4.08</td>
<td>4.20 ± 4.25</td>
</tr>
</tbody>
</table>

CONCLUSIONS: Morphokinetics of embryos derived from patients with unexplained infertility showed a delay in all time-points and resulted in higher pregnancy and implantation rates, while rapid motion of development showed by morphokinetics of embryos derived from patients with male factor infertility may negatively affect the pregnancy and implantation rates.

References:

P-518 Wednesday, October 19, 2016

PRELIMINARY EXPERIENCE WITH THE NOVEL LAPAROSCOPIC SINGLE-SITE EXTRAPERITONEAL (LESS-EP) VARICOCELECTOMY.


OBJECTIVE: Minimally invasive varicocelectomy offers improved perioperative pain and cosmesis as compared to standard microsurgical approaches.(1-3) While standard multi-port laparoscopic varicocelectomy yields equivalent outcomes in terms of efficacy(4), an extraperitoneal approach decreases risk of bowel injury or post-operative gastrointestinal symptoms.(5, 6) We herein describe our initial results with an extraperitoneal approach coupled to single port laparoscopy (LESS-ep).

DESIGN: We performed an IRB approved retrospective chart review of patients undergoing varicocelectomy (CPT codes 55550, 55530) at our center with a single surgeon between 3/1/2013 to 3/1/2016.

MATERIALS AND METHODS: Microsurgical and laparoscopic varicocelectomies were performed in standard previously described fashion. LESS-EP was performed as follows; a 2 cm infra umbilical incision was made. The anterior rectus sheath was anchored with Vicryl sutures in parallel then divided. The rectus muscle was dissected laterally thereby exposing the posterior rectus sheath. The extraperitoneal space was developed using a balloon dissector under direct vision, and then the GelPort Mini Advanced Access (Applied Medical) was affixed. The GelPort was prepared with three trocars positioned in a tripod configuration as well as the Doppler probe. Varicocelectomy was performed under direct vision with a 5mm 30 degree bariatric laparoscope with dissection at the level of the internal inguinal ring. Manual chart review included patient history, lab values, and operative data. Data were analyzed with Student’s T-test.

RESULTS: Of the 75 patients in our cohort, 32 underwent microsurgical varicocelectomy, 18 had a standard laparoscopic varicocelectomy, and 25 underwent a less-ep repair. The average age was 39. There were no intraoperative complications in any group, nor EBL greater than 25 cc's. There was no difference in operative times between groups (97 vs 84 vs 101 minutes, respectively; p = 0.43). There were no instances of recurrent varicocele. In the LESS-EP cohort, there were no complications within 30 days; 2 patients received treatment for presumed epididymitis within the first 6 months of surgery. No statistically significant difference in change in sperm parameters was identified. Of 27 concomitant surgeries performed, all inguinal hernia repairs were performed with a standard laparoscopic technique and testicular sperm extraction was performed via microsurgical approach.

CONCLUSIONS: LESS-EP is a novel approach to varicocelectomy. We have found LESS-EP to be comparable to established methods in terms of safety, operative time and efficacy. It may be most appropriate in patients with bilateral disease or prior inguinal surgery. A microsurgical approach
may be most apropos in patients with unilateral disease and no prior groin surgery, and as well for whom concomitant surgeries are not required. Further study is ongoing to assess patient outcomes including long term improvement in semen analysis and pregnancy rates.

**References:**


**SPERM BIOLOGY**

**P-519 Wednesday, October 19, 2016**

**DOES SPERM ORIGIN HAVE AN IMPACT ON MORPHOKINETICS OF HUMAN ZYGOTES?**

- Kyono ART Clinic Takanawa, Minatoku, Tokyo, Japan; Universiti, Toho University, Ota-ku, Tokyo, Japan; Kyono ART Clinic, Sendai, Miyagi, Japan.

**OBJECTIVE:** ICSI with testicular sperm extraction (TESE) is the choice of treatment for azoospermic patients irrespective of testicular pathology, i.e., obstructive (OA) or non-obstructive azoospermia (NOA). However, lower fertilization and compromised embryonic development are often observed particularly with NOA patients compared to those with ejaculated spermatoozao (EJ). The objective of this study was to assess the effect of azoospermia etiology on morphokinetics of embryos fertilized with testicular sperm. To do so, zygotes in OA and NOA patients were compared with those in EJ patients by time-lapse monitoring (TM).

**DESIGN:** Comparative morphological assessment of ICSI zygotes.

**MATERIALS AND METHODS:** A total of 792 mature oocytes from 145 patients were ICSI inseminated with OA (n = 272), NOA (n = 267) or EJ (n = 433) sperm. After ICSI, oocytes were individually cultured in a TM system (EmbryoScopeTM). Time points of each morphokinetic event were recorded up to the blastocyst stage, and the 3 groups were compared. Morphokinetic behavior was also compared between transferred embryos according to their implantation potential.

**RESULTS:** Average maternal age was 33.5 ± 4 years for NOA, which is the youngest out of the 3 groups, 36.4 ± 3 for OA, and 37.1 ± 4 for EJ. While fertilization rate in both NOA (54.3%) and OA (60.7%) were lower (P < 0.05) than EJ (69.7%), blastocyst formation and implantation rates were all comparable. Time points for PN disappearance, 2-cell stage, and 4-cell stage, as well as the blastocyst, were longest in NOA (P < 0.01), while the interval between the 4- and 5-cell stage was shortest in NOA (P < 0.01). Those in OA embryos were all similar to EJ, but PN appearance and time to morula were shorter. Although the maternal age of implanted embryos was younger than non-implanted counterparts, no significant difference was noted between the two. Among implanted zygotes across the three groups, intervals between the 2- and 3-cell, and the 4- and 5-cell in NOA were shorter than in EJ, but not different from that in OA.

**CONCLUSIONS:** NOA zygotes showed slower and less synchronized cell cleavage than OA, which was similar to EJ, indicating spermatozoic function has an impact on early embryonic development. However, NOA embryos that were suitable for transfer or capable of implantation developed similarly to EJ zygotes.

**P-520 Wednesday, October 19, 2016**

**NON-CODING RNA PROFILING AS AN INDICATOR OF MALE GAMETE REPRODUCTIVE POTENTIAL.**


**OBJECTIVE:** In men with unexplained infertility, supplementary tests may be pivotal to gain insight into the paternal contribution to the zygotic (non-coding RNA (ncRNA)) phenotype and its regulatory role. To date, molecules that are transcribed from DNA but not translated into proteins. We aimed to determine if sperm ncRNA have an influential role in profiling the fertile male partner and predict his ability to achieve a viable pregnancy.

**DESIGN:** In the course of a 15-month period, we assessed the RNA profile of men undergoing infertility screening with specific focus on ncRNA via next generation RNA-sequencing (RNA-Seq). RNA extraction was carried out on 25 men (9 samples per man, 25 consenting patients undergoing ICSI screening). The analysis was performed by measuring the abundance of small non-coding RNA (snRNA) and long non-coding RNA (lncRNA) in relation to ICSI reproductive outcome. A cohort of couples unable to sustain a pregnancy were compared to a men able to conceive naturally.

**MATERIALS AND METHODS:** Human semen specimens ranging in concentration from 7 to 25x10^6/mL were utilized to isolate total RNA using a spin column commercial kit. Their spermatozoon nucleic acid quality and concentration were measured. Expression values were calculated in fragments per kilobase of transcript per million mapped reads (FPKM).

**RESULTS:** Of the 25 men screened, 8 were selected for sperm RNA-Seq with an average female partner age of 34.8 ± 3 years and male age of 26 ± 5 years that presented with a sperm concentration of 27.3 ± 27x10^6/mL, motility of 46.6 ± 24%, and normal morphology. From the 25,260 genes assessed, statistical analysis evidenced 28 (0.12%) ncRNAs that were differentially expressed (P < 0.0005) between the control cohort (n = 3) and men (n = 5) treated by ICSI (female partner age 34.8 ± 3) achieving a fertilization of 71.4% (30/42) but not capable of sustaining a pregnancy. Additionally, these RNA genes (n = 16) were completely unexpressed in the cohort of men unable to conceive. Of these transcripts, 21/28 (75.0%) were long non-coding RNA and 7/25 (20.0%) were small non-coding RNA. In relation to their function, most of these (11/16, 68.8%) non-protein-coding RNA are considered to guide chemical modification of other RNAs, influence metabolism, and modulate stability and translation of messenger RNA. Interestingly, 13/16 (81.3%) of these ncRNA were located on autosomes, while only three genes were located on the sex chromosomes; following similar distribution of the spermatogenesis related genes.

**CONCLUSIONS:** The ncRNAs contributed by the spermatoozoan at the time of fertilization are chiefly regulatory molecules that can affect embryo development. Profiling men via RNA-Seq to supplement standard semen analysis may aid in the diagnosis and management of these couples with unexplained infertility. Screening men for an epigenetic imbalance of snRNA and lncRNA provides crucial information on the etiology of unexplained infertility and overall reproductive capacity of the infertile male.

**P-521 Wednesday, October 19, 2016**

**HYDROGEN MOLECULE TREATMENT ENHANCES ATP PRODUCTION IN HUMAN SPERMATOZOA.**

- K. Nakata, K. Yoshida, M. Yoshida, N. Yamashita, Reproductive Medicine Research Center, Yamashita Shonan Yume Clinic, Kanagawa, Japan; Biomedical Engineering Center, Toin University of Yokohama, Kanagawa, Japan; Misaki Marine Biological Station Graduate School of Science, University of Tokyo, Kanagawa, Japan.

**OBJECTIVE:** Asthenozoospermia, i.e., reduced sperm motility is one of major causes of male infertility. We have reported that H2 treatment of sperm remarkably increased the rate of forward motility of the frozen-thawed human spermatozoa, whereas N2 treatment did not. The H2 treatment also increased the membrane potential of human sperm mitochondria. In this study, in order to examine why the H2 treatment increases the rate of forward motility of the sperm, we investigated the effect of the H2 treatment on respiration in the spermatozoa.

**DESIGN:** We used frozen-thawed sperm from 172 normospermic patients in this study. Sperm motility and ATP content were measured on the sperm that were treated by H2 with or without oxidative phosphorylation inhibitors (antimycin, rotenone) and pentoxifylline.

**MATERIALS AND METHODS:** Sperm samples were frozen on the collected day. They were treated in the medium only (control (C)) or in the 75% H2-saturated medium (H2); with antimycin A (200uM) in C (C-A) or
were measured with Makler chamber and Sperm Class Analyser (SCA). Sperm concentration and motility was measured with an luminometer. Sperm concentration and motility than in H2+R in the parameters of VCL and ALH (P < 0.05, n = 12). Sperm treated in C+R showed significantly lower than in H2+R in the parameters of VCL and ALH (P < 0.05, n = 15). Sperm treated in Px showed significantly lower than in H2+R in the parameters of VSL, VAP and BCF (P < 0.05, n = 10). Sperm treated in C+R showed significantly lower than in H2+R in the parameters of VCL, VAP and BCF (P < 0.01, n=10), LIN, STR, WOB (P < 0.05, n=40). CONCLUSIONS: These clinical findings indicate that H2 treatment increases the intracellular ATP content of the normal sperms patients’ sperm. Possibly, men with severe sperm dysfunction could select IVF instead of ICSI by using H2 treatment. It may also be useful in the selection of good quality sperms for ICSI. This is a basic study on a relatively small sample size with limited conditions. The confirmation using larger samples under various conditions may be required. Furthermore, we need to check the safety of H2 treatment and sperm motility before ICSI. Supported by: This work was supported partly by a grant from the National Center for Child Health and Development to MY (grant number 26-21).

P-522 Wednesday, October 19, 2016

SEGMENTED HAIRPIN-LOOP ORGANIZATION OF CHROMOSOMES IN SPERM NUCLEI: IMPLICATIONS FOR FERTILIZATION AND EMBRYOGENESIS. D. Ioannou1, H. G. Tempest,2 #Human and Molecular Genetics, Assistant Professor, Miami, FL; 2Human and Molecular Genetics, Florida International University, Miami, FL.

OBJECTIVE: Genomes are nonrandomly organized within nuclei. Sperm cells are proposed to have a unique hairpin-loop arrangement that is hypothesized to be instrumental in the organization of the nuclear genome following fertilization. This model describes centromeres clustering in the center (chromocenter), with p- and q-chromosome arms stretching toward the nuclear periphery. This study examines whether evidence can be provided to support this model of organization in sperm using 3D modeling.

DESIGN: Transversal study in a laboratory environment.

MATERIALS AND METHODS: This study was approved by the local IRB, five normozoospermic males were recruited. Three color fluorescence in situ hybridization targeted the centromere and p- and q-arms of eight different chromosomes (2, 3, 6, 8, 10, 12, 16, and 18). 3D modeling was employed to investigate the radial organization of each targeted region by measuring the geometric center of each target to the nearest nuclear periphery. Furthermore, hairpin-loop configurations were determined by the angle created between p- and q-arms. A minimum of 30 cells per subject, per chromosome were studied. Nonrandom organization of was established using the Chi-squared goodness-of-fit test (p<0.05).

RESULTS: Distinct reproducible chromosome-specific patterns of organization emerge. All chromosomes were found to possess nonrandom radial organization (p<0.05). Chromosome arms were found to form discrete hairpin-loop configurations. Three reproducible categories of chromosome loops were observed: narrow (<40°: 10, 12), intermediate (40°-60°: 2, 8, 18), and wide (>60°: 3, 6, 12). Four centromeres (3, 6, 12, and 18) were found to be localized closer to the nuclear periphery than their chromosome arms.

CONCLUSIONS: We report reproducible nonrandom hairpin-loop organization of chromosomes that supports the proposed model. However, our findings do not support the existence of a centralized chromocenter with four centromeres being more proximal to the nuclear periphery than their chromosome arms. This suggests the sperm nucleus is more segmentally organized; resulting in specific genomic regions being exposed, remodeled and activated first following fertilization. The sequential exodus and remodeling could impact patterns of gene activation observed within the early embryo, perturbations in which, could negatively impact fertilization and early embryogenesis.
A COMPREHENSIVE STUDY INTO THE EFFECTS OF ADVANCING MALE AGE ON SEMEN PARAMETERS, SPERM GENETIC INTEGRITY AND THE OUTCOME OF ASSISTED REPRODUCTIVE TREATMENTS. A. Raberi, a,b G. Rozis, c S. Alfarrari, d K. Glynn, c L. Lansdowne, c S. Batha, d D. Wells, a,b “The Nuffield Department of Obstetrics & Gynaecology, Institute of Reproductive Sciences, Oxford, United Kingdom; b Reprogenetics UK, Oxford, United Kingdom; c List Fertility Clinic, London, United Kingdom.

OBJECTIVE: We undertook a detailed evaluation of a large number of sperm samples, aiming to determine the effect of advancing male age on a wide range of semen characteristics. Fertilisation capacity, embryo development and pregnancy were also assessed.

DESIGN: Retrospective analysis of clinical data.

MATERIALS AND METHODS: Results from 590 males undergoing fertility treatment were included. Data was available for 14 distinct parameters, descriptive of semen quality, sperm function, and treatment outcome. Together, this information allowed a comprehensive review of the impact of age on male reproductive function. Additionally, relationships between individual parameters, independent of age, were evaluated. Lifestyle factors and prior medical history were also considered. DNA fragmentation analysis utilized the Sperm Chromatin Dispersion (SCD) test, while cytogenetic analysis utilised fluorescence in situ hybridization (FISH). Statistical evaluation was performed using correlation (Pearson test) and linear regression.

RESULTS: Most traditional sperm parameters, such as concentration and motility, which declined with advancing age [F(1,197) = 7.98, p < 0.05, R² = 0.076]. Linear regression analysis showed that advanced male age is also associated with increasing sperm DNA fragmentation (SDF) [F(1,551) = 4.556, p < 0.05, R² = 0.008] and elevated DNA degradation [F(1,570) = 23.49, p < 0.001, R² = 0.064]. Regardless of age, alcohol intake was observed to adversely affect SDF rates [F(1,104) = 5.685, p < 0.05, R² = 0.052]. Furthermore, advancing male age was associated with a decrease in the average number of 2PN cleaved embryos (p < 0.05), fertilization rate (p < 0.05) and birth rate (p < 0.001) (partners aged more than 35 were excluded).

CONCLUSIONS: A negative impact of male age on assisted reproductive treatments was confirmed, ultimately leading to decreased birth rates. Results obtained provide evidence that factors such as sperm DNA damage may contribute to this age-effect, suggesting that measuring this parameter, and obtaining provide evidence that factors such as sperm DNA damage may contribute to this age-effect, suggesting that measuring this parameter, and

P-526 Wednesday, October 19, 2016

THE POTENTIAL APPLICATION OF THE INDUCED PLURIPOTENT STEM CELLS (iPS) INDUCED FROM URINE STEM CELLS IN MALE INFERTILITY. G. Liu, a J. Zhang, ’ a Z. Wang, a X. Liang. ’a Anatomical Science, Hiroshi University Graduate school of Medicine, Hiroshi, Japan; b Obstetrics and Gynecology, Hiroshi University, Graduate School of Medicine, Hiroshi, Japan; c Saint Mother Hospital, Kitakyusyu, Japan.}

OBJECTIVE: To minimize the risk to choose sperm with DNA fragmentation for ICSI, the most preferable sperm head size was determined, since it has been still difficult to select a sperm with genetically normal nucleus among sperm population on a microscope for ICSI.

DESIGN: TUNEL assay and measurement of the sperm head sizes in human semen samples.

MATERIALS AND METHODS: The semen samples showing normozoospermia were obtained from 21 infertile male patients who were subjected to IVF or ICSI. The sperm were washed with PBS, fixed by 4% paraformaldehyde and smeared on glass slides. One of the smear samples was stained with 2% giemsa’s solution. 100 sperm (except for amorphous sperm) were randomly selected, and the length and width of the heads were measured on their magnified digital images. The other sample was used for TUNEL assay. 100 TUNEL-positive cells, which have DNA fragmentation, were randomly selected and the head sizes were measured. Distribution of the head sizes was compared between the 100 sperm that were randomly selected and the 100 sperm with DNA fragmentation.

RESULTS: Sperm were classified into 9 groups based on the length and width of the heads (Table). In 21 samples, 50% or more of sperm population consisted of normal (classified according to WHO criteria, average 25.9%), small (average 24.3%) and narrow heads (average 52.1%). Narrow head sperm was predominant. Of the sperm with DNA fragmentation, 30.6% and 57.3% were normal and larger head (thick, elongated and huge) groups, respectively. Other groups occupied less than 4.9%. To compare the actual risk of DNA fragmentation, shares of each sperm head in total sperm and DNA-fragmentation sperm populations were multiplied. As a result, the relative risk of DNA fragmentation was 5 times lower in narrow head than normal head groups (0.24 versus 1.0). Almost all of the narrow group sperm have heads of which widths were more than 2 μm and less than 2.5 μm.
Distribution of sperm head sizes and DNA fragmentation

<table>
<thead>
<tr>
<th>Head shape</th>
<th>Head width (μm)</th>
<th>% Population, % DNA fragmentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thin</td>
<td>&lt;2.5</td>
<td>5.0%</td>
</tr>
<tr>
<td>Elongate</td>
<td>2.5-3.5</td>
<td>5.6%, 2.7%</td>
</tr>
<tr>
<td>Normal</td>
<td>4.0-5.0</td>
<td>3.4%, 23.0%</td>
</tr>
<tr>
<td>Thick</td>
<td>&gt;5.5</td>
<td>0.1%, 17.7%</td>
</tr>
<tr>
<td>Small</td>
<td>&lt;4.0</td>
<td>32.1%, 4.5%</td>
</tr>
<tr>
<td>Round</td>
<td>24.3%, 3.3%</td>
<td>25.9%, 30.6%</td>
</tr>
<tr>
<td>Flattten</td>
<td>8.2%, 4.9%</td>
<td>0.1%, 12.5%</td>
</tr>
</tbody>
</table>

CONCLUSIONS: The present results suggest that the narrow sperm is superior to the normal sperm for ICSI treatment in the points that they are frequently found on a microscope and their DNA is not highly damaged. The DNA integrity in the narrow head may be maintained by tighter DNA packing with protamine, responsible for sperm head compaction.

SPERM PREPARATION

P-529 Wednesday, October 19, 2016

BIOMARKERS FOR SPERM QUALITY ARE ASSOCIATED WITH FERTILITY RATES AND EMBRYO VIABILITY. E. Lopez-Bayghen, P. Tello-Mora, B. Quintanilla-Vega, Departamento de Toxicología, Cines-tav-IPN, Ciudad de Mexico, Mexico; Laboratorio de Investigación y Diagnóstico Molecular, Instituto Ingenes, Ciudad de Mexico, Mexico.

OBJECTIVE: Current World Health Organization (WHO) parameters for assessing sperm quality fail to accurately predict higher fertilization rates and the production of viable embryos, therefore we assessed the effectiveness of assays based on the function and integrity of spermatozoa: 1) spontaneous and induced acrosome reaction, and 2) DNA damage, to uncover associations with the fertilization rate and embryo viability for in vitro fertilization (IVF) and intra-cytoplasmic (ICSI) patients.

MATERIALS AND METHODS: Semen samples were collected and characterized as either normospermic (n=51) or abnormospermic (n=35), according to the WHO parameters. Semen was further assessed using fluorescence/cytometry-based techniques for the acrosome reaction [spontaneous (sAR) and induced (iAR), using anti-CD46-FITC; and the acrosome response to a ionophore challenge (ARIC) was calculated], and for DNA integrity [SCSA technique for DNA fragmentation index (%DFI)]. Fertilization was achieved by either a standard IVF or ICSI procedure. Embryo viability was determined at day 3 or 5, only ideal embryos were transferred and clinical pregnancy was confirmed by plasma β-hCG concentration (≤10 mU/mL) after day 20. Linear regression analysis was used to describe the associations between sAR, iAR, ARIC, %DFI and fertilization rate, embryo viability or pregnancy outcome.

RESULTS: Independent of sperm quality, sAR, iAR and ARIC were associated with the IVF rate (β=-0.54, p<0.0001; β=-0.83, p<0.001; and β=-2.10, p<0.0001, respectively); whereas, %DFI was associated with a decreased number of viable embryos for IVF (β=-0.87, p<0.001) and for ICSI treatment (β=0.059, p<0.05). When only normospermic samples were considered, sAR and iAR still correlated with fertilization rates (β=-0.54 and β=-0.40, respectively, p<0.01). WHO sperm quality did not predict male fertility success. Data of 67 pregnancy outcomes are complete but none of the parameters that were assessed predicted a clinical pregnancy.

CONCLUSIONS: WHO parameters were not good predictors of fertility, however, the acrosome reaction could predict spermatozoa with a high fertilization rate, whereas the DNA fragmentation was inversely associated with embryo viability.

Supported by: PEI-Conacyt 231793.

P-530 Wednesday, October 19, 2016

OPTIMAL TIMING FOR INTRAUTERINE INSEMINATION (IUI) AFTER ADMINISTERING HCG IN OVULATION INDUCTION IUI CYCLES. B. S. Hurst, K. Merriam, P. Marshburn, M. Matthews, R. S. Usadi, Ob/Gyn, Carolinas HealthCare System, Charlotte, NC; Caro-linas Medical Center, Charlotte, NC; Department of OB/GYN, Carolinas Healthcare System, Charlotte, NC; Carolinas Healthcare System, Charlotte, NC; Reproductive Endocrinology and Infertility, Carolinas Healthcare, Charlotte, NC.

OBJECTIVE: To determine if pregnancy and birth rates are higher for intrauterine insemination (IUI) at 24 or 36 hours (h) after HCG administration. A prior study of fewer than 210 patients found that outcomes were marginally better when IUI was performed at 36 compared to 24 hours (1).

DESIGN: Retrospective case-control study at an academic medical center.

MATERIALS AND METHODS: 1200 consecutive ovulation induction (OI) IUI cycles from January 2010 to October 2013 in 567 women, including 408 at 24h and 792 at 36h. The population studied included 404 women with AMH less than 1.0 ng/mL; 190 had unexplained infertility, 176 had polycystic ovarian syndrome (PCOS), 174 had endometriosis, 128 had male infertility, 120 had other ovulatory dysfunction, 118 had basal FSH over 15 mIU/mL, 102 had thyroid dysfunction, and 101 had fibroids. In our center, IUI at 24h or 36h was selected for convenience. Data was organized using REDCap and analyzed with SAS.
RESULTS: Pregnancy rates (PR) and live birth rates (LBR) were significantly higher with 36 h than 24 h IUI (16.5% and 11.7%, vs 12.0% and 7.6%, respectively). PR and LBR were higher (p<0.05) for clomiphene (14.1%, 10.0%) than letrozole (12.5%, 8%). LBR was 15.7% with gonadotropin IUI, and 13.9% with combined protocols. Asians experienced the highest LBR (15.5%) and African Americans the lowest (4.6%), p<0.005. The LBR was 15.5% for ages 25-29, 10.9% for 30-34, 11.3% for 35-39, and 7.7% for 40-44. No one conceived after age 45 or with a BMI over 50; otherwise there was no trend for BMI PR or LBR. Donor IUI LBR was 12.2%, and partner 10.1%. The mean age was 35.7, length of infertility 2.9±4.4 months, BMI 26.7, and AMH 2.6.

CONCLUSIONS: Since studies of timed intercourse on the day of or day before ovulation show comparable outcomes, we were surprised that the pregnancy rates and live birth rates are statistically and clinically significantly higher for 36 h IUI than 24 h after HCG administration. The LBR declines with age but OI-IUI still seems beneficial up to age 44. Clomiphene outperformed letrozole. While gonadotropins were most successful, use is discouraged due to the risk of multiple birth and high cost. In conclusion, pregnancy and live birth rates are higher when IUI is performed 36 h after HCG than at 24 h.

References:

Supported by: Carolinas HealthCare System Cannon Summer Research Scholars Program.

P-531 Wednesday, October 19, 2016

THE EFFECTIVENESS OF DIFFERENT MAGNETIC ACTIVATED CELL SORTING PROGRAMS IN DEPLETING APOPTOTIC SPERM CELLS. N. Azia, J. Novotny, J. Brezinova, I. Oborna. aGynaecology, Consultant, Liverpool Women’s Hospital and the University of Liverpool, Liverpool, United Kingdom; bFaculty of Medicine and Dentistry, Palacky University, Olomouc, Czech Republic; cSpermBank International Ltd., Olomouc, Czech Republic.

OBJECTIVE: To compare the effectiveness of different commercially available Magnetic Activated Cell Sorting (MACS) columns and AutoMACS Pro Separator pre-set separation programs in separating non-apoptotic human spermatozoa. To our knowledge this was not studied before.

DESIGN: Prospective study

MATERIALS AND METHODS: Sperm samples from 32 healthy donors and infertile men were prepared and incubated with paramagnetic Annexin V-conjugated microbeads. Three aliquots of each sample were subjected to MACS procedure using three different separation columns (MS, LS, LD). The procedure delivered two sperm fractions: Annexin-negative (non-apoptotic) and Annexin-positive (apoptotic). A lipophilic cationic dye was used to assess the integrity of the sperm mitochondrial membrane potential (MMP) as a marker of apoptosis in the non-apoptotic fractions and the unseparated sperm sample. Mitochondrial labeling was assessed using flow cytometry. A further 16 semen samples were prepared as above and subjected to MACS procedure using AutoMACS Pro Separator (Miltenyi Biotec). The LS column was used for all samples’ separation. Three aliquots of each sample were subjected to MACS procedure using AutoMACS Pro Separator (Miltenyi Biotec). The LS column was used for all samples’ separation. Three aliquots of each sample were subjected to MACS procedure using AutoMACS Pro Separator (Miltenyi Biotec).

Table 1: Sperm with intact MMP % in un-separated sperm samples and the non-apoptotic fractions

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean sperm with intact MMP% (±SD) using three different columns (n=32)</th>
<th>Mean sperm with intact MMP% (±SD) using three different pre-set programs (n=16)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Unseparated samples</td>
<td>Unseparated samples</td>
</tr>
<tr>
<td></td>
<td>MS column</td>
<td>LS column</td>
</tr>
<tr>
<td></td>
<td>42.7 ± 16</td>
<td>46.1 ± 16</td>
</tr>
<tr>
<td></td>
<td>Deplete</td>
<td>Depletes</td>
</tr>
<tr>
<td></td>
<td>52.2 ± 11.9</td>
<td>63.3 ± 10</td>
</tr>
</tbody>
</table>

designated Deplete, Depletes, Depletes025. The integrity of the MMP in all non-apoptotic fractions was assessed as above. The study was IRB approved.

RESULTS: The mean (±SD) of the percentages of sperm cells with intact MMP in the unseparated semen samples and the non-apoptotic fractions are given in table 1. Pairwise comparison of the three treatments using MS, LS, and LD columns revealed that the use of LD column yielded a significantly higher percentage of sperm with intact MMP compared to MS column (P < 0.0001) and LS column (P = 0.0006). LS and MS columns yielded similar results (P = 0.67). Among the pre-set programs Depletes setting yielded significantly less sperm cells with intact MMP than Depletes setting (P = 0.006) and Depletes025 setting (P = 0.01). Depletes and Depletes025 settings yielded similar results (P = 0.8).

CONCLUSIONS: The LD column and also pre-set programs Depletes and Depletes025 yielded the highest percentages of intact sperm in separated fractions. Our findings should help assisted conception labs in choosing the right tools for MACS separation.

References:
LF_2016_014
Supported by: Internal Grant of Palacky University.

P-532 Wednesday, October 19, 2016

MICROSURGICAL TESTICULAR SPERM EXTRACTION (MICROTESE) SPERM RETRIEVAL RATE (SRR) POST TESTICULAR SPERM ASPIRATION (TESA). A. H. AlMalki, A. Zini. aUrology, McGill University, Montreal, QC, Canada; bUrology, McGill University.

OBJECTIVE: Studies have shown that MicroTESE (Microsurgical Testicular Sperm Extraction) outcome may be adversely influenced by a prior MicroTESE (performed in the preceding 6 months). We sought to evaluate MicroTESE sperm retrieval rate (SRR) post-TESA (Testicular Sperm Aspiration) in a cohort of infertile men.

DESIGN: We conducted a retrospective study of 39 consecutive men with NOA (non-obstructive azoospermia), cryptozoospermia and severe oligo-thenoazoospermia who underwent MicroTESE post-failed TESA between July 2007 and April 2016.

MATERIALS AND METHODS: MicroTESE sperm retrieval rates (SRR) were recorded. Patients were grouped based on whether they had TESA within 6 months (≤6 months) (group 1) or more than 6 months (>6 months) (group 2).

CLINICAL CHARACTERISTICS OF MEN THAT UNDERWENT MICROTESE POST TESA

<table>
<thead>
<tr>
<th>Parameter</th>
<th>≤ 6 months</th>
<th>&gt; 6 months</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>18</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>Mean (±SD) Male Age</td>
<td>36 ± 8</td>
<td>39 ± 6</td>
<td>NS</td>
</tr>
<tr>
<td>Mean (±SD) PSH (IU/L)</td>
<td>8 ± 6</td>
<td>16 ± 17</td>
<td>NS</td>
</tr>
<tr>
<td>Mean (±SD) Total Testosterone (nmol/L)</td>
<td>13 ± 6</td>
<td>13 ± 8</td>
<td>NS</td>
</tr>
<tr>
<td>Mean (±SD) Right Testicular Volume (ml)</td>
<td>16 ± 3</td>
<td>13 ± 5</td>
<td>NS</td>
</tr>
<tr>
<td>Mean (±SD) Left Testicular Volume (ml)</td>
<td>16 ± 3</td>
<td>13 ± 5</td>
<td>NS</td>
</tr>
<tr>
<td>Unilateral Procedures (%)</td>
<td>15/18 (83%)</td>
<td>14/21 (67%)</td>
<td>NS</td>
</tr>
<tr>
<td>Successful Sperm Retrievals (%)</td>
<td>15/18 (83%)</td>
<td>14/21 (67%)</td>
<td>NS</td>
</tr>
<tr>
<td>Salvage MicroTESE post failed TESA</td>
<td>12/15 (80%)</td>
<td>11/18 (61%)</td>
<td>NS</td>
</tr>
</tbody>
</table>

*NS - not significant (P > 0.05)  
*Fisher’s exact test  
Mann Whitney Rank Sum Test  
Defined as positive identification of ≥ 5 spermatozoa
A SIMPLE NEW METHOD FOR THE FREEZE-DRYING AND STORAGE OF HUMAN SPERM. P. Patrizio, Y. Natan, Y. Barak, P. Levi Setti, A. Arav. Obstetrics, Gynecology & Reproductive Sciences, Yale Fertility Center & Fertility Preservati, New Haven, CT; 2FertileSafe Ltd., Nes-Ziona, Israel; 3Clinical Embryologist, Rosh Haayin, Israel; 4Dept. Gynecology, Division of Gynecology and Reproductive Medicine, Humanitas Fertility Center-Humanitas Research Hospital, Rozzano (Milano), Italy; 5Fertilesafe Ltd, Nes-Ziona, Israel.

OBJECTIVE: Cryopreservation and long term storage of biological samples in LN is demanding and costly. We explored a new method, freeze/drying (lyophilization) and storage of human sperm, as an alternative.

DESIGN: Basic experimental research of human sperm vitrification and lyophilization.

MATERIALS AND METHODS: Fresh human sperm samples donated to research (n=3) were first diluted 1:1 (v/v) in lyophilization solution (LyoS: α-MEM Eagle- 0.25% sucrose, 0.25% trehalose and 0.6% (w/v) HSA) and then cryopreserved by direct exposure to sterile liquid air. Frozen pellets were kept closed in 10 mL glass vials and moved into a sterile drying device (Darya, FertileSafe, Israel) immersed in liquid air. After 48 hrs the sperm pellets were dried and stored at 4°C for 1 week until rehydration (0.2 mL of LyoS α-MEM Eagle warmed). Sperm DNA integrity of rehydrated sperm was evaluated by Halosperm test (Halotech, Spain) and morphology was assessed using IMSI parameters under inverted microscope with Nomarski optics, at a magnification of x6100.

RESULTS: Rehydrated human sperm showed no significant cell loss and no increased DNA damage despite being kept lyophilized in sealed glass vials for up to one week at 4°C. Fresh sperm concentration was 10^10^ cells/mL and motility was >50%, DNA integrity was 81.06±9.2%. Post thaw motility of the same samples (without drying) was 35%. After drying and rehydration, sperm concentration of the samples rehydrated with LyoS was 8.25±0.8 cells/mL and DNA integrity was 81.35±3.5%; while sperm concentration of the samples rehydrated with α-MEM Eagle was 5.375±0.8 cells/mL and DNA integrity was 71.19±7.7%. Sperm morphology by IMSI (6% of the cells) were consistent with scores of 4-6 based on head shape, its base and the presence of vacuoles, compatible with high quality rehydrated spermatozoa usable for ICNI (1). Taken together these results show no cell loss and no additional damage to the DNA integrity due to the drying process and that rehydration with LyoS was better than with medium only.

CONCLUSIONS: We have developed a novel, simple method for the freeze/drying of human sperm and for storage at 4°C. Rehydrated sperm droplets can be directly dissolved into culture medium without any need of sperm pre-washing, and, since high DNA integrity and IMSI scores are maintained, these sperm could be used for ICNI. Current research is evaluating storage at room temperature.

References:


OBJECTIVE: PICSI has been demonstrated to positively select sperm with less aneuploidies, DNA fragmentation and adequate maturation features. However, their impact on the development and quality of embryos is unknown. To evaluate whether microinjection with sperm selected by PICSI (hyaluronic acid receptor binding ability) show any improvement on embryo quality based on morphokinetic analysis in comparison with classic sperm selection.

DESIGN: Secondary analysis from an ongoing prospective, randomized and triple-blinded trial, including a total of 144 infertile couples undergoing oocyte donation.

MATERIALS AND METHODS: Embryo quality parameters and in vitro fertilization outcomes were compared between PICSI (72 patients) and control group, conventional ICSI (72 patients). A total of 535 embryos were analyzed in PICSI and 613 embryos in control group with Embryoscope® or Eeva® for the main morphokinetic parameters. Also, the proportion of embryos classified according to aneuploidy risk, blastocyst prediction and implantational potential (based on published algorithms) were compared.

RESULTS: Statistically significant differences between PICSI and ICSI groups were found when morphokinetic parameters were analyzed, e4: 22.4h (95% CI=22.0-22.8) vs. 21.8h (95% CI=21.4-22.2), t2: 29.6h (95% CI=28.3-29.7) vs. 30.24h (95% CI=29.4-31.1), t3: 38.5h (95% CI=37.8-39.2) vs. 39.7h (95% CI=38.9-40.6), t4: 41.5h (95% CI=40.8-42.2) vs. 43.0h (95% CI=42.1-43.8), t8: 65.2h (95% CI=63.8-66.6) vs. 67.5h (95% CI=66-6.88), t9*: 75.0h (95% CI=73.4-76.5) vs. 78.6h (95% CI=77.1-80.1), tEB: 111.6h (95% CI=110.3-112.8) vs. 113.9h (95% CI=112.3-115.5) PICSI and control group respectively. Regarding the embryo quality, expressed as the categories of aneuploidy risk and implantation potential, normal groups, aneuploidy likelihood (low, A type embryo) was 22% (95% CI=18.3-25.6) vs. 17% (95% CI=14.1-20.4), and D type embryo (high aneuploidy likelihood) was 29% (95% CI=24.7-32.7) vs. 35% (95% CI=30.6-38.6) for PICSI and ICSI respectively. Implantation potential classification between PICSI and control group was 17% (95% CI=14.2-20.7) vs. 16% (95% CI=13.4-19.3) (High likelihood, A type embryo) and 39% (95% CI=35-43.4) vs. 42% (95% CI=38-45.9) (Low likelihood, E type embryo). Statistical differences were found in the proportion of high quality embryos 18% in PICSI group vs. 13% in control group based on Eeva algorithm.

CONCLUSIONS: PICSI leads to a significant improvement of embryo quality, as reflected in the higher implantation potential and lower risk of aneuploides. The better embryo quality obtained after its application the higher clinical outcome would be expected with large scale randomized control trials.

Supported by: PI14/00523, Spanish Ministry of Economy and Competitiveness, Instituto de Salud Carlos III program.


OBJECTIVE: Magnetic activated cell sorting (MACS) procedure is able to separate reactive/positive sperm and inject no apoptotic spermatoza in the oocyte. Our objective was to determine if MACS-Anexin V selection improved embryo morphokinetic parameters, development or implantation outcome, over the conventional swim-up technique.

DESIGN: Secondary analysis from a prospective, randomized and double-blinded study. A total of 80 sperm samples from patients undergoing ovum donation were included.

MATERIALS AND METHODS: We generated two groups: MACS (Swim-up + MACS) and Swim-up group, before ICSI treatment. The MACS group included 37 couples and Swim-up 43. A total of 258 and 243 oocytes were analyzed respectively. With the use of Time-lapse technology we did a complete embryo follow-up until transfer with further morphokinetic analysis.

RESULTS: Similar results were obtained in implantation rates in both groups 39.19% (C95% 24.42-53.96) vs. 41.86% (C95% 28.46-55.26).
Direct division from 1 to 3 cells embryos incidence was 22.90% (CI95% 17.74_27.99) vs. 24.30% (CI95% 18.89_29.67) comparing MACS vs Swim-up groups respectively. Significant differences were found in morphokinetic parameters, particularly at cleavage stage embryos, results in MACS and Swim-up groups respectively were compared; t2: 27.05h (CI95% 26.54_27.56) vs. 28.55h (CI95% 27.98_29.12), t3: 37.11h (CI95% 36.26_37.95) vs. 38.62h (CI95% 37.69_39.55), t4: 39.71h (CI95% 38.85_40.57) vs. 42.04h (CI95% 40.97_43.11), t6: 54.50h (CI95% 53.18_55.82) vs. 51.69h (CI95% 50.45_52.92), t7: 57.04h (CI95% 55.73_58.34) vs. 54.08h (CI95% 52.93_55.24).

CONCLUSIONS: MACS technology application in unselected males undergoing ICSI on donors affects cleavage stage embryos, results in faster cleaving embryos that may affect implantation potential. Further study should be performed to understand the insights of this selection and whether this effect could be observed in the outcome by large scale studies.

<table>
<thead>
<tr>
<th>Morphokinetic parameters and statistical significance between groups (hours).</th>
<th>MACS (95%CI)</th>
<th>Swim-up (95%CI)</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>t2</td>
<td>27.05h (26.54_27.56)</td>
<td>28.55h (27.98_29.12)</td>
<td>0.000</td>
</tr>
<tr>
<td>t3</td>
<td>37.11h (36.26_37.95)</td>
<td>38.62h (37.69_39.55)</td>
<td>0.018</td>
</tr>
<tr>
<td>t4</td>
<td>39.71h (38.85_40.57)</td>
<td>42.04h (40.97_43.11)</td>
<td>0.001</td>
</tr>
<tr>
<td>t6</td>
<td>54.50h (53.18_55.82)</td>
<td>51.69h (50.45_52.92)</td>
<td>0.002</td>
</tr>
<tr>
<td>t7</td>
<td>57.04h (55.73_58.34)</td>
<td>54.08h (52.93_55.24)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Supported by: PI14/00523. Spanish Ministry of Economy and Competitiveness. Instituto de Salud Carlos III program.

CLINICAL REPRODUCTIVE LABORATORY

P-536 Wednesday, October 19, 2016

CAN USE OF TIME-LAPSE MONITORING COMPARED TO CONVENTIONAL MORPHOLOGIC ASSESSMENT IMPROVE 3-DAY EMBRYO SELECTION AMONG EXPERIENCED EMBRYOLOGISTS AND INEXPERIENCED TRAINEES? A PILOT STUDY. I. Okeigwe, D. E. Ikhena, R. Confino, M. Pavone, J. Robins, J. X. Zhang. Obstetrics & Gynecology, Division of Reproductive Endocrinology & Infertility, Northwestern University, Chicago, IL.

OBJECTIVE: Choosing the best embryo to transfer has a major impact on an IVF program’s success. Using conventional morphologic assessment (CMA) for embryo selection requires the expertise of an experienced embryologist. Time-lapse monitoring (TLM) may simplify decision-making in the lab and allow those with less experience to identify the best embryo to transfer. The objective of this study was to evaluate the impact of TLM compared to CMA on decision-making among experienced embryologists and inexperienced trainees.

DESIGN: Cross-sectional analysis.

MATERIALS AND METHODS: We selected IVF cycles that resulted in at least 3 embryos with ≥ 6 cells on day 3 and at least one embryo that was transferred and implanted or frozen on day 5. A maximum of 6 embryos were evaluated per cycle. Three experienced embryologists and three inexperienced trainees independently graded all embryos and selected their best embryo based on still images taken at four focal planes on day 3. After submitting their CMA score sheets, evaluators then graded and selected their best TLM embryo. Evaluators recorded the time spent per cycle. The Cohen’s kappa statistic was used to determine inter-observer agreement. Odds ratios were calculated to determine the impact of TLM and experience on embryo selection.

RESULTS: A total of 108 embryos from 23 cycles were evaluated. Approximately 40% of cycles were single embryo transfers. Among all evaluators, there were no statistically significant differences in time spent evaluating embryos. Compared to CMA, TLM improved the inter-observer agreement in embryo selection among both inexperienced trainees and experienced embryologists (k 0.47 vs. 0.58). TLM also improved the performance of all evaluators except one inexperienced trainee. However, when single embryo transfer cycles were examined, TLM improved the performance of experienced embryologists (OR 1.75) but not inexperienced trainees (OR 0.63). Analysis was performed to determine if experience was predictive of performance. Experience did not predict performance using CMA; however, experience consistently improved the odds of choosing the correct embryo to transfer for all graded cycles (OR 2; p=0.05) and single embryo transfer cycles (OR 3.9; p=0.03) evaluated by TLM.

CONCLUSIONS: Our findings show that time-lapse monitoring helps to improve identification of the best embryo to transfer on day 3 compared to conventional morphologic assessment. The impact of time-lapse monitoring was greatest among experienced embryologists, particularly when selecting single embryo transfers. The poorer performance of inexperienced trainees when data were stratified by number of embryos transferred suggests that time-lapse monitoring cannot substitute the skill set of experienced embryologists. Further investigation is needed to determine whether these findings hold true in a larger cohort of subjects.

MATERNAL PREDICTORS OF MORPHOKINETIC EMBRYO PARAMETERS USING TIME-LAPSE (TL) IMAGING. I. Souter, I. Dimitriadi, C. L. Bormann, R. Hauser, C. Messerlian. Obstetrics & Gynecology/REI Division, Harvard Medical School-Massachusetts General Hospital, Boston, MA; Tufts Medical Center, Boston, MA; Massachusetts General Hospital-Harvard Medical School, Boston, MA; Harvard Chan School of Public Health, Boston, MA; Environmental Health, Harvard T.H. Chan School of Public Health, Boston, MA.

OBJECTIVE: To determine how certain maternal factors, such as age, body mass index (BMI), antral follicle count (AFC), anti-mullerian hormone (AMH), and basal follicle stimulating hormone (FSH) influence timing of embryonic morphokinetic parameters thought to predict embryonic development and implantation potential.

DESIGN: Retrospective cohort of women undergoing assisted reproduction at a large academic fertility center.

MATERIALS AND METHODS: We abstracted maternal age, BMI, AFC, AMH, and basal FSH from 358 women providing 1863 embryos with embryonic kinetic data. We measured duration (hours) of 2- to 3-cell (P2) and 3- to 4-cell (P3) stage. We estimated adjusted Hazard Ratios (HR) and 95% CI for maternal factors of interest using Cox regression models. We also assessed whether HR differed between women <38 years and women ≥38 years of age.

RESULTS: Morphokinetic parameters P2 and P3 from 358 women with median (IQR) age of 35.8 (33.2, 39.2) years were analyzed. Median (IQR) P2 and P3 times for viable embryos (either transferred and/or frozen at the blastocyst stage) were 11.1 (10.0, 12.1) and 0.84 (0.5, 2.0) hours, respectively. In the overall sample, maternal characteristics did not predict morphokinetics. However, the relationship between AMH and P2 differed between women <38 years and women ≥38 years. For every unit increase in AMH, time to P2 increased by 13% among women <38 years, and decreased by 6% among women ≥38 years (HR (95%CI): 1.13 (1.05, 1.20), P<0.005; and 0.94 (0.88, 1.01), P<0.005). However, the relationship between AMH and P3 was opposite. For every unit increase in AMH, time to P3 decreased by 5% among women <38 years, and increased by 9% among women ≥38 years (HR (95%CI): 0.95 (0.89, 1.0), P=0.06; and 1.09 (1.02, 1.16), P=0.02). The remaining factors examined were not related to the timing of either P2 or P3.

CONCLUSIONS: Maternal age, BMI, AFC, and FSH were not associated with the duration of either P2 or P3. AMH predicted the length of time to P2 and P3, however, the direction of the effect differed between younger and older women.

P-538 Wednesday, October 19, 2016


OBJECTIVE: As the use of frozen donor oocytes becomes more prevalent, we wanted to look into the possibility of the vitrification process causing damage to the oocyte resulting in an increase in aneuploidy.

DESIGN: Retrospective study.

MATERIALS AND METHODS: We reviewed all donor oocyte cycles utilizing preimplantation genetic screening (PGS) from 2014 to 2016. Aneuploidy rates were calculated for cycles using fresh donor oocytes and for cycles using frozen donor oocytes. A Chi-squared test was used to calculate
statistical significance of aneuploidy. A one-tailed t-test was used to calculate the significance of the mean oocytes retrieved between the groups. RESULTS: 62 cycles utilizing fresh donor oocytes and PGS produced a total of 331 tested embryos with 249 being euploid and 82 aneuploid. Fresh donor oocytes resulted in 44.8% and 38.5% aneuploid embryos, 55 cycles utilizing a frozen donor oocytes and PGS produced a total of 136 tested embryos with 89 being euploid and 47 aneuploid. Frozen donor oocytes resulted in 34.6% aneuploid embryos. This is a statistically significant difference with a p < 0.05. No significant difference was seen between the mean age of donors for fresh egg cycles versus frozen egg cycles at 25.8 and 25 years old, respectively. The average number of oocytes retrieved in fresh egg cycles was 29.4 while the average number of oocytes retrieved in frozen egg cycles was 20.4. A t-test revealed a significant difference with a p < 0.0001.

CONCLUSIONS: The vitrification and warming of oocytes could possibly be increasing the number of aneuploid embryos in these donor oocyte cases. However, the donors being stimulated for these vitrification cycles are subjected to more aggressive stimulations to produce a larger quantity of eggs. This may also be increasing aneuploidy rates. While these numbers are still small, the significant difference in aneuploidy between fresh donor oocyte cycles and frozen donor oocyte cycles encourages further investigation into specific causes and future ramifications.

<table>
<thead>
<tr>
<th></th>
<th>Mean Number of Euploid</th>
<th>Mean Number of Aneuploid</th>
<th>Oocytes Retrieved</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fresh Donor Oocytes</td>
<td>249</td>
<td>82</td>
<td>25.8</td>
</tr>
<tr>
<td>Frozen Donor Oocytes</td>
<td>89</td>
<td>47</td>
<td>25</td>
</tr>
</tbody>
</table>

P-539 Wednesday, October 19, 2016

A SYSTEMATIC STUDY USING A LASER REVEALS DIFFERENCES IN THE BLASTOCYST HATCHING RATE AND CLINICAL OUTCOMES BETWEEN TWO DIFFERENT METHODS: CLASSIC ASSISTED HATCHING (AH) AND ZONA THINNING (ZT). L. Herrero, a N. Basile, a J. Garcia Velasco, a N. Costa Borges, a G. Calderon. a IVF laboratory, IVI Madrid, madrid, Spain; bIVI Madrid, Madrid, Spain; cEmbryotools, Barcelona, Spain.

OBJECTIVE: To compare the effect of two laser assisted hatching techniques on the blastocyst formation and hatching rates, and clinical outcomes.

DESIGN: Retrospective observational uncenter study.

MATERIALS AND METHODS: Patients undergoing autologous IVF cycles (n=270) with fresh embryo transfer on day 5 and embryo culture in a time-lapse system were included. Assisted hatching was performed using a laser (Navilase®, OCTAX Microscience GmbH, Germany) on day 3 of development. Patients were divided in 3 groups according to the type of hatching technique applied: Group AH (n=22, 116 embryos): classic assisted hatching technique involving 2 laser pulses that opened a hole in the zona pellucida (ZP). The hole was 1.5 times wider than the thickness of the ZP of each embryo. Group ZT (n=26, 169 embryos): classic assisted hatching technique involving 2 laser pulses that opened a hole in the zona pellucida (ZP). The hole was 1.5 times wider than the thickness of the ZP of each embryo.

RESULTS: No differences were found in patients’ baseline characteristics or in the embryo quality on Day 2, Day 3 and Day 5 of development. Blastocyst formation rate was statistically higher in AH group (73.3%) when compared to ZT (56.5%, p=0.0033) or control (60.5%, p=0.0064). Similarly, blastocyst hatching rate was significantly higher in AH vs. ZT and control groups (38.8%, 7.2% and 6.2% respectively; p<0.0001). With respect to kinetic markers, we found statistical differences in the time to hatching, especially in the BiH-IBSI (4.0) (10.2±4.7 h for AH, 18.2±4.3 h for ZT and 20.2±4.5 h for control; p<0.0001). When analyzing clinical outcomes, implantation rate in AH group (45.7%) showed to be significantly (p=0.0344) higher than ZT group (33.3%). No differences were found when both groups were compared to control (42.2%). Clinical pregnancy rate was significantly higher in AH group vs. control (77.3% vs. 50.2%; p=0.0152) but no difference was found between AH and ZT groups (77.3% vs. 65.2%). Ongoing pregnancy rate was also higher in the study groups: 63.6% in AH group vs. 38.1% in control group; p=0.0078 and 65.2% in ZT group vs. 38.1% in control group; p=0.0201.

CONCLUSIONS: These preliminary results suggest that: 1) Assisted hatching using a systematic laser methodology is safe and does not impair embryo development. 2) Assisted hatching in general, increases the rate of blastocyst hatching and AH appears to be more efficient than ZT. 3) AH may help improving implantation rates, however, results must be confirmed in a larger study.

P-540 Wednesday, October 19, 2016

ENDOMETRIAL CELL GROWTH ON TAILORED AMORPHOUS MULTI-POREOUS SCAFFOLDS: A NOVEL PLATFORM FOR AUTOLOGOUS ENDOMETRIAL CULTURE. L. E. Eisman, a L. I. Barmat, a M. Falk, a T. J. Kowal, a H. Jain, d S. G. Somkuti. bOb/Gyn, Abington Jefferson Health, Abington, PA; cReproductive Endocrinology, Abington Reproductive Medicine, Abington, PA; dBiological Sciences, Lehigh University, Bethlehem, PA; eMaterials Science and Engineering, Lehigh University, Bethlehem, PA.

OBJECTIVE: To evaluate a novel in vitro endometrial cell scaffold substrate.

The use of autologous endometrial coculture (AECC) in vitro fertilization improves embryo quality and pregnancy outcome by embryo exposure to cytokines and growth factors secreted by endometrial cells 1. Present AECC techniques results in endometrial cells losing their polarity when grown on plastic tissue culture. AECC using polarized endometrial cells may more closely mimic the in vivo environment and result in enhanced embryo development.

Tailored amorphous multi-porous (TAMP) bioactive sterilizable 30% CaO-70%SiO2 glass scaffolds contain interconnected nano- and macro-pores that facilitate cell adhesion, in-growth, and fluid exchange and reacquisition of three-dimensionality. The purpose of this study is to determine if endometrial cells, when grown on TAMPs, will exhibit polarity.

DESIGN: Basic science research.

MATERIALS AND METHODS: Tissue was obtained by random Pipelle endometrial biopsy from infertility patients (age greater than 21 years), with no history of uterine abnormalities or spontaneous abortion. Tissue was digested using collagenase, and cells were plated using previously published protocol 1. Upon reaching confluence, cells were cryopreserved for future use. Sterile TAMP scaffolds were pre-incubated in phosphate-buffered saline. Scaffolds and coverslips were placed in wells and each seeded with 500,000 cells that were allowed to grow to confluence. Cellular morphology was observed by immunofluorescence using Alexa 488-phalloidin to stain filamentous actin (cytoskeleton) and 4',6-diamidino-2-phenylindole (DAPI) to detect chromatin (nuclei). Primary-secondary antibody pairing was used to detect: acetylated tubulin (cilia), as well as tubulin (centrosomes) andGranulocyte Macrophage-Colony Stimulating Factor production by co-culture versus conventional medium: A randomized trial. Fertil and Steril 1998;70:1109-1113.


References:
   nwaks Z: Interleukin-1 levels in the supernatant of conditioned media of
   embryos grown in autologous endometrial coculture: Correlation with
   embryonic development and outcome for patients with a history of

   SS, Rosenwaks Z: Autologous endometrial coculture in patients with in
   vitro-fertilization (IVF) failure: Correlations of outcome with leukemia

Supported by: Abington Hospital Innovators’ Circle grant.

P-541 Wednesday, October 19, 2016

CENTER SPECIFIC VARIATIONS OF TRIPLOID EMBRYOS. K. Bauckman,a C. Welch,b G. Garrison,c M. G. Garrison,d C. Wagner Coughlin,e B. Kaplan,f T. Lemma,g S. Munne.b aReprogenetics, Highland Park, IL; bReprogenetics, Livingston, NJ; cInstitute for Reproduc-
   tive Medicine and Science at Saint Barnabas, Livingston, NJ; dOb-Gyn, IRMS at Saint Barnabas, Livingston, NJ; eAparent IVF Laboratory, Highland
   Park, IL; fFCI, Highland Park, IL; gMolecular PGD, Reprogenetics, Living-
   ston, NJ.

OBJECTIVE: High Resolution Next Generation Sequencing (hr-NGS) can
   identify certain forms of polyploidy. Here we determine the percentage of em-
   bryos classified as triploids in a large data set, identify inter-center variations
   in triploid rates, and determine the most likely cause of triploid generation.

<table>
<thead>
<tr>
<th>Percent Triplet (rate)</th>
<th>Number of Centers</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-0.5%</td>
<td>4</td>
</tr>
<tr>
<td>0.5-1.11%</td>
<td>7</td>
</tr>
<tr>
<td>1.11-2%</td>
<td>4</td>
</tr>
<tr>
<td>2.5-3.5%</td>
<td>4</td>
</tr>
</tbody>
</table>

RESULTS: 178 embryos were consistent with a triploid diagnosis, giving a
   general triploid rate of 1.11% across all centers. 19 IVF centers were
   included in the center-specific analysis. The triploid rate varies greatly
   between centers, between 0% and 5.43% (table). 4 centers with varying rates
   of triploid presentation self-reported insemination primarily via ICSI.

8 embryos were diagnosed triploid via karyomapping for single gene dis-
   orders (total rate 0.35%). Excess maternal alleles were identified in 7 of those
   embryos, paternal in 1.

CONCLUSIONS: hr-NGS technology allows reliable identification of triploid
   XXXY or XYXY embryos. After the IVF lab has checked for signs of triploid
   zygotes (3PNs or 1PB), more than 1% of blastocysts are identifiably triploid by
   hr-NGS; the data also suggests that polar body retention is the most common
   triploidy escaping QC at the fertility center. We theorize that the true rate of tri-
   ploid blastocysts should be approximately double what is observed, as eggs with
   retained polar bodies can fertilize with X or Y sperm. Based on the inter-center
   variation seen, it is possible that the overall triploid rate can be lowered by
   improvement in QC at the fertility center. This is especially important given
   that 69,XXX embryos cannot be identified via hr-NGS.

P-542 Wednesday, October 19, 2016

ANALYSIS OF VEGF AND FGF IN HUMAN SERUM AND FOLLIC-
   ULAR FLUID AS MARKERS OF IVF CYCLE RESPONSE. A. Kotlyar,a R. Baird,b R. Flyckt. c aOb/Gyn and Women’s Health Institute, The Cleveland Clinic Foundation, Cleveland, OH; bOb/Gyn
   and Women’s Health Institute, Cleveland Clinic Lerner College of Medicine, Cleveland, OH; cCleveland Clinic Beachwood, OH.

OBJECTIVE: To determine if serum and/or follicular fluid VEGF and
   FGF across an IVF cycle are associated with IVF cycle response.

DESIGN: Single-institution prospective cohort.

MATERIALS AND METHODS: 15 patients underwent a standard long
   lupron in-vitro fertilization protocol and had serum samples taken at their
   IVF baseline (BL), on the day of hCG trigger (T), and at the time of their
   post-IVF pregnancy test (PT). Follicular fluid was collected from the first fol-
   licle puncture at the time of egg retrieval. VEGF and FGF were measured us-
   ing ELISA (Quantikine VEGF/FGF ELISA Kit, RND Systems Inc.).

Continuous measures were analyzed using single-sample t-tests, one-way
   analysis of variance (ANOVA), and non-parametric regression. Predictive models were performed using nominal logistic regression modeling. All analyses were performed with JMP v12.2.0 (SAS).

RESULTS: Our cohort had an average age of 32.3±3.7, BMI of 24.2±3.0
   kg/m², with an average AMH value of 3.86±2.58 ng/mL. 10/15 of the pa-
   tients had at least three sequential serum samples for analysis. The clinical
   pregnancy rate was 30.8%. No significant differences were seen in serum
   values of VEGF or FGF between any of the time points by one-way ANOVA.
   Correlation analysis is shown in table 1. Comparisons of serum VEGF and
   FGF values in sequential samples were performed. Only the difference in
   serum FGF from IVF baseline to time of trigger approached significance
   and this was used for logistic regression analysis also outlined in Table 1.

Table 1: Correlation of serum and follicular fluid VEGF and FGF with markers of IVF cycle response.* Nominal logistic regression for FGF Trigger-Initial is also
   included.

<table>
<thead>
<tr>
<th>Marker</th>
<th>BL</th>
<th>T</th>
<th>PT</th>
<th></th>
<th>BL</th>
<th>T</th>
<th>PT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak E2</td>
<td>0.006(0.99)</td>
<td>0.035(0.91)</td>
<td>0.018(0.96)</td>
<td>0.247(0.41)</td>
<td>0.161(0.62)</td>
<td>0.588(0.074)</td>
<td></td>
</tr>
<tr>
<td>Total Number of Eggs</td>
<td>0.047(0.88)</td>
<td>0.151(0.64)</td>
<td>0.383(0.27)</td>
<td>0.193(0.53)</td>
<td>0.459(0.13)</td>
<td>0.201(0.58)</td>
<td></td>
</tr>
<tr>
<td>Total Number of Fertilized Embryos</td>
<td>0.259(0.39)</td>
<td>0.641(0.02)</td>
<td>0.693(0.03)</td>
<td>0.107(0.73)</td>
<td>0.165(0.61)</td>
<td>0.4745(0.17)</td>
<td></td>
</tr>
<tr>
<td>Total Number of Blastocysts</td>
<td>0.082(0.79)</td>
<td>0.462(0.13)</td>
<td>0.716(0.02)</td>
<td>0.241(0.43)</td>
<td>0.273(0.39)</td>
<td>0.414(0.23)</td>
<td></td>
</tr>
<tr>
<td>Follicular Fluid VEGF</td>
<td>-0.280(0.38)</td>
<td>-0.291(0.38)</td>
<td>-0.297(0.40)</td>
<td>-0.636(0.03)</td>
<td>-0.590(0.11)</td>
<td>-0.854(0.002)</td>
<td></td>
</tr>
<tr>
<td>Follicular Fluid FGF</td>
<td>-0.427(0.17)</td>
<td>-0.254(0.45)</td>
<td>-0.030(0.93)</td>
<td>-0.133(0.68)</td>
<td>-0.154(0.65)</td>
<td>-0.370(0.29)</td>
<td></td>
</tr>
</tbody>
</table>

HCG POSITIVE

<table>
<thead>
<tr>
<th>Serum VEGF</th>
<th>Serum FGF</th>
</tr>
</thead>
<tbody>
<tr>
<td>BL</td>
<td>T</td>
</tr>
<tr>
<td>0.0624</td>
<td>0.032*</td>
</tr>
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</table>

CLINICAL PREGNANCY

<table>
<thead>
<tr>
<th>FGF TRIGGER-INITIAL</th>
<th>Odds Ratio</th>
<th>p-value</th>
<th>Odds Ratio</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Logistic Regression</td>
<td>2.22±4.00</td>
<td>6.02±2.33</td>
<td>0.2223</td>
<td></td>
</tr>
<tr>
<td>FGF TRIGGER-INITIAL</td>
<td>1.54</td>
<td>0.032*</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

AUC 0.857

*Correlation expressed as Spearman’s rho coefficient with p-value in parentheses.
CONCLUSIONS: Peak stimulation serum VEGF is associated with increased fertilization and blastocyst formation in a standard long lutenizing hormone IVF cycle. In addition, increasing FGF values during stimulation showed some predictive value for HCG positivity and clinical pregnancy. Further studies could focus on within-subject differences in this growth factor rather than absolute values.

References:

Supported by: Internal

P-543 Wednesday, October 19, 2016


OBJECTIVE: To evaluate the impact of ovarian reserve on early embryo morphokinetic parameters in a time lapse monitoring system.

DESIGN: Retrospective study comparing time lapse monitoring analysis of embryos from three groups of patients according to the ovarian reserve.

MATERIALS AND METHODS: A total of 200 infertile couples including patients with diminished ovarian reserve (Group1; n=41), normal ovarian reserve (Group2; n=62) and polycystic ovary syndrome (Group3; n=97) were included in the study. The exclusion criteria were male factor, endometriosis and recurrent implantation failure. All oocytes were fertilized by intracytoplasmic sperm injection and embryos were incubated in incubatory scope taking images every 20 minutes. The time from insemination to the following events were analyzed: pronuclear fading (tpnf), and cleavage to 2,3,4,5 cells. The intervals between two consecutive cleavages (the duration of second cell cycle (cc2); t5-t2; second synchrony (s2); t5-t2) and optimal ranges for morphokinetic parameters of t5, s2 and cc2 in each group were also evaluated. The results were analyzed using one way anova to compare timings and chi-square test to compare proportion. A p-value of less than 0.05 was considered to be statistically significant.

RESULTS: The morphokinetic parameters including time to tpnf, t2, t3, t4, t5, cc2, s2, cc3, t5-t2 were not statistically different between groups (p>0.05) (Table). Data was analyzed according to different age groups including patients under and over 35 years. The morphokinetic parameters were not statistically different in patients with different age groups (p>0.05). The percentage of optimal embryos according to t5, s2 and cc2 were not statistically different between groups(p>0.05)

CONCLUSIONS: The ovarian reserve status does not seem to affect the embryo morphokinetic parameters.

Supported by: Internal

P-544 Wednesday, October 19, 2016

PARTHENOGENETIC ACTIVATION AND DEVELOPMENTAL POTENTIAL OF MOUSE OO CYTES AFTER INTRACYTOPLASMIC INJECTION (ICSI) OF PVP (POLYVINYL PYRROLIDONE) AND HA (HYALURONIC ACID). S. Roychoudhury, 1, A. Maldonado-Rosas, 2, A. Agarwal, 3, S. Esteves, 4, R. Sharma, 5, S. Gupta, 6, M. Assisi. 7American Center for Reproductive Medicine, Department of Urology, Cleveland Clinic, Cleveland, OH; 8Citrum IVF Clinic, Miguel de Cervantes, Mexico City, Mexico; 9ANDROFERT, Andrology & Human Reproduction Clinic, São Paulo, Brazil; 9Center of Excellence in Genome Medicine Research, KFMRG, Jeddah, Saudi Arabia.

OBJECTIVE: During ICSI, a small amount of PVP medium is unavoidably injected into the oocyte cytoplasm, raising concerns about its safety and possible adverse effects on embryo development. HA-based products are physiologic alternatives to PVP as they are thought to be safer but the literature is mixed in regards to the validity of replacing PVP with HA. The objective of this study was to assess parthenogenetic activation and the developmental competence of mouse oocytes after ICSI of PVP and HA.

DESIGN: In vitro experimental study.

MATERIALS AND METHODS: B6C3F1 frozen-thawed metaphase II mouse oocytes (n =102) were divided into 3 groups: PVP (n = 36); HA (n = 34) and control (n = 32). In the respective groups, 2-3 picoliters of PVP, HA or culture medium were microinjected into the oocyte cytoplasm. Oocytes were then parthenogenetically activated with calcium ionomycin A23187 solution for 15 minutes. Parthenogenetic activation of mouse oocytes was recorded as a percentage of surviving embryos at the two-cell stage 24 hours after microinjection; embryo development was recorded until the blastocyst stage. Chi-square or Fisher exact tests were used to compare the outcome measures.

RESULTS: The parthenogenetic activation and developmental potential of mouse oocytes after ICSI of PVP, HA or culture medium is presented in Table 1. No significant differences were seen among the groups with regard to these outcome measures. Results are expressed as mean and 95% confidence interval. Differences were not significant among the groups at p < 0.05. (Table 1)

CONCLUSIONS: In this experimental study in which sperm factors have been controlled, neither PVP nor HA seemed to adversely affect the developmental competence of parthenogenetically activated mouse oocytes.

Supported by: Internal

**Morphokinetic parameters of the study groups**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group1</th>
<th>Group2</th>
<th>Group3</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>tpnf</td>
<td>25.59 (3.83)</td>
<td>25.13 (3.60)</td>
<td>24.77 (4.31)</td>
<td>0.477</td>
</tr>
<tr>
<td>t2</td>
<td>27.86 (3.96)</td>
<td>27.63 (3.86)</td>
<td>27.29 (4.53)</td>
<td>0.454</td>
</tr>
<tr>
<td>t3</td>
<td>35.98 (5.33)</td>
<td>36.09 (5.03)</td>
<td>35.10 (5.28)</td>
<td>0.765</td>
</tr>
<tr>
<td>t4</td>
<td>38.35 (5.35)</td>
<td>37.94 (5.03)</td>
<td>37.73 (4.84)</td>
<td>0.732</td>
</tr>
<tr>
<td>t5</td>
<td>47.93 (7.42)</td>
<td>46.23 (7.21)</td>
<td>47.08 (7.61)</td>
<td>0.410</td>
</tr>
<tr>
<td>cc2</td>
<td>8.36 (4.91)</td>
<td>8.18 (4.82)</td>
<td>8.08 (4.64)</td>
<td>0.717</td>
</tr>
<tr>
<td>s2</td>
<td>2.73 (3.39)</td>
<td>2.70 (3.30)</td>
<td>2.98 (3.76)</td>
<td>0.265</td>
</tr>
<tr>
<td>cc3</td>
<td>11.91 (4.76)</td>
<td>11.47 (5.26)</td>
<td>11.59 (5.43)</td>
<td>0.750</td>
</tr>
<tr>
<td>t5-t2</td>
<td>20.27 (7.85)</td>
<td>19.66 (8.05)</td>
<td>19.68 (7.48)</td>
<td>0.718</td>
</tr>
</tbody>
</table>

**Parameter**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>PVP (n = 36)</th>
<th>HA (n = 34)</th>
<th>Control (n = 32)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oocyte degeneration rate (%)</td>
<td>33.33; 18.56-50.97 (12/36)</td>
<td>26.47; 12.88-44.36 (9/34)</td>
<td>34.38; 18.57-53.19 (11/32)</td>
</tr>
<tr>
<td>Surviving embryos at 2-cell stage (%)</td>
<td>62.50; 40.59-81.18 (15/24)</td>
<td>68.0; 46.5-85.05 (17/25)</td>
<td>61.90; 46.5-85.05 (13/21)</td>
</tr>
<tr>
<td>Surviving embryos at 4-cell stage (%)</td>
<td>53.33; 26.57-78.73 (8/15)</td>
<td>52.94; 27.81-77.02 (9/17)</td>
<td>53.85; 25.14-80.78 (7/13)</td>
</tr>
<tr>
<td>Surviving embryos at morula stage (%)</td>
<td>53.33; 26.57-78.73 (8/15)</td>
<td>52.94; 27.81-77.02 (9/17)</td>
<td>46.15; 19.22-74.86 (6/13)</td>
</tr>
<tr>
<td>Blastocyst development rate (%)</td>
<td>33.33; 11.82-61.62 (5/15)</td>
<td>35.29; 14.21-61.67 (6/17)</td>
<td>38.46; 13.86-68.42 (5/13)</td>
</tr>
</tbody>
</table>
OBJECTIVE: To investigate trends and factors in ICSI utilization among fertility clinics in the United States.

DESIGN: Retrospective data analysis of CDC annual ART report 2000-2013 (latest published data)

MATERIALS AND METHODS: Fresh non-donor cycles were analyzed. Longitudinal trends of ICSI practice, and effects of patient volume, geographic region, male factor diagnosis, and insurance coverage mandates on utilization, were compared. T-tests and Pearson’s correlation coefficients were used to analyze all trends and differences in proportions between categories.

RESULTS: The number of fresh non-donor ICSI cycles continued to increase from 33,378 in 2000 to 67,693 in 2012, followed by a slight decrease to 64,425 in 2013. The percent of cycles using ICSI in all fertility centers increased from average 44.8% in 2000 to average 72.3% in 2013 despite the fluctuation of total cycles and no significant change in the prevalence of male factor related infertility (35.0-38.2%). Nationwide inter-clinic data showed no significant correlation between ICSI utilization and male factor related diagnosis in general. In recent years, programs with smaller patient volume consistently showed a higher percentage of ICSI compared to larger programs (p < .05). This is in contrast to 2000 data which showed larger clinics performing a higher percentage of ICSI cycles (p < .05). Overall pregnancy, implantation, and live birth rates were similar between programs with low and high ICSI utilization rates. Differences among geographic regions were found with local trends of utilization gradually shifting throughout the years, without change in the incidence of male factor diagnosis rates. Many programs in states with insurance mandates showed higher ICSI rates, but generally a lower incidence of male factor infertility diagnosis. CONCLUSIONS: ICSI utilization rates in the United States have increased from average 44.8% in 2000 to average 72.3% in 2013 despite the fluctuation of total cycles and no significant change in the prevalence of male factor related infertility (35.0-38.2%). Nationwide inter-clinic data showed no significant correlation between ICSI utilization and male factor related diagnosis in general. In recent years, programs with smaller patient volume consistently showed a higher percentage of ICSI compared to larger programs (p < .05). This is in contrast to 2000 data which showed larger clinics performing a higher percentage of ICSI cycles (p < .05). Overall pregnancy, implantation, and live birth rates were similar between programs with low and high ICSI utilization rates. Differences among geographic regions were found with local trends of utilization gradually shifting throughout the years, without change in the incidence of male factor diagnosis rates. Many programs in states with insurance mandates showed higher ICSI rates, but generally a lower incidence of male factor infertility diagnosis. CONCLUSIONS: ICSI utilization rates in the United States have continued to increase, with significant variation based on factors including male factor diagnosis, clinic sizes and geographic regions. However, the increase in ICSI use did not correlate to clinical outcomes. These findings warrant further investigations regarding the appropriate use of ICSI for non-male factor infertility.

ART OUTCOME PREDICTORS - LABORATORY

P-546 Wednesday, October 19, 2016

EEVA™ PREGNANCY PILOT STUDY: A RANDOMIZED CONTROLLED TRIAL OF SINGLE EMBRYO TRANSFER (SET) ON DAY 3 OR DAY 5 WITH OR WITHOUT TIME-LAPSE IMAGING (TLI) SELECTION. D. J. Kaster, C. L. Bornmann, S. A. Missmer, L. V. Farland, E. S. Ginsburg, C. Racowsky, Obstetrics, Gynecology & Reproductive Biology, Brigham & Women’s Hospital, Harvard Medical School, Boston, MA; Epidemiology, Harvard Chan School, Boston, MA.

OBJECTIVE: TLI is increasingly used for embryo selection, despite relatively sparse high-quality evidence supporting its utility. This study was designed to assess the value of the EEVA™ test [times in the 2-cell (P2) and 3-cell (P3) stages] for embryo selection when used as an adjunct to conventional morphology (CM) for day 3 or day 5 transfer.

DESIGN: Randomized controlled trial.

MATERIALS AND METHODS: Patients with a planned fresh SET < 3 prior retrievals, and ≥ 4 zygotes were blocked on age (<35, 35-37, 38-40 y) and randomized by closed envelope immediately after the fertilization check to one of 3 arms: Arm 1: Day 3 with EEVA™+CM; Arm 2: Day 5 with EEVA™+CM; Arm 3: Day 5 with CM alone. Other TLI parameters used for selection included abnormal and direct cleavage. Exclusion criteria were use of donor egg, gestational carrier or PGD/PGS, and presence of an uninterrupted hydrosalpinx or history of intrauterine adhesions. Embryos in all 3 arms were imaged continuously by EEVA™ version 2.2 in the same type of incubator. Intention-to-treat and as-treated analyses of the primary endpoint (clinical pregnancy rate [CPR] at 7 weeks) and secondary endpoint (ongoing pregnancy rate [OPR] at 12 weeks) were performed. Multivariate regression adjusted for age, body mass index (BMI), and number of embryos on day 1. Sensitivity, specificity, PPV, and NPV of the EEVA™ test (High/Medium vs. Low) for predicting ongoing pregnancy at 12 weeks were calculated.

RESULTS: Of 217 patients consented, 163 were randomized. Demographic and cycle characteristics were similar among the three study arms. Neither CPR nor OPR differed significantly between randomization arms in both intention-to-treat and as-treated analyses; notably, selection of a day 5 embryo with only CM resulted in the highest pregnancy rates (Table). While the sensitivity of EEVA™ High/Medium was the same on day 3 vs. day 5 (95.2% vs. 95.4%), the specificity (5.9% vs. 17.0%), PPV (38.5% vs. 46.6%) and NPV (66.7% vs. 83.3%) were all lower for day 3. CONCLUSIONS: Addition of the EEVA™ test to CM did not improve clinical outcomes compared with CM alone, despite a 95% sensitivity of a High/Medium embryo resulting in ongoing pregnancy. This study was not powered to detect statistical difference, though the observed trend favoring selection on day 5 with CM alone challenges the use of P2 and P3 for time-lapse selection. These findings do not preclude the utility of P2 and P3 for embryo selection when used in conjunction with other time-lapse markers.

Supported by: Progyny, Inc.

P-547 Wednesday, October 19, 2016

METABOLOMIC PROFILE OF FOLLICULAR FLUID AS A PREDICTIVE TOOL FOR PREGNANCY OUTCOMES. D. A. Montani, J. Camillo, A. Rodrigues-Oliveira, D. Oliveira-Silva, E. G. Lo Turco, R. Faietta. Department of Surgery, Division of Urology, Human Reproduction Sector, Sao Paulo Federal University, Sao Paulo, Brazil; Sao Paulo Federal University, Diadema, Brazil; Department of Surgery, Division of Urology, Human, Sao Paulo Federal University, Sao Paulo, Brazil.

OBJECTIVE: This study evaluated the metabolic profile of follicular fluid from women who underwent in vitro fertilization treatments as a potential predictive approach for pregnancy.

DESIGN: Prospective study including follicular fluid samples from 91 women.

MATERIALS AND METHODS: According to the β-hCG levels measured 14 days after the embryo transfer the samples were divided...
into two groups: (i) pregnant patients (n=33) and (ii) non-pregnant patients (n=58). The metabolic extraction was performed by Bligh-Dyer protocol. The following analyses were performed on a micotOF-QII mass spectrometer equipped with an Apollo II electrospray ion source (Bruker, Billerica, USA) and coupled to a UFLC Prominence binary liquid chromatograph (Shimadzu, Kyoto, Japan). The data were acquired with the ESI source set as follows: nebulizer gas at 2.0 bar, dry gas at 8.0 L/min, dry temperature at 180°C and voltage at 4.5 kV. The mass/charge ratios of the metabolites were scanned (m/z 50-1200 Da) in positive and negative modes. The spectral data of m/z and intensity were processed and statistically analyzed using MetaboAnalysis 3.0 software. The ROC Curve was built based on biomarkers potentials, which were selected by VIP scores through PLS-DA.

RESULTS: Among 30 potential biomarkers, 26 metabolites were identified using Metlin database. These metabolites both from positive (AUC=0.937) and negative (AUC=0.713) mode were associated with enrichment analysis and pathway topology analysis of Glyoxylate, Dicarboxylate, Purine, Pyruvate, Galactose and Vitamin B6 metabolism, Citrate cycle (TCA cycle), Fatty acid biosynthesis and Steroid hormone biosynthesis.

CONCLUSIONS: In conclusion this study showed that this particular predictive model can possibly ensure that a patient undergoing an Assisted Reproduction Technology (ART) treatment can achieve 93.7% chances of pregnancy. Even though most studies of ART combine the knowledge of oocytes, sperm and endometrial receptivity, this study demonstrated that the oocyte alone, plays a crucial role for the establishment of pregnancy. We hope that our findings can stimulate further investigations for the development of prognostic tests using blood plasma of patients.

Supported by: Funding was received by the Coordenação de Aperfeiçoamento de Pessoal de Ensino Superior, Brazil.

P-548 Wednesday, October 19, 2016


OBJECTIVE: The Eeva Test’s TLM software automatically analyzes time-lapse images and generates a trinary result (high, medium, low) that prognosticates which embryos on day 3 are more likely to blastulate. The goal of the present analysis is to determine if this scoring system is associated with ploidy status and/or delivery of euploid embryos.

DESIGN: Prospective, blinded observational.

P-549 Wednesday, October 19, 2016

THE EFFECT OF BLASTOCYST MORPHOLOGY AND QUANTITATIVE PARAMETERS OF EMBRYO ON THE CLINICAL OUTCOMES. S. Saribal, G. Kuspinar, Y. Yalim, G. Uncu, B. Ata, B. A.V.C.T. Department of Histology and Embryology, Department of Gynecology and Obstetric IVF Center, Uludag University Medical Faculty, Bursa, Turkey; Department of History and Embryology, Uludag University Medical Faculty, Bursa, Turkey; Department of Gynecology and Obstetric IVF Center, Uludag University Medical Faculty, Bursa, Turkey; Department of Gynecology and Obstetric, Koc University School of Medicine, Istanbul, Turkey.

OBJECTIVE: Determination of the relevance of the size of a blastocyst and inner cell mass (ICM) and the other quantitative blastocysts parameters as predictor of its potential to survive following implantation and lead to a clinical pregnancy.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: 104 women (166 embryos) who had no implantation (hCG < 5IU/L) following single or double blastocyst transfers (Group I), 22 women (22 embryos) who had a biochemical pregnancy (hCG > 10IU/L) following a single blastocyst transfer (Group II), and 64 women (88 embryos) who had clinical pregnancies (heart beat in the 6th week) with 100% implantation rate following single or double blastocyst transfers (Group III) were matched for age and IVF cycle rank. PC running...
RESULTS: Blastocysts quality score, trophoeotoderm cell number, perimeter and area of blastocyst, blastocyst excluding zona pellucida (ZP) and blastocoele were significantly different between the three groups. When the groups were compared with each other, only blastocyst quality score was significantly different between Groups I and II. However, all parameters were significantly different between Groups I and III, but similar in Groups II and III (Table I).

CONCLUSIONS: The morphology of the blastocyst as well as the cell number of the trophoeotoderm are related with the implantation potential of an expanded blastocyst. Prior studies reported that a round shaped ICM with a longer diameter could be associated with higher chances of implantation and occurrence of clinical pregnancy with a heartbeat. Our observations suggest that a larger blastocyst with better morphology is more likely to lead to a clinical pregnancy but the size and roundness index of ICM not effective.

References:

P-551 Wednesday, October 19, 2016

EFFECTICITY OF ASSISTED HATCHING BASED ON EMBRYO QUALITY IN IVF CYCLES WITH FRESH TRANSFERS. T. A. Chang, a J. F. Knudson, b Y. T. Su, b E. S. Jacoby, a R. D. Robinson, a R. S. Schenken, a Obstetrics and Gynecology, University of Texas Health Science Center, San Antonio, TX, 3Research Consultant, Helotes, TX.

OBJECTIVE: To investigate the effect of assisted hatching (AH) on embryos while controlling for maternal age, day of transfer, and embryo quality. DESIGN: Retrospective data analysis of Society of Assisted Reproductive Technologies Clinical Outcomes Reporting System (SART CORS) datasets 2009-2013 (latest published data).

MATERIALS AND METHODS: The latest five years of SART CORS data, 2009-2013, were used to study the effect of assisted hatching (AH) in the United States. Autologous IVF cycles with fresh transfers excluding PGT, oocyte banking, and embryo banking, were selected for analysis. Only cycles in which all transferred embryos were of similar quality and all or none (AH-all vs. AH-none) of the transferred embryos underwent AH were included to assess the effect of AH based on embryo quality. Pregnancy rates were assessed based on embryo quality (good, fair, and poor), maternal age according to SART Clinical Summary Report format (<35, 35-37, 38-40, 41-42, and >42) and stage of embryo transfer (day 3, day 5 and day 6). Chi-square test was applied with p < .05 considered significant.

RESULTS: Pregnancy rates between all embryos undergoing AH and those without did not differ significantly. Good quality embryos receiving AH had significantly lower pregnancy rates (p < .05) in all maternal age groups having day 3 and 5 transfers when compared with those without AH. In fair and poor quality embryos, AH had mixed effect on pregnancy rates in different age groups having day 3 and 5 transfers. In addition, AH did result in better outcomes in all age groups having day 6 transfers.

CONCLUSIONS: Our findings indicate that AH of fair and poor quality embryos has variable effects on pregnancy rates in different age groups; whereas AH of good quality embryos resulted in lower pregnancy rates in all age groups. These findings suggest that assisted hatching of good quality embryos adversely affects pregnancy rates.

OBJECTIVE: To determine the influence of follicular size (large and small) in synchronous and asynchronous follicle development during stimulation on morphokinetic parameters of embryo development.

RESULTS: Embryos developing from small follicles were found to develop 1.8h faster than those from large follicles (p=0.0036). Next we looked at the timings of embryos with known implantation data (KID). For implanting blastocysts (KID positive) a statistically significant difference was observed for Tb values were compared, blastocysts from small follicles developed 1.8h faster than those from large follicles (p=0.003). Implantation rate and pregnancy rates (IR and PR) for Group 1 were 81.8% (9/11). All pregnancies were singleton. IR and PR for Group 2 were 49.2% (95/193) and 47.7% (92/193) respectively. Group 2 had three sets of monzygotic twins (MZT). While both IR and PR were better in the ZP-free group, only PR reached statistical difference.

CONCLUSIONS: 1. ZP-free euploid blastocysts resulted in a significantly higher pregnancy rate compared to ZP-intact blastocysts.

2. These findings, especially if confirmed by larger series, may indicate that the ZP’s role in production is completed when the embryo reaches the blastocyst stage.

3. Our study raises the question of whether deliberate removal of the ZP can potentially increase pregnancy rates.

P-555 Wednesday, October 19, 2016

IMPLANTATION RATE AND PREGNANCY RATE IN ZONA FREE GROUP VS. ZONA INTACT GROUP

<table>
<thead>
<tr>
<th>Zona Free</th>
<th>Zona-Intact</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1 (n=11)</td>
<td>Group 2 (n=193)</td>
</tr>
<tr>
<td>Implantation Rate</td>
<td>Pregnancy Rate</td>
</tr>
<tr>
<td>81.8% (9/11)</td>
<td>81.8% (9/11)</td>
</tr>
<tr>
<td>49.2% (95/193)</td>
<td>47.7% (92/193)</td>
</tr>
</tbody>
</table>

P-554 Wednesday, October 19, 2016

CHANGES IN SERUM INHIBIN B LEVELS THROUGHOUT CONTROLLED OVARIAN HYPERSTIMULATION, RATHER THAN INITIAL CONCENTRATIONS, ARE BETTER PREDICTORS OF OVARIAN RESPONSE. E. Haikin Herzberger, A. Hershko Klement, S. Mazaki-Tovi, H. Kanety, R. Hemi, N. Zada, A. Shulman, A. Wiser, "IVF Unit, Department of Obstetrics and Gynecology, Meir Medical Center, Kfar-Saba, Israel; Sheba Medical Center, Ramat-Gan, Israel; "Institute of Endocrinology, Sheba Medical Center, Tel-Hashomer, Sackler School of Medicine, Ramat-Gan, Israel; "Institute of Endocrinology, Sheba Medical Center, Tel-Hashomer, Sackler School of Medicine, Ramat-Gan, Israel.

OBJECTIVE: To determine whether alternations of inhibin B and anti-mullerian hormone (AMH) throughout controlled ovarian hyperstimulation (COH) are associated with in vitro fertilization (IVF) outcomes.

DESIGN: This was a longitudinal study conducted at a single tertiary care center between April 2014 and August 2014.

MATERIALS AND METHODS: Patients undergoing IVF, ages 18-42 years, were enrolled. Inhibin B and AMH levels were measured before ovarian stimulation (lowest estradiol level) and on hCG administration day (highest estradiol level). The difference in serum levels between these two points was calculated for both inhibin B and AMH. Spearman correlations were calculated for delta serum inhibin B and AMH levels and cycle outcomes.

RESULTS: A total of 27 patients were included. Serum inhibin B levels were significantly higher on day of hCG administration compared to starting point (544.64 pg/ml [IQR 272.59-1000.00 pg/ml] vs. 65.09 pg/ml [IQR 20.67-31.48 pg/ml], p<0.0001, respectively). No correlation was found be-
tween basal inhibin B and the number of oocytes retrieved (r = 0.29, P = 0.14). However, the increase in inhibin B was strongly correlated with the number of oocytes (r = 0.76, P < 0.001). Serum AMH levels were significantly lower on day of hCG administration compared to the starting point (1.73 ng/mL [IQR 0.53-4.94 ng/mL] vs. 2.54 ng/mL [IQR 1.05-5.38 ng/mL]; P < 0.001, respectively). Basal AMH levels were positively correlated with the number of oocytes retrieved (r = 0.72, P < 0.001). Unlike inhibin B results, a weaker positive correlation was found between the absolute degree of AMH change and the number of oocytes retrieved (r = 0.57, P = 0.02).

CONCLUSIONS: The study cohort demonstrated that serum inhibin B levels increase and serum AMH levels decrease during IVF treatment. The degrees of changes in inhibin B levels were better predictors of ovarian response than were basal levels.

P-555 Wednesday, October 19, 2016


OBJECTIVE: The purpose of this study was to assess the beneficial effect of fragment removal on the subsequent development and pregnancy outcome of the fragmented human day 2 embryos.

DESIGN: The study included 96 patients who underwent day 3 ET program from March 2015 to October 2015. The patients were divided into two groups; Fragment removal (FR) group (n=48) and control group (n=48). There were no differences between the FR and the control groups in the number of blastomeres (4.0±1.3 vs. 4.0±1.3) and the morphological grade of embryos (3.1±0.6 vs. 3.1±0.5) before fragment removal on day 2.

MATERIALS AND METHODS: Fragment removal was performed on the grade 3 embryos (10% < degree of fragmentation <25%) of the FR group. We performed assisted hatching with laser and fragments removal on day 2. Before fragment removal, the fragmented embryos were incubated in GPGD medium (Vitrolife) under paraffin oil (Ovolit, Vitrolife) for 30 minutes. Microsurgical fragment removal was performed with handheld suction micro-pipet with outer diameter of 30μm.

RESULTS: There were no differences in the characteristics of the patients between the FR and the control groups; mean age of the patients (36.2±4.3 vs. 36.2±4.1), endometrial thickness (10.4±2.5 vs. 10.0±2.0), AMH levels (4.4±4.5 vs. 4.2±2.9), and mean number of retrieved oocytes (8.7±5.7 vs. 9.2±4.8). No differences were also observed between the two groups in fertilization rate (76.0±17 vs. 71.0±22%) and mean number of ET (2.0±0.4 vs. 2.0±0.3). After fragment removal and 24 h culture in vitro, although the number of blastomeres (7.0±1.6 vs. 6.8±1.6) was comparable in the two groups, embryo morphological grade (2.9±0.8) of the FR group was significantly improved compared to that (3.2±0.5; p < 0.01) of the control group. Clinical pregnancy (43.8%) and implantation rates (28.0%) in the FR group were significantly higher than the rates (23.0 and 14.7%, respectively, P<0.05) of the control group.

CONCLUSIONS: Early fragment removal on day 2 significantly improved the subsequent development and pregnancy outcomes of the fragmented embryos. These results suggest that early fragment removal effectively prevents secondary degeneration of fragmented embryos by eliminating the release of toxic substances as soon as possible.

References:

Supported by: Mamanpapa&baby OB/GY

P-556 Wednesday, October 19, 2016

DIFFERENTIAL EXPRESSION OF TRP CHANNELS MODULATE ART OUTCOME. L. Samanta, N. Swain, S. Kar. "Zoolology, Ravenshaw University, Cuttack, India; Redox Biology Lab, Department of Zoology, Ravenshaw University, Cuttack, India; Consultant Gynaecologist, Kar Clinic & Hospital Pvt. Ltd., Bhubaneswar, India.

OBJECTIVE: Extensive research has led to the identification of several calcium channels as as mediators of sperm function. Sperm functions like motility, capacitation and acrosomal reaction require decoding a variety of signals in the form of intracellular Ca2+ changes. Transient receptor potential (TRP) protein super family are a diverse group of calcium-permeable cation channels expressed in mammalian cells. The presence and functional importance of TRP channels in the sperm of worms and mammals suggest that TRP channels are broadly utilized across the phyla and might help in constituting an evolutionarily conserved biological pathway, including human. They are reported to act as transducers of thermal, chemical, and mechanical signals and thereby regulating intracellular Calcium ion (Ca2+) in sperm cells. They are also modulated by reactive oxygen species.

DESIGN: A prospective cohort study was undertaken to correlate the differential expression profile of TRP channel to ART outcome.

MATERIALS AND METHODS: Actively motile spermatozoa were collected from patients undergoing ICSI (n=16) by density gradient separation. TRP channel expression was monitored by indirect immunofluorescence and FACS. Out of the six super-families of TRP channels, members of four superfamilies documented to be thermosensitive as well as associated with oxidative stress (OS) were targeted for expression studies : TRPA1 (ankyrin), TRPM8 (melastatin) and TRPV 1 and V4 (vanilloid). Further the fertilization rate, cleavage rate, number of Grade 1 embryos formed, serum beta-HCG level and live birth rate were recorded.

RESULTS: All semen samples used were normozoospermic. Of the 16 patients recruited 4 get pregnant and have live birth. There was no report of miscarriage. Expression profile of TRPM8 was lower in non-pregnant patients. TRPV1 expression was more in the acrosomal region in pregnant group while that in non-pregnant group is down the equatorial region and neck piece. TRPA1 showed an increasing trend while a decline in TRPV1 was noticed in non-pregnant group though not statistically significant (may be due smaller sample size).

CONCLUSIONS: The results surmise that a detailed evaluation of TRP channel expression in spermatozoa of patients undergoing ART will help us in identifying good quality sperms for insemination and increase in pregnancy outcome.

P-555 Wednesday, October 19, 2016

CLINICAL PERFORMANCE OF DIAFERT® TO DETERMINE GRANULOCYTE COLONY-STIMULATING FACTOR (G-CSF) CONCENTRATION IN FOLLICULAR FLUID (FF) AS A PREDICTOR OF IMPLANTATION DURING IN VITRO FERTILIZATION (IVF). J. Foidart, H. Tournaye, T. D’Hooghe, G. Verheyen, K. Reape, F. Devreker, S. Perrier d’Hauterive, F. Somers. "CPMA-Université de Liège, CHR Citadelle, Liège, Belgium; Université Libre de Bruxelles, Brussels, Belgium; Leuven University Hospital (during study), Leuven, Belgium; Allergan plc (during study), Jersey City, NJ; Université Libre de Bruxelles, Brussels, Belgium; Allergan plc, Jersey City, NJ.

OBJECTIVE: To assess the clinical performance of Diafert to determine FF G-CSF concentration as a predictor of implantation

DESIGN: Prospective, non-interventional, observational study (Prospect 1)

MATERIALS AND METHODS: Women 18-36 years of age with good response to ovarian stimulation undergoing first and/or second IVF attempt and eligible for Day 3 (D3) or D5 single embryo transfer (SET) were included. FF was individually collected and analyzed for G-CSF concentration using the Diafert immunoassay kit. Embryo morphology was evaluated using established criteria. Implantation was confirmed by visualization, using transvaginal ultrasound, of the number of gestational sacs containing a fetus with cardiac activity at 12 weeks of gestation (10 weeks after SET). As a non-interventional, diagnostic study, no safety data were collected.

RESULTS: Among 465 subjects enrolled, 396 SETs were performed (288 D3 and 108 D5). Implantation rates (ROC) curve analysis, G-CSF thresholds were identified (17.5 and 48.0 pg/mL). Implantation probabilities were calculated for all morphology categories and functional importance of TRP channels in the sperm of worms and mammals suggest that TRP channels are broadly utilized across the phyla and functional importance of TRP channels in the sperm of worms and mammals suggest that TRP channels are broadly utilized across the phyla.
University of North Carolina, Chapel Hill, NC; UNC Fertility, Raleigh, NC; University of Pennsylvania, Philadelphia, PA.

OBJECTIVE: To determine if progesterone level (P4) at time of trigger impacts oocyte maturity, fertilization, embryo development rate, and clinical pregnancy rate after IVF.

DESIGN: Retrospective study.

MATERIALS AND METHODS: Women ages 21-43 years, contributed 443 autologous fresh IVF cycles from 2013-2015. Oocyte maturity, fertilization, and embryo development rate (number of normally fertilized embryos which progressed to day 5 and were suitable for transfer or cryopreservation) were all determined by standard embryology protocols at our institution. Clinical pregnancy was an ultrasound confirmed intrauterine gestation with cardiac activity. P4 levels (ng/mL) on the day of trigger were analyzed on an Immulite 1000, with a limit of detection of 0.2 ng/mL, and categorized into quartiles (<21.4, 21.4-27.5, 27.5-33.5, >33.5) using a Bayesian beta-binomial model.

RESULTS: 44% of women achieved clinical pregnancy. Mean P4 level was 1.17 ng/mL. There was no difference in rates of oocyte maturity, fertilization, or embryo development between highest and lowest quartiles of P4 (29.9% versus 32.3%, p = 0.13; 64% versus 69%, p = 0.08; and 38% versus 37%, p = 0.85, respectively). The odds of clinical pregnancy decreased with increasing P4, as women in the highest quartile of P4 had less than half the odds of pregnancy as women in the lowest quartile, even in the adjusted model (Table 1).

CONCLUSIONS: Although there was no association seen between P4 on day of trigger and the rates of oocyte maturity, fertilization, or embryo development, a higher P4 level was associated with decreased odds of clinical pregnancy. Thus, the negative impact on pregnancy rates seen with high P4 is likely due to etiologies other than oocyte maturity or function.

PROCEDURES AND TECHNIQUES - LABORATORY: ART

OB/GYN, University of Hawaii School of Medicine, Honolulu, HI; Office of Biostatistics and Quantitative Health Science, University of Hawaii School of Medicine, Honolulu, HI.

OBJECTIVE: The purpose of the study was to describe and to compare the morphokinetics of blastocyst expansion in double embryo transfers resulting in either sustained singleton or twin pregnancies.

DESIGN: A retrospective descriptive study designed to control for confounding factors of endometrial receptivity and/or embryo transfer difficulties.

MATERIALS AND METHODS: This study compared 64 patients (32 pairs of blastocysts) having a 100% implantation rate (IR) with 52 patients (26 pairs) having a 50% IR defined as having either two or one heartbeat at 7 weeks gestation. After ICSI, all embryos were cultured continuously in an Embryoscope until D5 transfer. Hourly cross sectional area (CSA)
measurements were retrospectively measured over 12 hours beginning from the time of blastocyst formation (Tb). Embryo pairs were further stratified into “fast” or “slow” subgroups as follows: “100% IR fast”, “100% IR slow”, “50% IR fast”, and “50% IR slow”. Their expansion rates were compared at 4, 8, and 12 hours from Tb (Kenny et al., 2006).

RESULTS: Slope comparisons between the four groups over the 3 time intervals resulted in several patterns having potential clinical implications: 1) The rank order of slope values (from highest to lowest) was consistent at all 3 time intervals: “100% IR fast”, “50% IR fast”, “100% IR slow”, and “50% IR slow”. 2) Comparisons of the stratified “fast” and “slow” embryos within either the “100% IR” or the “50% IR” groups always showed significant expansion slope differences beginning at 6 hours (P < 0.01). Comparisons between the “fast” and “slow” embryos from either the “100% IR” or the “50% IR” group showed a significant expansion slope difference between only the “100% IR fast” and “50% IR slow” (P < 0.002). 4) The expansion slope curve for the “50% IR slow” group was always outside of the range defined by the “100% fast” and “100% slow” groups; in contrast, that curve for the “50% IR fast” group was always inside of that range. These results were used to define a range of average expansion rates for implanting donor egg blastocysts from the 100% IR group (e.g. 822-1036 μm/h at 8 hours). The “fast” expansion embryo rates within the 50% IR group were always within this range (899 μm/h) while the “slow” embryo rates in this 50% IR group were outside of that range (657 μm/h).

CONCLUSIONS: These results first describe blastocyst expansion morphokinetics over the first 12 hours for egg donor blastocysts and compared rates in implantations that form one versus two sustained ongoing heartbeats. In pregnancies with a 50% implantation rate, trailing embryos expanded at a rate outside that of those having positive implantation, while their leading embryos expanded within the range having positive implantation. The results are consistent with an optimal expansion rate range and time to choose a single embryo for transfer.

References:

Supported by: This work was supported by the Division of Research of Department of Obstetrics and Gynecology of the John A. Burns School of Medicine and an intramural grant U54MD007584.
disease risk visibility. For example, DHCR7-related disease risk was observed with one well known pathogenic variant (c.964-1G>C) and a second previously uncharacterized variant (p.R362H). At-risk pairs for Niemann-Pick disease (SPMD1), Charcot-Marie-Tooth neuropathy type 4F (PRX), and a second Smith-Lemli-Opitz syndrome (DHCR7) case were all uniquely identified through VPA with two previously uncharacterized variants.

CONCLUSIONS: Donors and recipients carry a wide range of known and novel variants that cause a spectrum of damage to the underlying gene. VPA is an effective methodology for expanding visibility into recessive disease risk for recipients of donor gametes. We suggest that consideration be given to augmenting or replacing existing carrier screening methods with joint comprehensive analysis of both donor and recipient variants.

Supported by: GenePeeks, Inc.

P-562 Wednesday, October 19, 2016

KINETICS OF THE EARLY IN VITRO DEVELOPMENT OF HUMAN HAPLOID ANDROGENOTES. L. Escrich, a N. Grau, a Y. Galiana, a M. F. Insua, a J. Remohi Gimenez, a M. Escriba, a IVF Laboratory, University Institute IVI Valencia, Valencia, Spain; bIVI Valencia, Valencia, Spain; cIVI- Fundation, Valencia, Spain.

OBJECTIVE: To describe the early development of human haploid androgonotes and to compare it to that of correctly fertilized (control) embryos.

DESIGN: Kinetic description of the early in vitro development of 16 haploid androgonotes compared with that of 20 control embryos.

MATERIALS AND METHODS: Androgonotes were produced by in vitro fertilization of enucleated MI oocytes. Enucleation was performed using PolScope technology. Once the spindle had been identified, it was removed by aspiration using an ICSI pipette. Ooplasm were then microinjected according to the ICSI procedure. Data from control embryos were retrospectively collected from infertile couples enrolled in our ovum donation program. In all cases, oocytes were cryopreserved by vitrification. Androgonotes and control embryos were cultured in a time-lapse incubator for 3 days. The following kinetic variables were evaluated: timing of cleavage from the 2–8-cell stage, and duration of the second (cc2) and third cell cycles (cc3).

RESULTS: Timings of cleavage to the 2–3-, 4–5-, 6–7-, and 8-cell stage were statistically comparable in androgonotes and control embryos. In relation to indirect variables, cc2 was comparable in both groups (averaged cc2: 11.9±0.2h; 95CI: 11.5-12.3h), while cc3 lasted longer in control embryos than in androgonotes (15.5±4.5 hrs vs. 17.7±3.6hrs; p<0.05).

CONCLUSIONS: The kinetics of haploid androgonotes are comparable to those of correctly fertilized biparental embryos during the second cell cycle, but not the third cell cycle.

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P-563 Wednesday, October 19, 2016

OPTIMIZATION OF ESTRADIOL ASSAY FOR USE DURING OVARIAN STIMULATION FOR IN VITRO FERTILIZATION. M. Peavey, a N. Akbas, a W. E. Gibbons, a S. Devaraj, a P. W. Zarutskie, a Reproductive Endocrinology and Infertility, Department of Ob/Gyn, Baylor College of Medicine, Houston, TX; aPathology and Immunology, Texas Children’s Hospital, Houston, TX.

OBJECTIVE: Measurement of estradiol is an integral component for management of ovarian stimulation for in vitro fertilization (IVF). Automated immunoassays commonly used in assisted reproductive clinics offer fast assay times and high throughput, but sacrifice sensitivity and specificity. The aim of this study is to compare estradiol values obtained using the current platform and another commercially available platform compared to the gold standard, tandem mass spectrometry, in patients undergoing ovarian stimulation for IVF in an effort to optimize the utility of estradiol assays in this clinical setting.

DESIGN: Prospective collection and analysis of serum estradiol levels from patients undergoing ovarian stimulation for IVF.

MATERIALS AND METHODS: Serum samples for estradiol measurement were prospectively collected and analyzed using the current platform (ADVIA Centaur® CP Immunoassay), as well as the Abbott Architect i1000® and ABSciex 5500 LC/MS/MS mass spectrometry systems, in close collaboration with the clinical pathology team. Samples analyzed on ADVIA Centaur® CP system are currently being used for clinical decision making. Precision studies and comparison studies were performed for Centaur and the new Architect systems, using the LC/MS/MS as a gold standard.

RESULTS: Comparison studies of estradiol values between ADVIA Centaur® CP and Abbott Architect i1000® systems revealed the ADVIA Centaur® CP had an overall, significant positive bias of 20%, while the Abbott Architect i1000® had a small and non-significant, negative bias of 0.3%, when compared to gold standard of LC/MS/MS. The greater bias of ADVIA Centaur® CP was similar in both lower estradiol ranges (<1000 pg/mL) and higher (>1000 pg/mL) values.

CONCLUSIONS: Our work demonstrates that with collaborative, prospective collection and comparison across several platforms, optimization of the clinical estradiol assay can be achieved. Clinicians should be aware of possible variations in estradiol levels in clinical practice and understand mechanisms to discover and correct estradiol value variances, via collaboration with the laboratory scientists using the assay platforms. We conclude that the Abbott Architect i1000® estradiol assay exhibits improved precision and significantly smaller bias when compared to LC/MS/MS, providing impetus for change within our estradiol testing platforms.

P-564 Wednesday, October 19, 2016

ARTIFICIAL SHRINKAGE OF FRESH BLASTOCYST: IMPACT ON SUCCESS RATES IN IVF/ICSI. S. Baillet, a A. Gala, a V. Loup, a S. Bringet, a T. Anahory, a S. Hamamah, a ART/PGD Department, Montpellier-1 University, UFR of Medicine, Montpellier Cedex 5, France; bCHU Montpellier, Montpellier, France; cMedical Doctor, Montpellier, France; dGynécologie Obstétrique, Medecine de la Reproduction, Montpellier, France.

OBJECTIVE: To determine if artificial shrinkage (AS) before transfer of fresh blastocysts impact clinical pregnancy rate in single blastocyst embryo transfer (SBET) cycle.

DESIGN: This is a prospective randomized study performed between November 2014 and July 2015. Clinical pregnancy rates were compared in 32 cycles with fresh blastocyst transfer after collapse (n=15) or transfer of fresh blastocysts with no intervention on blastocyst cavity (n=17).

MATERIALS AND METHODS: Cycles (n=32) with women aged 37 years old or less in their first or first post-partum attempt elected for SBET were randomized on transfer day in two arms: the AS group (n=15) where blastocoeic cavity was artificially reduced by a laser pulse prior to transfer and a control group (n=17). Clinical pregnancy rates were compared. Secondarily, rate of monozygotic twin pregnancy and Cell free DNA concentration in culture medium was evaluated in the two groups.

RESULTS: Clinical pregnancy rate in the AS group was slightly higher ([8/15] 53%) than in the control group ([8/17] 47%) but not significantly. One monzygotic twin pregnancy was observed in the AS group. The median rate of cell free DNA (cfDNA), evaluated by ALU quantitative PCR, is 91 [45-332] ng/ml and 42 [21-171] ng/ml in the AS and the control group respectively (p=0.05).

CONCLUSIONS: This study reveals that AS before fresh blastocyst replacement is not harmful and could improve clinical pregnancy. CFDNA seems to be an relevant biomarker in IVF/ICSI and might explain the benefit of collapsing either after fresh or frozen blastocyst replacement. These results need to be confirmed in a larger study.

References:
EMBRYO DONATION: NATIONAL TRENDS AND OUTCOMES, 2000-2013. J. F. Kawwass, S. Crawford, H. Hipp, S. Boulet, D. M. Kissin, D. J. Jamieson. Reproductive Endocrinology and Infertility, Emory University Reproductive Center & CDC, Atlanta, GA; CDC, Atlanta, GA; Gynecology and Obstetrics, Emory University School of Medicine, Atlanta, GA; Centers for Disease Control and Prevention, Atlanta, GA; Division of Reproductive Health, Centers for Disease Control and Prevention, Atlanta, GA.

OBJECTIVE: To quantify trends in donor embryo cycles in the United States, to characterize donor embryo recipients, and to report transfer, pregnancy, and birth outcomes of frozen donor embryo transfers.


MATERIALS AND METHODS: Linear and binomial regression were used to explore trends in the use of donor embryos and corresponding rates of pregnancy and live birth during 2000-2013. We investigated recipient and cycle characteristics and outcomes of frozen donor embryo transfers performed between 2007-2013, years reflective of current practice and for which age of the donor oocyte source was collected. We report rates of cancellation, intrauterine pregnancy, miscarriage, live birth, singleton live birth, twin live birth, and delivery of full term singleton infant of normal birthweight (>37 weeks, weighing >2500 grams) among donor embryo cycles.

RESULTS: Among all frozen transfers between 2000 and 2013 (n=391,662), the annual number of donor embryo transfers increased significantly from 332 to 1,374; however, the proportion of donor embryo transfers among all frozen transfers did not change significantly (2.3% to 2.6%). The overall donor embryo cycle cancellation rate prior to transfer between 2007 and 2013 was 7.1%. Among all donor embryo transfers between 2007 and 2013 (n=6,773), 3,193 (47.2%) resulted in pregnancy and 2,589 (38.2%) resulted in a live birth. Both overall pregnancy and live birth rates per frozen donor embryo transfer increased significantly (33.3% to 49.1% and 26.5% to 40.8%, respectively) (p<0.01). Among all pregnancies, 535 (16.9%) resulted in a miscarriage. Among all live births, 1,929 (74.5%) delivered a singleton of which 1,482 (76.8%) were full term and had normal birthweight.

CONCLUSIONS: The increasing availability of donor embryos, low chance of cancellation, and increasing likelihood of achieving live birth can inform consumers and health care providers who are considering ART options. Collection of data surrounding donated embryo formation would allow for additional studies that can elucidate predictors of success among donor embryo transfers.

EMBRYO CRYOPRESERVATION WITH WARMING INCREASES PREECLAMPSIA COMPARED TO FRESH EMBRYO TRANSFER. M. Barsky, D. Wilson, D. Bernson, Y. Zhang, C. K. Sites. Obstetrics and Gynecology, Baystate Medical Center, Springfield, MA; Baystate Health, Springfield, MA; Massachusetts Department of Public Health, Boston, MA; Division of Reproductive Health, CDC, Mathematical Statistician, Chamblee, GA.

OBJECTIVE: To compare preeclampsia rates, including those associated with preterm delivery, in fresh compared to cryopreserved-warmed embryo transfers.

DESIGN: We used SMART Collaborative linked datasets to link ART records from the National Reproductive Surveillance System (NASS) with state-level birth certificate and maternal hospital discharge data in Massachusetts. Resident singleton births from 2005 to 2010 were included.

MATERIALS AND METHODS: Descriptive statistics were compiled and stratified by the type of embryo transfer. Chi square tests were performed to determine the association between preeclampsia diagnosis and embryo transfer type. Generalized estimating equations were then fit using preeclampsia status as the outcome and type of embryo transfer as the predictor of interest.

RESULTS: A total of 9,417 singleton births were identified: 7,453 following fresh non-egg donor, 1,052 following cryopreserved-warmed non-egg donor cycles, 643 following fresh egg donor, and 269 following cryopreserved-warmed egg donor cycles. The incidence of preeclampsia was 4.29% in fresh non-donor cycles vs. 7.51% in cryopreserved-warmed non-donor cycles (OR=1.81, p<0.0001). Preeclampsia with preterm delivery was more common following transfer of cryopreserved-warmed non-donor embryos compared to transfer of fresh non-donor embryos (2.76% vs. 1.48%, OR=1.81, p<0.0001; 0.43% vs. 0.95%, p=0.0329, respectively). In donor egg cycles, the rate of preeclampsia was not different between fresh and cryopreserved-warmed transfers (12.13% vs. 10.78%, p=0.56), yet there was a higher rate of preeclampsia following all donor egg cycles vs. non-egg donor cycles (OR=2.7, p=0.0001).

CONCLUSIONS: Following cycles with autologous eggs, the rate of preeclampsia including that associated with preterm delivery, is higher following cryopreserved-warmed embryo transfer compared to fresh embryo transfer in singleton gestations. The rate of preeclampsia is higher in egg donor cycles compared to non-donor cycles, but is not different between donor egg transfer types. Fresh embryo transfers should be considered while alternative options in couples using autologous eggs to reduce the incidence of preeclampsia with preterm delivery.

ART - CLINICAL

Infectious Disease Screening of Semen for Surrogacy Cases. A. A. Kiessling. Bedford Research Foundation, Bedford, MA.

OBJECTIVE: To prevent transmission of HIV and other infectious agents to gestational carriers.

DESIGN: Semen specimens collected within 7 days of blood and urine tests mandated by the Food and Drug Administration for tissue donors are screened for HIV, cytomegalovirus (CMV), bacteria and T pallidum, if indicated by serology. Gestational carriers are counseled about risks and confidentiality before the embryo transfer, and tested for HIV antibodies three times after the transfer whether or not pregnancy is achieved. Babies are tested for HIV sometime during their first year of life.

MATERIALS AND METHODS: Semen specimens are divided into three parts, sperm from one part are washed and cryopreserved in a vapor-phase nitrogen quarantine tank. The second part is aldehyde-prepared, and the third part is tested for HIV, cytomegalovirus (CMV), bacteria and T pallidum, if indicated by serology. Gestational carriers are counseled about risks and confidentiality before the embryo transfer, and tested for HIV antibodies three times after the transfer whether or not pregnancy is achieved. Babies are tested for HIV sometime during their first year of life.

RESULTS: Among all frozen transfers between 2000 and 2013 (n=391,662), the annual number of donor embryo transfers increased significantly from 332 to 1,374; however, the proportion of donor embryo transfers among all frozen transfers did not change significantly (2.3% to 2.6%). The overall donor embryo cycle cancellation rate prior to transfer between 2007 and 2013 was 7.1%. Among all donor embryo transfers between 2007 and 2013 (n=6,773), 3,193 (47.2%) resulted in pregnancy and 2,589 (38.2%) resulted in a live birth. Both overall pregnancy and live birth rates per frozen donor embryo transfer increased significantly (33.3% to 49.1% and 26.5% to 40.8%, respectively) (p<0.01). Among all pregnancies, 535 (16.9%) resulted in a miscarriage. Among all live births, 1,929 (74.5%) delivered a singleton of which 1,482 (76.8%) were full term and had normal birthweight.

CONCLUSIONS: The increasing availability of donor embryos, low chance of cancellation, and increasing likelihood of achieving live birth can inform consumers and health care providers who are considering ART options. Collection of data surrounding donated embryo formation would allow for additional studies that can elucidate predictors of success among donor embryo transfers.
CONTRIBUTION OF CRYOPRESERVATION CYCLES TO CUMULATIVE LIVE BIRTH OUTCOMES FOLLOWING OOCYTE DONATION WITH PREIMPLANTATION GENETIC SCREENING (PGS) IN THE UNITED STATES: 2005 TO 2013. D. H. Barad, a,b S. Darmon, c V. A. Kushner, d,e E. Lazzaroni-Tealdi, d Q. Wang, c D. Albertini, c N. Gleicher. c Center for Human Reproduction, New York, NY; Albert Einstein College of Medicine, Bronx, NY; Wake Forest School of Medicine, Winston-Salem, NC; University of Kansas Medical Center, Kansas City, KS; Rockefeller University, New York, NY.

OBJECTIVE: To assess the impact of frozen-thawed embryo transfers (FET) on live birth rates following initial fresh oocyte donation (OD) cycles with or without PGS.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: SART data suggest that OD represents about 12% of assisted reproduction (ART) cycles. OD, comparatively, utilizes PGS only rarely. To explore trends in third party reproduction, we obtained data from the Assisted Reproductive Technology Database developed by SART on all donor oocyte cycles performed in the United States from 2005 through 2013. The SART database is de-identified and represents more than 90% of all ART cycles in the United States. Live Births after initial fresh oocyte donation cycle and subsequent FET were calculated to provide estimates of cumulative live birth rates.

RESULTS: 33,266 patients began first oocyte donation cycles during the study period. PGS was performed in 1,528 (3.1%). FETs were performed in 348 (23%) PGS and 8,113 (25%) non-PGS OD cycles. Live birth rates were significantly lower among donor oocyte recipients whose embryos underwent PGS after fresh transfers (55.1% vs 46.9%, P < 0.001). The cumulative pregnancy rate after 3 cycles of FET (Table) remained significantly higher in the non-PGS group (P < 0.001).

CONCLUSIONS: Although transfer of cryopreserved embryos does increase cumulative live birth rates, even after 3 FETs overall live birth rates remain significantly lower among donor oocyte recipients whose embryos have been subjected to PGS.

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Supported by: Intramural funds from The Center for Human Reproduction and grants from The Foundation for Reproductive Medicine.

P-568 Wednesday, October 19, 2016

ARE BLASTOCYST ANEUPLOIDY RATES DIFFERENT BETWEEN FERTILE AND INFERTILE POPULATIONS? J. Kort, a R. C. McCoy, Z. Demko, c R. Lathi. a Reproductive Endocrinology and Infertility, Stanford University, Stanford, CA; bGenome Sciences, University of Washington, Seattle, WA; cNatera, Inc., San Carlos, CA.

OBJECTIVE: This study aimed to determine if patients with infertility or recurrent pregnancy loss have higher rates of embryo aneuploidy than age-matched fertile controls.

DESIGN: Retrospective chart review.

MATERIALS AND METHODS: This was a retrospective chart review of all pre-implantation genetic screening (PGS) cases processed by a single reference lab prior to March 2014 after a blastocyst biopsy. Cases were excluded if no indication for PGS was designated or patients were translocation carriers. The fertile control group consisted of patients undergoing IVF with PGS for gender selection only. The comparison cohorts included those with recurrent pregnancy loss, male factor infertility, unexplained infertility, prior failed IVF and previous aneuploid conceptions. A logistic regression model was created to assess the dependent variable, aneuploidy rates, related to independent variables, maternal age and reason for PGS. A quasi-Poisson regression model was created to evaluate the correlation of similar independent variables and the number of blastocysts available for biopsy.

RESULTS: The initial study population consisted of 3,378 IVF-PGS cycles and 18,387 analyzed blastocysts. There was an age-independent increased rate of aneuploidy among patients with recurrent pregnancy loss, prior aneuploid pregnancy or failed IVF cycles compared to fertile controls. Patients with unexplained and male factor infertility did not have a significantly different aneuploidy rate than controls. (Table 1). The increase in aneuploidy in patients with RPL and prior IVF failure was driven by both an increase in meiotic (OR 1.488 and 1.508, p < 0.05) and mitotic errors (1.269 and 1.393, p < 0.05) relative to fertile controls, while patients with prior aneuploid pregnancies had only an increased risk of meiotic error aneuploidies (OR 1.650, p < 0.05).

CONCLUSIONS: Patients with recurrent pregnancy loss, previous IVF failures and prior aneuploid pregnancies have a significantly higher, age-independent, aneuploidy rate compared to patients without infertility. Counseling regarding estimated aneuploidy rates should be tailored to a patient’s age and diagnosis.

Adjusted Odds Ratio for blastocyst aneuploidy rates relative to fertile controls:

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Adj. OR</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male factor</td>
<td>1.036</td>
<td>0.854, 1.257</td>
<td>0.721</td>
</tr>
<tr>
<td>Unexplained infertility</td>
<td>1.061</td>
<td>0.809, 1.295</td>
<td>0.563</td>
</tr>
<tr>
<td>Recurrent Pregnancy Loss</td>
<td>1.330</td>
<td>1.132, 1.565</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Previous IVF failure</td>
<td>1.356</td>
<td>1.129, 1.629</td>
<td>0.0012</td>
</tr>
<tr>
<td>Previous aneuploidy</td>
<td>1.439</td>
<td>1.170, 1.772</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Supported by: None, data provided by Natera.

P-570 Wednesday, October 19, 2016

EXAMINING PATERNAL AGE AS A RISK FACTOR FOR POORER OUTCOMES IN DONOR OOCYTE CYCLES. T. C. Powley, N. Banks, M. J. Hill, G. Patounakis, E. Levens, K. Devine, A. DeCherney, B. W. Whitcomb. aPRAE, NIH, Bethesda, MD; bShady Grove Fertility Reproductive Science Center, Rockville, MD; cBiostatistics and Epidemiology, University of Massachusetts Amherst, Amherst, MA.

OBJECTIVE: To assess the independent effects of increasing recipient and paternal age on clinical pregnancy, livebirth, and spontaneous abortion (SAB) in oocyte donor treatment cycles.

DESIGN: Retrospective cohort study

MATERIALS AND METHODS: Data from 5873 cycles from 4309 couples undergoing donor oocyte cycles at Shady Grove Fertility Center from 2004 - 2014 included paternal and recipient age and semen parameters. Mixed models were used to assess relations of semen parameters and other continuous variables with paternal age categories. Log-binomial regression models were used to assess relations of paternal and recipient age with risk of clinical pregnancy, live birth, and SAB in first treatment cycles as primary analysis; generalized estimating equations were used for analysis using all cycles.

RESULTS: Mean recipient age was 41.0 years (SD=4.4, range: 23-53) and mean paternal age was 42.0 years (SD=6.4, range: 24-84). In analysis restricted to first cycles (n=4309), increasing male age was associated with lower semen volume (P<0.0001) and motility (P<0.0001), as well as with increasing recipient age (P<0.0001). In log-binomial regression models including both paternal and recipient age as predictors, paternal age was consistently unassociated with considered outcomes. In contrast, recipient age was associated with lower live birth rates (P<0.001) and higher rates of SAB (P=0.006). Compared to recipients age <35, those 35-44 had 12% reduced likelihood of livebirth (RR=0.88, P=0.02); women ≥45 had even...
further reduced likelihood of livebirth (RR = 0.82, P = 0.003). Taking recipient age into account, none of the paternal age categories had reduced likelihood of livebirth compared to those < 35 (P = 0.80).

CONCLUSIONS: In this large cohort of oocyte donor cycles, increasing paternal age was associated with poorer semen quality; however, increasing paternal age was not associated with pregnancy. Conversely, increasing recipient age was associated with poorer clinical pregnancy rates, live birth rates, and SAB rates. Poorer outcomes related to increasing recipient age were independent of paternal age and oocyte quality and warrant further investigation.

Supported by: This research was supported, in part, by the Intramural Research Program of NICHD.

P-571 Wednesday, October 19, 2016

SUBENDOMETRIAL VASCULARITY AND HIGH SENSITIVE C-REACTIVE PROTEIN IN PATIENTS WITH UNEXPLAINEDINFERTILITY UNDERGOING ENDOMETRIAL SCRATCHING PRIOR TO INTRAUTERINE INSEMINATION. H. Hamza, 1 M. Rezk, 1 A. Saad. 1

 OBJECTIVE: to assess the correlation between subendometrial vascularity, high-sensitive C-reactive protein (HS-CRP) and endometrial scratching in patients with unexplained infertility undergoing intrauterine insemination (IUI).

 DESIGN: A randomized controlled trial included a total of 146 couples with unexplained infertility. Sample size The assumed total sample size of the study was actually calculated according to a proposed type I error of 5% with an expected difference between rates of clinical pregnancy in study groups of 10%. Type II error was proposed to be 20% (b = 20%) hence the power was set at (1-b, 80%). Accordingly, 72 women were needed in each group. Randomization and blinding Enrolled patients were randomly assigned into two groups according to the method of intervention. Randomization in 1:1 ratio was carried out using computer-generated simple random tables.

 Clinical trial registration number at Pan African Clinical Trials Registry (http://www.pactr.org). PACTR201509001264171 Date of registration: 2015/09/12.

 MATERIALS AND METHODS: Patients were randomly allocated into two groups: group 1 comprised 72 women who underwent endometrial scratching in the luteal phase of a spontaneous menstrual cycle; and group 2 included 74 women who underwent a placebo procedure. HS-CRP was measured 48 hours after scratching with transvaginal Doppler studies performed on the day of hCG administration followed by IUI. Primary outcome was clinical pregnancy rate.

 RESULTS: There were statistically significant differences between the two groups regarding the serum level of HS-CRP (p < 0.001), endometrial thickness (p < 0.001), positive vascularization pattern (p < 0.001) and clinical pregnancy rate (p < 0.001) being higher in the study (scratching) group. Serum level of HS-CRP higher than 1.5 mg/L, endometrial thickness greater than 7 mm and the presence of subendometrial-endometrial vascularization were associated with higher chance of achieving pregnancy.

 CONCLUSIONS: endometrial scratching induces a state of endometrial inflammation and increases the clinical pregnancy in couples with unexplained infertility undergoing IUI. Further studies are warranted to confirm or refute these findings.

P-572 Wednesday, October 19, 2016

PLANNING FOR THE FUTURE: HOW MANY EGGS DO PATIENTS NEED TO HARVEST TO ACHIEVE THEIR FERTILITY GOALS? A. Coates, 1* E. Mounts, 1 A. Kung, 1 B. J. Bankowski, 1 S. Munne. 1Oregon Reproductive Medicine, Portland, OR; 2School of Biosciences, University of Kent, Canterbury, United Kingdom; 3Reprogenetics, Portland, OR; 4Reprogenetics, Livingston, NJ.

 OBJECTIVE: To establish the number of mature eggs needed to create one euploid blastocyst according to maternal age. This metric can be extrapolated to estimate how many eggs may be required to potentially completely a family of more than one child.

 DESIGN: Retrospective single center data analysis.

 MATERIALS AND METHODS: Retrospective data analysis of embryos generated as part of clinical IVF cycles and tested for aneuploidy using high resolution Next Generation Sequencing (hrNGS). The total number of mature eggs retrieved for each maternal age group was divided by the final number of euploid blastocysts available post- biopsy, resulting in the number of mature eggs retrieved per euploid blastocyst. Blastocysts with an inconclusive result were omitted from the analysis which accounted for 2.5% of the total number of blastocysts available.

 RESULTS:

*as 90% of vitrified eggs survive the warming process then one would need 10% extra mature eggs to compensate for any post warm losses.

 CONCLUSIONS: As maternal age increases so does the number of eggs anticipated to be needed to result in one euploid blastocyst. As the live birth rate per euploid blastocyst is around 65% (own data) the number of embryos projected to achieve the goal of one live born child would be approximately a minimum of 2. This equation is useful when counsellings patients vitrifying eggs for fertility preservation, to facilitate an informed decision regarding the number of egg retrieval cycles they may require to achieve their future fertility goals. This would also apply to infertile patients to aid in planning the number of cycles they may take for them to complete their family. It also illustrates the effects of delaying reproduction without fertility preservation.

 Supported by: Oregon Reproductive Medicine.

<table>
<thead>
<tr>
<th>HS-CRP (mg/L)</th>
<th>Endometrial thickness(mm)</th>
<th>Positive vascularization pattern</th>
<th>Clinical pregnancy rate</th>
<th>Odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.89 ± 0.87</td>
<td>9.8 ± 1.9</td>
<td>42</td>
<td>38</td>
<td>6</td>
</tr>
<tr>
<td>0.51 ± 0.39</td>
<td>7.1 ± 1.4</td>
<td>16</td>
<td>9</td>
<td>1</td>
</tr>
<tr>
<td>12.42</td>
<td>19.04*</td>
<td>25.75*</td>
<td>6</td>
<td></td>
</tr>
</tbody>
</table>

*Chi square test, HS-CRP = High sensitive C-reactive protein, IUI = Intrauterine insemination, OR = Odd’s ratio, 95% CI = Confidence interval at 95%.
CONCLUSIONS: As opposite as we previously assumed, subcutaneous progesterone is clearly preferred to vaginal route in patients that have used both treatments. We suggest that discomfort of vaginal route is being underestimated.

### Table 1

<table>
<thead>
<tr>
<th>Vaginal versus subcutaneous routes. (p&lt;0.05 in all rows)</th>
<th>Much better</th>
<th>Better</th>
<th>Similar</th>
<th>Better</th>
<th>Much better</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comfortable</td>
<td>8 (18%)</td>
<td>7 (16%)</td>
<td>5 (11%)</td>
<td>13 (29%)</td>
<td>12 (27%)</td>
</tr>
<tr>
<td>Easiness</td>
<td>6 (13%)</td>
<td>9 (20%)</td>
<td>10 (22%)</td>
<td>15 (33%)</td>
<td>5 (11%)</td>
</tr>
<tr>
<td>Local discomfort</td>
<td>3 (7%)</td>
<td>6 (13%)</td>
<td>13 (29%)</td>
<td>14 (31%)</td>
<td>9 (20%)</td>
</tr>
<tr>
<td>Frequency</td>
<td>0</td>
<td>2 (4%)</td>
<td>6 (13%)</td>
<td>15 (33%)</td>
<td>22 (49%)</td>
</tr>
<tr>
<td>Lost of product</td>
<td>0</td>
<td>3 (7%)</td>
<td>14 (31%)</td>
<td>18 (40%)</td>
<td>10 (22%)</td>
</tr>
<tr>
<td>Feeling dirty</td>
<td>1 (2%)</td>
<td>0</td>
<td>5 (11%)</td>
<td>15 (33%)</td>
<td>24 (53%)</td>
</tr>
<tr>
<td>Home activity interference</td>
<td>1 (2%)</td>
<td>2 (4%)</td>
<td>15 (33%)</td>
<td>12 (27%)</td>
<td>15 (33%)</td>
</tr>
<tr>
<td>Laboral activity interference</td>
<td>1 (2%)</td>
<td>0</td>
<td>17 (38%)</td>
<td>12 (27%)</td>
<td>15 (33%)</td>
</tr>
<tr>
<td>Sexual interference</td>
<td>0</td>
<td>0</td>
<td>10 (22%)</td>
<td>14 (31%)</td>
<td>21 (47%)</td>
</tr>
</tbody>
</table>

**P-573** Wednesday, October 19, 2016

**PATIENTS PREFER SUBCUTANEOUS PROGESTERONE OVER VAGINAL ADMINISTRATION. UNEXPECTED RESULTS OF A PROSPECTIVE TRIAL.** A. Gosalvez-Vega, a,b E. Ninchritz, a E. Fernandez-Sanchez.*a Unit of Reproductive Medicine, Hospital Universitario Quironsalud Madrid, Pozuelo de Alarcón, Madrid, Spain; bUnidad Europea de Madrid, Villaviciosa de Odón, Spain.

OBJECTIVE: To determine if subcutaneous or transvaginal progesterone are preferred by patients after the use of both, based on the influence on their sexual life, global comfort and interference on their normal activities.

DESIGN: An open-label crossover study to determine patients preference for luteal phase support between Prolutex® and Utrogestan® for vitrified embryo transfer treatment.

As we could not find any similar study, a 10 item questionnaire was developed (global comfort, easiness, unexpected problems, local inconveniences, self confidence, feeling dirty, interference with home activities, interference with work, interference with sexual activity, global preference) with 5 possible answers (much better vaginal, better vaginal, similar, better subcutaneous, much better subcutaneous).

MATERIALS AND METHODS: 45 patients under estrogen treatment for frozen embryo transfer were asked to use subcutaneous progesterone for 7 days (Prolutex® aqueous preparation of progesterone 25mg, once a day) and another 7 days of transvaginal natural micronized progesterone (Utrogestan 200® 400 mg every 12 h). After completing both treatments patients were asked to fulfill a questionnaire with 10 items related with their feelings and preferences about subcutaneous and vaginal routes. As the study is focused on patient’s acceptance, no medical or clinical results were recorded, and preferences about subcutaneous and vaginal routes. As we could not find any similar study, a 10 item questionnaire was developed (global comfort, easiness, unexpected problems, local inconveniences, self confidence, feeling dirty, interference with home activities, interference with work, interference with sexual activity, global preference) with 5 possible answers (much better vaginal, better vaginal, similar, better subcutaneous, much better subcutaneous).

RESULTS: Unexpectedly, subcutaneous progesterone was preferred in all categories. Strongest preferences were found in better genital hygiene (87%) frequency of use (82%) and less sexual interference (78%). Medium preferences in feeling secure of not losing product (62%) and interference in home (60%) or laboral activity (60%). Also was preferred in comfort (56%) less negative symptoms (51%) and easiness of administration (44%).

Finally, 73% will choose subcutaneous route if offered. Main questions and answers are showed in Table 1.

### Table 1

<table>
<thead>
<tr>
<th>Donor egg (25)</th>
<th>&lt;30</th>
<th>30-34</th>
<th>35</th>
<th>36</th>
<th>37</th>
<th>38</th>
<th>39</th>
<th>40</th>
<th>41</th>
<th>42</th>
<th>43</th>
<th>44-46</th>
</tr>
</thead>
<tbody>
<tr>
<td># cycles</td>
<td>534</td>
<td>47</td>
<td>169</td>
<td>75</td>
<td>68</td>
<td>81</td>
<td>86</td>
<td>101</td>
<td>92</td>
<td>81</td>
<td>37</td>
<td>27</td>
</tr>
<tr>
<td>Ave # M2/cycle</td>
<td>21.8</td>
<td>15.7</td>
<td>15.2</td>
<td>14.2</td>
<td>16.3</td>
<td>13</td>
<td>12</td>
<td>11.3</td>
<td>13</td>
<td>12.2</td>
<td>12.8</td>
<td>11.2</td>
</tr>
<tr>
<td>Ave # embryos</td>
<td>7.6</td>
<td>6.4</td>
<td>5.6</td>
<td>5.2</td>
<td>6.2</td>
<td>5.1</td>
<td>4.7</td>
<td>3.7</td>
<td>4.1</td>
<td>3.6</td>
<td>4</td>
<td>2.7</td>
</tr>
<tr>
<td>Ave # euploid/</td>
<td>5.6</td>
<td>6.4</td>
<td>3.5</td>
<td>3.5</td>
<td>3.5</td>
<td>3.5</td>
<td>2.9</td>
<td>2.2</td>
<td>1.6</td>
<td>1.6</td>
<td>1.3</td>
<td>1.1</td>
</tr>
<tr>
<td>cycle</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>0.1</td>
</tr>
<tr>
<td># mature eggs</td>
<td>3.9 (7.8)</td>
<td>3.4 (6.8)</td>
<td>4 (8)</td>
<td>4 (8)</td>
<td>4.3 (8.6)</td>
<td>4.5 (9)</td>
<td>5.5 (11)</td>
<td>7.3 (14.6)</td>
<td>8.1 (16.2)</td>
<td>9.7 (19.4)</td>
<td>11.3 (22.6)</td>
<td>19 (38)</td>
</tr>
<tr>
<td>to make one</td>
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<tr>
<td>euploid</td>
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<td></td>
<td></td>
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</tr>
<tr>
<td>blastocyst</td>
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<tr>
<td>(% to make 1</td>
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<td></td>
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<tr>
<td>child)</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of egg</td>
<td>4.29</td>
<td>3.74</td>
<td>4.4</td>
<td>4.4</td>
<td>4.73</td>
<td>4.95</td>
<td>6.05</td>
<td>8.03</td>
<td>8.91</td>
<td>10.67</td>
<td>11.4</td>
<td>20.9</td>
</tr>
</tbody>
</table>

**P-574** Wednesday, October 19, 2016

**NONCOMPLIANCE WITH ASRM/SART GUIDELINES CONTINUE TO BE HIGH IN 2013 COMPARED TO 2011-2012 IN DONOR OOCYTE CYCLES WITH BLASTOCYST TRANSFER.** K. S. Acharya,a S. Keyhan,b C. R. Acharya,a S. J. Li,b S. J. Mussher,a Duke University Obstetrics and Gynecology, Duke University Obstetrics and Gynecology, Durham, NC; aObstetrics and Gynecology, Reproductive Endocrinology and Infertility Fellow, Durham, NC; bDept. Of Biostatistics and Bioinformatics, Duke Computational Biology and Bioinformatics, Durham, NC; aObstetrics and Gynecology - Duke Fertility Center, Duke University Medical Center, Durham, NC; bDuke University, Chapel Hill, NC.

OBJECTIVE: ASRM/SART published guidelines in 2013 for the number of embryos to transfer in IVF. In donor oocyte IVF with donor age <35, the recommendation is for single embryo blastocyst transfer. Our group previously found a >70% noncompliance rate with this guideline for 2011-2012. With the newest available 2013 SART data (2014 data not available at time of submission), we sought to determine trends in embryo transfer noncompliance in donor IVF cycles to determine whether compliance has improved over time and the implications of this on multiple pregnancy rates.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: 12,998 donor-oocyte IVF cycles with fresh blastocyst transfer were analyzed. Cycles were excluded if donor age was >35 years old. Cycles were classified as noncompliant if >1 blastocyst was transferred. Main outcomes were the percentage of noncompliant cycles in 2011-12 vs 2013 as well as the MPR (>2 fetal heart beats on ultrasound) in each of these time frames. P-values were obtained from t-tests and chi-square test and were adjusted for multiple comparisons using the Benjamini-Hochberg method.
RESULTS: We found that the noncompliance rate stayed virtually the same between 2011-12 and 2013; in both time frames, >70% of donor IVF cycles were noncompliant and transferred 2 or more blastocyst embryos. The clinical pregnancy rates, live birth rates, and multiple pregnancy rates showed no difference between the two time frames.

<table>
<thead>
<tr>
<th>Noncompliant donor IVF cycles from 2011-12 compared with 2013, with fresh blastocyst transfer</th>
<th>2011-12</th>
<th>2013</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>10238</td>
<td>2760</td>
<td>NA</td>
</tr>
<tr>
<td>% noncompliant</td>
<td>72.4</td>
<td>71.2</td>
<td>0.23</td>
</tr>
<tr>
<td>Oocytes, mean (SD)</td>
<td>22 (9.9)</td>
<td>22 (10.2)</td>
<td>0.1</td>
</tr>
<tr>
<td>ET, mean (SD)</td>
<td>2.1 (0.3)</td>
<td>2.0 (0.3)</td>
<td>0.09</td>
</tr>
<tr>
<td>ET, range</td>
<td>2-6</td>
<td>2-11</td>
<td>NA</td>
</tr>
<tr>
<td>Cryopreserved, mean (SD)</td>
<td>4.2 (4.1)</td>
<td>4.4 (4.3)</td>
<td>0.14</td>
</tr>
<tr>
<td>CPR, %</td>
<td>72.0</td>
<td>70.6</td>
<td>0.21</td>
</tr>
<tr>
<td>LBR, %</td>
<td>63.0</td>
<td>60.7</td>
<td>0.23</td>
</tr>
<tr>
<td>Singleton %</td>
<td>47.2</td>
<td>48.0</td>
<td>0.67</td>
</tr>
<tr>
<td>MPR, %</td>
<td>52.8</td>
<td>52.0</td>
<td>0.67</td>
</tr>
<tr>
<td>Multiple LB, %</td>
<td>46.2</td>
<td>48.0</td>
<td>0.29</td>
</tr>
</tbody>
</table>

ET = embryos transferred; CPR = clinical pregnancy rate; LBR = live birth rate; MPR = multiple pregnancy rate; LB = live births.

CONCLUSIONS: In donor-oocyte IVF cycles, which inherently have a very favorable prognosis, we continue to see a high level of embryo transfer noncompliance and a high rate of multiple pregnancies. Despite the recommendation for single embryo transfer in this population, the majority of IVF cycles in the US underwent transfer of 2 donor-oocyte blastocysts in 2013. The multiple pregnancy rate remains unacceptably high at over 50%. The 2014 data was not available to us at the time of submission, and we plan to update the results accordingly.

P-575 Wednesday, October 19, 2016

THE SUCCESS RATE OF INTRAUTERINE INSEMINATION AFTER FAILED OOCYTE RETRIEVAL.

M. Irani, V. Gunnala, I. Kligman, Z. Rosenwaks.

OBJECTIVE: There are few available options for patients undergoing IVF and who did not have oocytes recovered during oocyte retrieval; these include intra-uterine insemination (IUI), intercourse, or no intervention. In the present study, we aim to determine the success rate of intra-uterine insemination (IUI) performed within an hour after failed oocyte retrieval.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Among patients who underwent autologous fresh IVF cycles between January 2004 and May 2013, those who underwent IUI after failed oocyte retrieval were included. Patients with history of male factor or tubal factor infertility were excluded. Values were expressed as mean ± SEM.

RESULTS: A total of 19709 IVF cycles were reviewed; 60 cycles (0.3 %) had no recovered oocytes during oocyte retrieval. 24/60 patients underwent IUI within an hour after failed retrieval; none of them achieved a clinical pregnancy. The age of patients who had failed oocyte retrieval was 38.8 ± 0.6 years. Estradiol level was 661 ± 81 pg/mL on the day of HCG trigger and 775 ± 99 pg/mL on the day after HCG trigger. LH was not elevated on the day of HCG trigger (5 ± 0.3 mIU/mL). β-hCG levels were normal (200 ± 17 mIU/mL) on the day after HCG trigger.

CONCLUSIONS: The success rate of IUI rescuing failed oocyte retrieval is negligible. Patients need to be educated about the low expectations of rescue IUI.

P-576 Wednesday, October 19, 2016

ELECTIVE SINGLE EMBRYO TRANSFER IN WOMEN UNDER AGE 38 REDUCES MULTIPLE BIRTH RATES BUT NOT LIVE BIRTH RATES IN UNITED STATES FERTILITY CLINICS.

A. Mancuso, S. Boulet, E. Duran, E. M. Munch, D. M. Kissin, B. J. Van Voorhis, Obstetrics and Gynecology, University of Iowa Hospitals and Clinics, Iowa City, IA; Division of Reproductive Health, Centers for Disease Control and Prevention, Atlanta, GA.

OBJECTIVE: To determine the effect of elective single embryo transfer (eSET) rates on live birth rates and multiple birth rates in United States IVF clinics.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Data were collected on all autologous fresh IVF cycles performed in 2013 and reported to the National Assisted Reproductive Technology Surveillance System (NASS). Cycles using preimplantation genetic diagnosis or screening were excluded. The analysis was stratified by patient age (<35 and 35-37). Clinics were divided into groups based on eSET rates: 0-9%, 10-19%, 20-29%, 30-39%, 40-49%, >=50% for age <35 and 0-9%, 10-19%, 20-29%, >=30% for age 35-37. Aggregate rates of live birth per embryo transfer and multiple birth per delivery were calculated for each eSET group after controlling for significant confounding variables (number of cycles per year, ICSI rate, blastocyst versus cleavage stage embryo transfer, average patient age, number of prior ART cycles, parity, race).

RESULTS: 464 clinics were analyzed for the age <35 group and 450 clinics for the age 35-37 group. There was a linear decrease in multiple birth rate with increasing eSET rate and no significant difference in clinic-level live birth rates (Table). Clinics with a higher average eSET rate tended to perform more blastocyst embryo transfers (day 5-6 of culture) and had higher average embryo implantation rates.

CONCLUSIONS: Our study showed a marked and linear reduction in multiple birth rates and importantly, little to no effect on live birth rates with increasing rates of eSET. This study supports the growing evidence that eSET is effective in decreasing the high multiple birth rates associated with IVF and suggests eSET should be utilized more frequently than is currently practiced.

Clinic eSET rate (Age <35) 0-9% 10-19% 20-29% 30-39% 40-49% >=50% P-value

<table>
<thead>
<tr>
<th>Number of clinics</th>
<th>Clinics eSET rate (%)</th>
<th>Multiple birth rate (%)</th>
<th>Clinical eSET rate (Age 35-37)</th>
<th>Number of clinics</th>
<th>Live birth rate (%)</th>
<th>Multiple birth rate (%)</th>
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<td>45.2</td>
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<td>32.8</td>
<td>26.3</td>
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<td>&lt;0.001</td>
</tr>
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</table>
MATERIALS AND METHODS: All fresh and frozen IVF cycles performed at an IVF center between Feb. 2006 and Aug. 2011 that resulted in a live birth were included in the study. Outcomes of interest included rates of gestational hypertension (GHTN), preeclampsia, small for gestational age (SGA), preterm delivery, gestational diabetes (GDM), and neonatal intensive care unit (NICU) admission. IVF data was obtained from the IVF program’s SART database and outcome data was abstracted using ICD-9 codes from patient medical records. For patients with more than one birth during the study period, only the first delivery was included in the analysis. Chi-squared analysis was used to analyze the differences in rates of the outcomes of interest between groups.

RESULTS: A total of 669 live births following fresh transfer and 197 births following frozen transfer were analyzed. The groups were similar in terms of age, nulliparity, and rates of chronic hypertension. Multiple gestations were more common in pregnancies following fresh transfer than after frozen transfer (36.4% vs. 24.9%, p = 0.0025). Ethnic distribution of patients also varied between the groups (p = 0.0405). When including all gestations, there was a significantly higher rate of GHTN following frozen transfers when compared to fresh transfers (25.3% vs. 13.5%, p < 0.0001). Among only singleton gestations, the rate of GHTN was still significantly higher following frozen transfer (27.0% vs 10.8%, p < 0.0001). The difference in the rate of preeclampsia was not as pronounced after frozen transfers vs fresh transfers (10.8% vs 6.1%, p = 0.0592). Rates of GDM, SGA, preterm delivery, or NICU admission were similar for all gestations and singletons, and there were no significant differences in outcomes among only multiple gestations.

CONCLUSIONS: Our data suggest that frozen embryo transfers were associated with a significantly higher rate of GHTN compared to fresh transfers. Patients should be counseled that pregnancies following frozen transfers may be at a higher risk for developing hypertensive disorders of pregnancy. Additional risk factors should be identified to further stratify patients at higher risk.

References:

P-579 Wednesday, October 19, 2016

SPINDLE POSTION AND SECOND POLAR BODY ORIENTATION ENABLES THE PREDICTION OF EMBRYONIC DEVELOPMENTAL POTENTIAL AFTER ICSI. S. Kim, J. Eum, W. Y Choi, S. Paek, S. Kwon, J. Kim, R. Kim, Y Hur, T. K. Yoon, W. Lee, D. Lee. Fertility Center, CHA Gangnam Medical Center, College of Medicine, CHA University, Seoul, Korea, Republic of.

OBJECTIVE: Previous studies have shown that the angle of spindle is associated with fertilization and embryo development. Also, second polar body (2nd pb) orientation was related to the early cleavage which affects the embryo development. However, the correlation between spindle and 2nd polar body orientation was unknown. In present study, we investigated the correlation between the angle of spindle and the angle between the PN axis and the 2nd pb, and the effect of such correlation on embryo quality.

DESIGN: This study was performed from February 2016 to April 2016 in the Fertility center of CHA Gangnam Medical Center. We analyzed 150 matured oocytes from 27 patients. The metaphase spindles were assessed by Polyscope before intracytoplasmic sperm injection (ICSI). Injected oocytes were cultured individually in continuous single culture medium (CSC medium, Irvine scientific, CA). After 16-18 hours, we measured the angle between the PN axis and the 2nd PB. Then, the early cleavage was checked on day 2 and embryo development was checked on day 3.

MATERIALS AND METHODS: After checking the angle of spindle in mature oocytes, the oocytes were divided into five groups according to the angle of spindle deviation from the PB position (0-5°, 6-15°, 16-45°, >46° and non-visible). And then, the angle between the PN axis and 2nd pb position was measured in pronuclear zygotes.

RESULTS: The angle between the PN axis and the 2nd pb was increased with increasing angle of spindle (0-5°, 15.4°; 6-15°, 17.9°; 16-45°, 22.8°; >46°, 77.1°). Also, the rate of early cleavage and good quality embryos has declined with increasing angle of spindle and angle between the PN axis and the 2nd pb. However, non-visible oocytes showed a lower incidence of the angle between the PN axis and the 2nd pb (49.3% versus 77.1%) and higher incidence of the rate of early cleavage (32.0% versus 14.3%) and good quality embryos (32.0% versus 14.26%) as compared with >46° oocytes. To note that there was a tendency to be related to the rate of good quality embryos with embryo score of Embryoscope.

CONCLUSIONS: A significant relationship was examined between the angle of spindle and the angle between the PN axis and the 2nd pb in the oocytes. In addition, these correlated angles were associated with embryo quality. Thus, this observation may give a new indicator which can be used to predict the developmental fate of embryos.

Supported by: Grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (HI12C0055).

P-578 Wednesday, October 19, 2016

TRENDS IN EMBRYO TRANSFER RATE, MULTIPLE BIRTH RATE, AND PREGNANCY RATE IN RESPONSE TO THE AMERICAN SOCIETY OF REPRODUCTIVE MEDICINE’S RECOMMENDATION TO LIMIT EMBRYO TRANSFER. M. Bazzi, N. Abdullah, P. Karabon, J. Chick, A. A. Dabaja. Wayne State University School of Medicine, dearborn, MI; Henry Ford Health System, Detroit, MI; Urology, Biostatistician, Detroit, MI; Wayne State University School of Medicine, Detroit, MI; Department of Urology, Henry Ford Health System, Detroit, MI.

OBJECTIVE: Multiple embryo transfer during in vitro fertilization (IVF) can lead to higher order pregnancy, and can complicate fetal and maternal health. The American Society for Reproductive Medicine (ASRM) passed recommendation in 1977 to reduce the number of embryos transferred during IVF. We evaluated the long-term impact of ASRM’s recommendation on embryo transfer rate (ETR), multiple birth rate (MBR), and pregnancy rate (PR) from 1997 to 2012.

DESIGN: Retrospective analysis of previously published ETR.

MATERIALS AND METHODS: Using publicly available data from the Centers for Disease Control and Prevention (CDC), we calculated the national ETR, MBR, and PR for a given year. The fertility success reports provided data stratified by the following age groups: less than 35 years old, between 35 and 40 years old and greater than 40 years old. For statistical analysis, we used a multilevel linear mixed effects model to assess temporal/time trends. Temporal trends were tested using the Estimated Annual Percentage Change (EAPC) methodology. All statistical analysis was performed using SAS 9.4 (Cary, North Carolina; SAS Institute).

RESULTS: Analyses from our study showed that the estimated annual percent change in embryo transfer rate and multiple birth rate is -3.36% and -1.90%, respectively (p-value <0.01) from 1997 to 2012. The pregnancy rate has improved between 1997 and 2012 with an estimated average percent change of 1.90% (p-value <0.01).

CONCLUSIONS: Professional societies’ recommendation to reduce the number of embryos transferred has effectively reduced national embryo transfer rate without compromising pregnancy rates.

References:

P-550 Wednesday, October 19, 2016

ABDOMINAL ECTOPIC PREGNANCY CASES AFTER IN VITRO FERTILIZATION: A SYSTEMATIC REVIEW OF A RARE COMPLICATION. N. Yoder, R. Tal, J. Martin. Obstetrics, Gynecology & Reproductive Sciences, Yale University School of Medicine, New Haven, CT.

OBJECTIVE: Ectopic pregnancy is the leading cause of maternal morbidity and mortality during the first trimester and the incidence increases dramatically with assisted-reproductive technology (ART), occurring in approximately 1.5-2.1 percent of patients undergoing IVF. Abdominal ectopic pregnancy is a rare yet clinically significant form of ectopic pregnancy due to potentially high maternal morbidity. While risks for ectopic pregnancy after IVF have been studied, little is known about risk factors specific to abdominal ectopic pregnancy. We performed a systematic review of
in PGS-OD decreased by 23% (OR 0.767, 95%CI 0.668 to 0.881) and in significantly better IVF outcomes than PGS-OD cycles, with odds of pregnancy and P while IVF outcomes in nPGS-OD remained remarkably stable (P

CONCLUSIONS: Our systematic review has revealed several trends in reported cases of abdominal ectopic pregnancy after IVF including tubal factor infertility, history of tubal ectopic and tubal surgery, higher number of embryos transferred, and fresh embryo transfers. These are consistent with known risk factors for ectopic pregnancy following IVF. A limitation of this review is the heterogeneity of reported cases and IVF practices which encompass several decades. Further research focusing on more homogeneous population may help in better characterizing this rare IVF complication and its risks.

P-581 Wednesday, October 19, 2016

EFFECT OF TIME TRENDS OF PREIMPLANTATION GENETIC SCREENING (PGS) UTILIZATION ON OOCYTE DONATION CYCLE LIVE BIRTH RATES IN THE UNITED STATES: 2005 TO 2013. D. H. Barad, a, b S. Darmon, a V. A. Kushnir, a, c E. Lazzaroni-Tealdi, a Q. Wang, a L. Zhang, a D. Albertini, a N. Gleicher, b Center for Human Reproduction, New York, NY; bAlbert Einstein College of Medicine, Bronx, NY; cWake Forest School of Medicine, Winston-Salem, NC; The Center for Human Reproduction, New York, NY; University of Kansas Medical Center, Kansas City, KS; Rockefeller University, New York, NY.

OBJECTIVE: Over the last decade PGS techniques changed from day-3 blastomere biopsy (PGS 1.0) to day-5 trophoderm biopsy (PGS 2.0), and from limited number chromosome analyses by FISH to full chromosome complement platforms of much higher accuracy. How these changes affected outcomes in IVF is, however, unknown. Donor oocyte (OD) cycles usually utilize young, healthy and carefully selected women and, therefore, should allow for a controlled assessment of PGS effects.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: We obtained data from the ART Database developed by SART on OD/recipient cycles performed in the U.S. from 2005 through 2013. Birth outcomes were assessed from initial fresh OD cycles and subsequent frozen-thawed (FET) cycles. Mixed Model Logistic regression adjusted for patient age, donor age, number of oocytes retrieved and number of embryos transferred was used to compare live birth rates between PGS oocyte donation (PGS-OD) and non-PGS oocyte donation (nPGS-OD) cycles in three reporting period categories.

RESULTS: 33,756 patients initiated a first oocyte donation cycle, among which 1,528 (4.5%) underwent PGS. Controlling for patient age, donor age, oocytes retrieved, embryos transferred and reporting year, pregnancy and live birth rates in PGS-OD patients continuously improved from earliest to latest time period (P=0.012 and P=0.015, respectively), while IVF outcomes in nPGS-OD remained remarkably stable (P=0.521 and P=0.628), nPGS-OD cycles, however, persistently produced significantly better IVF outcomes than PGS-OD cycles, with odds of pregnancy in PGS-OD decreased by 23% (OR 0.767, 95%CI 0.668 to 0.881) and in live birth by 25.8% (OR 0.742, 95% CI 0.661 to 0.832; both P<0.001) (Table).

CONCLUSIONS: The switch from PGS 1.0 to PGS 2.0 improved PGS outcomes in association with IVF but only slightly diminished the outcome advantage with nPGS-OD. Indeed, even in most recent years, when PGS 2.0 has been used almost exclusively, nPGS-OD, still, demonstrates significant outcome advantages over PGS-OD. These data raise serious additional questions about the utility of PGS in IVF.

P-S82 Wednesday, October 19, 2016

PROGESTERONE SUPPLEMENTATION FOR LUTEAL PHASE SUPPORT IN NON-ASSISTED REPRODUCTIVE TECHNOLOGY TREATMENTS - PREVALENCE OF USE AND PRACTICE PATTERNS AMONG INFERTILITY SPECIALISTS. E. Weedin, a J. Kort,b A. Quaas,c V. L. Baker, d K. R. Hansen. aObstetrics and Gynecology, The University of Oklahoma Health Sciences Center, Oklahoma City, OK; bDivision of OB-GYN, University of Nebraska Medical Center, Omaha, NE; cDepartment of Obstetrics and Gynecology, University of Oklahoma Health Sciences Center, Oklahoma City, OK; dDivision of REI, Department of Obstetrics and Gynecology, Stanford University, Stanford, CA; aObstetrics and Gynecology, University of Oklahoma Health Sciences Center, Oklahoma City, OK.

OBJECTIVE: To examine the prevalence of and indications for progesterone supplementation for luteal phase support in non-assisted reproductive technology (non-ART) infertility treatments.

DESIGN: Survey investigation.

MATERIALS AND METHODS: Using a web-based tool, we surveyed reproductive endocrinology and infertility (REI) specialists regarding use of progesterone supplementation for non-ART infertility treatments. The anonymous survey was sent to members of the Society for Reproductive Endocrinology and Infertility (SREI). Comparisons between indications and treatment types were performed with StatView v5.0 (SAS Institute, Cary, NC) using Chi-square and Fishers exact tests with a nominal p-value of <0.05 being considered statistically significant. Institutional Review Board approval was obtained for this study.

RESULTS: Sixty-four REI physicians completed the survey (a 9% response rate). Greater than 98% of all respondents offered non-ART treatments, including clomiphene citrate, letrozole, gonadotropins, and intrauterine insemination. All physicians reported supplementing the luteal phase with progesterone in non-ART cycles for one or more indications. Frequency of prescription by indication was reported as follows: unexplained infertility (46%), polycystic ovarian syndrome (with ovulation induction, 34%), hypothalamic amenorrhea (with ovulation induction, 34%), recurrent pregnancy loss (70%), short luteal phase (73%), and patient request (75%) (p <0.0001 for difference in frequencies of use based on indication). In treatment cycles limited to clomiphene citrate and letrozole, 24% always used progesterone supplementation and 59% would if one or more indications were present, suggesting widespread use in the clinical setting. More REI physicians reported using vaginal progesterone (100%) than intramuscular (89%) or oral (22%) (p <0.0001).

CONCLUSIONS: The impact of luteal-phase progesterone supplementation on non-ART treatment cycle outcomes is uncertain. Nevertheless, our survey demonstrates that the empiric use of luteal-phase progesterone supplementation in these treatments is widespread among REI practitioners in spite of lack of evidence supporting its effectiveness. Indications for use also varied significantly among REIs. These findings point to the lack of...
standardization and suggest the need for prospective trials to examine the role of progesterone supplementation in non-ART treatments.

Supported by: Departmental, SREI.

**P-583 Wednesday, October 19, 2016**

**HYPERMETHYLATION SUPPRESSES EXPRESSION OF HUMAN SYNCTIN 2 IN PLACENTA OF PREECLAMPSIA.** C. Feng. The Second Affiliated Hospital, School of Medicine, Zhejiang University, Hangzhou, China.

OBJECTIVE: Our previous retrospective cohort study found a significant increase of preeclampsia in pregnancies conceived through in vitro fertilization - embryo transfer (IVF-ET) compared to naturally conceived pregnancies (OR: 1.9, 95% CI 1.5-2.5). IVF-ET manipulates gametes and embryos during the pivotal stage of methylation reprogramming, so it is likely to induce inappropriate methylation and lead to preeclampsia. Considering syncytin 2 encoded by HERV-FRD plays a key role in trophoblast cell fusion and placenta invasion, deficiency of syncytin 2 might contribute to the development of preeclampsia. Therefore, we aimed to elucidate 1) whether the expression of syncytin 2 is disregulated in placentae of preeclampsia and 2) the regulation of DNA methylation on the expression of syncytin 2.

DESIGN: Eight early pregnant women, 7 preeclampsia patients, and 14 age-matched term-delivered healthy controls were recruited. The first trimester placenta (1N) were collected during legally induced abortion, and the third trimester placenta (3P and 3N) were obtained during cesarean section.

MATERIALS AND METHODS: Real-time RT-PCR, western blot, and immunohistochemistry (IHC) were conducted to investigate the expression of HERV-FRD in the pathogenesis of preeclampsia. Bisulfite restriction analysis (COBRA) and bisulfate sequencing PCR (BSP) were carried out to explore the role of DNA methylation in the regulation of HERV-FRD. Furthermore, BeWo cells with ADC treatment were adopted to validate the DNA methylation regulation in HERV-FRD.

RESULTS: The mRNA expression of HERV-FRD was found to be remarkably elevated in 3N placentae than that in 1N placenta. Both the mRNA expression and protein expression of syncytin 2 decreased significantly in 3P placentae compared to that in 3N placentae. The methylation status varied significantly in promoter, exon, and 3’LTR regions of HERV-FRD gene. The promoter region was mildly methylated, the exon region was moderately methylated, and the 3’LTR region was highly methylated. The methylation levels of promoter and exon were similar between preeclampsia and control, while differential methylation was found in 3’LTR region of HERV-FRD. BeWo cells treatment with ADC proved that the expression of HERV-FRD increased following the reduction of 3’LTR methylation.

CONCLUSIONS: In conclusion, the present study proved that the expression of syncytin 2 increased in placenta in the third trimester. The expression of syncytin 2 is decreased in preeclampsia, and this reduction may attribute to the development of preeclampsia. Therefore, we aimed to elucidate 1) whether the expression of syncytin 2 is disregulated in placentae of preeclampsia and 2) the regulation of DNA methylation on the expression of syncytin 2.

**Supported by:** The National Natural Science Foundation of China (No. 81200446) and the Special Fund for Scientific Research in the Public Interest (201402004), the National Natural Science Foundation of China (81370765), and the Science and Technology Program of Guangzhou (20130000097).

**Comparison of laboratory data and clinical outcomes between the two groups**

<table>
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<th>Indication</th>
<th>Group A (n=92)</th>
<th>Group B (n=95)</th>
<th>P value</th>
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<td>No. of retrieved oocytes</td>
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<td>14.6±4.9</td>
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<tr>
<td>No. of transferred embryos</td>
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<td>50.5%</td>
<td>NS</td>
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<td>Implantation rate (%)</td>
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<td>Live birth rate/ET cycle(%)</td>
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<td>46.3%</td>
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**References:**


**Supported by:** This study was sponsored by grants listed as follows: National Science Foundation of China (No. 81200446 to C.F.)

**P-584 Wednesday, October 19, 2016**

**INITIATION OF PROGESTERONE SUPPLEMENTATION ONE DAY AFTER OOCYTE RETRIEVAL DID NOT DECREASE LIVE BIRTH RATE: A PROSPECTIVE RANDOMIZED CONTROLLED TRIAL.** J. Gao, F. Fu, C. Zhou, B. Miao, Y. Yu. "Reproductive Center, First Affiliated Hospital, Sun Yat-sen University, Guangzhou, China; Guangdong Provincial Key Laboratory of Reproductive Medicine, Guangzhou, China.

OBJECTIVE: The study aimed to analyze the influence of the start point of luteal support on clinical pregnancy rate, implantation rate, and live birth rate of in vitro fertilization and embryo transfer (IVF-ET) cycles.

DESIGN: This single-center prospective randomized controlled trial was conducted on 187 patients who underwent long-protocol treatment from 1 Oct 2014 to 31 Jan 2015 at our hospital. Our study was registered in the Chinese Clinical Trial Registry (registration number: ChiCTR-IPR-14005293).

MATERIALS AND METHODS: A total of 187 women aged ≤35 years undergoing IVF were recruited for this study and received ovarian stimulation using a GnRH agonist long protocol. Computer-based randomization divided the recipients into two groups at HCG trigger day. The first group (group A) started progesterone supplementation one day after oocyte retrieval; the second group (group B) started progesterone supplementation on the day of oocyte retrieval. Both of them received embryo transfer 72 to 120 h after oocyte retrieval.

RESULTS: The live birth rate did not differ significantly between the two groups. There were no significant differences with regard to serum estrogen and progesterone levels on the day of HCG trigger, the number of oocytes retrieved, or available embryos. The clinical pregnancy rate (group A 54.3% vs. group B 50.5%), implantation rate (group A 37.1% vs. group B 37.0%), and miscarriage rate (group A 8.0% vs. group B 6.2%) were similar between the two groups.

CONCLUSIONS: Initiation of progesterone supplementation on day +1 of oocyte retrieval did not decrease clinical pregnancy rate, implantation rate, or live birth rate.

**Supported by:** The Guangdong Provincial Key Laboratory of Reproductive Medicine (2012A061400003) and the Special Fund for Scientific Research in the Public Interest (201402004), the National Natural Science Foundation of China (81370765), and the Science and Technology Program of Guangzhou (201300000097).

**P-585 Wednesday, October 19, 2016**


OBJECTIVE: Anecdotal evidence suggests that US practice patterns for ART differ by geographic region. The purpose of this study was to determine whether use of ICSI differs by region and to evaluate whether these rates are correlated with differences in live birth rates.

DESIGN: Retrospective database analysis.

MATERIALS AND METHODS: Publically available data for 2012 from the National Assisted Reproductive Technology Surveillance System (NASS) were downloaded from the Centers for Disease Control and Prevention (CDC) website [1]. Clinics with ≥100 fresh, non-donor, cycles were selected by region according to the 10 nationally recognized Department of Health & Human Services (HHS) regions [2] as well as for 9 metropolitan Megaregions [3] containing 8 or more clinics per service area or region and compared for use of ICSI and for live birth rate in women ≤35 years via ANOVA. Regional ICSI rates were compared with live birth rates in women ≤35 using correlation coefficients.
RESULTS: There were 274 clinics with >100 fresh autologous cycles in the 10 HHS regions. Number of clinics per region ranged from 8 to 55. Mean rates of ICSI/cycle were between 52.5% and 78.2% of all clinic cycles (P<0.0001). Live birth rates in women <35 years of age also differed (range 34.2–47.6%; P<0.0001) but did not correlate with rates of ICSI (r=0.057). For Megaregions there were 239 clinics included with 9 to 79 clinics per region. Again, mean rates of ICSI/cycle differed (range 63.4%-83.1%, P<0.0001) as did live birth rates for women <35 (range 36.1%-45.7%, P=0.001) but there was no correlation between the two (r=0.0731). Highest mean rates of ICSI utilization occurred in Gulf Coast (83.1%) and Southern California (82.3%) Megaregions. Lowest rates occurred in the Northeast (36.1%) and Florida (38.6%) Megaregions. Lowest rates of ICSI/clinic were between 52.5% and 78.2% of all clinic cycles but no ART LB had the greatest number of cycles. All groups had HDD 34.2-47.6%; P<0.0001) but did not correlate with rates of ICSI (r<0.057).

CONCLUSIONS: ICSI utilization rates and live birth rates per clinic were significantly different across geographical regions of the continental U.S. Despite these differences, higher utilization rates of ICSI were not correlated with higher live birth rates for women in the <35 year old age group. Studies are ongoing to understand factors that might influence ICSI utilization rates in these regions.

References:
3. https://en.wikipedia.org/wiki/Megaregions_of_the_United_States

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NON-ART DELIVERIES FOR WOMEN WITH AND WITHOUT ART LIVE BIRTH: ANALYSIS OF SART CORS CYCLES LINKED TO INPATIENT HOSPITAL DISCHARGES IN MASSACHUSETTS. J. E. Stern, a D. Gopal, a H. Diop, b B. Luke, a Obstetrics and Gynecology, Dartmouth-Hitchcock, Lebanon, NH; aDepartment of Community Health Sciences, BUSPH, Boston, MA; aMass Department of Public Health, Mass Department of Public Health, Boston, MA; bObstetrics, Gynecology, and Reproductive Biology, Michigan State University, East Lansing, MI.

OBJECTIVE: To evaluate rates of delivery hospitalization before, during and after ART treatment according to whether or not women achieved a pregnancy or live birth (LB) during their ART cycles.

MATERIALS AND METHODS: A total of 6,130 women residing in Massachusetts undergoing 17,135 cycles of ART reported to the Society for Assisted Reproductive Technology Clinic Outcome Reporting System (SART CORS) from 2004-2011 were linked to hospital discharge records in the state vital records under Memorandum of Understanding and IRB approval using encrypted SS#. Women were grouped according to cycle outcome as having had no ART pregnancy in any cycle, one or more ART pregnancies but no LB in any cycle, or one or more ART singleton but no LB. Hospital delivery discharges (HDD) during fiscal years 1998-2011 were identified according to whether they occurred before (prior to the first ART start date), during (between first and last ART start dates), or after (after the last start date and may include ART deliveries) the ART treatment. Live births were identified through ICD9 codes. Groups were compared using chi square test and data were analyzed using SAS 9.3 software.

RESULTS: Shown below are the characteristics, cycles, and HDD for each group. Women with ART LB deliveries were younger; women with pregnancies but no ART LB had the greatest number of cycles. All groups had HDD before, during and after ART treatment and more than 95% of these were LB.

CONCLUSIONS: All three groups of women had deliveries and LB during the study period suggesting a significant contribution of non-ART treatment or spontaneous conception to overall delivery and LBs in this population even in women whose ART cycles do not result in pregnancy or delivery.

Supported by: NICHD: RO1HD06727001.

P-587 Wednesday, October 19, 2016

A STUDY ON THE TIMING OF THE INITIATION OF LUTEAL PHASE PROGESTERONE SUPPLEMENTATION IN FROZEN EMBRYO TRANSFER CYCLE AFTER SPONTANEOUS OVULATION. Y. Fukushima, A. Moriyama, M. Kitamura, Y. Katagiri, M. Morita, Obstetrics and Gynecology, Toho University Medical Center Omori Hospital, Tokyo, Japan.

OBJECTIVE: It is a well-known fact that luteal phase progesterone supplementation after embryo transfer increases pregnancy rate. We studied whether the timing of the initiation of luteal phase progesterone supplementation in frozen embryo transfer cycle after spontaneous ovulation could influence pregnancy rate.

DESIGN: Retrospective cohort study, University-based hospital Single-center study.

MATERIALS AND METHODS: We investigated 44 cycles which underwent frozen embryo transfer after spontaneous ovulation at our hospital from January 2015 to March 2016. A total of 27 cycles started to receive luteal phase progesterone supplementation at the time of embryo transfer (f-ET group), and 17 cycles started to receive one on the second day after ovulation (b-ET group). For luteal phase progesterone supplementation, 100 mg vaginal tablet was used transvaginally twice daily. All the cycles underwent transvaginal ultrasound and blood test (estradiol [E2], luteinizing hormone [LH], and progesterone) around ovulation to determine the timing of ovulation, following which they underwent transfer of a single blastocyst embryo. We compared the groups with the use of t-test and chi-square test to evaluate progesterone and E2 levels at the time of embryo transfer; and progesterone and E2 levels, positive human chorionic gonadotropin (bCG) rates, positive gestational sac (GS) rates, and positive fetal heart beat (FHB) rates after transfer.

RESULTS: Baseline characteristics, including the mean age and endometrium thickness before embryo transfer, showed no significant differences between the groups: the mean age of f-ET group was 35.7 years, and that of b-ET group was 36.4; the mean thickness of endometrium at 10.4 mm in f-ET group, and 10.9 mm in b-ET group. Progesterone level at the time of embryo transfer was significantly higher in b-ET group (p<0.05) at 20.43 ng/mL than in f-ET group at 14.76 ng/mL. E2 level after transfer was significantly lower in b-ET group at 168.2 pg/mL than in f-ET group at 248.3 pg/mL. Positive rates of bCG, GS, and FHB in f-ET group were 48.1%, 29.6%, and 29.6%, respectively, and those in b-ET group were 36.4%; 41.2%, and 35.3%, respectively; all the positive rates were significantly higher in b-ET group, which started to receive luteal phase progesterone supplementation on the second day after ovulation, than in f-ET group (p<0.01), which started to receive one at the time of embryo transfer.

CONCLUSIONS: Regarding the timing of the initiation of luteal phase progesterone supplementation in frozen embryo transfer cycle after spontaneous ovulation, the initiation before embryo transfer was shown to increase pregnancy rate more than that at the time of the transfer.
P-588 Wednesday, October 19, 2016

PREGNANCY RATE AFTER ENDOMETRIAL SCRATCHING IN COUPLES WITH UNEXPLAINED INFERTILITY IN OVULATION INDUCTION & IUI CYCLES: A RANDOMISED CONTROLLED TRIAL. A. Kripalani, T. Goel, R. Mahey, K. Garima, J. B. Sharma, N. Bhatia, Obstetrics & Gynaecology, All India Institute of Medical Sciences, New Delhi, India; 2AIIMS, New Delhi, New Delhi, India; 3All India Institute of Medical Sciences, New Delhi, New Delhi, India; 4Obstetrics and Gynaecology, All India Institute of Medical Sciences, New Delhi, India; 5Obstetrics & Gynaecology, All India Institute of Medical Sciences, New Delhi, New Delhi, India; 6Department of Obstetrics & Gynaecology, New Delhi, India.

OBJECTIVE: To compare pregnancy rates during ovulation induction and IUI cycles with or without endometrial scratching in couples with unexplained infertility.

DESIGN: A prospective randomized controlled study.

MATERIALS AND METHODS: The study was conducted in the Department of Obstetrics and Gynaecology, AIIMS, New Delhi. One hundred twenty four couples with unexplained infertility were recruited during March 2014 to March 2016 (excluding exclusion & inclusion criteria) and were randomized into two groups. Group I (n=62) included patients who underwent endometrial scratching on day 8 of the same menstrual cycle after receiving 7 days of ovulation induction with clomiphene citrate 50mg (day 2 to day 6) and Inj hMG 75 IU on day 6, and Group II (n=60), the control group included those who did not undergo endometrial scratching during ovulation induction and IUI. Primary outcome was measured by conception rate and secondary outcome was measured by abortion rate and ongoing pregnancy rate (>12wks) and ectopic pregnancy rate.

RESULTS: The baseline characteristics (age, BMI, baseline hormone profile and husband semen analysis) were comparable in two groups. The type of infertility in group I was primary 73.3% (40/60); secondary 26.7% (22/60) and in group II - primary 80% (44/22); secondary 20% (8/62). There was no difference in the dose of gonadotropin requirement in two groups. Sixty patients in each group completed the entire course of treatment. Total number of pregnancies in scratching group in cycle 1 was 12/62 (19.35%); cycle II 5/ 49 (10.2%); cycle III-1/43 (2.3%); 2/42 (4.76%) conceived in third wash out cycle. Number of pregnancies in control group were cycle I-2/62 (3.22%); cycle II- 4/58 (6.9%); cycle III- 4/54 (7.41%).

CONCLUSIONS: Though the scratching group had higher ongoing pregnancies than control group, the difference was not statistically significant. Further large number trials are required to document the role of endometrial scratching in IUI cycles.

P-590 Wednesday, October 19, 2016

THE RELEVANCE OF PRECONCEPTIONAL CARRIER SCREENING (PCS) AND GENETIC MATCHING OF DONATED OCYTES AND SPERM ON LIVEBIRTH RATES. RETROSPECTIVE ANALYSIS OF 1934 CONSECUTIVE EMBRYO TRANSFERS. R. Rivera Egea, E. Bosch, P. Alama, J. Martin, J. Remohi Gimenez, N. Garrido, Andrology Laboratory, Instituto Universitario IVI Valencia, Valencia, Spain; 2Medical Director of IVI Valencia, Instituto Universitario IVI Valencia, Valencia, Spain; 3Director of the Ovodonation Programme, Instituto Universitario IVI Valencia, Valencia, Spain; 4Lab Director CGT & PGD, Igenomix, Paterna (Valencia), Spain; 5IVI Valencia, Valencia, Spain; 6Andrology Laboratory, Instituto Valenciano IVI Valencia, Valencia, Spain.

OBJECTIVE: We want to show that PCS change reproductive chances of infertile couples in addition of diminishing the risk of genetically inherited diseases in oocyte donation with donor sperm cycles, obtaining better reproductive results.

DESIGN: Retrospective study, comparing the reproductive outcome between couples since December 2013, the date when we introduced this technique for our patients. Results were compared by beta hCG positive results, clinical and ongoing pregnancy rate per cycle. 1934 consecutive oocyte and sperm donation cycles were included.

MATERIALS AND METHODS: Data were obtained from medical charts of couples, undergoing oocyte and sperm donation in 15 clinics from IVI group, thus including only private practices, in the above mentioned time period. Data were categorized depending on the existence of PCS in order to select the sperm donor (n=171), or not (n=1763). Chi square tests and logistic regression were employed in order to compare proportions for the main outcome measures, while T-tests were employed to compare between means.

RESULTS: SPSS version 22 was used to conduct the statistical analysis, and p < 0.05 was considered as statistically significant. Data were expressed as means or proportions, and odds ratios (OR) with their corresponding 95% confidence interval (95%CI).

CONCLUSIONS: Although the rate of 4-cell stage embryo formation was similar in the two groups, transfer of sequentially assessed embryos resulted in significantly higher rates of biochemical pregnancy, clinical pregnancy, abortion and ectopic pregnancy. Therefore the sequential embryo assessment on day 2 and day 3 could be a simple and non-invasive method for embryo selection in human IVF.
Miscarriage rates were 16.9% 95%CI(14.8-18.2) in control group and 14.6% 95%CI(9.3-19.9) in PCS group. The role of chance is very limited, given the elevated number of treatments included in our research.

CONCLUSIONS: Apart from diminishing the risk for the offspring, implementing PCS provides a clear trend to have ongoing pregnancy rates improved and miscarriage rates decreased on the cases where PCS has been performed.

P-591 Wednesday, October 19, 2016

PREVALENCE AND EFFECT OF PREIMPLANTATION GENETIC SCREENING (PGS) ON OOCYTE DONATION CYCLES IN THE UNITED STATES: 2005 TO 2013. D. H. Barad, S. Darmon, V. A. Kushnir, E. Lazzarini-Tealdi, Q. Wang, L. Zhang, D. Albertini, N. Gleicher. Center for Human Reproduction, New York, NY; Albert Einstein College of Medicine, Bronx, NY; Wake Forest School of Medicine, Winston-Salem, NC; University of Kansas Medical Center, Kansas City, KS; Rockefeller University, New York, NY.

OBJECTIVE: Since overall benefits of PGS on in vitro fertilization (IVF) have remained controversial, we evaluated the utilization and effects on live birth rates of PGS in donor-recipient cycles in the U.S. As donor oocyte cycles usually involve young, healthy women, their cycles should allow a clearer assessment of effects of PGS.

DESIGN: Retrospective national cohort study.

MATERIALS AND METHODS: To explore trends in third party reproduction, we obtained data from the Assisted Reproductive Technology Database developed by SART on all donor oocyte, sperm, embryo and gestational carrier cycles performed in the United States between 2005 through 2013. Birth outcomes were assessed from all first fresh oocyte donation cycles. Logistic regression adjusted for patient age, donor age, number of oocytes retrieved, number of embryos transferred and reporting year, were used to compare live birth rates between PGS- (PGS-OD) and non-PGS-oocyte donation (nPGS-OD).

RESULTS: 33,756 patients initiated a first oocyte donation cycle, among which 1,528 (4.5%) underwent PGS. Average age of nPGS recipients was 41.8 ± 5.6 and of PGS recipients 42.6 ± 6.7 years (P<0.001). Interestingly, fewer PGS-OD recipients demonstrated low ovarian reserve (58.0%) than nPGS-OD (75.2%, P<0.001). Live birth rates were significantly lower for PGS-OD (46.9%) than nPGS-OD (55.1%, P<0.001). Controlling for patient age, donor age, oocytes retrieved, embryos transferred and reporting year, odds of live birth decreased for PGS-OD 28.6% (OR 0.71, 95% CI 0.638 to 0.800, P<0.001).

CONCLUSIONS: In donor recipient cycles, national IVF data (SART Registry) suggest that PGS significantly reduces live birth rates. These data raise further questions about the increasing indiscriminate utilization of PGS in IVF.

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P-593 Wednesday, October 19, 2016

DIFFERENT ESTROGEN ROUTE ADMINISTRATION DOES NOT INFLUENCE CLINICAL PREGNANCY RATES IN FROZEN EMBRYO TRANSFER. M. Cavagnoli, C. Gomes, F. Torelli, T. C. Bonetti, P. C. Serafini, E. Motta. Clinical, Huntington Medicina Reprotiva, Sao Paulo, Brazil; Gynecology, Federal University of Sao Paulo, Sao Paulo, Brazil; Discipline of Gynecology, Hospital das Clinicas, Un, Sao Paulo, Brazil; Huntington Medicina Reprotiva, Sao Paulo, Brazil.

OBJECTIVE: The aim of this study was to evaluate different routes of estrogen (E2) administration for endometrium preparation and the correspondent clinical pregnancy rates (CPR) in frozen embryo transfer (FET) cycles.

DESIGN: This is a retrospective cohort study including FET cycles between July 2014 and November 2015 in a private reproductive medicine center. Patients were allocated into three groups according to route of estrogen administration.

MATERIALS AND METHODS: This study included 280 women undergoing FET cycles with vitrified-warmed blastocysts who underwent endometrium preparation using estradiol valerate at day 02 of the menstrual cycle plus progesterone support when appropriate. Women were divided in three groups according to administration route of estrogen for endometrium preparation: oral daily (Or, n=111), oral daily + transdermal each 48 hours (Or+Tr, n=123), intramuscular twice a week (IM, n=57).

RESULTS: We compared groups according to age (Or: 37.1±4.4; Or+Tr: 36.0±4.3; IM: 39.7±5.0; p=0.003), number of ET (Or: 1.8±0.7; Or+Tr: 1.7±0.6; IM: 1.9±0.7; p=0.225) and endometrial thickness (Or: 8.8±1.6; Or+Tr: 9.1±1.8; IM: 8.6±1.3; p=0.211). Clinical pregnancy rate was statistically similar among groups (Or: 47.7%; Or+Tr: 56.8%; IM: 64.9%; p=0.141), although CPR seen in women with intramuscular administration was numerically higher. Regarding to estradiol levels on the day of FET, the three groups were statistically different and the IM group presented higher levels (Or: 422.71 ng/ml; Or+Tr: 580.81 ng/ml; IM: 799.74 ng/ml; p<0.001). Multivariate logistic regression models were built to evaluate the association of IM route of E2 (OR: 1.7; p=0.162) or E2 levels on the day of FET (OR: 1.0; p=0.742) with the clinical pregnancy, adjusted for patients age, number of ET and endometrial thickness, but we did not observe any significant differences.

CONCLUSIONS: There are no differences between the route of estradiol valerate supplementation if compared the Oral, Oral + Transdermal or Intramuscular administration and considering the clinical pregnancy rate in FET cycles. Costs and patient’s convenience must be considered by clinicians to select an individualized protocol for endometrial preparation with estrogen administration according to specific patient’s characteristics. This is a retrospective study and the number of patients included in the IM group is small; hence a prospective and randomized study should be carried out to investigate if the IM route of E2 in FET cycles result in better CPR.
WHAT INFLUENCES ANTI-MULLERIAN HORMONE LEVELS? ASSOCIATIONS WITH GENOTYPE COMBINATIONS. M. Gold,a S. L. Bristow,a R. Shraga,a M. Berliss,a J. Luk.b aRecombine, New York, NY; bReproductive Endocrinology and Infertility, Neway Fertility Center, New York City, NY.

OBJECTIVE: Previous studies have identified single nucleotide polymorphisms that impact hormones involved in the hypothalamic-pituitary-ovarian (HPO) axis. However, these genetic variants may present concurrently, the significance of which is not well understood. This study aimed to identify combinations of genetic variants that affect clinically relevant hormones, such as AMH, in ways that singularly occurring variants do not.

MATERIALS AND METHODS: AMH levels and genotypes for 18 variants were recorded for 413 women; informed consent was obtained. To investigate joint effects of mutations on AMH, we ran a conditional association analysis as follows. For all pairs of mutations, we conditioned on the first mutation and tested for association on the second. For example, from our original 413 women, 95 women are wildtype (Ser/Ser) for the FSHR p.Ser680Asn mutation. We considered only the subset of 95 wildtype women, and ran association tests between AMH levels and genotype for each of the remaining 17 mutations. We repeated this process 54 times, conditioning on all 3 different genotypes for each of the 18 mutations. To account for multiple testing, we adjusted the p-value using a randomized permutation procedure.

RESULTS: We found a few significant genotype combinations associated with AMH levels. For example, we identified the TP53 p.Pro72Arg mutation within the subset of patients that have Ser/Ser for the FSHR p.Ser680Asn mutation. The Ser/Ser/Pro/Arg group has significantly higher AMH levels (mean = 5.88) than the Ser/Ser/Pro/Arg and the Ser/Ser/Arg/Arg group combined (mean = 2.85). No significant difference in age between the two groups was observed.

CONCLUSIONS: The FSHR Ser allele and the TP53 Pro allele are associated with less active forms of their respective proteins. FSHR is responsible for promoting follicle growth and TP53 is associated with cell cycle control, including apoptosis. Individually, these mutations may not sufficiently disrupt folliculogenesis to alter AMH levels, but jointly this threshold may be reached, highlighting the importance of focusing analysis on genotyping combinations. Further investigation of such combinations may clarify the complex biological processes influencing AMH levels, as their significance is not well understood. Ultimately, a greater understanding may help to refine predictions of ovarian response.

P-595 Wednesday, October 19, 2016

IS IMMUNOTHERAPY USEFUL IN RECURRENT IMPLANTATION FAILURE PATIENTS; ESPECIALLY WITH HIGH NATURAL KILLER CELL? H. Sun,a K. Lee,c I. Park,a S. Kim,a H. Chi,a J. Kim,a J. Cho. aMamapapa & Baby OB&GY Clinic, Ulsan, Korea, Republic of; cEillemed Women’s Hospital, Changwon, Korea, Republic of.

OBJECTIVE: IVIG is an established treatment in several autoimmune and inflammatory diseases and has been tested in several RCTs in recurrent miscarriage (RM) patients. Although clinically different disorders, RIF has been suggested to share many characteristics with early RM. Immunological parameters that seem associated with both RIF and RM are increased numbers of peripheral blood natural killer cells. There were several reviews of IVIG efficacy in RM patients with high NK cell, but there were few studies in RIF patients.

DESIGN: This retrospective study included 295 cases third IVF cycles between January 2011 and October 2015.

MATERIALS AND METHODS: In 295 cases with previous two IVF-ET failure cycles, 81 women had blood tests for NK cell assay and were treated with intravenous immunoglobulin (IVIG) 400mg/kg on ET day and repeated if pregnancy test was positive (IVIG group). We divided IVIG group into two groups with high NK cell (≥12%) group and normal NK cell (<12%) group.

RESULTS: Total pregnancy rate of third IVF cycle was 29.8% (88/295). In 81 cases, patients had blood tests for NK cell assay and were treated with intravenous immunoglobulin (IVIG group). Among IVIG group, patients with high NK cell (≥12%) were 58.0% (47/81) and normal NK cell (<12%) were 42.0% (34/81). Pregnancy rate was significantly higher in high NK cell group than in normal NK cell group [55.3% (26/47) vs. 26.5% (9/34), p = 0.018]. And pregnancy rate was significantly higher in IVIG group with high NK cell than in no IVIG treatment patients [55.3% (26/47) vs. 24.8% (53/214), p = 0.015]. But pregnancy rate showed no significant difference between normal NK cell IVIG group and no IVIG treatment patients [26.5% (9/34) vs. 24.8% (53/214), p = 0.926]. IVIG treated patients with high NK cell showed improved IVF outcome than patients without IVIG treatment. But IVIG treatment with normal NK cell did not affect IVF outcome.

CONCLUSIONS: IVIG treatment enhances pregnancy rate in RIF patients with high NK cell, but do not affect IVF outcome in patients with normal NK cell. Our results showed that more than half of RIF patients had increased NK cell level. In these patients, IVIG treatment was resulted in increasing more than twice pregnancy rate. Therefore if clinicians encounter repeated IVF failure, we recommend proper evaluation and treatment about RIF causes including NK cell.

P-596 Wednesday, October 19, 2016

DOES ANTAGONIST ADMINISTRATION ON THE DAY OF HCG IN ICSI/IVF CYCLES WITH PREMATURITY PROGESTERONE RISE (PPR)-USING LONG AGONIST PROTOCOL- IMPROVES PREGNANCY OUTCOME? S. A. Hebisha,a B. A. Aboelazm,a H. M. Adel,a A. I. Ahmed. aGynecology, Alexandria University - Faculty of Medicine, Alexandria, Egypt; bObstetric and Gynecology, MEM Division, Department of Medical Genetics, Wayne State University, Detroit, MI.

OBJECTIVE: To evaluate the effect of antagonist administration (Cetrorelix) on the day of human chorionic gonadotrophin (hCG), in high responder patients with premature progesterone rise PPR, during long agonist protocol for IVF/ICSI cycles on pregnancy outcome.

DESIGN: Prospective controlled study.

MATERIALS AND METHODS: The study included ninety six high responder patients undergoing IVF/ICSI treatment with long agonist protocol with serum estradiol level more than 3000 pg/ml at the day of hCG. Patients were divided into three groups according to serum progesterone level on the day of hCG administration; (group A) 36 patients with progesterone level at or below 1.5 ng/ml (group B) 30 patients with progesterone level more than 1.5 ng/ml and (group C) 30 patients with progesterone level more than 1.5 ng/ml and they were administered single dose of 0.25 mg Cetrorelix on the day of hCG administration. Clinical pregnancy rate was compared among the three study groups.

RESULTS: There was no significant difference in the clinical pregnancy rate between (group A) with progesterone level below 1.5 ng/ml and (group C) with high progesterone level who received Cetrorelix (61.11% (22/36) vs 53.33% (16/30) respectively, p = 0.249). While the clinical pregnancy rate was significantly higher in (group C) with high progesterone who received Cetrorelix compared to (group B) with high progesterone who didn’t receive it (53.33% (16/30) vs 33.3 % (10/30) respectively, p = 0.002*).

CONCLUSIONS: Administration of a single dose of 0.25 mg Cetrorelix on the day of hCG in high responder patients with premature progesterone rise PPR-more than 1.5 ng/ml-during long agonist protocol for IVF/ICSI enhances the clinical pregnancy rate.

References:


P-597 Wednesday, October 19, 2016

MONO-Hp-hMG IN OVARIAN STIMULATION FOR ART IS ASSOCIATED WITH A SIGNIFICANTLY LOWER INCIDENCE OF PREMATURE PROGESTERONE RISE COMPARED TO MIXED FSH-Hp-hMG: IS HCG-DERIVED LH ACTIVITY PROTECTIVE? F. Sharara1,2, M. R. Goodwin.1,2 Virginina Center for Reproductive Medicine, Reston, VA;1Virginia Center for Reproductive Medicine, Reston, VA;2Ob/gyne, George Washington University, Washington, DC.

OBJECTIVE: The role of elevated progesterone (P₄) levels on implantation success is controversial. Some studies have suggested that premature progesterone rise (PPR) (defined as peak P₄ levels > 1.5 ng/ml) has a detrimental effect on IVF success, while others have been unable to demonstrate a negative effect. Recent data demonstrated that using ovarian stimulation with an LH/FSH ratio in the range of 0.3-0.6 yielded the lowest chance of spontaneous ovarian hyperstimulation syndrome while others have been unable to demonstrate a mental effect on IVF success, while others have been unable to demonstrate a mental effect on IVF success.

MATERIALS AND METHODS: Clinical data from all couples with unexplained infertility residing in the Grampian region of Scotland who attended Aberdeen Fertility Clinic from 1998-2011. A dynamic prediction modelling approach was used to predict a live birth pregnancy within one year from registration at the fertility clinic and from every subsequent month for a period of two years. Predictors included female age, duration of infertility, previous pregnancy status, male age, sperm motile density, year of registration at the fertility clinic, and initiation of fertility treatment (clomifene, intrauterine insemination or in-vitro fertilisation), the latter as a time-varying covariate. Treatment allocation bias was investigated by adjusting for propensity to treat at the clinic level.

RESULTS: Out of 1521 women with unexplained infertility, 911 (60%) achieved at least one live birth pregnancy over a maximum of 14 years, of which 640 (70%) were treatment independent pregnancies. The adjusted dynamic prediction model showed that the age of 32 the chances of pregnancy decrease by 11% with increasing year of age (Hazard Ratio (95% CI) = 0.89 (0.87 to 0.92)). Increasing duration of infertility was also associated with a decreased chance of pregnancy. Three months after the first visit to the fertility clinic the average chances of a pregnancy within one year with and without treatment were 23% and 31% respectively. Twelve months post registration these decreased to 18% and 25% respectively. The effect of treatment on pregnancy was highly significant (Hazard Ratio (95% CI) = 1.67 (1.34 to 2.09). Notably, this effect did not vary with time. There was no statistically significant evidence of treatment allocation bias.

CONCLUSIONS: This model estimates the diminishing chances of pregnancy over time and shows that early initiation of treatment is always more beneficial than expectant management. These results will inform individualised patient care pathways. Future work will involve external validation on other centres and the development of a decision rule to determine the optimum time to start treatment taking into account treatment burden, costs, waiting time and associated reduction in fertility.

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P-599 Wednesday, October 19, 2016

BODY MASS INDEX AND NUMBER OF MATURE EGGS RETRIEVED VERSUS NUMBER EXPECTED: IS THERE A GREATER DISCREPANCY IN OVERWEIGHT AND OBESE PATIENTS? S. Kim, L. R. Goodman, R. Flyckt. Cleveland Clinic, Beachwood, OH.

OBJECTIVE: As rates of obesity have increased worldwide, oocyte retrieval in overweight and obese patients has become more common. This scenario poses technical challenges both for the surgeon and the anesthesiologist. The objective of this abstract is to compare whether the expected number of mature eggs is different than the collected number of mature eggs in overweight and obese patients.

MATERIALS AND METHODS: 121 consecutive egg retrievals in 2012 from day one of stimulation. > 90% of the LH activity in HP-hMG is HCG-derived. The incidence of PPR was compared to 249 cycles using a mixed uFSH-Hp-hMG at 0.5 ratio reported earlier (Sharara, ASRM 2015).

RESULTS: Characteristics of the mono-Hp-hMG were as follows (mean ± SD): age = 35.3 years ± 3.7, BMI = 23.7 ± 4.1, AMH = 3.64 ± 3.52 ng/ml, FSH = 8.4 ± 5.5 IU/L, stimulation days = 9.5 ± 1.1, total HP-hMG dose (IU) = 3,559 ± 1,091, oocytes = 10.6 ± 5.1, MII = 7.8 ± 4.2, 2PN = 7.0 ± 3.8, peak E₂ = 1,578.5 ± 976.7 pg/ml, and peak P₄ = 0.81 ± 0.46 ng/ml. Cycles were divided into peak (day of hCG administration) P₄ < 1.5 ng/ml compared to P₄ > 1.5 ng/ml. The incidence of PPR was only 3.8% (4/157) in the mono-hMG group, compared to 16.4% (41/249) in the mixed FSH-hMG group (P = 0.0001).

CONCLUSIONS: The 2.5% incidence of PPR with mono-hMG is significantly lower than any reported PPR with FSH only (40%) or FSH/LH at 0.3-0.6 ratio (20% in the Warner study and 16.4% in our study). The use of mono-hMG seems protective against the potential negative effect of elevated P₄ on implantation compared to mixed protocols. Whether there are differences between HP-hMG using HCG-derived LH activity and other hMGs where the LH activity is not HCG-driven remains to be studied.


2. Sharara F. ArSM 2015.
to patients with both BMI $\geq 25$ (overweight) and BMI $\geq 30$ (obese) by t-test and among groups with ANOVA.

RESULTS: The average age of the cohort was 33.2 +/- 3.0 years, mean BMI was 25.5 +/- 5.5 kg/m$^2$, and the average number of mature oocytes collected was 11.6 +/- 3.9. When stratified into three groups of BMI $< 25$, 25-29 and $\geq 30$ kg/m$^2$, there was no difference in age, number of mature oocytes expected or retrieved between groups. The delta value in BMI $< 25$ patient cohort (n = 69) was 2.3 +/- 4.8 oocytes, delta value in the BMI 25-30 cohort (n = 32) was 3.3 +/- 4.3 oocytes, and delta value in the BMI $\geq 30$ (n = 20) was 2.0 +/- 4.8 oocytes, with no difference among groups (p = 0.51). There was no statistically significant difference between the delta values in the BMI $< 25$ and BMI $\geq 25$ groups (2.3 +/- 4.8 vs. 2.8 +/- 4.5; p = 0.55), and no difference was found between the delta values in the BMI $< 25$ and BMI $\geq 30$ groups (2.3 +/- 4.8 vs. 2.0 +/- 4.8 oocytes; p = 0.80).

CONCLUSIONS: Although technically more challenging, there may be no difference in oocyte retrieval rate in patients with higher BMI. Further studies are needed with larger sample sizes in the future.

P-600 Wednesday, October 19, 2016

UTILIZATION AND EFFECTS OF EMBRYO BANKING ON ART OUTCOME REPORTING IN THE U.S. A. Kashmir, D. H. Barad, S. Darmon, D. Albertini, N. Gleicher. Center for Human Reproduction, New York, NY; Wake Forest School of Medicine, Winston-Salem, NC; Albert Einstein College of Medicine, Bronx, NY; University of Kansas Medical Center, Kansas City, KS; Rockefeller University, Bronx, NY.

OBJECTIVE: Assisted Reproductive Technology (ART) reports generated by the Centers for Disease Control and Prevention (CDC) exclude embryo banking cycles from outcome calculations.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: We examined 2013 CDC data for impact of cycle exclusions from reporting on national ART outcomes due to embryo banking by recalculating live birth rates for autologous oocyte cycles. Inflation of reported live birth rates was assessed for all age groups of infertile women as the difference between fresh cycle live births in reference to number of initiated fresh cycles (excluding embryo banking cycles), as typically reported by the CDC and, again, with reference fresh ART cycles (i.e., “intent to treat”), including embryo banking cycles.

RESULTS: Out of 121,351 fresh non-donor ART cycles 27,564 (22.7%) involved in 2013 embryo banking. The proportion of banking cycles increased with female age from 15.5% in women <35 years to 56.5% in women >44 years. Concomitantly, the proportion of thawed cycles decreased with advancing female age (P <0.0001). Exclusion of embryo banking cycles led to inflation of live birth rates in fresh ART cycles, increasing in parallel to advancing female age, with utilization of embryo banking reaching 56.3% in women >44. Inflation of live birth rates in thawed cycles could not be reliably calculated from publically available CDC data but appears even larger.

CONCLUSIONS: Utilization of embryo banking increased during 2013 with advancing female age, suggesting a potential age selection bias. Exclusion of embryo banking cycles from national ART outcome reports significantly inflates national ART success rates, especially among older women.

Supported by: Intramural funds from The Center for Human Reproduction and grants from The Foundation for Reproductive Medicine.

P-601 Wednesday, October 19, 2016


OBJECTIVE: To determine if the type of IVF cycle (fresh versus frozen) influences IVF live birth rates (LBR) in different ethnic groups.

RESULTS: Age, BMI, day 3 FSH, AMH, gravidity, parity, infertility diagnoses, previous fresh cycles, oocytes retrieved, LBR and number of embryos transferred.

MATERIALS AND METHODS: Women under age 40 who underwent fresh IVF or FET, day 3 blastocyst transfer of fewer than 3 embryos from 2010 to 2015, with fewer than two prior IVF retrievals, were included in the study. We included four ethnic groups: Caucasian, African American, Asian and Hispanic, which were dichotomized into two main groups: Caucasian (n=1918, 76.4%) and non-Caucasian(n=593, 23.6%). Primary outcome was live birth rate. Variables were analyzed using Chi-square, ANOVA, Student’s t-test and logistic regression. A p-value < 0.05 was considered statistically significant.

RESULTS: The average age of the cohort was 33.2 +/- 3.0 years, mean BMI was 25.5 +/- 5.5 kg/m$^2$, and the average number of mature oocytes collected was 11.6 +/- 3.9. When stratified into three groups of BMI $< 25$, 25-29 and $\geq 30$ kg/m$^2$, there was no difference in age, number of mature oocytes expected or retrieved between groups. The delta value in BMI $< 25$ patient cohort (n = 69) was 2.3 +/- 4.8 oocytes, delta value in the BMI 25-30 cohort (n = 32) was 3.3 +/- 4.3 oocytes, and delta value in the BMI $\geq 30$ (n = 20) was 2.0 +/- 4.8 oocytes, with no difference among groups (p = 0.51). There was no statistically significant difference between the delta values in the BMI $< 25$ and BMI $\geq 25$ groups (2.3 +/- 4.8 vs. 2.8 +/- 4.5; p = 0.55), and no difference was found between the delta values in the BMI $< 25$ and BMI $\geq 30$ groups (2.3 +/- 4.8 vs. 2.0 +/- 4.8 oocytes; p = 0.80).

CONCLUSIONS: Although technically more challenging, there may be no difference in oocyte retrieval rate in patients with higher BMI. Further studies are needed with larger sample sizes in the future.

P-602 Wednesday, October 19, 2016

OUTCOMES FOR IN VITRO FERTILIZATION IN UTERINE ADENOMYSIS: A RETROSPECTIVE COHORT STUDY. D. O’Connor, M. A. Bedaiwy, C. Dunne, B. Taylor, J. Havelock.


CONCLUSIONS: Minority women have a significantly higher LBR in FET cycles compared to fresh IVF cycles, regardless of age. Caucasian women have higher LBR in fresh vs FET cycles in SET but not in DET. Further research is needed to identify confounding factors and to determine if minority women would benefit from double FET in selected cases.

Supported by: Intramural funds from The Center for Human Reproduction and grants from The Foundation for Reproductive Medicine.
conflicting results in the current literature and to date no definitive association has been found. This objective of this study was to compare IVF outcomes in subjects with adenomyosis to subjects without adenomyosis. 

**DESIGN:** This was a retrospective cohort study.

**MATERIALS AND METHODS:** We used the transvaginal ultrasonograms of 400 subjects undergoing fresh embryo IVF cycles during 2014 in two fertility centres. Adenomyosis was diagnosed on ultrasonograms performed during controlled ovarian hyperstimulation using validated morphological criteria. Our primary outcome was clinical pregnancy before 12 weeks.

**RESULTS:** Adenomyosis was found in 34 out of 400 (8.5%) subjects. The clinical pregnancy rate of women undergoing IVF with adenomyosis was not statistically different than those without adenomyosis (47% vs 41.2%, p=0.591). Spontaneous miscarriage rate was also not statistically different between the two groups (19.1% vs 14.7%, p = 0.528). No differences in outcome were found when controlled for age, number of embryos transferred, or day of transfer.

**CONCLUSIONS:** Our study found no difference in IVF outcomes in women with adenomyosis compared to those without adenomyosis. A limitation of this study is the small sample size; however, the results of our study and the current literature to date demonstrate that there is insufficient evidence to recommend the routine screening and treatment of adenomyosis before IVF cycles.

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**P-604 Wednesday, October 19, 2016**

**SHORT INTERPREGNANCY INTERVAL (IPI) AND OBSTETRIC OUTCOMES IN ASSISTED REPRODUCTION.** M. Quinn, M. Cedars, V. Y. Fujimoto. Department of Obstetrics, Gynecology and Reproductive Sciences, University of California, San Francisco, San Francisco, CA.

**OBJECTIVE:** Research has demonstrated an association between short IPI and poor obstetric outcomes, prompting the World Health Organization (WHO) to recommend an IPI of 18 months. Many patients undergoing assisted reproduction desire a shorter IPI, particularly in the setting of advanced maternal age. We aim to determine whether the association between short IPI and adverse pregnancy outcome exists within the population undergoing assisted reproduction.

**DESIGN:** Retrospective cohort analysis of all patients who had a live birth following assisted reproduction at a single academic center and returned for a subsequent IVF cycle between 2003-2015.

**MATERIALS AND METHODS:** Delivery-to-cycle interval (DCI) was calculated as time elapsed from delivery to first cycle start. For those subjects who conceived on their first cycle this was defined as IPI. A short DCI or IPI was defined as < 18 months. Chi-squared analyses were used to evaluate dichotomized pregnancy outcomes while t-tests were used to compare differences in means for continuous pregnancy outcomes among those with short vs. recommended IPI. A multivariate regression was utilized to evaluate the impact of age on outcomes of interest.

**RESULTS:** 1,054 subjects returned for an attempt at a second conception. 508 (48.2%) had a DCI <18 months. 461 subjects conceived in their first cycle including 339 who had a live birth. There was no difference in rate of spontaneous or live birth among those with and without a short DCI (45.9% vs. 41.7% p-value 0.17 and 33.7% vs. 32.5% p-value 0.68). There was no difference in rate of miscarriage among those with a short vs. recommended IPI (25.4% vs. 19.56% p-value 0.13). Among subjects with a singleton live birth and a short or recommended IPI there was no difference in gestational age at delivery (38.6 ± 0.17 vs. 38.9 ± 0.10 weeks p-value 0.08), preterm delivery rate (<37 weeks) (13.9% vs. 12.7% p-value 0.70) or birth weight (3398.5 ± 512.1 vs. 3373.3 ± 317.7 grams p-value 0.67). Among subjects with a live birth of a multiple gestation (n=105), gestational age at delivery was decreased in the short compared to recommended IPI group (35.49±0.49 vs. 36.77±0.25 p=0.005) although there was no difference in preterm delivery rate (60.5% vs. 46.2% p-value 0.16).

**CONCLUSIONS:** A short IPI does not appear to have a dramatic impact on patients undergoing assisted reproduction with respect to the most commonly measured obstetric outcomes. A larger dataset is needed to address the validity of the WHO recommendation for an 18 month IPI in this population.
EMT was associated with live birth in univariate models (OR 1.04, 95% CI 1.01-1.09) but not in adjusted models (1.03, 95% CI 0.98-1.08). In univariate and adjusted models, C endometrial pattern had significantly lower live birth (OR 0.63, 95% CI 0.46-0.87) compared to A and B patterns.

CONCLUSIONS: The endometrial pattern was associated with age and endometrial thickness, but not with P on the day of trigger. C graded endometrial pattern was associated with lower live birth, even when controlling for other confounders.

P-606 Wednesday, October 19, 2016
RE-PUNC TURE TO PREVENT OCTO EE DEGENERATION DOES NOT INFLUENCE PIEZ I-ICSI PREGNANCY RATES OR EMBRYO VIABILITY. R. Matsunaga, a S. Watanabe, a M. Miura, a Y. Kobayashi, a N. Yamanaka, a K. Kamihata, a K. Wakahata, a T. Horiuchi. a Ochi Yume Clinic, Nago, Japan; a Department of Life Science, Prefectural University of Hiroshima, Shobara, Japan.

OBJECTIVE: In cases where the oolemma is punctures without a piezo pulse due to the low elasticity of the oolemma at the time of insertion of the injection pipette previous reports indicate that the direct injection of sperm into such oocytes increases their degeneration rate.However, occasionally this abnormal puncture can be corrected by re-puncturing at a different injection site resulting in a decreased oocyte degeneration rate.

DESIGN: Retrospective study.

MATERIALS AND METHODS: We collected 2248 mature oocytes from 604 women (treatment cycle: 968, average age: 39.4) between July 2015 and December 2015 and performed piezo-ICSI. In cases where the oolemma was punctured using a pipette inserted into less than 50% of the oocyte diameter without a piezo pulse (defined as an abnormal puncture), re-puncturing was performed at a different injection site. Oocytes were re-punctured a maximum of three times, and oocyte degeneration rate was measured in each case. The oocyte blastocyst development rate and implantation and pregnancy rate were also compared in embryos that had, and had not been, re-punctured.

RESULTS: Of 243 re-punctured mature eggs (11% of the total), 147 (60%) were successfully punctured by applying a piezo pulse or using a pipette inserted into marathon 50% of the oocyte diameter without a piezo pulse (defined as a normal puncture). Outcomes were classified into three groups: "the first attempt resulting in a normal puncture", "the second or third attempt resulting in a normal puncture", and "the second or third attempt resulting in an abnormal puncture". The oocyte degeneration rate in each group was 1.7% (n=472), 12% (17/147), and 29% (28/96), respectively. These results indicate that there is a significant difference in oocyte degeneration rate between the three groups (P<0.05). In embryos that needed re-puncture, the blastocyst development rate was 37% (49/133), and implantation and pregnancy rate of a single blastocyst was 59% (10/17). In embryos which did not need re-puncture, the implantation and pregnancy rate was 34% (472/ 1405) and 47% (771/165), respectively. These results indicate that there is no significant difference between implantation and pregnancy rates in normal puncture and re-punctured embryos.

CONCLUSIONS: Abnormal oocyte punctures can be corrected by re-puncturing and suppresses an increase in oocyte degeneration rate. Re-puncturing did not influence embryo development and pregnancy rates and is thus thought to be and effective technique to prevent oocyte degeneration.

P-607 Wednesday, October 19, 2016
SYMPTOMS OF ANXIETY AND DEPRESSION AMONG INFERTILE WOMEN, WOMEN PREGNANT AFTER INFERTILITY TREATMENT, AND SPONTANEOUSLY PREGNANT WOMEN. L. S. Joelsson, a A. Berglund. a K. Wanggren. a T. Tyden. b Department of Women's and Children's, Obstetrics and Gynecology, Uppsala, Sweden; a Department of Clinical Science, Intervention and Technology, Obstetrics and Gynecology, Karolinska Institutet, Stockholm, Sweden; a Department of Public Health and Caring Sciences, Uppsala University, Uppsala, Sweden.

OBJECTIVE: Fertility problems and assisted reproductive technology (ART) treatments have been associated with psychological stress. Little is known whether these symptoms persist when treatment results in a pregnancy. The aim of the study was to investigate symptoms of anxiety and depression among sub-fertile women seeking for infertility and assess to what extent they differ from women who conceived after infertility treatment and/or women who conceived naturally.

DESIGN: A cross-sectional study; participants completed a self reported questionnaire.

MATERIALS AND METHODS: Sub-fertile women (n = 468) answered a questionnaire at their first visit to the fertility clinic and pregnant women (n = 3290) upon their registration at antenatal clinics. The Hospital Anxiety Scale (HADS) and Edinburgh Depression Scale (EDS) were used. Data were analyzed using Pearson’s chi-squared test.

RESULTS: A total of 468 infertile women and 3290 pregnant women were included in the study. Among the pregnant women, 151 had conceived after infertility treatment and 3005 had conceived naturally. One out of four (23.3%, n=108) sub-fertile women had HADS-A scores > 10 compared to 7.7% (n=11) of pregnant women who conceived after infertility treatment and 6.9% (n=203) of pregnant women who conceived naturally (P<0.001). The EDS scores among infertile women were > 12 in 16.1% and 8.5% of pregnant women after infertility treatment (P<0.001). Women who conceived after infertility treatment did not score differently for anxiety and depression compared to women having conceived naturally.

CONCLUSIONS: Women showed a decrease in anxiety and depression when treatment successfully resulted in a pregnancy. However, the high scores among infertile women can pose challenges not only for the patient, but also for the infertility treatment team. Early psychological counseling and interventions are advisable to decrease the surge in depression/anxiety, and could presumably lead to increased pregnancy rates and improvement in infertile women's quality of life.

Supported by: Funding of the study was received from the Foundation Family Planning Fund in Uppsala, the College of Medicine at Uppsala University, Sweden and the Uppsala-Örebro Regional Research Council, Sweden. None of the authors have any conflict of interest to declare.

P-608 Wednesday, October 19, 2016
DOES PRESENCE OF HUMAN PAPILLOMAVIRUS (HPV) INFEC TION INFLUENCE THE RESULTS OF IN VITRO FERTILIZATION (IVF) TREATMENT? I. Oborna, a H. Ondryasova, a B. Zborilova, a J. Brezina, a J. Vrbкова. a Faculty of Medicine and Dentistry, Palacky University, Olomouc, Czech Republic; a Fertimed Ltd, Olomouc, Czech Republic; a Arleta, Ltd, Kostelec nad Orlici, Czech Republic.

OBJECTIVE: To find out the prevalence of HPV in oocyte donors and in women from infertile couples and to examine whether there is any relation between HPV status and IVF results.

DESIGN: Prospective study.

MATERIALS AND METHODS: Cervical smears of oocyte donors (n=207) and women from infertile couples (n=946) were taken from March 2013 to October 2015 and analyzed for the presence of 14 high-risk HPV genotypes (Cobas 4800, Roche). Prevalence of HPV in both groups was compared. In those who underwent IVF treatment within the next 6 months after sampling (47 oocyte donors and 362 women from infertile couples), number of pregnancies and abortions was evaluated in relation to their HPV status. Only embryo transfers (ET) with one or two fresh embryos were included. All participants signed written consent, filled a questionnaire focused on their health status and sexual behavior. Study was approved by ethical board of the university.
RESULTS: Average age of oocyte donors (OD) was 27.0 and of women from infertile couples (IW) was 32.7 (p = 0.001). Average age of oocyte recipients was 40.6. The incidence of HPV increased with the number of sexual partners in both groups. HPV was detected in 90 IQ (15%) and increased in the number of sexual partners (median 4 for IQ group vs. 5 for IW HPV+; p = 0.002); and in 57 OD (27%) where number of sexual partners (median 3 for OD group vs. 4 for OD HPV+; p = 0.074). HPV prevalence in OD was 28% compared to 15% in IW (p = 0.024). HPV+ OD (n = 57) were younger (24.3 vs. 27 in HPV−; p = 0.001) and more often childless (44% vs. 20%; p = 0.001) than HPV−. OD oocytes obtained were used for one to three synchronized recipients. There were 46 spontaneous pregnancies in IW group (5%); 9 in HPV+ IW (6%), 37 in HPV− IW (4.6%) with one abortion (AB) in each group (11% vs 3%). IVF results are given in the table.

CONCLUSIONS: HPV positivity may have a negative influence on fertility and may be a risk factor for pregnancy. From that point significantly higher prevalence of HPV infection within OD is disconcerting. No statistical significance in pregnancy rate and number of abortions between HPV+ and HPV− women undergoing IVF treatment was found.

<table>
<thead>
<tr>
<th>IVF+ET</th>
<th>HPV Status</th>
<th>Pregnancy/ ET (%)</th>
<th>p</th>
<th>Abortion (%)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>IW HPV+ (n=45)</td>
<td>18/45 (40%)</td>
<td>0.131</td>
<td>3/18 (16.7%)</td>
<td>0.722</td>
<td></td>
</tr>
<tr>
<td>OD HPV+ (n=10)</td>
<td>1.000</td>
<td>0.927</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OD HPV− (n=362)</td>
<td>HPV− (n=317)</td>
<td>88/317 (27.8%)</td>
<td>21/88 (23.9%)</td>
<td>0.710</td>
<td></td>
</tr>
<tr>
<td>Recipient (n=47)</td>
<td>Recipient (n=16)</td>
<td>6/16 (37.5%)</td>
<td>2/6 (33.3%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recipient (n=87)</td>
<td>HPV− (n=37)</td>
<td>24/71 (33.8%)</td>
<td>11/24 (45.8%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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P-610 Wednesday, October 19, 2016

PROGESTERONE LEVELS AND IVF PREGNANCY. I. Rybkina,a G. Barcia,b K. Wei,c J. D. Jacobson,b J. Corselli,a P. J. Chan.a aGynecology and Obstetrics, Loma Linda University School of Medicine, Loma Linda, CA; bLoma Linda University, Yucaipa, CA.

OBJECTIVE: Premature luteinizing hormone (LH) surge causes a 5-30% probability of preovulatory rise in serum progesterone (P4) during IVF cycle stimulation and is associated with negative pregnancy outcome. We evaluated the probability of preovulatory rise in serum progesterone (P4) during IVF cycle stimulation and is associated with negative pregnancy outcome. The objectives were: (1) to correlate P4 measured 3-4 days before IVF with pregnancy outcome and (2) to determine the ability of measuring P4 level 1-week after embryo transfer in predicting pregnancy outcome.

DESIGN: Retrospective study in a tertiary academic center.

MATERIALS AND METHODS: With IRB approval, chart reviews of 171 cases of IVF/ICSI cycles from 2013-2014 were carried out. 74 female patients were >35 years old. Day of P4 measurement either before egg retrieval or post-embryo transfer and the corresponding P4 levels were recorded and analyzed with pregnancy outcome. Exclusion criteria were missing data, P4 drawn >4 days before egg retrieval or <9 days post-embryo transfer. Clinical pregnancy was defined as ultrasound and serum beta human chorionic gonadotrophin administration. Data were analyzed by ANOVA and t-test adjusted for unequal variance.

RESULTS: The results were analyzed based on patient age and reproductive outcome. In pregnant patient who were <35 years old, P4 levels were 0.7±0.3, 1.0±0.4, 0.7±0.2 ng/mL (mean±1st.dev.) for 4, 3 or 2 days before egg retrieval respectively. In the non-pregnant group who were ≥35 years old, P4 levels were 1.0±0.2, 1.1±0.5, 0.9±0.4 ng/mL respectively. The means were not different (p > 0.05). In pregnant patients who were >35 years old, P4 were 1.1±0.5, 1.0±0.4, 1.3±0.9 ng/mL for 4, 3 or 2 days before egg retrieval respectively. In the non-pregnant group P4 were 0.6±1.2, 1.2±0.7, 1.0±0.6 ng/mL respectively. For the <35 years group, P4 on day 7 post-transfer for the pregnant versus non-pregnant groups were 78.7±39.1 versus 61.0±21.0 ng/mL while the ≥35 years group, the P4 were 106.2±92.8 versus 85.4±42.0 ng/mL. The means were not significantly different.

CONCLUSIONS: The results demonstrated P4 measurements 3-4 days before oocyte retrieval were not associated with pregnancy outcome. Furthermore, P4 levels on day 7 post-transfer were not useful in predicting outcome and testing considered wasted resource. The findings suggested either early follicular P4 was an ineffective marker for uterine receptivity or differences between local and systemic P4 existed. Limitations of the study included data from a single center, observational design and patient subpopulation residing in a Blue Zone region. In summary, P4 testing 3-4 days before retrieval was not useful in predicting outcome.

References:
OBJECTIVE: Inferfertile couples seek ART treatment with the goal of achieving the birth of a healthy child. A growing number of clinicians propose an IVF, PGS and freeze-all plan, a strategy that has shown to be efficient in improving the efficiency of the treatment process. Amidst these benefits a pivotal question lingers when ≥2 embryos are available for ET: transfer 2 embryos in one cycle, or transfer 2 single embryos in sequential cycles.

DESIGN: Retrospective.

MATERIALS AND METHODS: A total of 1,907 IVF cycles were identified, and 832 met the inclusion criteria of use of a freeze-all protocol with PGS testing in 2010-2015. Cohorts were segregated into: Group 1) two SET cycles (n=663); Group 2) one DET cycle (n=169). Cycle outcome (no pregnancy, biochemical pregnancy, clinical loss (after detection of gestational sac) and ongoing pregnancy (OPR)) and the multiples rate were calculated, along with the empirical cumulative percentage of patients who achieved OP on each treatment path. 95% CI were reported for all calculations. The average cost of live birth for each path was computed as the sum of the cumulative costs associated with having a singleton ($26,922) or twins ($115,238) weighted by their respective probabilities of occurring conditional on a live birth occurring, along with the weighted cost of miscarriages ($596), PGS use ($5,000), and the weighted cost of FETs ($2,800) required in each path.

RESULTS: There was no statistical difference between age, BAFC, AMH, day 3 FSH and BMI between groups. The cumulative ongoing pregnancy rate (OPR) in Group 1 was 75% [71-80] with a 97.3% [96-99] singleton rate. Per cycle, the OPR in cycle 1 was 52% [48-56], and in cycle 2 was 49% [42-56]. The cumulatively achieved singleton OPR was 73% [69-78]. From the 48% that did not achieve a OP in the 1st cycle, 44% had a loss (biochemical loss 24% [19-28]; clinical loss 20.7% [17-25]); and 56% [51-61] were not pregnant. The expected cost for a live birth in this group was $38,063 and for no live birth: $10,852. In Group 2 59% [52-66] achieved OP with 38% [31-46%] of patients achieving a singleton gestation. Among those who had OP, 35% [26-45%] had twins. The expected cost for a live birth was $65,910 and for no live birth: $7,911.

CONCLUSIONS: It is well established that SET with PGS reduces multiple births and improves neonatal end points. However, there is a paucity of data when considering economic impact of such decisions. Compared to one DET cycle with PGS, this study showed patients who pursued two SET cycles with euploid embryos achieved 16% higher cumulative OPR, 35% higher singleton OPR, 32% lower multiple rate and $27,847 less dollars spent on a live birth when ≥2 euploid embryos were available for transfer.

Probabilty of ongoing clinical pregnancy in relation to serum HCG levels 9 days post-ET

<table>
<thead>
<tr>
<th>HCG (mIU/mL)</th>
<th>Probability (%)</th>
<th>Serum HCG 9 days post-transfer</th>
</tr>
</thead>
<tbody>
<tr>
<td>50</td>
<td>26.5</td>
<td></td>
</tr>
<tr>
<td>75</td>
<td>67.1</td>
<td></td>
</tr>
<tr>
<td>80</td>
<td>80.6</td>
<td></td>
</tr>
<tr>
<td>90</td>
<td>107.6</td>
<td></td>
</tr>
<tr>
<td>95</td>
<td>134.6</td>
<td></td>
</tr>
<tr>
<td>&gt;99</td>
<td>185.3</td>
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</tr>
</tbody>
</table>

P-612 Wednesday, October 19, 2016


OBJECTIVE: Despite the increasing utilization of single, euploid frozen blastocyst transfer (FET) as a treatment strategy, prognostic thresholds for the initial serum hCG level have yet to be established. This study seeks to identify the hCG thresholds correlative of successful intrauterine pregnancy.

DESIGN: Retrospective cohort analysis.

MATERIALS AND METHODS: Patients that underwent single, euploid FET resulting in a positive serum hCG (>2 mIU/ml) from June 2011 to March 2016, were included. Serum hCG levels (unit: mIU/ml) were measured 9 days post FET and analyzed with respect to maternal age, BMI, blastocyst expansion grade, implantation and clinical pregnancy rates.

All embryos were biopsied at the blastocyst stage, with ploidy determined by PCR. Data was analyzed by student’s t-test, Chi-square, Kruskal-Wallis, linear and binary logistic regression.

RESULTS: Of the 876 single euploid FETs, 91% (n=802) had a serum hCG >2 mIU/ml. Serum hCG levels were drawn 9 days after FET in 649 patients with 77.8% implantation (n=505) and 71.8% clinical pregnancy rate (n=466). Neither odds of implantation nor clinical pregnancy were influenced by maternal age, BMI or blastocyst expansion grade. Serum hCG levels were lower in patients with BMI>30 (OR -4.39 [95% CI (-6.3)-(-2.46), p=0.0012]. Serum HCG levels significantly predicted the probability of implantation (OR 1.02 [95% CI 1.02-1.03], p<0.0001) and clinical pregnancy (OR 1.03 [95% CI 1.02-1.04], p<0.0001. HCG thresholds for clinical pregnancy (Table) were not correlated with maternal age, degree of blastocyst expansion or BMI.

CONCLUSIONS: Serum hCG levels measured 9 days after transfer are a predictive marker for implantation and clinical pregnancy. Half of patients with hCG <26.5 mIU/ml ultimately had an early pregnancy loss, while nearly 90% of those with initial HCG >100 mIU/ml had an ongoing clinical pregnancy. In a well controlled population if patients undergoing SET of euploid embryos, initial HCG level are a powerful prognostic indicator of embryonic health and of the likelihood of a positive reproductive outcome.
CONCLUSIONS: Intra lipid has been introduced to improve pregnancy rates in women with implantation failure. Based on these results there is no difference in outcomes once confounding factors have been allowed for. Our study concludes that, at present, intra lipid should not be advocated for as a beneficial therapy and future use should only be as part of a randomised controlled trial. The safety of intra lipid also needs investigation.

References:

P-614 Wednesday, October 19, 2016

OBJECTIVE: The euploid embryo has on average a 50-60% implantation rate. The purpose of this study was to determine whether blastocyst development rate and/or morphology were independently associated with implantation of a euploid embryo.

DESIGN: Retrospective study.

MATERIALS AND METHODS: A total of 3,646 blastocysts were biopsied and analyzed. All embryos were biopsied once expanded and cryopreserved the same day. 1,475 blastocysts were biopsied on day 5 and 2,171 on day 6. Morphology was determined using Gardner's classification and subsequently categorized into four grades: good (BB); fair (BB) and poor (C+). All embryos were vitrified after biopsy. 647 euploid embryos were studied.

RESULTS: The average patient age of day 5 and day 6 blastocyst transfer cycles was 37.7 ± 3.3 and 37.9 ± 3.3 years, respectively. The percent of euploid embryos were euploid on day 5 and day 6 was 51% and 42% (P < 0.001), respectively. The implantation rate for day 5 vs day 6 euploid embryos was 62% and 45% (p < 0.05), respectively.

Table 1. The association between euploidy implantation rate, day of biopsy and morphology

<table>
<thead>
<tr>
<th>Blast grading</th>
<th>Day 5 IR</th>
<th>Day 6 IR</th>
</tr>
</thead>
<tbody>
<tr>
<td>AA</td>
<td>0.67</td>
<td>0.58</td>
</tr>
<tr>
<td>AB/BA</td>
<td>0.60</td>
<td>0.43</td>
</tr>
<tr>
<td>BB</td>
<td>0.64</td>
<td>0.46</td>
</tr>
<tr>
<td>C+</td>
<td>0.40</td>
<td>0.33</td>
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</table>

CONCLUSIONS: This study indicates that the development rate is the most important predictor of implantation rate in a euploid embryo. These findings suggest that not all euploid embryos are equal. Thus, when determining which euploid embryo to transfer, the development rate should be the primary factor and morphology the secondary factor.

P-615 Wednesday, October 19, 2016
EARLY GROWTH RESPONSE 1 (EGR1) IS REQUIRED FOR PROPER EPITHELIAL-STROMAL CROSS-TALKS TO RESPOND TO E2 AND P4 FOR SUCCESSFUL EMBRYO IMPLANTATION IN THE UTERUS. H. Kim,a Y. Kim,a K. Kang,b H. Choi,a M. Koong,a I. Kang,b T. K. Yoon,b H. Song,a,b aBiomedical Science, CHA University, Seongnam, Korea, Republic of; bCHA Seoul Fertility Center, CHA University, Seoul, Korea, Republic of.

OBJECTIVE: Harmonized actions of ovarian estrogen (E2) and progesterone (P4) regulate cell proliferation and differentiation in the uterus with a spatiotemporal manner. Imbalance between the actions and levels of two major regulators often lead to infertility and gynecological diseases. While numerous works have shown that reduced expression and/or deletion of uterine factors participating in P4 signaling could disturb uterine physiology, a few local factor(s) to mediate E2 actions in the uterus has been revealed. Recently, we reported that Egr1 is an immediately early response gene induced by E2 in the uterus. In this study, we have examined whether early growth response 1 (Egr1) is required to maintain coordinated actions of E2 and P4 for successful embryo implantation by characterizing Egr1(-/-) female mice with multiple approaches.

DESIGN: Animal study on mouse uterus with a series of experiments in cell culture.

MATERIALS AND METHODS: real-time RT-PCR, Western blotting, immunostaining, histological analyses, hormone assays, epithelial-stromal cell co-culture were performed with wildtype and/or Egr1(-/-) mice.

RESULTS: Given exogenous gonadotrophins to overcome LHβ deficiency in the pituitary of Egr1(-/-) mice, ovulation, fertilization and embryo development normally occurred in these mice. However, they showed compromised development rate of embryo implantation with reduced uterine responses to artificial decidualization stimuli. While serum levels of E2 and P4 in Egr1(-/-) mice were comparable, genes regulated by E2 or P4 in uterine epithelial cells (ECs) were aberrantly expressed on day 4 of pregnancy. Impaired P4 signaling in ECs caused hypersensitive E2 responses shown as enhanced expression of E2-responsive genes such Muc1 and Ltf as well as reduced levels of P4-dependent genes, such as Ihh and Areg, in Egr1(-/-) ECs.

This is consistent with persistent proliferation in ECs and severely compromised proliferation in stromal cells (SCs) in Egr1(-/-) mice treated with E2+P4. Furthermore, primary co-culture of Egr1(-/-) ECs with Egr1(+/+) SCs and vice versa supported a notion that Egr1 is required for epithelial-stromal cross-talks with respect to proper responses to E2 and/or P4 in both uterine cell compartments.

CONCLUSIONS: Egr1 is an essential transcription factor for epithelial-stromal cross-talks with properly responses to E2 and P4 for successful embryo implantation in the uterus.

Supported by: This work was supported in part by grants from the National Research Foundation of Korea (NRF) grant funded by the Korean government (MEST) (NRF-2012R1A1A2A01011274 and NRF-2015R1A2A20106714).

P-616 Wednesday, October 19, 2016
IMPACT OF TRANSCRIPTOMIC BASIS OF LOCAL ENDOMETRIAL INJURY ON IMPLANTATION RATE AMONG PREVIOUSLY FAILED IVF-ICSI CYCLES. N. Singh, M. Bhat, D. Ghosh; aDepartment of Obstetrics & Gynaecology & IVF, All India Institute Of Medical Sciences, Delhi, India; bSenior Research Fellow, Department of Physiology, All India Institute Of Medical Sciences, Delhi, India; cDepartment of Physiology, All India Institute Of Medical Sciences, Delhi, India.

OBJECTIVE: To assess the impact of transcriptomic basis of local endometrial injury on implantation rate among the women with previously failed attempts of IVF-ICSI cycles.

DESIGN: Prospective non randomized intervention study was performed in IVF Center, Department of Obstetrics and Gynaecology, and Molecular Biology Laboratory, Department of Physiology of a tertiary care hospital.

MATERIALS AND METHODS: A total of 20 women with previously failed attempts of IVF were recruited in the ethically approved study during the period January 2014-December 2015. Endometrial samples were obtained by gentle scratching of the endometrium using karmen’s cannula no.4 at cycle day 14-18 and endometrial tissue was subjected to mRNA extraction using standard protocol (Khan et al 2012). IVF-ET was done in subsequent cycles. Based on pregnancy outcome, the subjects were classified into groups; those who became pregnant and those who did not become pregnant. High quality (RIN > 8.0) RNA were employed for microarray-based expression analysis using 4X44K human whole genome chips and agilent microarray platform. Exploratory and differentials display analysis of gene expression data were performed using Gene Spring software (Khan et al 2012).
RESULTS: Clustering analysis of 20 samples revealed that endometrial samples collected from women who became pregnant (n=9) displayed expression cluster segregated from the samples of non-pregnant women (n=11). Further, differential display analysis of the expression data identified 415 genes showing >3-fold changes in expression between the two groups at \( P<0.01 \).

CONCLUSIONS: The study concluded that injury to the endometrium resulted in improved pregnancy rate and there were differential mRNA expression profile in endometrium between the pregnant and non-pregnant women. Further, study of different genes identified from expression microarray will assist in prediction of implantation competence of patients with recurrent implantation failure.

References:

Supported by: Institutional Research Grant.

P-617  Wednesday, October 19, 2016

DOES AN ENDOMETRIAL SCRATCH AFFECT PREGNANCY RATES IN EGG-DONATION TREATMENT PATIENTS WITH OR WITHOUT PREVIOUS IMPLANTATION FAILURES?
A. Izquierdo, a J. Rayward, a M. Moschetta, b M. Calomarde Rees, b

OBJECTIVE: Endometrial scratch (ES) has been described as a simple technique that may increase the endometrial receptivity when performed in the mid-luteal phase of the precedent cycle to embryo transfer. Our aim was to assess the effects of an endometrial scratch in patients undergoing an egg donation cycle.

DESIGN: All patients with uterine anomalies, severe male factor or recurrent miscarriage were excluded. We retrospectively reviewed 142 egg donation cycles and analyzed their results in terms of pregnancy rate (PR) and ongoing pregnancy rate (OPR) considering whether they had done previous embryo transfers and/or had an ES prior to the embryo transfer cycle. We compared women who had their first embryo transfer to those who had previous embryo transfers and had not succeeded.

MATERIALS AND METHODS: Proportions were compared with Chi-Squared test, and continuous variables were analyzed with the ANOVA among the 4 groups.

RESULTS: A total of 142 cycles of egg-donor fresh embryo transfer were reviewed. 29 of them had had an ES with a Cournier Pipelle during the luteal phase of the previous cycle. Once they had their period, patients started taking either 2 mg Estradiol Valerate orally every 8 hours or two 100 mg Estradiol patches every 48 hours. They had a scan to check the endometrial thickness 10 to 12 days after the cycle started. If the lining was thicker than 6 mm they continued with the same protocol. If the endometrial thickness was lower, we added another patch or more oral estradiol. The day of the egg retrieval of the donor, recipients began with 200 mg vaginal progesterone pessaries and continued both meds until the pregnancy test at least. The overall PR was 67% for the patients who did not undergo an ES and 51.7% for the patients who did receive it. PR for patients who had had a previous ART treatment and had an ES was 56%. PR for patients who had had a previous ART treatment but did not have an endometrial scratch was 63.3%. None of these differences was statistically significant. Other results are summarized in this table:

<table>
<thead>
<tr>
<th></th>
<th>No Previous Treatment + No ES</th>
<th>No Previous Treatment + ES</th>
<th>Previous Treatment + No ES</th>
<th>Previous Treatment + ES</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>45</td>
<td>6</td>
<td>55</td>
<td>23</td>
<td>0.679</td>
</tr>
<tr>
<td>AGE years (SD)</td>
<td>40 (6.2)</td>
<td>43,2 (1.94)</td>
<td>41 (4.05)</td>
<td>41,4 (4.91)</td>
<td></td>
</tr>
<tr>
<td>Donor Sperm (%)</td>
<td>4 (8.9)</td>
<td>0 (0)</td>
<td>4 (7,1)</td>
<td>1 (4.6)</td>
<td>0.824</td>
</tr>
<tr>
<td>Partner Sperm (%)</td>
<td>41 (91,1)</td>
<td>100 (100)</td>
<td>52 (92,9)</td>
<td>21 (95,4)</td>
<td>0.824</td>
</tr>
<tr>
<td>Endometrial Thickness mm (SD)</td>
<td>7,82 (2,13)</td>
<td>7,55 (1,09)</td>
<td>8,4 (2,15)</td>
<td>7,55 (1,90)</td>
<td>0.291</td>
</tr>
<tr>
<td>Pregnancy Rate (%)</td>
<td>32 (71,1)</td>
<td>2 (33,3)</td>
<td>35 (63,3)</td>
<td>13 (56,5)</td>
<td>0.265</td>
</tr>
<tr>
<td>Ongoing Pregnancy Rate (%)</td>
<td>33 (94,3)</td>
<td>2 (100)</td>
<td>30 (93,8)</td>
<td>11 (84,6)</td>
<td>0.662</td>
</tr>
<tr>
<td>Miscarriage Rate (%)</td>
<td>2 (5,7)</td>
<td>0 (0)</td>
<td>2 (6,2)</td>
<td>2 (15,4)</td>
<td>0.662</td>
</tr>
</tbody>
</table>

OBJECTIVE: To determine the degree of negative impact of transferring fresh embryos despite a serum progesterone (P) >2 ng/mL on the day of human chorionic gonadotropin (hCG) injection vs. purposeful cryopreservation with a deferred frozen embryo transfer (ET) in women with diminished ovarian reserve (DOR). Furthermore, to determine if the negative effect in more on actual implantation or live birth.

DESIGN: Prospective quasi-controlled (patient option) comparative study.

MATERIALS AND METHODS: Women aged \( \leq 39 \) whose day 3 follicle stimulating hormone (FSH) was \( >12 \) mIU/mL, who following controlled ovarian stimulation using a gonadotropin releasing hormone antagonist-gonadotropin protocol had a serum P \( >2 \) ng/mL were advised of the general consensus that an increased serum P \( >2 \) ng/mL on day of hCG is associated with a lower pregnancy rate following ET in fresh cycles probably by advancing the window of implantation (WOI). Further advice was that the adverse effect was on the endometrium not the embryo, thus deferring to frozen ET was expected to be more successful. Nevertheless, they were informed that live deliveries have occurred following fresh ET with serum P level \( >2 \) ng/mL and the only advantage of transferring fresh embryos were for financial savings. All ETs were on day 3.

RESULTS: Pregnancy and implantation rates for patients aged \( \leq 39 \) with P levels \( >2 \) ng/mL on day of hCG and DOR. Fresh ETs vs. patients that deferred for frozen ET.

P-618  Wednesday, October 19, 2016

PREGNANCY OUTCOME FOLLOWING FRESH VS. FROZEN EMBRYO TRANSFER ON EMBRYOS CREATED WITH THE SERUM PROGESTERONE >2 NG/ML ON THE DAY OF THE HUMAN CHORIONIC GONADOTROPIN TRIGGER IN WOMEN WITH DECREASED EGG RESERVE. J. H. Check, a R. Cohen, b C. Watson.

aDept. OB/GYN, Cooper Medical School of Rowan University, Melrose Park, PA; bCooper Institute for Reproductive and Hormonal Disorders, P.C., Mt. Laurel, NJ.

OBJECTIVE: To determine the degree of negative impact of transferring fresh embryos despite a serum progesterone (P) >2 ng/mL on the day of human chorionic gonadotropin (hCG) injection vs. purposeful cryopreservation with a deferred frozen embryo transfer (ET) in women with diminished ovarian reserve (DOR). Furthermore, to determine if the negative effect in more on actual implantation or live birth.

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RESULTS: Pregnancy and implantation rates for patients aged \( \leq 39 \) with P levels \( >2 \) ng/mL on day of hCG and DOR. Fresh ETs vs. patients that deferred for frozen ET.
Surprisingly, out of 32 cases, 19 (59.3%) chose fresh ET. The only significant difference was in the live delivered pregnancy rate (p<.05, chi-square analysis) with the frozen ET almost 5 times higher. There was only a slight trend for lower implantation rates in those choosing fresh ET.

CONCLUSIONS: A priori we hypothesized that the main adverse effect of advancing the WOI would be on implantation. Instead the main adverse effect was on live deliveries. Thus it appears that advancing the WOI does not seem to prevent implantation but causes an adverse endometrial milieu that adversely affects fetal survival. A poll of women who chose fresh ET found that the large majority were considering donor oocytes for their next ET and they wanted to minimize their costs related to low expectation for a successful outcome. The slightly higher age may have had a mild contribution to the lower live delivered pregnancy rate. These data should greatly influence our staff to encourage women with DOR and increased serum P on day of hCG not to cancel the IVF but cryopreserve the embryos.

P-619 Wednesday, October 19, 2016

ESTROGEN INDUCES C-KIT VIA EGR1-DEPENDENT TRANSCRIPTIONAL REGULATION FOR SUCCESSFUL IMPLANTATION IN MOUSE UTERUS. M. Park, a K. Kang, a H. Choi, b M. Koong, a I. Kang, a T. K. Yoon, b H. Kim, b H. Song, a,b "Biomedical Science, CHA University, Seongnam, Korea, Republic of; CHA Seoul Fertility Center, CHA University, Seoul, Korea, Republic of.

OBJECTIVE: Estrogen (E2) induces expression of an array of genes including early growth response 1 (Egr1) to make the uterus receptive for embryo implantation. Egr1 is spatiotemporally regulated by E2 in the uterus. Furthermore, Egr1 knock-out female mice do not support embryo implantation. Our in silico analyses previously showed that c-Kit is one of putative EGR1 direct target genes in the uterus. In this study, we have performed a series of experiments to demonstrate that estrogen induces EGR1 as a local transcription factor to control transcription of genes, such as c-Kit, important for implantation.

DESIGN: Animal study on mouse uterus with a series of experiments in cell culture.

MATERIALS AND METHODS: RT-PCR, real-time RT-PCR, Western blotting, immunostaining, histological analyses, promoter assays with mutagenesis, and chromatin immunoprecipitation were performed.

RESULTS: Realtime RT-PCR and immunostaining for c-KIT and EGR1 showed that spatiotemporal expression of c-Kit followed that of Egr1 in uteri of ovariectomized (OVX) mice at various time points after E2 treatment. Pretreatment of ICI 182,780 (an estrogen receptor antagonist) before E2 injection inhibited E2-dependent induction of c-Kit as well as Egr1 in the uterus. Furthermore, pretreatment with RU486 [a progestosterone (P2) receptor antagonist] interfered with P2 action to inhibit E2-dependent c-Kit induction. Experiments with pharmacological inhibitors for various signaling pathways showed that c-KIT expression is controlled by estrogen-induced activation of ERK1/2 and p38 followed by EGR1 induction in the uterus. During early pregnancy, c-Kit expression is significantly increased in mouse uterus on days 4 and 5. Administration of Masitinib (a pharmacologic inhibitor of c-KIT) on day 4 effectively interfered with embryo implantation on day 5 while unimplanted blastocysts were recovered. Transfection of EGR1 expression vectors produced rapid and transient induction of c-KIT as well as EGR1 in time- and dose-dependent manners. Furthermore, site-directed mutagenesis for EGR1 binding site(s) (EBS) of c-Kit promoter demonstrated that the EBS at -818/-805 is critical for EGR1-dependent c-Kit transcription. Chromatin immunoprecipitation for EGR1 reinforced that this EBS physically interacts with EGR1 for c-KIT transcription.

CONCLUSIONS: Collectively, our results clearly show that estrogen induces EGR1 to control transcription of c-Kit critical for embryo implantation in the uterus.

Supported by: This work was supported in part by grants from the National Research Foundation of Korea (NRF) grant funded by the Korea government (MEST) (NRF-2012R1A2A2A01011274).

P-620 Wednesday, October 19, 2016

USING A HISTOLOGICAL MARKER TO DETERMINE ENDOMETRIAL RECEPTIVITY NONINVASIVELY - PROOF OF PRINCIPLE. F. Meng a U. T. Meier. a OB/GYN and Women's Health, Montefiore Medical Center/Albert Einstein College of Medicine, Hurstdale, NY. a Anatomy and Structural Biology, Albert Einstein College of Medicine, Bronx, NY.

OBJECTIVE: To determine endometrial receptivity in a fashion that is compatible with same-day embryo transfer.

DESIGN: The prevalence of nuclear channel systems (NCSs) - transient, micron-sized organelles in the nuclei of endometrial epithelial cells (EECs) of the midluteal phase - in endometrial biopsies has been established as a bona fide marker of the window of implantation. The goal of this study is to take NCS detection from endometrial biopsy to that in exfoliated EECs of uterine secretions. Uterine secretion aspiration has been shown compatible with same-day embryo transfer.

MATERIALS AND METHODS: Women of reproductive age who require endometrial biopsy for medical reasons are being enrolled in the study and undergo uterine secretion aspiration right before biopsy. Exfoliated cells in uterine secretions are cytospun onto slides, fixed and labeled with antibody markers for epithelial cells and NCSs, cytokeratin and certain nuclear pore complex proteins, respectively, followed by fluorescently labeled secondary antibody and DNA staining. NCS prevalence in biopsies is determined as described in several prior studies. The present study was approved by the IRB of the Montefiore Medical Center and the Albert Einstein College of Medicine.

RESULTS: A sufficient number of endometrial epithelial and stromal cells can be harvested from uterine secretions and preserved on slides for indirect immunofluorescence analysis. EECs stain specifically with antibodies to cytokeratin. The anti-nuclear pore complex monoclonal antibody, mAb414, detects NCSs in EECs of midluteal aspirations. Specifically, NCSs were detected in EECs of 3 aspirations, 2 of which were classified as high NCS prevalence according to biopsy analysis (the third biopsy is awaiting analysis). Significantly, EECs of the aspiration from a fourth patient (self reported as midluteal) lacked NCSs; however, this sample was subsequently identified as proliferative based on biopsy analysis. As expected, all EECs in aspirations from 3 additional patients taking OCPs were NCS-negative.

CONCLUSIONS: NCS-positive EECs in uterine secretions are readily detected and are representative of the NCS status in situ. Our methodology can now be applied to determine prospectively if the window of NCSs is truly identical to that of implantation. Eventually, an NCS-positive uterine secretion can serve as indicator for same-day embryo transfer in a frozen transfer cycle opening the door to personalized embryo transfer.

References:

OBJECTIVE: Early placentation is regulated by uterine natural killer cells which mediate access to the maternal vasculature during trophoblast invasion. These cells contain a variable combination of inhibiting and activating receptors, or KIRs. Activity of these cells is modulated by interactions between KIRs and trophoblastic HLA-C ligands. Prior studies suggest that certain KIR/HLA-C combinations result in increased miscarriage risk. However, these studies were limited by lack of direct embryo data, relying instead on supposition of HLA status by parental genotypes. Thus, this study sought to evaluate whether KIR/HLA-C combinations altered risk of pregnancy loss by directly evaluating HLA-C alleles in trophoderm biopsy (TEBx) samples and controlling for aneuploidy.

DESIGN: Retrospective study.

MATERIALS AND METHODS: All single embryo transfer (SET) cycles in which stored maternal DNA and residual preimplantation DNA from TEBx samples could be genotyped were analyzed. Only the first euploid SET resulting in a positive β-hCG for each patient was evaluated. Maternal samples were evaluated for 16 KIR genotypes. KIRs were then separated into Haplotype AA (only inhibitory genotypes present) and Haplotype B (activating genotypes also present) by standard criteria. DNA from TEBx samples was genotyped for HLA-C1 or HLA-C2 alleles and embryos were separated by biallelic pair (C2/C2, C1/C1, or C2/C1). All HLA/KIR combinations were evaluated.

RESULTS: 668 transfers resulting in pregnancy were analyzed. The overall pregnancy loss rate (including biochemical and clinical losses) was 24.7%. There was no difference in loss risk among HLA-C biallelic groups. KIR AA patients were overall less likely to experience pregnancy loss (p<0.01). However among KIR AA patients, homozygous C2/C2 embryos resulted in a significantly higher rate of pregnancy loss than C1/C1 or C1/C2 (p<0.05)**. CONCLUSIONS: Maternal KIR haplotype influences risk of pregnancy loss. In KIR AA patients, transfer of C2/C2 embryo significantly increases the risk of pregnancy loss. This is the first study to obtain direct embryo data on HLA-C alleles and the first to control for aneuploidy when characterizing the contribution of HLA/KIR combinations to pregnancy loss risk. While this phenomenon needs further study, these findings have significant implications for embryo selection among KIR AA women, in whom selection against the transfer of C2/C2 embryos may decrease loss risk.

References:

Supported by: Foundation for Embryonic Competence.

Loss risk by KIR Haplotype alone and KIR/HLA combinations

<table>
<thead>
<tr>
<th>KIR AA</th>
<th>KIR B</th>
</tr>
</thead>
<tbody>
<tr>
<td>C1/C1</td>
<td>16%* (28/176)</td>
</tr>
<tr>
<td>C2/C2</td>
<td>12.3% (10/81)</td>
</tr>
<tr>
<td>C1/C2</td>
<td>33%** (8/24)</td>
</tr>
<tr>
<td>14.1% (10/71)</td>
<td>27.8% (137/492)</td>
</tr>
<tr>
<td>16% (28/176)</td>
<td>32% (58/181)</td>
</tr>
<tr>
<td>C2/C2</td>
<td>26.7% (24/90)</td>
</tr>
<tr>
<td>C1/C2</td>
<td>25.3% (56/221)</td>
</tr>
</tbody>
</table>

ARE MATERNAL THYROID ANTIBODIES ASSOCIATED WITH EUPOLOID MISCARRIAGE IN WOMEN WITH RECUPRRENT PREGNANCY LOSS (RPL)? S. Cueva, D. McQueen, M. S. Barkoff, M. Stephenson. University of Illinois at Chicago, Chicago, IL.

OBJECTIVE: An association between RPL and overt hypothyroidism is well documented, however, ongoing controversy exists in regard to thyroid autoimmunity. We hypothesize that if an association exists between Autoimmune Thyroid Disease(AITD) and RPL, the frequency of euploid miscarriage would be increased in women with thyroid autoantibodies. Therefore, the objective of this study is to evaluate whether maternal thyroid autoantibodies are associated with euploid miscarriage in RPL.

DESIGN: Observational cohort study using prospectively collected data.

MATERIALS AND METHODS: IRB approval was obtained. Inclusion criteria included: women seen between July 2004 - September 2015 with a history of ≥2 pregnancy losses <10 weeks size; euthyroid (TSH 0.3-2.5mIU/L) or subclinical hypothyroidism (TSH >2.5, with normal free thyroxine or free thyroxine index); serum testing for antithyroid peroxidase (anti-TPO) and/or antithyroglobulin (anti-Tg) antibodies; and at least one subsequent pregnancy loss <10 weeks size. AITD was defined as anti-TPO antibodies >4 IU/ml or anti-Tg antibodies >9 IU/ml. Women with eu-thyroid AITD did not receive thyroid supplementation. Cytogenetic analysis of miscarriage tissue was performed; with a 46, XX result, microarrays were used. The frequency of euploid miscarriage was compared between women with and without AITD. T-test was used to compare continuous variables and chi-square or Fisher’s Exact tests for categorical variables.

RESULTS: 74 women with 112 subsequent pregnancy losses met criteria. 17.6% (n=113) had AITD. Subjects with AITD had a mean age at miscarriage of 36.3 years (SD 4.1, range 25-41), mean BMI at miscarriage of 25.4kg/m2 (SD 4.4, range 17.9-33.4) and a mean of 5.3 (SD 1.5, range 3-9) prior pregnancy losses. The subjects without AITD had a mean age at miscarriage of 35.8 years (SD 3.8, range 27-45), mean BMI at miscarriage of 26.7kg/m2 (SD 5.8, range 18-4.549) and a mean of 6.1 (SD 2.41, range 3-13) prior pregnancy losses. There were no significant differences in the above demographics between women with and without AITD. T-test was significantly higher in the AITD group, 2.6 vs. 1.7, P<0.001. The type of subsequent pregnancy losses was significantly different, as women with AITD had less nonvalidated pregnancy losses and more embryonic miscarriages than women without AITD, P=0.05. The frequency of euploid miscarriage did not differ between groups, 56% (5/9) in women with AITD and 48% (21/44) in women without AITD.

CONCLUSIONS: This is a novel study assessing whether the presence of maternal thyroid autoantibodies increases the frequency of euploid miscarriage in women with RPL, who are euthyroid or have subclinical hypothyroidism. The prevalence of AITD in this RPL cohort was similar to the prevalence of AITD in the general reproductive population (17.6% vs. 5-15%) (DeGroot et al. J Clin Endocrinol Metab 2012). The presence of thyroid antibodies was not associated with the frequency of euploid miscarriage.

References:
OBJECTIVE: The often quoted minimal serum HCG doubling time of early gestations (66% rise in 2 days) is based on a study with an 85% confidence interval in a cohort of only 20 female patients. More recent studies examining HCG dynamics in ART pregnancies are often confounded by multiple embryo transfer, replacement of unsectored embryos, and variation in the day of embryo development and normalization of endometrial transformation. The minimal HCG rise in early pregnancies conceived after single, euploid, frozen-thawed blastocyst transfer (FET) that correlates with good reproductive outcome has yet to be determined.

DESIGN: Retrospective cohort analysis.

MATERIALS AND METHODS: Patients that underwent single, euploid FET, from June 2011 to March 2016, were included. Oocyte donor cycles were excluded. Serum HCG levels were monitored on day 9 post FET, and if positive, on day 11. The rise was then correlated with implantation and ongoing pregnancy rates. Data was analyzed by student’s t-test, Chi-square, Kruskal-Wallis, linear and binary logistic regression.

RESULTS: A total of 458 single, euploid FETs were included. HCG rise of ongoing pregnancies (mean: 158.7 ± 57%; range: 9.5-698.32%) did not differ by maternal age (x^2=1.55, p=0.82), BMI (x^2=7.13, p=0.13) or blastocyst expansion grade (x^2=0.69, p=0.71). The degree of HCG rise significantly correlated to successful implantation (OR 4.101 [95% CI 2.39-7.21], P=0.0001) and ongoing pregnancy (OR 3.51 [95% CI 1.83-6.74], P=0.0002), with a minimal threshold of 10.8% rise conferring a 50% probability of ongoing pregnancy (Table 1). This association was not influenced by maternal age (x^2=5.09, p=0.28), BMI (x^2=1.78, p=0.078) or blastocyst expansion stage (x^2=0.03, p=0.98).

CONCLUSIONS: This is the largest study to date which establishes thresholds for initial HCG rise in normal pregnancies resulting from single, euploid FET. HCG dynamics have long been used to establish prognosis. By thresholding for initial HCG rise in normal pregnancies resulting from single, it is a cost effective therapy.

OBJECTIVE: Intralipid infusions have been used to improve clinical outcomes in patients with repeat implantation failure or recurrent pregnancy loss. Nonetheless, studies have not demonstrated a benefit. The primary aim of this study was to determine if intralipid infusion improves live birth rates and if use based on anecdotal evidence online. The objectives of this study are to determine if intralipid infusion improves live birth rates and if it is a cost effective therapy.

mGSD-CRL and first trimester pregnancy loss following IVF

<table>
<thead>
<tr>
<th>mGSD-CRL (mm)</th>
<th>Unadjusted rate of pregnancy loss (%)</th>
<th>Adjusted odds of pregnancy loss (AOR, 95% CI)</th>
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<tbody>
<tr>
<td>&lt;5</td>
<td>5-9</td>
<td>10-14.9</td>
</tr>
<tr>
<td>n=31</td>
<td>n=154</td>
<td>n=163</td>
</tr>
<tr>
<td>61.3</td>
<td>18.2</td>
<td>9.8</td>
</tr>
<tr>
<td>40.43 (8.52-191.94)</td>
<td>2.11 (0.84-5.29)</td>
<td>Referent</td>
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<tr>
<td>(AOR, 95% CI)</td>
<td></td>
<td>0.39 (0.05-3.38)</td>
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</tbody>
</table>

DESIGN: Retrospective cohort study and cost effectiveness analysis.

MATERIALS AND METHODS: IRB approval was obtained. A total of 127 patients were identified who received intralipid infusion based on elevated peripheral NK cells at a large REI practice from 2012-2015. Two authors validated the data obtained via database query. The majority conceived using ART. Chi square analysis was used to compare pregnancy rate. T tests were used for patient characteristics. Cost effectiveness analysis was performed from a societal perspective and used our practice costs, with adjustment to costs when only charges were available, and our institution pregnancy rates. Tree Age software was used for decision analysis. One-way sensitivity analysis was conducted. p values < 0.05 were considered significant.

RESULTS: Sixty-five patients, 35.9 ± 4.2 years old, BMI 26.3 ± 6.1 mg/m² had a positive serum βHCG. Forty-seven patients, 35.8 ± 4.1 years old, BMI 25.6 ± 5.6 mg/m² had an ongoing pregnancy. Sixty-five of the 127 patients (51.2%) receiving intralipid infusions had a positive serum βHCG test (p<0.01) and 47/127 (37.0%) (p=0.71) receiving intralipid therapy had an ongoing pregnancy. Thus only patients with positive serum βHCG whom received intralipid therapy had a statistically increased pregnancy rate. No differences were noted in demographics of those receiving intralipids when comparing those that conceived with those that did not. Power calculation demonstrated need for 271 patients in each group to demonstrate 10% increase in ongoing pregnancy rate. Cost analysis was done demonstrating that intralipid therapy increased costs by $681 per live birth. Yet sensitivity analysis demonstrated if pregnancy rates were > 40% for the intralipid infusion group and < 51% for the control group that neither strategy was favored.

CONCLUSIONS: Intralipid infusion for patients with RIF/RPL with elevated NK cells does not improve live birth rates. Moreover, despite the low cost of the intervention it is not cost effective in the majority of patients with repeat implantation failure or recurrent pregnancy loss.

P-625 Wednesday, October 19, 2016

MEAN GESTATIONAL SAC DIAMETER TO CROWN-RUMP LENGTH DIFFERENCE AS A MARKER OF FIRST TRIMESTER PREGNANCY LOSS AFTER IN VITRO FERTILIZATION.


OBJECTIVE: Pregnancy loss rates as high as 94% have been reported when the mean gestational sac diameter (mGSD) to crown-rump length (CRL) difference (mGSD-CRL) measures <5mm on first trimester ultrasound (1-3). This association has not been specifically examined in the infertile population, nor has it been correlated with other pregnancy outcomes. This study evaluates the association between mGSD-CRL and pregnancy loss, gestational age at delivery, and birth weight after in vitro fertilization (IVF).

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Data were abstracted from autologous IVF cycles performed at the University of Iowa from November 2011-December 2014 resulting in a singleton gestation. Crown-rump length and mGSD (average of measurements in 3 dimensions) were routinely measured on ultrasound performed between 6 and 8 weeks gestation. Based on prior data and the population distribution, mGSD-CRL groups were categorized as <5mm, 5-9.9mm, 10-14.9mm, and ≥15mm. Outcomes including pregnancy loss, gestational age at delivery, and birth weight were assessed for each group. Covariates considered included age, parity, body mass index, use of preimplantation genetic testing, intracytoplasmic sperm injection, fresh versus frozen transfer, day of transfer, history of recurrent pregnancy loss, and presence of a concurrent subchorionic hematoma. Covariates with significant associations (p<0.05) in bivariate analyses were included in a subsequent logistic regression model.
RESULTS: 391 singleton pregnancies conceived following autologous IVF cycles met inclusion criteria and were included in the analyses. The mean patient age was 32.8 and 88.5% were white. There was a significant association between increasing rates of first trimester pregnancy loss and decreasing mGSD-CRL (p<0.001). The combined loss rate in the entire sample was 16.6%, and the highest loss rate of 61.3% was seen with mGSD-CRL <5mm. For pregnancies that progressed beyond the first trimester, there was no association between mGSD-CRL difference and gestational age at time of delivery or infant birth weight.

CONCLUSIONS: Risk of first trimester pregnancy loss in IVF-conceived pregnancies is inversely proportional to mGSD-CRL. A similar association between mGSD-CRL and risk of preterm delivery or low birthweight was not seen. First trimester measurement of mGSD-CRL may be a useful sonographic marker of early pregnancy loss in the infertile population.

References:

P-626 Wednesday, October 19, 2016

REPRODUCTIVE OUTCOMES OF COUPLES WITH RECURRENT PREGNANCY LOSS DUE TO PARENTAL CHROMOSOME REARRANGEMENT. M. A. Bedaiwy, a S. I. Maithripala, b U. S. Durland, b J. Havelock, d S. Kashyap, e J. Hitkari, f S. Lisonkova, e aDepartment of Obstetrics and Gynecology, University of British Columbia, Vancouver, BC, Canada; bDepartment of Medical Genetics, University of British Columbia, Vancouver, BC, Canada; cPCRM, Burnaby, BC, Canada; dPacific Centre for Reproductive Medicine, Vancouver, BC, Canada; eGeneva Fertility Centre, Vancouver, BC, Canada; fOlive Fertility Centre, Vancouver, BC, Canada; gUniversity of British Columbia, Vancouver, BC, Canada.

OBJECTIVE: To evaluate pregnancy outcomes of patients pursuing Preimplantation Genetic Diagnosis (PGD) or clinical management for recurrent pregnancy loss (RPL) due to parental chromosome rearrangement.

MATERIALS AND METHODS: 2321 couples referred due to history of recurrent pregnancy loss to a specialty clinic for assessment and clinical management who were found to have parental chromosome rearrangement between January 2005 and December 2013 (n=23). Couples pursuing PGD through private fertility centers in this time period (n=13). The primary outcome measure used is successful live birth incidence following cytogenetic diagnosis. Secondary outcomes include time to first live birth, miscarriage rate, and delivery method. Analysis on discrete variables was performed using Fisher’s exact tests and time to first live birth was assessed using Wilcoxon rank-sum test.

RESULTS: 32 cases of recurrent pregnancy loss to a specialty clinic for assessment and clinical management who were found to have parental chromosome rearrangement between January 2005 and December 2013 (n=23). Couples pursuing PGD through private fertility centers in this time period (n=13). The primary outcome measure used is successful live birth incidence following cytogenetic diagnosis. Secondary outcomes include time to first live birth, miscarriage rate, and delivery method. Analysis on discrete variables was performed using Fisher’s exact tests and time to first live birth was assessed using Wilcoxon rank-sum test.

RESULTS: 23 out of 2321 (1.0%) couples referred for clinical assessment of RPL were found to have a causative chromosome rearrangement with pericentric inversion, reciprocal translocation or Robertsonian translocation. No significant differences were observed in live birth rate between PGD and clinical management (66.6% vs. 53.3%, p=0.717) following genetic diagnosis.

With PGD management, 6 live birth outcomes were observed, with an incidence of 1/5.631 person-years. With clinical management, 24 live birth outcomes were observed, with an incidence of 1/4.65 person-years. Mean time to live birth was 17.5 months and 23.3 months in clinical management and PGD groups respectively. Preterm births were more common in patients pursuing PGD when compared to clinical management (50% vs. 4.2%, p=0.018).

CONCLUSIONS: There is no significant difference between PGD and clinical management in live birth rate outcomes following cytogenetic diagnosis of parental chromosome rearrangement. In addition, significant differences were not seen in miscarriage rate, or time to live birth between these groups. Patients with PGD management were more likely to deliver preterm.

P-627 Thursday, October 20, 2016

KARMIN CANNULA ASPIRATION: AN ALTERNATIVE TO PRECUMPTIVE METHOTREXATE FOR PREGNANCY OF UNKNOWN LOCATION AFTER IVF. I. Insogna, a S. A. Misserm, b L. V. Farland, c E. S. Ginsburg, d P. Brady, e f Department of Obstetrics & Gynecology, Brigham & Women’s Hospital and Harvard Medical School, Boston, MA; g Department of Epidemiology, Harvard Chan School, Boston, MA.

OBJECTIVE: To evaluate the utility of an endometrial sampling protocol for the diagnosis of pregnancies of unknown location (PUL) following in vitro fertilization (IVF).

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: All fresh and frozen autologous IVF cycles from 10/2007 to 9/2015 were reviewed (n=14,505). PUL was defined as a positive serum beta-human chorionic gonadotropin (hCG, ≥3IU/L) and pelvic ultrasound without evidence of intrauterine pregnancy (IUP) or ectopic pregnancy (EP). Patients with PUL and an abnormal hCG trend (<53% rise or <15% fall in 2 days) underwent outpatient endometrial sampling with Karman cannula aspiration (n=112). Patients with hCG decline ≥15% within 24 hours of sampling and/or villi detected on pathologic analysis were diagnosed with failing IUP and had weekly hCG measurements thereafter; those with <15% hCG decline and no villi identified were diagnosed with EP and treated with intramuscular methotrexate (MTX, 50 mg/m2) or laparoscopy. Logistic regression adjusted a priori for oocyte age and number of hCG measurements before sampling was used to estimate the association between demographic and cycle characteristics and diagnosis with EP. RESULTS: Failed IUP was diagnosed in 47 patients (42%), and EP in 65 patients (58%) of all autologous IVF cycles. Whether the cycle was fresh or frozen, day of embryo transfer, serum hCG at the time of sampling, endometrial thickness, and presence of an adnexal mass were not significantly different among patients with failed IUP or EP. In patients with failed IUP, 100% demonstrated post-sampling hCG declines ≥15%, while villi were identified in just 47% (n=22). Fifty-seven patients (92%) with EP received MTX, while 5 underwent laparoscopy due to pain or patient preference. Patients with failed IUP had significantly shorter time to resolution after sampling (negative hCG, <2IU/L) compared to patients with EP (12.6 vs 26.2 days, p-value<0.001). One patient required a repeat procedure due to inadequate sampling; no other complications occurred.

CONCLUSIONS: Using this safe and effective Karman cannula aspiration protocol, a large proportion of women with PUL after IVF/ICSI are spared MTX, with a shorter time to negative serum hCG than those receiving MTX. Even in the absence of confirmatory pathology, Karman cannula aspiration is effective for diagnosis of pregnancy location using pre- and post-sampling serum hCG.

PROCEDURES AND TECHNIQUES - CLINICAL: ART

P-628 Wednesday, October 19, 2016

EVALUATING CHANGE IN GHONADOTROPIN-RELASING HORMONE (GnRH) USE IN A US REAL-WORLD DATABASE STUDY OF 96,446 IN VITRO FERTILIZATION CYCLES OVER 6.5 YEARS. G. L. Motlla, a K. S. Richter, b B. Kaplan, e B. Hayward, e M. C. Mahony, d aResearch, Shady Grove Fertility Reproductive Science Center, Annapolis, MD; bResearch, Shady Grove Fertility Reproductive Science Center, Rockville, MD; cFertility Centers of Illinois, Chicago, IL; dEMD Serono, Inc., Rockland, MA.

OBJECTIVE: To evaluate the change in use of GnRH analogs over time in IVF cycles for women in the US by primary diagnosis from a large US real-world database.

DESIGN: Non-randomized, observational, retrospective database analysis.

MATERIALS AND METHODS: Data from all autologous IVF cycles with fresh embryo transfer between Jul 2009 and Dec 2015 within a large US clinical dataset were analyzed by primary diagnosis.

RESULTS: From a total of 96,446 treatment cycles, 36,048 (37.4%) used a GnRH agonist to prevent a premature LH surge and 58,364 (60.5%) used a GnRH antagonist. Mean (SD) age in the two groups was 34.8 (4.61) years and 35.2 (4.64) years, respectively; mean (SD) antral follicle count (AFC) values were 12.87 (5.75) and 15.20 (6.69) respectively. The GnRH antagonist use was 15.8% in 2009, 23.4% in 2010, 24.9% in 2011, 24.6% in 2012, 24.9% in 2013, and 24.8% in 2014. From Jul 2009 to Dec 2015, GnRH analog use increased from 61.2% to 75.1% (p<0.0001).

CONCLUSIONS: The GnRH antagonist use increased significantly from 2009 to 2015.
EFFECT OF ENDOMETRIAL BIOPSY ON IN VITRO FERTILIZATION CLINICAL PREGNANCY RATES - A RANDOMIZED MULTI-CENTRE STUDY.
J. L. Hilton,1 K. Liu,2 C. A. Laskin,3 J. Havelock,4 1Division of Reproductive Endocrinology and Infertility. Department of Obstetrics and Gynecology, University of British Columbia, Vancouver, BC, Canada; 2Centre for Fertility & Reproductive Health, Toronto, ON, Canada; 3Medicine Obstetrics & Gynecology, LifeQuest Centre for Reproductive Medicine, Toronto, ON, Canada; 4Pacific Centre for Reproductive Medicine, Burnaby, BC, Canada.

OBJECTIVE: The purpose of this study was to determine if endometrial biopsy immediately prior to an in vitro fertilization (IVF) cycle affects IVF clinical pregnancy rates in the first or second IVF cycle.

DESIGN: A Canadian, multicenter, randomized, controlled open-label study.

MATERIALS AND METHODS: The intervention was a single endometrial biopsy performed 5-10 days prior to the start of gonadotropin in a standard IVF cycle compared to no biopsy. Primary outcome was clinical pregnancy rate. Live birth rate, implantation rate, endometrial thickness on day of trigger injection, number of oocytes retrieved and rate of embryo cryopreservation were secondary outcomes. Starting and total gonadotropin doses were also compared. Statistical analysis included; Fisher’s Exact, t-tests, and Mann-Whitney U tests using SPSS statistical software. Primary analysis was performed as intention to treat.

RESULTS: This study ended with 51/332 women randomized due to slow recruitment (25 endometrial biopsy group and 26 no biopsy/control group). Groups were similar at baseline for; age, duration of infertility, BMI, day 3 FSH, and number having first IVF cycle. The clinical pregnancy rate in the endometrial biopsy group was 52% (13/25) and 46% (12/26) in the control group (p=0.45). Live birth rate in the endometrial biopsy group was 52% (13/25) and 35% (9/26) in the control group (p=0.17). The implantation rate was also similar in the endometrial biopsy (21/36 embryos; 58%) and the control groups (18/40 embryos; 45%, p=0.17). The groups were similar for endometrial thickness on day of trigger, number of oocytes retrieved and embryo cryopreservation rate. Starting and total gonadotropin doses did not differ between the groups. The majority of embryo transfers were performed on day 5 (endometrial biopsy group 21/25 and control group 21/26). Per-protocol analysis on patients proceeding to embryo transfer also showed no difference in clinical pregnancy rate between the groups (12/23 Endometrial biopsy and 12/24 control group; p=0.48).

CONCLUSIONS: Further study is required to determine if the live birth rate is greater with endometrial biopsy compared to no endometrial biopsy in initial IVF cycles with fresh embryo transfer. The lack of difference between endometrial biopsy groups and control groups in clinical pregnancy and live birth rate in this study may be because it is underpowered.

Supported by: Unrestricted Educational Grant from Ferring Inc. (Canada)
SPERM RETRIEVAL RATES (SRR) AT REDO TESTICULAR SPERM ASPIRATION (REDO-TESA). A. H. AlMutairi, A. Zini. *Urology, McGill University, Montreal, QC, Canada; #McGill University.

OBJECTIVE: The aim of the study was to evaluate redo-testicular sperm aspiration (redo-TESA) sperm retrieval rate (SRR) in a cohort of infertile men.

DESIGN: We conducted a retrospective study of 100 consecutive men who underwent redo-TESA between June 2011 and April 2016. These men had different indications for TESA: obstructive azospermia (OA), hypospermato genesis (severe oligoasthenoteratozoospermia, cryzptozoospermia, non obstructive azospermia) and other conditions (complete asthenozoospermia, anejaculation, retrograde ejaculation, high DNA fragmentation index).

MATERIALS AND METHODS: Redo-TESA sperm retrieval rates (SRR) were recorded. Men were deemed to have a successful retrieval if ≥5 spermatozoa were rapidly identified on microscopic examination of the testicular aspirates. Patients were grouped based on whether they had 1 (Group 1), 2 (Group 2) or ≥3 prior TESAs (Group 3) in the same testicular unit.

RESULTS: Mean (±SD) male age was 40 ± 8 years. Sperm recovery by TESA was successful in 100% (100/100) of the men with a mean (±SD) of 1.4 ± 0.6 aspirations per procedure. The mean FSH and testosterone values were 8 ± 8 U/L and 15 ± 9 nmol/L, respectively. The mean right and left testicular volumes were 18 ± 3 and 17 ± 3mL, respectively. 75% of the procedures were performed on the right with the remaining 25% performed on the left side. The number of prior TESA procedures did not affect sperm recovery rates. The mean (±SD) number of aspirates per procedure in men with 1, 2 or ≥3 prior TESAs were 1.4 ± 0.6, 1.3 ± 0.5 and 1.6 ± 0.5, respectively (P>0.05).

CONCLUSIONS: Our data indicate that redo-TESA yields high (100%) sperm retrieval rates. The data also show that the number of previous TESAs does not affect sperm recovery.

Table 1. Clinical Characteristics of the 100 Redo TESA Cases

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Group 1 (n=33)</th>
<th>Group 2 (n=67)</th>
<th>Group 3 (n=6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (±SD) Male Age</td>
<td>40 ± 8</td>
<td>40 ± 7</td>
<td>40 ± 8</td>
</tr>
<tr>
<td>Mean (±SD) FSH (IU/L)</td>
<td>8 ± 8</td>
<td>8 ± 6</td>
<td>8 ± 7</td>
</tr>
<tr>
<td>Mean (±SD) Total Testosterone (nmol/L)</td>
<td>15 ± 9</td>
<td>15 ± 9</td>
<td>15 ± 9</td>
</tr>
<tr>
<td>Mean (±SD) Right Testicular Volume (ml)</td>
<td>18 ± 3</td>
<td>18 ± 3</td>
<td>18 ± 3</td>
</tr>
<tr>
<td>Mean (±SD) Left Testicular Volume (ml)</td>
<td>17 ± 3</td>
<td>17 ± 3</td>
<td>17 ± 3</td>
</tr>
<tr>
<td>Right Testicular biopsy (no.)</td>
<td>75</td>
<td>75</td>
<td>75</td>
</tr>
<tr>
<td>Left Testicular biopsy (no.)</td>
<td>25</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>Mean (±SD) Testicular Aspiration per procedure</td>
<td>1.4 ± 0.6</td>
<td>1.4 ± 0.6</td>
<td>1.4 ± 0.6</td>
</tr>
</tbody>
</table>

‡**Defined as positive identification of ≥ 5 spermatozoa**

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THE EFFECT OF PROPOFOL DOSAGE DURING OOCYTE RETRIEVAL ON IN VITRO FERTILIZATION OUTCOMES. A. C. Petrini, N. Pereira, S. D. Spandorfer. The Ronald O. Perelman and 1.030 FETs). Statistical analyses were carried out by SPSS version 19.0. The normality of quantitative data was tested both by Kolmogorov-Smirnova test and Shapiro-Wilk test, and the Mann-Whitney U test, Chi-square test or Fisher’s exact test were applied to purpose of the study, a successful IVF cycle was one that resulted in live birth. The baseline demographics and IVF cycle characteristics between the two groups were compared. Anesthesia characteristics included duration of anesthesia (min) and dosages of propofol (mg/kg/min), midazolam (mg/kg/min), and fentanyl (mcg/kg/min) were also compared.

RESULTS: To detect a 10% difference in mean propofol dosage with power of 80%, alpha of 0.05, a sample size of 370 per group was deemed necessary. There was no difference in the baseline demographics between patients with successful and unsuccessful IVF cycles. Patients with live births had more supernumerary embryos cryopreserved (1 vs. 0.3; P<0.009), but otherwise, cycle characteristics were not different between the two groups. The duration of anesthesia was similar in both groups (5.9 vs. 6.4 min). The mean propofol dose per MII oocyte in the live birth group (0.04 mg/kg/min) was similar to non-pregnancy group (0.03 mg/kg/min). Similarly, there were no differences in the mean doses of midazolam or fentanyl per MII oocyte between the two groups.

CONCLUSIONS: While previous studies have reported a deleterious effect of propofol on oocytes¹ and a potential lower clinical pregnancy rate when oocytes are exposed to a higher propofol concentration at the time of retrieval,² our study suggests that this may not be the case. Specifically, we showed no significant difference in the mean propofol dose per MII oocyte between those with and without live birth after fresh IVF-ET.

References:

P-633 Wednesday, October 19, 2016

EFFECTS OF DIFFERENT ENDOMETRIAL PREPARATIONS ON THE OUTCOMES OF FROZEN EMBRYO TRANSFER CYCLES OF IN VITRO FERTILIZATION/INTRACYTOPLASMIC SPERM INJECTION: A STUDY BASED ON MORE THAN 30,000 CYCLES. T. Du, Q. Chen, Q. Lyu, Y. Kuang. Department of Assisted Reproduction, Shanghai Ninth People’s Hospital, Shanghai, China.

OBJECTIVE: To evaluate the effects of different endometrial preparations on the outcomes of frozen embryo transfer (FET) cycles of in vitro fertilization (IVF)/intracytoplasmic sperm injection (ICSI).

DESIGN: Strictly controlled retrospective cohort study.

MATERIALS AND METHODS: Women undergoing 31,871 FET cycles of IVF/ICSI in the period between March 2003 and May 2015 were enrolled, and those with uterine abnormalities, uterine disorders or disorder history, uterine or uterine cavity surgery and other conditions that were not suitable for matching were excluded. After that, women undergoing different endometrial preparations including natural cycles, hormone therapy cycles and stimulated cycles were strictly matched by age, number of cycles, number of prior full-term births, type of infertility, presence of Fallopian tubal diseases, previous Fallopian tubal surgery, previous ectopic pregnancy, polycystic ovary syndrome, endometriosis and male factor infertility, number of embryos transferred, stage of embryos transferred and endometrial thickness on embryo transfer (ET) day, and then divided into three groups according to the type of endometrial preparations: natural cycle group (n=4,098 FETs), hormone therapy cycle group (n=4,098 FETs) and stimulated cycle group (n=4,098 FETs). Statistical analyses were carried out by SPSS version 19.0. The normality of quantitative data was tested both by Kolmogorov-Smirnova test and Shapiro-Wilk test, and the Mann-Whitney U test, Chi-square test or Fisher’s exact test were applied to obtain group comparisons as appropriate. P<0.05 was considered statistically significant.

RESULTS: Main baseline characteristics including age, body mass index, number of cycles, number of prior full-term births, profiles of type
of infertility, indications for IVF/ICSI and preexisting conditions including previous Fallopian tube surgery and previous ectopic pregnancy, and FET characteristics including number of embryos transferred, number of good-quality embryos transferred, stage of embryos transferred and endometrial thickness on ET day had no statistically significant differences among the three groups. As for pregnancy outcome, the ectopic pregnancy rates and miscarriage rates also had no statistically significant differences among the three groups. However, the clinical pregnancy rate (47.6% vs. 44.0%, p=0.001, 47.6% vs. 43.3%, p<0.001, respectively) and live birth delivery rate (31.1% vs. 28.2%, p=0.004, 31.1% vs. 26.4%, p<0.001, respectively) were statistically significant higher in stimulated cycle group both than in natural cycle group and in hormone therapy cycle group while no statistically significant differences were detected between the latter two groups.

CONCLUSIONS: Stimulated cycles are associated with significant higher clinical pregnancy rate and live birth delivery rate both than natural cycles and hormone therapy cycles in FET cycles of IVF/ICSI.

Supported by: National Natural Science Foundation of China.

Table 1: Comparison between conventional ICSI and PICSI parameters

<table>
<thead>
<tr>
<th>Oocytes</th>
<th>Age yrs (ICSI)</th>
<th>Fertilization ICSI %</th>
<th>D-3 Embryos ICSI %</th>
<th>Age yrs (PICSI)</th>
<th>Fertilization PICSI %</th>
<th>D-3 Embryos PICSI %</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 5</td>
<td>39.8 ± 4.3</td>
<td>89 ± 10</td>
<td>80.8 ± 32</td>
<td>36 ± 3</td>
<td>81 ± 20</td>
<td>78 ± 28</td>
</tr>
<tr>
<td>5 to 10</td>
<td>36.5 ± 5.3</td>
<td>76 ± 18</td>
<td>78 ± 28</td>
<td>36 ± 3</td>
<td>73 ± 23</td>
<td>72 ± 28</td>
</tr>
<tr>
<td>≥ 10</td>
<td>33 ± 4.7</td>
<td>69 ± 15</td>
<td>71 ± 27</td>
<td>35 ± 4</td>
<td>71 ± 17</td>
<td>70 ± 24</td>
</tr>
<tr>
<td>Overall</td>
<td>34.6 ± 5.3</td>
<td>72 ± 17</td>
<td>73.6 ± 28</td>
<td>35 ± 4.3</td>
<td>73 ± 20</td>
<td>70 ± 26</td>
</tr>
</tbody>
</table>

P-635 Wednesday, October 19, 2016


OBJECTIVE: to evaluate the effect of prewashing the insemination catheter before performing the IUI on pregnancy outcome.

DESIGN: Double-blind randomized controlled study.

MATERIALS AND METHODS: Setting: McGill university reproductive center, Montreal, Canada. Patients: 450 Infertile patients, 18-40 years, undergoing IUI with fresh or frozen sperm, during stimulated and unstimulated cycles.

Interventions: Flushing the insemination catheter with sperm washing media prior to IUI. Main Outcome Measures: Primary outcome: Pregnancy rate Secondary outcome: Clinical pregnancy, miscarriage & live birth rates. Statistics: Sample-size calculation was derived from the study of Pont JC et al, assuming a 5% Type-I error rate, 450 patients per group was needed to achieve an 80% power in order to detect a difference in the pregnancy rate of 7.3%. After obtaining approval from the research ethics board (13-158-SDR), the patients were randomized on the day of IUI & the catheters were prepared by the andrology lab technician to eliminate the risk of non-blinding.

RESULTS: The 2 study arms had similar demographics, causes & duration of infertility. The lab & ultrasound finding, type of treatment & cycle parameters were also comparable between the 2 groups. The pregnancy rate was (14.7% Vs. 11.59%, p=0.4), clinical pregnancy (11.34 % Vs. 10.14 %, p=0.82), miscarriage rate (0.41 Vs. 0.97%, p=0.46) & the live birth rate (8.54 % Vs. 8.21%, p=0.8) in the intervention group compared to the control group, respectively.

CONCLUSIONS: Although washing the Insemination catheter prior to IUI seemed to improve the pregnancy & miscarriage rates, yet it had no statistically significant effect on the clinical pregnancy & the live birth rate. This may lead to the modification of IUI protocols & to propose adapted guidelines for insemination as those for IVF during embryo transfer.

References:

REPRODUCTIVE BIOLOGY - ANIMAL AND EXPERIMENTAL MODELS

P-636 Wednesday, October 19, 2016


OBJECTIVE: Rnf8 and Scml2 are two essential genes for epigenetic programming of meiotic sex chromosomes that independently regulate gene activation in spermatids through distinct ubiquitination pathways. The aim of this study is to demonstrate there is genetic interplay of Rnf8; Scml2 and Rnf8; Scml2- double knockout (dKO) mouse model.

DESIGN: Basic research IACUC approved animal study.

MATERIALS AND METHODS: Experimental groups included C57BL/6 male mice; wild-type (WT) (n=3), Rnf8 knockout (KO) (n=3), Scml2-KO (n=3), and Rnf8; Scml2-dKO (n=3). All genotypes were confirmed by PCR. Mice were sacrificed at 5-11 weeks of life and testes were removed. Chromosome spread slides from testicular cell suspensions were prepared. Immunocytochemistry was performed with antibodies for mono- and poly-ubiquitination: histone H2A at Lys119 (H2AK119ub), ubiquitin conjugate monocolonal antibody (FK2), and monoubiquitinated histone H2A clone E6C5. Stages of primary spermatocytes were determined by staining for
SYCP3. All slides were mounted in Vectashield with 4’,6-Diamidino-2-Phe- 
nylindole. Dihydrochloride (DAPI). Germ cell images were acquired with a 
TE2000-E microscope (Nikon). A minimum of 30 spermatocyte nuclei im-
ages per sub-stage of meiotic prophase I were captured for analysis. Analysis 
included comparison of accumulation, depletion, and relative intensity of 
ubiquitination on sex chromosomes.

RESULTS: *Rnf8*;*Scml2*;*KO* had less testicular tissue when compared to 
WT, *Rnf8*;KO and *Scml2*;KO. H2AK119ub had a markedly different accumu-
lation pattern on the sex chromosomes in *Rnf8*;*Scml2*;dKO in comparison to 
WT, *Rnf8*;KO, and *Scml2*;KO. In early pachynema *Scml2*;KO demonstrates 
an intense accumulation of H2AK119ub on sex chromosomes, while *Rnf8*; 
KO demonstrates depletion starting in middle pachynema. Accumulation in 
*Scml2*;KO and depletion in *Rnf8*;KO continues until early diplonema. The 
*Rnf8*;*Scml2*;dKO has an intermediate intensity of ubiquitination starting in 
the transition from early to middle pachynema that continues until early diplonema.

CONCLUSIONS: Though *Rnf8* and *Scml2* independently regulate gene 
activation in spermatids through distinct ubiquitination pathways, the ubiqui-
tin phenotype in *Rnf8*;*Scml2*;dKO is markedly different in comparison. Our 
results suggest a genetic interplay between *Rnf8* and *Scml2* in the early sub-
estages of meiotic prophase I. However, further molecular analysis needs to be 
performed to fully elucidate this mechanism.

Supported by: NIGMS Grant.

P-637 Wednesday, October 19, 2016

EFFECTS OF RESVERATROL ON DIABETES-INDUCED DNA 
DAMAGE AND MODULATION OF POLY (ADP-RIBOSE) POLY-
MERASE SIGNALING IN RAT TESTIS. N. Kilarkaje,a A. Abdelali,a 
M. Al-Bader.a bDepartment of Anatomy, Kuwait University, Kuwait, Kuwait; 
Msc, Kuwait, Kuwait; bDepartment of Physiology, Kuwait University, 
Kuwait, Kuwait.

OBJECTIVE: To investigate modulatory effects of Resveratrol on dia-
betes-induced DNA damage and alterations in poly (ADP-ribose) polymer-
ase (PARP) signaling in rat testis.

DESIGN: An in vivo study.

MATERIALS AND METHODS: Adult male Wistar rats (n=6-8) were 
segregated into 1) control, 2) Resveratrol-treated (5 mg/kg; ip), 3) Streptozo-
toxin (55 mg/kg; ip)-induced diabetic, and 4) diabetic+ Resveratrol-treated 
groups. The rats in groups 2 and 4 received Resveratrol from days 22 to 
42. The rats were killed on day 42 after the induction of diabetes. Total anti-
oxidant and oxidant levels (plate reader assays), oxidative DNA damage in 
sperm and testes (8-oxo-dG labeling) and DNA double strand breaks 
(DNA fragmentation assay) were estimated in testes samples. The PARP 
signaling pathway proteins [total PARP, PARP1, sirtuin 1 (SirT1), PAR-
glycohydrolase (PARG), poly-ADP-ribose polymers (pPARG), apoptosis-
inducing factor (AIF) and aminoaacyl tRNA synthetase complex-interacting 
multifunctional protein 2 (AIMP2)] were quantified by Western blotting and 
immunohistochemistry. Data were analyzed by one way ANOVA and 
Least Square Difference test and P<0.05 was considered significant.

RESULTS: Resveratrol recovered diabetes-induced oxidative stress, de-
creases in DNA synthesis, oxidative DNA damage, and DNA double-strand 
brakes in the testes. Resveratrol did not affect diabetes-induced increases in 
total PARP and decreases in PARP1, however, it did recover decreased SirT1 
levels. Administration of Resveratrol alone resulted in decreased accumula-
tion of PpARG, but did not affect its increased levels in diabetic rats. Diabetes 
did not affect PARP levels, but Resveratrol supplementation reduced levels 
of its 60kDa fragment in diabetic rats. Resveratrol aggravated diabetes-
duced up-regulation of AIMP2 and AIF expression in the testis, although 
there was no nuclear re-localization of AIF in any testicular cells suggesting 
the lack of induction of parthanatos. The PARP signaling was well expressed 
in spermatids in the testes of rats belonging to all groups.

CONCLUSIONS: Resveratrol inhibits diabetes-induced DNA damage and 
modulates alterations in PARP signaling pathway in the testis, but neither 
diabetes nor Resveratrol induces parthanatos of testicular cells.

Supported by: Kuwait University grant # RM01/12, YM10/13, College of 
Graduate Studies and SRUL02/13.

P-638 Wednesday, October 19, 2016

ABSTRACT WITHDRAWN

FERTILITY & STERILITY®

P-639 Wednesday, October 19, 2016

ZP1 CONtributes TO THE PREVENTION OF POLYSPerMY IN 
MICE. N. Banks, a M. Avella,b B. Baibakov,b K. Tokuhiro,b J. Dean,b 
NICHHD, Bethesda, MD; bNIDDK, Bethesda, MD.

OBJECTIVE: The zona pellucida (ZP) plays an important role in oocyte 
development, gamete recognition, prevention of polyspermy, and protection 
of early embryos prior to implantation. The mouse zona pellucida is 
composed of three glycoproteins, ZP1, ZP2, and ZP3. Female mice lacking 
ZP1 are fertile with decreased fecundity. Secreted ZP1 (571 amino acids) 
contains a zona domain for oligomerization and a trefoil domain of unknown 
function. We hypothesise that the trefoil domain contributes to the structural 
integrity of the normal mouse zona pellucida and that zonae pellucidae lacking 
this domain may be more porous and vulnerable to polyspermy. This may 
explain, in part, the decreased fecundity observed in Zp1 null female mice.

DESIGN: Transgenic mouse model.

MATERIALS AND METHODS: Egg-free zonae pellucidae from wild-
type and Zp1 null mice were inseminated with capacitated mouse epididymal 
sperm. Egg-free zonae from wild-type activated eggs with cleaved ZP2 pro-
vided a negative sperm-binding control. In vitro fertilization of wild-type and 
Zp1 null mouse eggs was performed and the number of penetrating sperm 
was assessed by confocal microscopy. A mouse line is under development 
to replace Zp1 with a modified transgene expressing an isoform that lacks 
the trefoil domain.

RESULTS: Using the egg-free zona assay, we observed that 15.8 ± 2.1 
(mean ± s.e.m) sperm crossed the zona matrix in Zp1 null compared to 
5.1 ± 0.6 sperm in wild-type mice. No sperm accumulated in the egg-free 
zone from the negative controls (n=3 for each group). During 24 hour in 
vitro fertilization, Zp1 null eggs were penetrated by 2.1 ± 0.9 sperm and 
wild-type eggs were penetrated by 0.8 ± 0.1 (n=3 for each group). Sperm 
penetration and fertility results of the modified mouse lines with Zp1 lacking 
the trefoil domain are pending.

CONCLUSIONS: ZP1 contributes to the prevention of polyspermy in an 
in vitro mouse model. Further studies will use transgenic mice to investigate 
the molecular basis for the critical role of Zp1 in ensuring zona pellucida 
integrity. Defects in ZP1 may provide an etiologic basis for recurrent molar 
pregnancies in human patients.

Supported by: Work supported in part by the NICHD and NIDDK intramu-
ral research programs.
**P-640** Wednesday, October 19, 2016

**ACTIVATION OF MOUSE OOCYTES AFTER INTRACYTOPLASMIC INJECTION OF HUMAN SPERM WITH LINEAR AND ROTATIONAL MOTION.** S. Roychoudhury, I. Maldonado-Rosas, A. Agarwal, S. Esteves, R. Sharma, S. Gupta.

**OBJECTIVE:** During the journey through the female reproductive tract, sperm exhibit a variety of motility modes and swimming patterns including linear and rotational motion. Currently, only those sperm that show rotational motion are chosen for intracytoplasmic sperm injection (ICSI). Whether this leads to better oocyte activation and embryo development competence after ICSI, however, is unknown. The objective of this study was to compare the activation of mouse oocytes after ICSI of human sperm with linear and rotational motion.

**DESIGN:** In vitro experimental study.

**MATERIALS AND METHODS:** Fresh human semen samples (n = 2) from fertile normozoospermic men according to 2010 WHO guidelines and B6C3F1 frozen metaphase II mouse oocytes (n = 88) were used. Sperm were prepared with density gradient centrifugation and selected for ICSI based on either linear or rotational motion in deep regions of a PVP microdroplet. Sperm with linear motion changed their position, but not their location, by exhibiting two-dimensional movement in the bottom of a PVP droplet. Sperm with rotational motion changed position by gyration over their own axis. After thawing, surviving oocytes (n = 42) were randomly assigned into two groups: in group 1 (n = 39) sperm with linear motion were microinjected into oocyte cytoplasm; in group 2 (n = 42) sperm with rotational motion were injected. In both cases, selected sperm were immobilized by squeezing the tail using an injection micropipette prior to injection. After injection, the oocyte degeneration rates and oocyte activation rates (recorded as a percentage of surviving embryos at the two-cell stage 24 hours after microinjection) were assessed. Chi-square or Fisher exact tests were used to compare the outcome measures (expressed as mean and 95% confidence interval) using an alpha level of p < 0.05.

**RESULTS:** The oocyte degeneration rates were not statistically different between the mouse oocytes microinjected with human sperm with linear motion (46.1%; 95% CI: 30.1%-62.8%) and those injected with sperm with rotational motion (42.8%; 27.7%-59.0%). The oocyte activation rate was higher in the group of oocytes injected with sperm with rotational motion (52.4%; 95% CI: 29.8%-74.3%) than in the group of oocytes injected with sperm with linear motion (79.16%; 57.8%-92.9%) than in the group of oocytes injected with sperm with linear motion (52.4%; 95% CI: 29.8%-74.3%; these differences trended toward significance (p = 0.057).

**CONCLUSIONS:** Our results indicate that selection of human sperm with rotational motion may be beneficial to oocyte activation.

**REFERENCES:**


**REPRODUCTIVE BIOLOGY - HUMAN STUDIES**

**P-642** Wednesday, October 19, 2016


**OBJECTIVE:** The in vitro proliferative capacity of human TE cells has been previously reported to be successful. The objective of this research is the successful transplantation and rapid proliferation of TE cells in blastocysts with low numbers of TE cells.

**DESIGN:** Research ongoing study.

**MATERIALS AND METHODS:** Patients consented the use of non-viable day-6 embryos for the same cohort with varying TE quality. Embryos designated as non-viable were graded to be poor quality embryo not suitable for transfer or freezing by non-study embryologists. A total of 11 TE transplantations were performed. Two different blastocysts were selected for each transplantation: one with a high number of TE cells (Donor) and one with a low number of TE cells (Receptor). ATE biopsy was performed to remove approximately 10 TE cells. Subsequently, Receptor blastocysts received these Donor TE cells. This procedure consisted on making a 30 μm hole on the zona pellucida. TE cells were placed gently inside Receptor blastocysts. After TE cell transplantation, embryos were cultured individually with blastocyst culture media (G2 Plus, Vitrolife) in a time-lapse incubator (EmbryoScope) for approximately 22 hours. Each receptor transplanted blastocyst was monitored by viewing time-lapse videos to verify the characteristics of the cell attachment and proliferation.

**RESULTS:** TE cells were successfully introduced inside Receptor blastocysts. Donor TE cells were not rejected by any recipient embryos. Cell attachment was verified within 2 hours of incubation. After cell attachment, transplanted cells proliferated to varying degrees in the blastocysts. Approximately 50% of the transplanted blastocysts completely hatched with strong cell adhesion. One of the transplanted embryos showed two defined TE cell masses with no attachment between TE areas. 10 out of 11 (91%) Recipient blastocysts showed attachment and cell proliferation merging two different sources of TE cells in a single well, as observed by time-lapse videos.

**CONCLUSIONS:** TE cell number was increased in Receptor trophectoderm when two sources of TE cells were conjoined after TE transplantation. Proliferation of TE cells improved the grade of Receptor blastocysts. We hypothesized that TE proliferation on blastocysts could
possibly improve blastocyst cell trophectoderm morphology in which the development of TE is enhanced for robust implantation. In this ongoing study, more transplantations and genetic analyses of this merging layers of TE cells need to be conducted to elucidate the effects on the Receptor blastocysts.

References:

Supported by: EmbryoScope provided by Vitrolife AB.

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OBJECTIVE: The main causes of repeated failure in assisted reproduction such as IVF-embryo transfer are believed to be ooplasmic deficiencies, abnormalities and ageing rather than nuclear deficiencies. The percentage of fetal chromosomal abnormalities in miscarriages increases according to female age. Such chromosomal abnormalities are mainly induced by the chromosomal pre-division, in which homologous chromosomes fail to pair during meiosis I and segregate before it is complete. Recently it was found that in-vitro matured oocytes and aged oocytes resembled one another in terms of a high incidence of sister chromatid pre-division. This study evaluates the efficacy and safety of M-II cytoplasmic exchange at M-II between in-vitro matured oocytes (recipient karyoplast) as a model of aged oocytes and freshly ovulated oocytes (donor ooplasm).

DESIGN: Retrospective cohort study to cytoplasmic exchange.

MATERIALS AND METHODS: Each donor or recipient oocyte was held with the M-II chromosomes located in 3 o’clock position. The zona pellucida just above the M-II chromosomes was slit with a LАЗAR (Research Instruments, UK). Then karyoplast of donor oocyte was removed with an aspiration pipette. The recipient karyoplast removed by the same method as that of donor one was put into a microdrop containing inactiv- ated Sendai virus and injected into the perivitelline space of the enucle- ated donor oocyte. ICSI was performed to the newly constructed oocyte 3 hours after the fusion. Recipient karyoplasts were derived from immature oocytes, after ovarian stimulation. They were matured by culture in human tubal fluid (HTF) medium until the first polar body (IPB) extrusion was observed. Chromosome aberrations were analyzed according to the method described by Mikamo and Kamiguchi (New York: Alan R Liss Inc.; 1983, pp. 411-432). Donor ooplasm was prepared from consented IVF or ICSI patients. ICSI patients. The 8 cell stage was performed according to the method described by Mikamo and Kamiguchi (New York: Alan R Liss Inc.; 1983. pp. 411-432). Data was statistically analyzed by Fisher’s exact test.

RESULTS: Fusion rate, fertilization rate and 8 cell stage rate were 94.8% (55/58), 83.6% (46/55) and 40.0% (22/55) respectively. The rate of chromosomal abnormalities (PCS) decreased to 14.5% (12/83) from 95.5% (21/22). The incidence of aneuploidy was very low (2.4%; 2/83) in these oocytes, and none of them had structural ab- errations.

CONCLUSIONS: In conclusion, it has been demonstrated that oocytes constructed following the exchange of cytoplasmic of in-vitro matured MII oocytes with enucleated freshly ovulated M-II oocytes clearly had more efficient and chromosomally normal embryonic development than did in-vi- tro matured oocytes after ICSI. This new technique is promising for the rescue of low quality aged oocytes.

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ELEVATED BMI IN PATIENTS OF ADVANCED MATERNAL AGE DOES NOT AFFECT BLASTOCYST DEVELOPMENT OR CHROMOSOMAL COMPLEMENT, BUT HAS NEGATIVE CONSEQUENCES FOR EMBRYO METABOLISM AND IMPLANTATION, K. C. Barentsen, S. Lyons, J. M. Stevens, C. Broeckling, J. Kirkwood, R. L. Krischer, W. B. Schoolcraft. *Colorado Center for Reproductive Medicine, Lone Tree, CO; 2Colorado State University, Fort Collins, CO.

OBJECTIVE: Because of the societal trend for women to delay childbearing and the increasing incidence of obesity, women undergoing ART are often of advanced maternal age (AMA; ≥ 35 years) and are overweight or obese (BMI ≥ 25). Our objective was to elucidate the interaction of age and obesity on ART success.

DESIGN: Retrospective analysis.

MATERIALS AND METHODS: In the first study, patients were catego- rized into 4 groups: young (<35 years) with normal BMI, BMI = 22, 396 mature oocytes; young with elevated BMI, BMI = 8, 112 mature oo- cytes; AMA (>39 years) with normal BMI, BMI = 32, 330 mature oo- cytes; AMA with elevated BMI, BMI = 15, 159 mature oocytes. We then examined a larger dataset that included only AMA patients ≥ 35 (underweight (UW), BMI < 18.5, n = 6; normal weight (NRML), BMI 18.5-24.0, n = 172; overweight (OW), BMI 25-29, n = 112; obese (OB), BMI ≥ 30, n = 27). We also analyzed the effect of BMI on meta- bolism of D5 good quality blastocysts in a subset of these patients (n = 19; 39.5±0.6 years, 23.1±0.9 BMI). Metabolites were separated using a zwitterionic polymeric hydrophilic interaction liquid chroma- tography (ZIC-phILIC) column after MTBE extraction, followed by electrospray ionization (ESI) and triple quadrupole mass spectrometer (TOF) coupled to LC-MS/MS, and quantified using a standard curve (Skyline).

RESULTS: In young patients, elevated BMI decreased the number of oocytes retrieved (normal BMI 25.0 oocytes, elevated BMI 16.9 oo- cytes; p<0.05). Elevated BMI did not affect blastocyst production in either age group, although AMA had a negative impact on [RRK1] blastocyst development. AMA reduced the number of euploid embryos pro- duced; BMI had no effect. However, in AMA patients elevated BMI tended (p=0.09) to increase the probability that no euploid embryos would be produced. In AMA patients elevated BMI reduced embryo im- plantation (normal BMI 80%, elevated BMI 44%; p=0.045). Our exam- ination of a larger group of AMA patients determined conclusively that BMI does not affect the percentage of euploid embryos. Regression analysis established significant (p=0.007) relationships between BMI and glucose and tryptophan metabolism in AMA derived embryos. Glutamine and tryptophan uptake were reduced in OW patients, as was ALA-GLN, aspartic acid, serine, and threonine (p<0.05). Embryo im- plantation tended (p<0.09) to be reduced in OW compared to NRML (57.8%, 71.2%, respectively) AMA patients.

CONCLUSIONS: Maternal BMI does not adversely affect blastocyst development or chromosomal complement in ART. However, meta- bolism of blastocysts from overweight AMA patients is significantly altered, potentially contributing to the reduced implantation potential of euploid blastocysts in AMA women with elevated BMI.

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WHAT IS THE BEST LEAD FOLLICLE SIZE FOR OVULATION IN- DUCTION IN OLDER WOMEN ≥43 YEARS TO AVOID PREMATU- RE LUTEINIZATION OF FOLLICLES? Y. Wu, V. A. Kushnir, S. Darmon, Q. Wang, L. Zhang, D. Albertini, D. H. Barad, N. Gleicher. 1Center for Human Reproduction, New York, NY; 2Wake Forest School of Medicine, Winston-Salem, NC; 3University of Kansas Medical Center, Kansas City, KS; 4Albert Einstein College of Medicine, Bronx, NY; 5Rock- effeller University, New York, NY.

OBJECTIVE: To determine best lead follicle size for induction of ovula- tion with human chorionic gonadotropin (hCG) to avoid premature luteiniza- tion of follicles in women ≥ 43 years.

DESIGN: Cohort study.

MATERIALS AND METHODS: Early retrieval at ~16mm was demonstrated to avoid premature luteinisation and, thereby, improve clinical pregnancy rates in women ≥ 43.1 We here investigated whether retrievals at even smaller follicle sizes may add further bene- fits. We, therefore, investigated 56 patients, divided into three groups based on leading follicle sizes on day of hCG trigger: (1) Very early retrieval (VER), 13.5-15.5mm, n = 17; Early retrieval (ER): 16.00-18.0mm, n = 24; Standard retrieval (SR): 18.5mm-20.5mm, n = 15. All patients received identical stimulation protocols.1 Statistical comparisons
were made using Prism software. Student’s t-test with Welch’s correction was used for comparison of clinical data between VER, ER and SR patients. One-way ANOVA, followed by the Tukey Test, was used to analyze PCR results.

RESULTS: All three groups produced similar oocyte and embryo numbers, though good quality embryos were significantly more prevalent in the ER group (P<0.05). Concomitantly, clinical pregnancy rates basically tripled in the ER group from 5.9% (VER) and 6.7% (SR), respectively, to 16.7% in the ER group (P<0.05). Though FSH receptor (FSHR) and P450 aromatase (Cyp19a1) were not significantly affected by follicle sizes, progesterone receptor (PGR) and LH receptor (LHCGR) demonstrated significantly higher expression in ST than VET and ET (P<0.05), confirming that earlier retrieval avoids premature luteinization. Though VER patients’ GCs in vitro demonstrated least evidence of premature luteinization, embryo quality and clinical pregnancy rates in this group were equally poor to the SR group, both being significantly lower than the ER group.

CONCLUSIONS: Even at oldest female ages ER, defined as 16-18mm follicle size at hCG trigger, results in best clinical pregnancy rates. At >18mm, premature luteinization apparently negatively affects oocyte quality and pregnancy chances, while <16mm (VER), egg quality likely suffers from insufficient cytoplasmic maturation, a characteristic of small follicles.

References:

Supported by: Intramural funds from The Center for Human Reproduction and grants from The Foundation for Reproductive Medicine.

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GENE EXPRESSION LEVELS OF MMP 2, MMP 9, TIMP 1 AND ADAMTS 1 IN PLACENTAS OF IVF/ICSI PREGNANCIES. O. Gun-Eryilmaz, B. Urman, Y. Yuksetten, A. Boza, A. Sunurguzlu, Zekai Tahir Barak Ankara, Ankara, Turkey, Department of OB/GYN Koc University School of Med, Istanbul, Turkey, Ankara University, School of Medicine, Ankara, Turkey, American Hospital, Istanbul, Turkey, Medical Biology, Ankara University Faculty of Medicine, Ankara, Turkey.

OBJECTIVE: We compared gene expression of MMP2, MMP9 and ADAMTS 1, being the first identified member of this family, has an inhibitory activity (3). The aim of this study was to measure gene expression levels of MMP2, MMP9, TIMP1 and ADAMTS 1 in placentas of IVF/ICSI pregnancies and compare them to the gene expression levels of placentas obtained from control patients who had conceived spontaneously.

DESIGN: Prospective cross-sectional study.

MATERIALS AND METHODS: A total of eighteen tissue samples of placenta from IVF/ICSI (n=9) and spontaneous (n=9) pregnancies were obtained. We measured the gene expression levels of ADAMTS1, MMP2, MMP9 and TIMP1 by real-time polymerase chain reaction. Expression levels were analyzed using the delta threshold cycle method.

RESULTS: The levels of ADAMTS1, MMP2, MMP9 were increased in placentas obtained from IVF/ICSI pregnancies compared to controls (p<0.05 for all), TIMP1 values were not different.

CONCLUSIONS: Gene expression of MMP2, MMP9 and ADAMTS 1 were increased in the placentas of the pregnancies conceived via IVF/ICSI compared to those conceived spontaneously. Disturbed placental architecture as a result of the increased destructive actions of MMP and ADAMTS may be one of the reasons why IVF/ICSI pregnancies are more prone to gestational complications.

References:

EMBRYO BIOLOGY

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A NEW APPROACH TO EVALUATE THE INFLUENCE OF ADVANCING MATERNAL AGE UPON MEIOTIC SPINDEL MORAFOLOGY AND DEVELOPMENTAL COMPETENCE IN HUMAN OOCYTES. R. Matsunaga, S. Watanabe, Miura, Y. Kobayashi, N. Yamana, K. Kaminaha, K. Kuwahata, M. Ochi, T. Horiiuchi, Ochi Yume Clinic Nagoya, Nagoya, Japan; Department of Life Science, Prefectural University of Hiroshima, Shobara, Japan.

OBJECTIVE: The developmental competence of oocytes/embryos decreases with advancing maternal age, and meiotic errors gradually increase from when a woman reaches her late 30s. The evaluation of meiotic spindle morphology using a Polscope is an effective method for investigating the effect of maternal age. However, very little is known about the relationship between meiotic spindle morphology in oocytes and their developmental competence as maternal age advances.

DESIGN: Retrospective study.

MATERIALS AND METHODS: We analyzed 1496 mature oocytes from 461 patients undergoing letrozole stimulation cycles between September 2013 and January 2016. Oocyte spindle morphology was analyzed prior to intracytoplasmic sperm injection (ICSI) using a Polscope. We divided oocytes into two groups according to patient age: under 39 years (young, n=408) and over 39 years (old, n=945). We compared spindle abnormality rates (defined as visible, true (complete, irregular shape) between young and old groups. We also analyzed whether abnormal spindles affect fertilization rate, embryo developmental competence, and embryo morphokinetics (time to pronuclear fading and the two cell stage from ICSI [tPNf and t2, respectively] and abnormal cleavage rate of the first cleavage) in each group. Embryo morphokinetics were analyzed using a time-lapse incubator (EmbryoScope).

RESULTS: There was no significant difference in the total rate of abnormal spindles between the young and old groups (8.8% vs. 8.4%). However, the number of oocytes whose spindles were not vertical to the plane of the oocyte’s equator was increased in older oocytes (young vs. old: 2.5% vs. 5.0%). In the older group, abnormal fertilization rates (multipronuclear and monopronuclear) of oocytes with a non-visible spindle (38.5%) were significantly higher than oocytes with a normal spindle (5.9%). Embryo morphokinetics were not significantly different when compared between oocytes with normal or abnormal spindles. Oocytes with abnormal spindles were more prone to developmental arrest before the 8-cell stage than oocyte with a normal spindle. In the older group, blastocyst formation rates of oocytes with abnormal spindle (22.6%) were significantly lower than oocytes with normal spindles (55.6%).

CONCLUSIONS: Abnormal spindle location and morphology were more prevalent in oocytes of advancing maternal age. We suggest that the increased incidence of abnormal spindle is associated with a reduction in embryo developmental competence.

References:
1. Jessica Patel, Seang Lin Tan, Geraldine M. Hartsorne and Andrew D. McAnnish. Unique genometry of sister kinetochores in human oocytes during meiosis I may explain maternal

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OBJECTIVE: In recent years, there have been some reports suggesting that embryos are evaluated as no pronuclei and two polar bodies (0PN2PB) using conventional microscopic observation but the embryos observed by time-lapse shows that these 2PN break down before the time when we normally observe (2PN-BD). However there are very few articles discussing the process and impact from such PN break-down. Here, we report whether we can reduce the risk for incorrect observation of embryos following insemination by using time-lapse technology.

DESIGN: From July 2014 to September 2014, 448 cycles with 2338 oocytes were cultured for 6h following conventional IVF (cIVF) or ICSI and observed at 20h after insemination in Embryo Scope (Vitrolife) then we cultured the embryos into moist incubator until Day5. We used Veeck’s criteria and Gardner’s criteria for embryo evaluation. Treatments using TESE-ICSI and rescue-ICSI and calcium ionophore were excluded.

MATERIALS AND METHODS: We calculated the ratio for which embryos were evaluated as 0PN2PB by conventional microscopic observation but showed 2PN by time-lapse observation. We also studied the cleavage rate, Day3 good quality embryo rate, Day5 blastocyst rate, and Day5 good quality blastocyst rate of these embryos. Furthermore, we analyzed the time from PN appearance to its breakdown. All statistical analyses were performed using chi squared analysis.

RESULTS: Among 281 embryos which were evaluated as 0PN2PB using conventional microscopic observation, 141 embryos were evaluated as 2PN by time-lapse observation. The cIVF group has 2PN-BD embryos of 33.6% (38/113) and the ICSI group has the embryos of 61.3% (103/168). The 2PN-BD embryos show same development compared 2PN embryos in cIVF group. However, in the ICSI group, Day3 good quality rate, Day5 blastocyst rate and Day5 good quality blastocyst rate were significantly higher in the 2PN-BD group (P<0.01). For the 1825 embryos which were evaluated as 2PN by time-lapse observation, the time from insemination to 2PN appearance was as follow: 8.6h±0.1h (5.5h-19.4h) for the cIVF group, and 6.9h±0.1h (3.6h-22.3h) for the ICSI group. The embryos which developed into 2PN later than 15 hours following insemination did not grow into good quality blastocysts. Finally, the time of 2PN-BD was 15.9h (ICSI) and 17.2h (cIVF) following insemination at earliest.

CONCLUSIONS: It is very difficult to get the information of correct fertilization without using time-lapse system, because there are some embryos whose pronuclei break down early. Time-lapse technology can also help us improve workflow in the lab since actual observation does not need to be done at a specific time.

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TROPHECTODERM GRADE PREDICTS PREGNANCY OUTCOMES IN SINGLE BLASTOCYST TRANSFER CYCLES. M. Xia, L. Cai, Q. Zeng, J. Liu. The Clinical Center for Reproductive Medicine, The First Affiliated Hospital of Nanjing Medical University, Nanjing, China.

OBJECTIVE: To estimate the effect of trophectoderm (TE) morphology grade and inner cell mass (ICM) morphology grade on live birth in single-blastocyst transfer cycles.

DESIGN: A total of 675 frozen-thawed single blastocyst transfer cycles in our center between January 2013 and June 2015 were retrospectively studied.

MATERIALS AND METHODS: Morphological parameters were analyzed for all blastocysts including the inner cell mass (ICM) and the trophoderm (TE) grade. And score was divided as A, B and C grade according to morphology. Then the effects of the ICM and TE score on the clinical pregnancy outcomes were observed. Univariate and multiple logistic regression analysis were used to identify the confounders that statistically significantly affected live birth outcomes and to investigate the independent effect of significant morphological parameters. Stepwise logistic regression analysis was used to select the best independent morphological predictors of live birth.

RESULTS: Our data showed the blastocyst quality and TE score to be correlated with clinical pregnant and live birth rates. Live birth rates were 60.70%, 54.41%, and 34.00% for ICM grades A, B, and C, respectively. Yet there was no statistical difference between blastocysts of grade A and B. However, TE score was significantly positive correlated with live birth rate. The live birth rates of blastocysts with TE grade A, B, and C were 62.61%, 56.55%, and 42.42% respectively, there were significant differences among these groups (P<0.01). Multiple logistic regression analysis showed that TE grade was significantly associated with clinical pregnancy outcomes whereas ICM grade was not. The TE score had the strongest correlation with live birth.

CONCLUSIONS: In single blastocyst transfer cycles, the blastocysts of higher TE grade demonstrated a considerably higher live birth rate, which associated with maintaining persistent pregnancy. TE morphology grade is an essential independent predictor for live birth rate and could predict pregnancy outcomes during the earlier development stages contrasted to ICM.

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OBJECTIVE: To evaluate if day of blastocyst biopsy is associated with embryo chromosomal status as determined by high density oligonucleotide microarray comparative genomic hybridization (aCGH).

DESIGN: Retrospective cohort analysis at a private fertility center.

MATERIALS AND METHODS: In-vitro fertilization (IVF) cycles from January 2014 - December 2014 with blastocysts that underwent trophectoderm biopsy for comprehensive chromosomal screening (CCS) with aCGH were included. Both donor and autologous cycles were included. Repeat cycles from the same patient were excluded. Cycles were evaluated for oocyte age, blastocyst number, day of blastocyst biopsy (day 5, day 6 or day 7), and euploidy rate. Cycles were stratified by SART age group (donor, <35, 35-37, 38-40, 41-42, >42) and analyzed to determine whether day of trophectoderm biopsy is associated with euploidy rate. Statistical analysis was performed with a mixed model test of fixed effects.

RESULTS: A total of 388 IVF cycles and 2,132 biopsied blastocysts were evaluated (Table 1). Average patient age was 35. The percent of blastocysts biopsied on day 5, day 6, and day 7 were 62.5%, 35.8% and 1.7%, respectively. Average blastocyst euploidy rate on day 5, day 6, and day 7 were 62.5%, 35.8% and 36.9%, respectively. Earlier day of blastocyst biopsy was significantly associated with increased euploidy rate (p<0.0001). Younger maternal age (p<0.0001) and higher number of blastocysts biopsied per patient (p=0.0063) were both independently associated with greater euploidy. Donor status, infertility diagnosis, partner age and stimulation protocol were not significantly associated with euploidy after controlling for covariates.

<table>
<thead>
<tr>
<th>Embryo characteristics by SART age group</th>
<th>donor</th>
<th>&lt;35</th>
<th>35-37</th>
<th>38-40</th>
<th>41-42</th>
<th>&gt;43</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ave # oocytes retrieved</td>
<td>33.27</td>
<td>18.56</td>
<td>15.31</td>
<td>13.69</td>
<td>7.55</td>
<td>8.03</td>
</tr>
<tr>
<td>Ave # mature oocytes</td>
<td>21.8</td>
<td>13.23</td>
<td>9.95</td>
<td>9.35</td>
<td>5.64</td>
<td>6.23</td>
</tr>
<tr>
<td>Fertilization rate (%)</td>
<td>66.4</td>
<td>66.8</td>
<td>62.9</td>
<td>65.1</td>
<td>71.4</td>
<td>76.9</td>
</tr>
<tr>
<td>Blast rate (%)</td>
<td>62.8</td>
<td>64.2</td>
<td>63.2</td>
<td>60.3</td>
<td>52.6</td>
<td>45.0</td>
</tr>
<tr>
<td>Ave # D5 blast</td>
<td>8.32</td>
<td>4.57</td>
<td>3.12</td>
<td>2.97</td>
<td>1.28</td>
<td>1.13</td>
</tr>
<tr>
<td>Ave # D6 blast</td>
<td>5.26</td>
<td>2.94</td>
<td>2.41</td>
<td>1.96</td>
<td>1.15</td>
<td>1.42</td>
</tr>
<tr>
<td>Ave # D7 blast</td>
<td>0.23</td>
<td>0.13</td>
<td>0.03</td>
<td>0.09</td>
<td>0.06</td>
<td>0.03</td>
</tr>
<tr>
<td>Ave D5 euploid rate (%)</td>
<td>78.3</td>
<td>71.7</td>
<td>57.9</td>
<td>46.2</td>
<td>34.2</td>
<td>8.8</td>
</tr>
<tr>
<td>Ave D6 euploid rate (%)</td>
<td>63.8</td>
<td>58.1</td>
<td>41.5</td>
<td>33.0</td>
<td>21.1</td>
<td>1.4</td>
</tr>
<tr>
<td>Ave D7 euploid rate (%)</td>
<td>63.9</td>
<td>50.0</td>
<td>50.0</td>
<td>33.3</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Total Euploid rate (%)</td>
<td>76.1</td>
<td>65.7</td>
<td>49.7</td>
<td>42.8</td>
<td>28.2</td>
<td>10.0</td>
</tr>
</tbody>
</table>
CONCLUSIONS: Faster progression to the blastocyst stage, allowing for earlier trophectoderm biopsy, is independently associated with a higher percentage of euploid embryos. This relationship was shown for both autologous and donor embryos. For patients who choose not to biopsy, these data support selection of a day 5 blastocyst for transfer over a later-developing embryo. Additionally, these results can assist in counseling of patients undergoing IVF with CCS regarding expectations by utilizing not only maternal age and number of total blastocysts, but also day of biopsy to best predict likelihood of a euploid embryo for transfer. To our knowledge, this is the first study to examine day of blastocyst biopsy and euploidy rate presented by SART category.

Supported by: This research was supported by NIH/National Center for Advancing Translational Science (NCATS) UCLA CTSA Grant Number TL1TR00121.

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METABOLIC IMAGING AS A NON-INVASIVE TOOL FOR ASSESSING OOCYTE AND EMBRYO MITOCHONDRIAL FUNCTION. T. Sanchez,1 D. Needelman.1 Harvard, Cambridge, MA; Department of Molecular and Cellular Biology, Harvard, Cambridge, MA.

OBJECTIVE: Oocyte and embryo mitochondrial metabolism is a key determinant of viability in ART procedures; however, there are currently no methods of accurately assessing mitochondrial function in oocytes and embryos. NADH and FAD are naturally fluorescent and integral components of cellular respiration. Our aim was to develop a non-invasive method of assessing oocyte/embryo metabolism by measuring the fluorescence of NADH and FAD with Fluorescence Lifetime Imaging Microscopy (FLIM).

DESIGN: We perform metabolic assessment of mitochondrial function in oocytes and embryos using FLIM, optimized for NADH and FAD fluorescence. We collect data over the course of embryo development from 1-cell to blastocyst to determine correlations between metabolic signatures and successful blastocyst development. We performed appropriate controls to verify that FLIM measurements reflect real physiological changes in metabolism, varying oxygen availability and using metabolic chemical inhibitors of the electron transport chain (ETC).

MATERIALS AND METHODS: Mouse embryos were imaged in an on-stage incubation system to allow for continuous monitoring during development. Comprehensive metabolic measurements were taken of embryos every 2h for 4 days. We varied oxygen concentration by exchanging premixed gases into the sample chamber with different oxygen concentrations, measuring metabolic responses with FLIM. We also used potassium cyanide, an ETC inhibitor, and FCCP, an ETC uncoupler, to actively alter NADH and FAD levels.

RESULTS: Our results demonstrate that FLIM-based metabolic imaging is highly sensitive to differences in mitochondrial function. In monitoring metabolism during development, we observed distinct changes in metabolic profile as embryos grow. These shifts were highly conserved for all embryos that successfully developed to blastocyst. We observed the expected changes in NADH and FAD in response to O2 and chemical perturbations.

CONCLUSIONS: This fundamental work establishes a framework and methods for non-invasively monitoring embryo metabolism. This could facilitate numerous new research studies into the role of metabolism in embryo development. These results also indicate promise for the use of metabolic imaging as a potential embryo selection tool.

Supported by: Funding for this work was provided by the Blavatnik Biomedical Accelerator of Harvard

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ARE EARLY MORPHOGENETIC PARAMETERS PREDICTIVE OF MONOZYGOTIC SPLITTING AFTER SINGLE EMBRYO TRANSFER?1 L. Sekhon,2 M. Kon,4 J. Rodriguez-Parata,4 J. A. Lee,4 B. McAvey,4 A. B. Copperman.4 1 Reproductive Medicine Associates of New York, New York, NY; 2 Obstetrics, Gynecology and Reproductive Science, Icahn School of Medicine at Mount Sinai, New York, NY.

OBJECTIVE: Extended in vitro culture has improved the ability to select the optimal embryo for transfer from both a genomic and morphokinetic perspective, though some have suggested that the delay in transferring embryos back to the uterus may be a risk factor for monozygotic twinning (MZT). Due to its rare incidence and IVF’s longstanding practice to return multiple embryos at transfer, a clear link between blastocyst morphology and MZT has yet to be demonstrated. Since MZT gestations confer additional perinatal morbidity and mortality, we undertook this study to assess whether early morphokinetic findings were correlated with monozygotic twinning.

Design: Case control study.

Materials and Methods: All singleton and MZT clinical pregnancies from single, euploid frozen-thawed embryo transfers (FET) from July 2011 to April 2016 were included. All embryos underwent cleavage stage assisted hatching and day 5 FET. FETs were stratified by day of trophectoderm (TE) biopsy and blastocyst morphology (expansion, inner cell mass (ICM) and TE grade). Student’s t-test, chi-square, linear and binary logistic regression analysis were performed.

Results: Six hundred forty-five clinical pregnancies from 1238 FETs were eligible for the study. Baseline demographics and FET cycle characteristics are shown in Table 1. The incidence of monozygotic twinning was 3.7% (n = 24). The odds of monozygotic splitting was not influenced by endometrial thickness at transfer (OR 0.94 [95% CI 0.6-1.4], p = 0.79), peak estrogen level (OR 1.0 [95% CI 0.99-1.0], p = 0.86) or the day of blastocyst biopsy (x2 = 0.003, p = 0.96). No association between MZT and blastocyst expansion (x2 = 0.38, p = 0.94), ICM (x2 = 2.4, p = 0.49) or TE (x2 = 1.7, p = 0.65) was observed.

Conclusions: Controlling for the number of embryos transferred, the endometrial environment and laboratory manipulation of the preimplantation blastocyst, the incidence of monozygotic splitting was neither correlated with expansion, inner cell mass grade, nor trophectoderm score. Further research is required to examine the potential influence of laboratory procedures, such as assisted hatching and morula biopsy, on the odds of MZT. Furthermore, the use of time-lapse technology may be informative regarding the mechanism underlying early embryonic splitting.

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BLASTOCYST METABOLISM, AS DETERMINED BY A NOVEL QUANTITATIVE APPROACH, IS NOT IMPACTED BY CHROMOSOME COMPLEMENT OR GENDER BUT IS ALTERED WITH MATERNAL AGE. T. Schlenker, a A. Greene, a S. Lyons, b J. M. Stevens, a J. Herrick, a J. Premji, a J. Kirkwood, c C. Broeckling, c W. B. Schoolecraft, d R. L. Krisher, e Colorado Center for Reproductive Medicine, Lone Tree, CO; e Colorado State University, Fort Collins, CO.

Objective: To determine if the metabolic footprint of single human day 5 blastocysts is associated with chromosome complement, gender, or maternal age.

Design: Retrospective analysis.

Materials and Methods: Individual embryos were cultured to the blastocyst stage in 25 μL of CCRM (in house prepared sequential medium in the EmbryoScope®). Only medium collected from good quality blastocysts (grade 3BB and better) on D5 was included in the analysis, following biopsy for comprehensive chromosome screening.

Baseline demographics and FET cycle characteristics

<table>
<thead>
<tr>
<th></th>
<th>Singletons (n=621)</th>
<th>Monozygotic twins (n=24)</th>
<th>P value</th>
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</thead>
<tbody>
<tr>
<td>Patient age</td>
<td>36.0 ± 4.2</td>
<td>36.5 ± 4.6</td>
<td>NS</td>
</tr>
<tr>
<td>Endometrial Thickness at ET (mm)</td>
<td>9.2 ± 2.0</td>
<td>9.3 ± 2.5</td>
<td>NS</td>
</tr>
<tr>
<td>Blastocyst expansion grade=4</td>
<td>35.0% (217/620)</td>
<td>29.2% (7/24)</td>
<td>NS</td>
</tr>
<tr>
<td>Blastocyst expansion grade=5</td>
<td>28.4% (176/620)</td>
<td>29.2% (7/24)</td>
<td>NS</td>
</tr>
<tr>
<td>Blastocyst expansion grade=6</td>
<td>36.6% (227/620)</td>
<td>41.7% (10/24)</td>
<td>NS</td>
</tr>
<tr>
<td>Inner Cell Mass grade=A</td>
<td>75.5% (458/607)</td>
<td>70.8% (17/24)</td>
<td>NS</td>
</tr>
<tr>
<td>Inner Cell Mass grade=B</td>
<td>21.7% (132/607)</td>
<td>20.8% (5/24)</td>
<td>NS</td>
</tr>
<tr>
<td>Inner Cell Mass grade=C</td>
<td>2.8% (17/607)</td>
<td>8.3% (2/24)</td>
<td>NS</td>
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<tr>
<td>Trophoektoderm grade=A</td>
<td>35.3% (214/607)</td>
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<tr>
<td>Trophoektoderm grade=B</td>
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<tr>
<td>Trophoektoderm grade=C</td>
<td>16.1% (98/607)</td>
<td>12.5% (3/24)</td>
<td>NS</td>
</tr>
</tbody>
</table>

Supported by: Funding for this work was provided by the Blavatnik Biomedical Accelerator of Harvard

Supported by: This research was supported by NIH/National Center for Advancing Translational Science (NCATS) UCLA CTSA Grant Number TL1TR00121.
BLASTOCYST SCORING SYSTEMS PROVIDE EVIDENCE OF EUPLOID PREDICTABILITY. M. Katz-Jaffe,1,2 M. Schweitz,3 S. McReynolds,1,4 J. M. Stevens,5 W. B. Schoolcraft,4 1Colorado Center for Reproductive Medicine, Lone Tree, CO; 2Genetics, Fertility Genetics Inc., Lone Tree, CO; 3Fertility Genetics, Lone Tree, CO; 4Embryology, Fertility Labs of Colorado, Lone Tree, CO.

OBJECTIVE: During an in vitro fertilization (IVF) cycle it is routine to select embryos for transfer based on morphological indices. Detailed embryo morphology based grading systems have been established and are a critical component to the success of infertility treatment. With the utilization of comprehensive chromosome screening techniques, it is now possible to correlate embryo morphology with chromosome nomenclature. The aim of this study was to examine the relationship between blastocyst grading, chromosome constitution, and embryo selection.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: A large consecutive cohort of 2,796 IVF cycles with blastocyst culture, trophectoderm (TE) D5 biopsy, comprehensive chromosome screening and blastocyst vitrification were evaluated. Blastocysts were graded using a standard morphology based grading system following D5 biopsy, prior to vitrification. Analysis was performed to determine the association between D5 blastocyst morphology and chromosome constitution, including the total graded blastocyst in an embryo cohort. Chi squared test for independence, Student’s t-test and Fisher’s exact were utilized where appropriate, with significance at P < 0.05.

RESULTS: A significantly different proportion of euploid D5 blastocysts was observed for blastocyst stage and hatching: Grade 5 (68.4%), Grade 4 (56.3%) and Grade 3 (43.9%) blastocysts (P < 0.0001). Additionally, a significant association was observed between euploid D5 blastocysts and the quality of the inner cell mass (ICM) and TE: ‘AA’ = 69.2% (83/120) and ‘AB’ = 45% (76/169) (P < 0.0001). Examination of the ploidy state for the top grade D5 blastocyst in each of the 2,796 embryo cohorts revealed an aneuploid composition in 40% of the IVF cycles. Errors for all 23 pairs of chromosomes, including both losses and gains, were observed in these top grade D5 euploid blastocysts. Maternal age was a significant contributor to whether the top grade D5 blastocyst in an IVF embryo cohort was aneuploid (38.7 ± 3.6 vs. 36.1 ± 3.8 years for a top grade D5 euploid blastocyst; P < 0.05).

CONCLUSIONS: Blastocyst stage, hatching, ICM and TE grades all showed significant correlation for euploid predictability of D5 blastocysts in this large consecutive cohort of IVF cycles. Later stage hatching blastocysts and an ‘A’ quality TE grade resulted in the highest association with euploidy. In the absence of TE biopsy for comprehensive chromosome screening in these IVF cycles, a top grade D5 euploid blastocyst would have been selected in 40% of the frozen embryo transfers.

FERTILITY & STERILITY®

P-655 Wednesday, October 19, 2016

BLASTOMERE EXTRUSION AND ABNORMAL CLEAVAGE BEHAVIOR IN HUMAN EMBRYOS UNDER TIME-LAPSE MONITORING: POSSIBLE WAY OF EMBRYO SELF-CORRECTION? N. Zaninovic,1 Q. Zhan,2 C. Norberg,3 Z. Ye,4 R. Clarke,5 Z. Rosenwaks.1 1Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: To investigate the correlation between blastomere extrusions and abnormal cleavage behavior (direct uneven cleavage (DUC) and karyokinesis without cytokinesis (NUK)) in human preimplantation embryos.

DESIGN: A retrospective analysis of time-lapse and PGS data.

MATERIALS AND METHODS: In this study, 5300 embryos from 624 preimplantation genetic screening (PGS) cycles underwent blastocyst biopsy between January and December 2015. Blastomere extrusions (BEHVs) that did not participate in embryo proper during blastulation, DUCS, and NUKs were identified by time lapse monitoring (EmbryoScope®, Vitrolife, Sweden). Biopsied blastocysts (BL) were tested by aCGH or SNP array and results were classified as euploid (EUP), aneuploid (ANU) or complex abnormal (CxA). Data was analyzed using the χ² test.

RESULTS: The overall incidence of blastomere extrusions in PGS embryos was 16.5% (877/5300), which were significantly lower in embryos of women greater than or equal to age 42 (4.1%, 165/1170) and higher in age group 35-37 and 38-40 (18.2% (163/895) – 18.5% (222/1200), respectively). The extrusion incidences were significantly higher in BLs exhibiting DUC (66.8%, 152/232) and NUKs (50.3%, 81/161) when compared to BLs without abnormal behavior (8.9% (171/1933), all p < 0.0001). The same trends were confirmed among all oocyte age groups. DUC Daughter blastomere extrusions occurred in 85.2% (132/155) of DUC BLs. Similarly, NUK daughter blastomeres were extruded in 53.1% (43/81) of all NUK BLs. The total blastomere extrusion rate in all euploid blastocysts was significantly higher in both DUC BS (69.2%, 83/120) and NUK BS (41.6%, 32/77) compared to BLs without abnormal behavior (10.2% (79/755), all p < 0.0001). In euploid embryos, DUCS daughter blastomeres were extruded in 85.5% (71/83) of DUC BS and NUKs daughter blastomeres were extruded in 43.8% (14/32) of NUKs BS.

CONCLUSIONS: The incidence of blastomere extrusion was elevated in embryos exhibiting abnormal cytokinesis and karyokinesis. Euploid blastocysts derived from these embryos had a higher incidence of extrusions, especially daughter blastomeres resulting from abnormal cleavage behavior, suggesting a possible mechanism of embryo self-correction.
using a time-lapse embryo monitoring system. We report implantation outcomes and pregnancy prognosis.

**DESIGN:** Retrospective study.

**MATERIALS AND METHODS:** We collected eggs from 378 women (treatment cycle: 488, average age: 40.1) between January 2013 and June 2013 and offered blastocyst culture and dynamic analysis of 1217 embryos. We cultured embryos and then monitored their development using EmbryoScope (Vitrolife). We classified embryos into those: dividing first into three cells or more (AC1 group), dividing first into two cells, then five or more (AC2 group), and dividing first into two cells, then four (NC group). Successful blastocysts were frozen, and a single freeze thaw embryo transfer was performed. Blastocyst development, pregnancy, and miscarriage rates were compared between the three groups.

**RESULTS:** Successful blastocyst development rates were 11.5% (22/192, AC1 group), 23.2% (33/142, AC2 group), and 53.2% (470/883, NC group). There was a significant difference between the groups (P<0.05). Pregnancy rates were 33.3% (4/12, AC1 group), 41.2% (7/17, AC2 group), and 48.5% (141/291, NC group), and miscarriage rates were 50.0% (2/4, AC1 group), 28.6% (2/7, AC2 group), and 34.8% (49/141, NC group). Pregnancy, and miscarriage rates showed no significant difference between the groups. Birth defects and deformities were not observed.

**CONCLUSIONS:** Abnormally cleaved embryos seem inappropriate for early embryo transfer because they result in a low rate of blastocyst development and implantation. Successful blastocysts, on the other hand, develop into blastocysts, they result in good implantation outcomes and successful pregnancies. Therefore, we suggest that they should be considered as potential embryo transfer candidates.

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**P-657 Wednesday, October 19, 2016**

**EVALUATION OF EARLY CYTOKINETIC TIMEPOINTS BY TIME-LAPSE MICROSCOPY.** G. F. Celia, K. J. Fresa, T. F. Chi, D. J. Kotze, S. Bocca, S. Occhini, Ob/Gyn, The Jones Institute for Reproductive Medicine, Norfolk, VA.

**OBJECTIVE:** To use Time-Lapse Microscopy (TLM) to identify early cytokinetic time-points indicative of implantation potential.

**DESIGN:** Retrospective Data Analysis.

**MATERIALS AND METHODS:** 68 patients (average age 33.6 ± 4.9 years) were retrieved from January 2015-Mar 2016, underwent IVF with ICSI, TLM culture (EmbryoScope, Goeteborg, Sweden), and embryo transfers resulting in either 100% (Preg: 17) or 0% (NP: 52) implantation. These patients were selected as the fate of all transferred embryos was known. 129 embryos were transferred on day 3 (65) or day 5 (64) at the discretion of the physician. TLM records were reviewed to determine the timing of the first through third cytokinesis. The timing of divisions relative to fertilization and each other was compared between implanting and non-implanting embryos.

**RESULTS:** Review of TLM revealed an average time to first cytokinesis of 28.1 ± 3.2 (NP) and 27.5 ± 2.7 (Preg) hrs post ICSI. Comparisons between the groups did not reveal a significant difference in timing (P = 0.33). Time to second (37.9 ± 3.2 NP vs 27.5 ± 2.7 Preg) and third cytokinesis (28.1 ± 3.2 NP vs 27.5 ± 2.7 Preg), typically 2-cell to 3-cell and 3-cell to 4-cell, similarly did not show any difference between groups (P = 0.56 and P = 0.523, respectively). In 34 cases, the embryos were found to cleave directly from 2 to 4 cells, although the shutter speed (20 minutes) limited interpretation of these events. These embryos were found to have a significantly greater implantation potential (odds ratio = 2.59, P = 0.043). A final analysis of the time between 1st and 3rd cytokinesis in each group was made. Raw data showed no difference between groups (P = 0.347), however further investigation revealed complete implantation failure in embryos requiring >15 hours to complete these divisions. All significance was interpreted at P<0.05.

**CONCLUSIONS:** The purpose of this study was to identify specific time points during earlier embryo cleavage that are predictive of implantation potential. Although no raw time points demonstrated such a relationship, the increased implantation potential of embryos with a rapid 2 cell to 4 cell conversion, and the complete failure of all embryos which took >15 hours to complete 1st through 3rd cleavages are potential selection criteria with TLM. Furthermore, the latter marker may prove useful in laboratories lacking TLM culture, as minimal observation is required to identify and exclude these embryos from transfer.

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**P-658 Wednesday, October 19, 2016**

**IS ICSI WITH CALCIUM IONOPHORE AFFECTING HUMAN EMBRYO DEVELOPMENT?** J. A. Aguilar, M. Ojeda, E. Taboas, M. Perez, E. Munoz. 1st IVF Laboratory, IVI Vigo, Vigo, Spain; 2Gyneacology, IVI Vigo, Vigo, Spain.

**OBJECTIVE:** Artificial Oocyte Activation (AOA) with Calcium Ionophore (Ica), has shown to be a successful alternative choice for those patients with previous total fertilization failure after ICSI. However, the information concerning its impact on the embryo development is scarce. The aim of this study is to analyze the fertilization, pregnancy and implantation rates, as well as direct cleavage rate, blastomere multinucleation incidence, and embryo morphokinetics parameters in patients who underwent ICSI with AOA using an Ica.

**DESIGN:** Retrospective cohort study of 65 couples with severe male factor, under 1 mill/l spermatozoa. We compared 271 oocytes microinjected with an Ica from 36 patients who had a previous fertilization rate under 30% in previous ICSI cycles (Ica group), to 232 oocytes from 29 couples with similar sperm characteristics (concentration under 1mill/ml) (control group) between January 2011 and December 2015 in IVI Vigo Clinic.

**MATERIALS AND METHODS:** AOA was carried out by microinjecting the oocytes with spermatozoa in a Ica buffered solution. Then, they were incubated for twenty minutes in a culture media + Ica solution in a 37°C, 6%CO2 20%O2 atmosphere, and finally cultured in a time lapse monitoring incubator at 37°C 6% CO2, and 20%O2. X2, t-Student and Mann-Whitney tests were applied when suitable for statistical treatment of data.

**RESULTS:** Fertilization rate was similar among groups, 54.2% (Ica) vs 58.1% (p =0.06). Pregnancy rate was 54.2% in Ica group vs 58.1% in the control group (p =0.06). Implantation rate did not show any statistical differences neither. There were no differences between groups in abnormal fertilisation rate (1.3 and 4 pronuclei), although the proportion was higher in Ica group. The proportion of multinucleated blastomeres at two and four cells stage between groups was similar; p=0.8 and p=0.09 respectively, as well as the direct cleavage rate (p=0.447). Time at which second polar body was extruded (tPB2), was briefer at Ica group (p =0.001).

**CONCLUSIONS:** ICSI with AOA by Ica seems not to affect neither fertilization, pregnancy and implantation rates, nor the proportion of multinucleated blastomeres, or direct cleavage. Concerning morphokinetics, only tPB2 is affected by Ica, what could be related with the resumption of meiosis and calcium levels within the oocyte.

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**EMBRYO CULTURE**

**P-659 Wednesday, October 19, 2016**

**AFFIXING LABELS ON CULTURE DISHES DECREASE THE DEVELOPMENT RATE OF MOUSE EMBRYOS.** H. Kawano, K. Nakata, M. Kamoshita, J. Ito, N. Kashiwazaki, N. Yamashta. ¥¥Yamashita Syonan Yume Clinic, Fujisawa, Japan; Laboratory of Animal Reproduction Department of Animal Science & Biotechnology School of Veterinary, Azabu University, Sagamihara, Japan.

**OBJECTIVE:** Temperature, humidity, oxygen concentration, bacteria, and airborne volatile organic compounds (VOCs) have been reported to influence the development of mammalian embryos during in vitro culturing. Identifying and managing culture embryos, we are able to use a pen or labels for writing patient’s information on the plastic ware. There has been concern that the VOCs originated from the ink of felt-tip pens, which are too small to be removed with the HEPA filter, might cause the decrease of the developmental rate of culture embryos. On the other hand, verification report is less about the labels. This study was conducted to investigate effects of affixing labels on culture dishes on development of the embryos in the mouse.

**DESIGN:** Prospective experimental Animal study.
MATERIALS AND METHODS: We performed ovarian hyperstimulation on 8-week-old female BDF1 mice by administering eCG 7.5 IU or hCG 7.5 IU. After rearing these females in the same cage with males of the BDF1, fertilized eggs were collected from oviducts of the plug-positive females. Plastic dishes (Falcon) with a 35-mm aperture were prepared with five 20-μL drops of M16, covered with mineral oil (Vitrolife), placed in a 60-mm dish (Falcon), and then cultured at rest in an incubator (HC-3100 ASTEC). Five to ten embryos were cultured per drop. Labels using acrylic adhesive were affixed to the inside of the lid of the 60-mm dish, and culturing was performed at 37°C, 5% CO2, 5% O2, 90% N2, and saturated humidity. The number of affixed labels totaled 0 (control group), 1 (group A), 7 (group B), or 13 (group C), and development of the cultured mouse embryos from the 1-cell stage was investigated for 96 hours. Statistically analysis between experimental groups were determined by one-way ANOVA followed by Tukey test for multiple comparisons. Following the approval by the Animal Care and Use Committee of Azabu University, we used 263 mouse embryos in this study, which was performed at the Azabu University in the duration from September 2015 to December 2015.

RESULTS: The cleavage rate of the control group and groups A, B, and C were 97.5%, 97.1%, 12.0%, and 9.5%, respectively, with significant (P<0.001) decreases in groups B and C compared with the control; the developmental rate to the blastocyst stage were 88.6%, 0%, 0%, and 0%. As increasing the number of label, the incidences of cleavage of the cultured embryos were reduced, and there was no embryo developed to the blastocyst stage in all of the label-affixed groups.

CONCLUSIONS: Affixing labels using acrylic adhesive on culture dishes have detrimental effects on the development of mouse embryos at 1-cell stage. It is concluded that careful consideration should be given to the adhesives' components when using label stickers for culture dish management.

References:

P-660 Wednesday, October 19, 2016

WASHING MINERAL OIL, USED FOR MICRODROP OVERLAY DOES NOT IMPROVE STABILITY OF MEDIA OSMOLALITY.

J. E. Swain, A. E. Batcheller, W. B. Schooler, N. Bosser.

OBJECTIVE: Evaporation of culture media and the resulting increase in osmolality is a concern in some IVF laboratories, especially considering the increased use of non-humidified benchtop incubators. In this concern may be increased when using single-step embryo culture media and uninterupted culture over periods of up to 7 days. Some conjecture that washing of oil “saturates” the oil and prevents absorption of media components from microdrops, thereby possibly protecting growth conditions. The impact of extended uninterrupted culture and washing of mineral oil used for overlay on osmolarity of microdrops was examined.

DESIGN: Basic Clinical Research Study.

MATERIALS AND METHODS: Microdrops of media (25μL) were prepared in a laminar flow hood at room temperature by pipetting 12.5μL of media onto the surface of a 35mm dish, covering with 3.5μL of unwashed or washed mineral oil (Ovotol, Vitrolife), removing the media and adding 25μL of fresh media. Washed oil was prepared by adding culture media in a 1:5 ratio to the oil, inverting 30 times and allowing to settle. Dishes were made every 24hr over 7 consecutive days (168h) and placed into a non-humidified benchtop incubator at 37°C (GI85, K-systems). At the end of 7 days, all dishes were removed and osmolality of microdrops measured using a vapor pressure osmometer (Wescor). Positive controls included media directly out of the bottle (con) and microdrops under oil for 10min (con drops). The resulting 16 treatments were measured 3 times each. Data were analyzed using ANOVA and Tukey analysis and presented as the mean ±SEM, p<0.05.

RESULTS: Mean osmolality of con media and con drop were similar (263±1.0 and 265±2.1mOsm, respectively). Osmolality of microdrops under washed and unwashed mineral oil increased over time and were both significantly higher than con and con drops after 48h of culture. No significant differences were apparent between washed and unwashed oil within any time point examined.

CONCLUSIONS: Washing of mineral oil for use with microdrop overlay had no protective impact on stabilizing media osmolality compared to unwashed oil when utilized for up to 7 days in a non-humidified incubator environment. Both types of oil resulted in significant osmolality increase over time compared to controls after 48h of culture. This osmolality increase should be considered when trying to optimize growth conditions within the IVF laboratory.

P-661 Wednesday, October 19, 2016

UNSTABLE OSMOTIC PRESSURE IN MICRODROPS CULTURED UNDER MINERAL OIL IN NON-HUMIDIFIED INCUBATORS.


OBJECTIVE: Humidified incubators are widely used for culturing human embryos, but in recent years, non-humidified benchtop incubators have been widely used due to their small size and lower risk of fungal contamination. Mineral oil is typically used to cover microdrops of culture medium in dishes so as to prevent changes in the osmotic pressure, pH, and temperature of the medium. The stability of pH and temperature in microdrops in non-humidified incubators has been verified, but it is unclear whether osmotic pressure remains stable. In this study, we cultured different size microdrops in humidified and non-humidified incubators to determine the stability of the osmotic pressure.

DESIGN: Basic Clinical Research Study.

MATERIALS AND METHODS: We compared three incubators: (i) humidified benchtop, (ii) non-humidified benchtop, (iii) humidified water jacket. Microdrops (50μl, 100μl, 200μl) of a single step medium (A) [standard value (SV): 265±10 mOsm/kg] or a sequential medium (B) (SV: 290±10 mOsm/kg) were prepared in q535 mm culture dishes (Nunc), and then covered with mineral oil (Naka Medical Co. Japan). After one and two days incubation, the osmotic pressure of the microdrops was measured using a micro-sample osmometer (Fiske 210®).

RESULTS: In the humidified benchtop and water jacket incubators, there were slight but non-significant increases of up to 4 mOsm/kg over 1 and 2 days in both media, regardless of drop volume. In contrast, there were significant increases in osmotic pressure in the non-humidified benchtop incubator. In medium A, the 50μl drops increased from 277±0.6 mOsm/kg after 1 day to 296±0.7 mOsm/kg after 2 days, while in medium B, the 50μl drops increased from 289±0.7 mOsm/kg after 1 day and to 310±0.8 mOsm/kg after 2 days. The increase in osmotic pressure of the 100μl and 200μl drops was ~50% less than in the 50μl drops. In 100μl drops of medium A, osmotic pressure was 271±0.2 mOsm/kg after 1 day and 273±0.5 mOsm/kg after 2 days, while in medium B, it was 294±0.6 mOsm/kg after 1 day and 297±0.4 mOsm/kg after 2 day. In 200μl drops, the osmotic pressure was 271±0.7 mOsm/kg after 1 day and 274±0.4 mOsm/kg after 2 days, while in medium B, it was 293±0.6 mOsm/kg after 1 day and 299±0.5 mOsm/kg after 2 days. In the small drops (50μl), the increases in osmotic pressure in the non-humidified benchtop incubator were significantly greater than in the humidified incubators (P<0.01).

CONCLUSIONS: The osmotic pressure of microdrops incubated under a layer of mineral oil is stable in humidified incubators, but increased rapidly and significantly in the non-humidified benchtop incubator after only 1 or 2 days incubation. This suggests that a mineral oil overlay may not adequately protect small microdrops from evaporation in a non-humidified atmosphere. Furthermore, the significant increases in osmotic pressure observed in 50μl
drops may stress embryos and could compromise their viability during extended culture.

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BLASTOCYST FORMATION RATE CAN BE PREDICTED BY AN AUTOMATIC SYSTEM INDEPENDENTLY OF THE NUMBER OF OCYTES RETRIEVED AND THE MORPHOLOGY OF THE EMBRYOS ON DAY 3. N. Basile, 1 B. Aparicio-Ruiz, 1 J. Garcia Velasco, 1 M. de los Santos, 1 J. Remohi Gimenez, 1 M. Meseguer, 1 IVI Madrid, Madrid, Spain; 2IVI Valencia, Valencia, Spain; 1IVF, Embryology, Valencia, Spain; 2Clinical Embryology, Valencia, Spain.

OBJECTIVE: To correlate the different categories provided by an automatic diagnostic test (Eeva) with the blastocyst formation rate and to assess possible confounding factors associated to such correlation.

DESIGN: Observational, retrospective, multi-center cohort study.

MATERIALS AND METHODS: A total of 3002 embryos from patients undergoing egg donation cycles were imaged with the Eeva System. The Eeva system provides dark-field image and automatic cell-division tracking without the intervention of the embryologist. On Day 3 of development, the system utilizes information on specific division times (defined as P2 and P3) to automatically classify embryos into HIGH, MEDIUM, and LOW according to their probability of becoming a blastocyst. In addition, embryologists classified the same embryos according to standard morphological criteria defined by the Spanish Association of Embryologists (ASEBIR).

RESULTS: There was a straight correlation between the Eeva categories and the blastocyst formation rates. More specifically: blastocyst formation rate was 75.20% for embryos categorized as HIGH, 58.50% for embryos categorized as MEDIUM and 51.50% for embryos categorized as LOW. In addition, optimal blastocyst formation rate was 35.7% for HIGH, 27.2% for MEDIUM and 17.3% for LOW. A further logistic regression analysis was developed taking into account possible confounding factors thought as having a potential effect on clinical pregnancy including: number of oocytes retrieved and embryo morphology according to ASEBIR. Results of the model indicate that an embryo labeled as HIGH develops to blastocyst 2.014 times more than an embryo labeled as LOW (Table 1). Analysis of area under the curve revealed values of 0.728 CI95% (0.707-0.749) for blastocyst prediction according to Eeva and of 0.717 CI95% (0.703-0.732) according to ASEBIR classification. When Eeva and ASEBIR were combined the AUC value was of 0.788 (CI95% 0.768-0.808).

CONCLUSIONS: This study demonstrates in a large data set that there is a direct link between the Eeva categories and the blastocyst formation rate and quality. Embryos HIGH have a higher probability of becoming a blastocyst than embryos LOW and this is independent of the presented confounding factors. Both classification methods are independent from each other and have similar predictive value. However, when both are combined, the predictive value increases.

<table>
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<td>High vs. Low</td>
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References:

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BLASTOCYST DEVELOPMENT USING SEQUENTIAL MEDIA VERSUS ONE-STEP MEDIA IN EMBRYOSCOPE AND PLANER INCUBATORS. K. Kaskar, 1 D. P. Hamilton, 1 K. Miller, 1 P. W. Zarutskie, 1 W. E. Gibbons, 1 1Department Ob/Gyn, Baylor College of Medicine, Houston, TX; 2Family Fertility Center, Texas Children’s Hospital, Houston, TX.

OBJECTIVE: To compare the blastocyst development rate of embryos cultured in sequential media versus a one-step media.

DESIGN: Retrospective analysis of embryos of patients undergoing in-vitro fertilization treatment over a two-year period from April 2014 to April 2016.

MATERIALS AND METHODS: Only IVF patients with oocytes inseminated using intra-cytoplasmic sperm injection and whose embryos were cultured to Day 5 and did not have a Day 3 transfer were included in the study. From April 2014 to July 2015, embryos were cultured in sequential media (SM) using Quinn’s Advantage (QA) Cleavage Plus media up to Day 3 and transferred to QA Blastocyst Plus Media up to Day 6. From September 2015 to April 2016, embryos were cultured using Sage One-Step Media (OSM) up to Day 6 with no refreshing of media on Day 3. Embryos for both groups were incubated in either Embryoscope (ES) or Planer (PL) incubators. Fertilization rate, blastocyst development on Day 5 and Day 6, and total blastocyst development was compared for both culture media systems. Blastocyst development was calculated as the percentage of blastocysts formed from the number of fertilized oocytes (2pns). These parameters were also compared between the ES and PL incubation systems. Comparisons of blastocyst development rates were statistically analysed using a Chi-squared test and adjusted using a Bonferroni correction.

RESULTS: A total of 1152 oocytes (73 patients) were cultured with sequential media and a total of 1035 oocytes (67 patients) were cultured with One Step media. No differences in patient age or egg maturation rate were noted in each group. There was a significant increase in the total blastocyst development rate in OSM compared to SM (62.2% vs 54.4%; P < 0.035). No differences in blastocyst development were noted between the incubators irrespective of which culture media was used.

CONCLUSIONS: The data indicate that One Step Media significantly improves the overall blastocyst development rate and is capable of maintaining culture conditions from fertilization to blastocyst development in both ES and PL conditions, when compared to sequential media. The use of One Step media can greatly benefit the efficiency of the IVF lab, since it reduces the time for making dishes and changing media on Day 3, and also eliminating any disturbances to the embryo during culture.

<table>
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<tr>
<th>Blastocyst development in Sequential and One-Step media using Embryoscope and Planer incubators</th>
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<td>Sequential Media</td>
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<td>Blastocyst development rates on Day 6 (%)</td>
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<td>Total blastocyst development rate (%)</td>
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*P < 0.035.
OBJECTIVE: Traditional fixed-time evaluation (FTE) of fertilization at 18 hours after fertilization and embryo morphology on day 3 could miss information on fertilization status if the pronuclei appear (PNa) after 18 hours or pronuclei fade (PNf) before 18 hours after fertilization, as well as information on embryo development before day 3. This study examined the developmental potential of embryos with PNa >18 hours or PNf <18 hours after fertilization as well as embryos with ID (1 cell directly divided into 3 or 4 cells) or MN (at least blastomere was multinucleated) before day 3. Developmental potential was defined as development to 8-cell stage by day 3, blastocyst by day 6, and implantation rate after transfer of one embryo or two embryos with identical classification. Differences were analyzed by a Chi-squared test (Fisher's exact test).

RESULTS: A total of 1599 embryos from 291 cycles of IVF-ET were analyzed. The mean age of the patients was 36.2 years old with a std of 4.1. The overall clinical pregnancy (confirmed by ultrasound observation) rate: 14% vs 28%, p < 0.01; compared with embryos with PNf >18 hours (8-cell development: 32% vs 65%; blastocyst development: 20% vs 55%, and implantation rate: 14% vs 28%). Embryos with ID or MN during days 1 and 2 had much poorer developmental potential compared with embryos without these anomalies (8-cell development: 13% vs 77%, p < 0.001; blastocyst development: 4% vs 67%, p < 0.001; and implantation rate: 5% vs 29%, p < 0.05).

CONCLUSIONS: Compared to traditional, fixed-time evaluation (FTE) of in-vitro-produced embryos, time-lapse monitoring (TLM) can generate additional information on embryo development that FTE may miss. Compared to TLM, FTE may mis-read fertilization status on a small percentage of embryos that have limited developmental potential. Information on abnormal development during the first two days in culture can assist in the identification of those embryos that have very poor developmental potential.

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IS THE ADDITIONAL INFORMATION FROM TIME-LAPSE MONITORING USEFUL IN EMBRYO ASSESSMENT? I. X. Zhang, M. Pavone, A. K. Lawson, J. Robins. Obstetrics and Gynecology, Northwestern University Feinberg School of Medicine, Chicago, IL; Northwestern University, Chicago, IL; Northwestern University Feinberg School of Medicine, Chicago, IL.

OBJECTIVE: These embryos’ developmental potential was reduced by at least 50% by day 3 or blastocyst stage by day 6. None of these embryos were selected for FERTILE DEVELOPMENT.

DESIGN: In a prospective cohort study, patients attending for IVF treatment were randomized to control in control and LC supplemented medium. Full ethical and UK HFEA approval was obtained.

MATERIALS AND METHODS: Non-invasive measurements of embryo metabolism of glucose, pyruvate and lactate were performed using ultraflorometric techniques to quantify the consumption/release from spent droplets of culture medium. LC depletion and total triglyceride levels within individual embryos were also determined. Results were compared for normal weight and OWOB women and examined in relation to blastocyst development (BD) in the presence/absence of LC culture using regression methods to account for non-independence of data.

RESULTS: Embryos consumed LC from the medium, and at 0.05mM LC addition, embryos showed reduced intracellular triglyceride levels (p < 0.01), increased glucose consumption (p < 0.02) and higher odds of BD (p < 0.01). However, at 0.5mM LC addition; embryo viability was significantly compromised in cohorts of embryos from women with a BMI <25kg/m².

CONCLUSIONS: These data show that human embryos deplete LC from the culture medium, in a dose dependent manner. Supplementation with LC up to a concentration of 0.05mM led to lower triglyceride levels, suggesting β-oxidation had been enhanced. The data suggest that there are optimum levels of LC consumption that correspond with embryo viability, particularly for cohorts of embryos from women of above and below 25kg/m².

Supported by: The Hull IVF Charitable Trust/ Hull York Medical School.

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OBJECTIVE: Although the cryopreserved embryos may have the same morphological score at the time of cryopreservation (cryo), the stage of development (Day 5 vs. 6s vs 7) may differ. When presented with this unique circumstance, the clinical standard within this study’s site is to select day 5 embryos. We sought to determine whether the day of cryo of embryos of similar morphology at the time of cryo correlated to IVF outcomes.

DESIGN: Retrospective.

MATERIALS AND METHODS: Patients who underwent single euploid FET cycle between 2010-2016 were analyzed. Ploidy was determined by P-666 Wednesday, October 19, 2016

EVALUATION OF PREIMPLANTATION HUMAN EMBRYO METABOLISM IN EMBRYOS EXPOSED TO L-CARNITINE DURING IN-VITRO DEVELOPMENT. C. K. Leary, R. G. Sturkey. The Hull IVF Unit, Hull, United Kingdom; Hull York Medical School, Hull, United Kingdom.

CONCLUSIONS: These data show that human embryos deplete LC from the culture medium, in a dose dependent manner. Supplementation with LC up to a concentration of 0.05mM led to lower triglyceride levels, suggesting β-oxidation had been enhanced. The data suggest that there are optimum levels of LC consumption that correspond with embryo viability, particularly for cohorts of embryos from women of above and below 25kg/m².

Supported by: The Hull IVF Charitable Trust/ Hull York Medical School.

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trophectoderm biopsy and analyzed via SNP analysis, qPCR, or aCGH. Cycles were segregated on the context of the day they were vitrified: Day 5, 6 or 7. Cycles were binned in 6 sub-categories based on ICM and trophectoderm criteria of “high”, “medium”, and “low” quality and further sorted by expansion (modified Gardner classification). Embryos were only frozen once they achieved at least expansion 3. The main outcome measure was implantation rate. Bivariate associations were examined using Pearson’s Chi-square test, independent samples t-test, as appropriate. All statistical tests were two-sided and P value <0.05 was considered statistically significant. Clopper-Pearson interval was used to calculate binomial CI for all reported proportions.

RESULTS: A total of 1822 patients underwent 2336 SET FET cycles (Table 1). When raw data were analyzed, all sub-categories achieved higher IRs when frozen on Day 5 (highest 100%, lowest 66.7%) as compared to Day 6 (highest 61.6%, lowest 36.8%) or Day 7 (highest 33.3%, lowest 25.0%). Embryos 3BB to 6Aa frozen on Day 5 had statistically higher IRs than those frozen on Day 6 (P<0.05). Any embryo frozen on day 5 showed higher implantation rates than those frozen on day 6, although statistical significance was not achieved in all groups.

CONCLUSIONS: Blastocyst-stage ET has progressively become the norm in many ART clinics. Advancements in extended culture methods have successfully enabled the development of embryos to day 5, 6, or 7 in vitro, which has given embryologists more insight into implantation potential. This study suggests that faster developing euploid blastocysts cryopreserved on Day 5 showed a trend towards higher clinical outcomes following a FET cycle. Further large randomized control trials are needed to confirm these findings.

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A NOVEL, HIGHLY SENSITIVE TANDEM MASS SPECTROMETRY METABOLOMICS APPROACH PREDICTS OUTCOME OF POOR QUALITY DAY 5 BLASTOCYSTS. R. L. Krisher, a S. Lyons, a A. Greene, a J. M. Stevens, a J. Herrick, a J. Kirkwood, a J. Premni, a C. Broeckling, a W. B. Schoolcraft, a Colorado Center for Reproductive Medicine, Lone Tree, CO; bColorado State University, Fort Collins, CO.

OBJECTIVE: To investigate whether the metabolic footprint of single human blastocysts can differentiate between good quality day 5 blastocysts and poor quality day 5 blastocysts that are or are not capable of producing a good quality blastocyst on day 6.

DESIGN: Retrospective analysis

MATERIALS AND METHODS: Individual embryos were cultured to the blastocyst stage in 25 µL of CCRM (in house prepared) standard medium in the EmbryoScope®. Medium samples (n=88) were collected on day 5 following 48 hours of culture from wells containing a good quality (grade 3BB and better, vitrified/transferred) or poor quality (assessed again on day 5) embryos. A medium from wells without an embryo or the same dish were also collected. An internal standard containing 20 isotopically labeled substrates was added to all samples. A zwitterionic polymeric hydrophilic interaction liquid chromatography (ZIC-phILIC) column was used to separate polar metabolites after MTBE extraction, followed by electrospray ionization (ESI) prior to triple quadruple mass spectrometer (TQ-S) coupled to LC-MS/MS. A standard curve was used for absolute quantification of each compound (Skyline software). Metabolic activity was defined as the difference between the concentration of each metabolite in medium with and without an embryo. Data was analyzed using ANOVA (NCSS 10) and Fisher’s LSD MCT when P<0.05.

RESULTS: Patients (n=19; 39.5±0.6 years) produced an average of 4.6±0.7 blastocysts (range 1-10). Each blastocyst was categorized as good quality day 5 (G; n=41), poor quality day 5/good quality day 6 (PG; n=20) or poor quality day 6 (PP; n=27). Uptake or production of 29 metabolites was quantified, including 21 amino acids, glucose, lactate, pyruvate, citrate, alanine, glutamine, myo-inositol, ornithine and citrulline. The metabolic footprints of G and PG blastocysts were indistinguishable on pyruvate, citrate, alanyl-glutamine, myo-inositol, ornithine and citrulline. The metabolic footprints of G and PG blastocysts were indistinguishable on pyruvate, citrate, alanyl-glutamine, myo-inositol, ornithine and citrulline. All 29 metabolites by single human blastocysts. This analysis revealed significant metabolic differences in poor quality blastocysts on day 5 that are related to embryo competence, but that could not be determined by morphology alone.

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CAN THE LOCATION OF A TROPHECTODERM BIOPSY CONTRIBUTE TO HUMAN BLASTOCYST DEVELOPMENT? T. Takano, a M. Funabiki, a S. Taguchi, a F. Saji, a N. Amano, a L. Young, a Y. Nakamura. aOak Clinic, Osaka, Japan.

OBJECTIVE: To investigate the influence of the location of a trophectoderm biopsy in human blastocysts on the development of those blastocysts.

DESIGN: An experimental prospective cohort study.

MATERIALS AND METHODS: We conducted an experimental prospective study to investigate the influence of the location of trophectoderm biopsies within human blastocysts on the development of those blastocysts. The study involved 92 patients (median age 34.3 years old) with infertility that were treated in our clinic. Embryos used in the study were removed with the patients’ informed consent and were cultured until they reached the blastocyst stage. Blastocysts were either frozen on day 5 or the patient was assigned to one of the following three treatment groups as follows: Treatment Group A, location close to the inner cell mass (ICM) (n=29); Treatment Group B, location distant from the ICM (n=32); and Treatment Group C, location between A and B (n=31). The influence of the location of the trophectoderm biopsy within the human blastocysts on the development of those blastocysts was compared between pre- and post-trophectoderm biopsies, according to the Gardner and Schoolcraft scoring system. The time between the post-trophectoderm biopsies and the evaluation of the development of the human blastocysts was 24 hours. In addition, institutional review board (IRB) approval was obtained.

RESULTS: According to the Gardner and Schoolcraft scoring system, degree (one up to six) of expansion of the blastocoele indicates progress of blastocoele development. The rate of blastocysts that showed developmental progress in Treatment Group A was significantly higher (p=0.024, Fisher’s exact test) than in Treatment Group B: 25/29 (86.2%) versus 19/32 (59.4%), respectively. The location of the trophectoderm biopsy in the human blastocysts did not change the trophectoderm and ICM grading. Multivariate logistic regression analysis indicated that blastocoele development was influenced by the location of the trophectoderm biopsy (p=0.049) and by the type of human blastocyst used (fresh or thawed) (p=0.037), regardless of the patient’s age (p=0.507) and the number of days for the human blastocyst in the pre-trophectoderm biopsy (p=0.239).

CONCLUSIONS: The present study is the first to report that when a trophectoderm biopsy is close to the ICM in human blastocysts, it improves the progress of blastocoele development.

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ENMOTION: EMBRYO’S NATURAL MOTION. BLASTULATION IS NOT DIFFERENT BETWEEN STATIC AND DYNAMIC CULTURE SYSTEMS. C. R. Juneau, a J. M. Fransasiak, a S. J. Morin, a M. D. Werner, a K. M. Upham, a R. T. Scott. aRMANI, Basking Ridge, NJ.

OBJECTIVE: A major consideration in assisted reproduction is providing a laboratory environment that is as similar to in vivo conditions as possible during embryo development. In vivo, the embryo is constantly in motion due to gross movement of the carrier or more localized forces from tubal fluid flow and kinetic forces exerted by tubal cilia. Laboratories worldwide currently use static culture systems; however, a dynamic system may more closely mimic in vivo conditions. Reported benefits to dynamic culture include improved blastulation and pregnancy rates (1,2). This study seeks to determine if dynamic embryo culture impacts the reproductive potential of human embryos resulting from IVF.

DESIGN: Paired randomized control trial.

MATERIALS AND METHODS: IVF patients with normal ovarian reserve have been recruited for participation at a single center since 2015. IVF care is routine until fertilization is confirmed. 2-pronuclei (2PN) are then randomized, and half of each patient’s 2PN are cultured in static culture and half in dynamic culture. Preimplantation genetic screening (PGS) is being utilized to control for aneuploidy and allow for DNA-fingerprinting. The best euploid blastocyst from each culture system is selected, and an embryo is frozen 2-3 days before transfer. If a singleton gestation results, DNA-fingerprinting can determine which of the two blastocysts implanted. The dynamic platform being utilized is the NSSB-300 (Nepagene, Ichikawa, Japan). Outcomes including usable blastulation rate and pregnancy outcomes are being analyzed in a paired fashion. A usable blastocyst is suitable for transfer or vitrification for future use. This analysis was performed using a Wilcoxon signed-rank test.

RESULTS: To date, 55 patients have enrolled. 51 patients have completed vaginal oocyte retrieval and blastocyst vitrification for future transfer. The
mean age of patients is 34.8 ± 3.7 years. The mean day 3 follicle stimulating hormone level is 6.184 ± 2.20 IU/mL, and the median anti-mullerian hormone level is 3.71 ng/mL (range 1.27-27.36 ng/mL) in this cohort. The mean number of metaphase II oocytes retrieved was 15.4 ± 8.5 oocytes and the average rate of fertilization was normal (85.7%). 335 static 2PN and 331 dynamic 2PN were followed. 178 blastocysts developed in static culture and 154 blastocysts developed in dynamic culture. In the paired analysis, the rate of usable blastulation was not different between static culture (53.7%) and dynamic culture (52.8%), (p=0.20). After PGS, there was also no difference in the rate of euploidy between static culture (66.7%) and dynamic culture (66.5%), (p=0.46).

CONCLUSIONS: In this interim analysis, dynamic culture did not improve blastulation rate which is contrary to previously published data. Further investigation including a paired comparison of the sustained implantation rate between static and dynamic culture systems is needed.

References:

Supported by: Foundation for Embryonic Competence.

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SUCCESSFUL PREGNANCIES AFTER VITRIFIED EMBRYO TRANSFER OF HUMAN EMBRYOS CULTURED IN RECOMBINED ALBUMIN.

OBJECTIVE: Human serum albumin (HSA), a commonly used protein source for ART, can contribute to biological variation and possibly disease transmission. Additionally, mammalian embryos cultured in blood serum are known to have impaired qualities. Recombinant human albumin (rHA) might reduce these risks, but little is known about neonatal data after transferring embryos cultured in rHA. Our previous randomized controlled trials (RCTs) revealed that the replacement of HSA with lower amounts of rHA during human embryo culture yielded good quality (GQ) embryos (1, 2). Here, clinical data, including perinatal outcomes associated with vitrified ET of these embryos, were analyzed.

DESIGN: Follow-up study of previously conducted RCTs.

MATERIALS AND METHODS: Our RCTs included a total of 136 patients who underwent IVF/ICSI treatment at our clinic between July 2012 and March 2015, and each patient had ≥ 4 2PN oocytes 18 h after insemination (1, 2). Embryo culture (n=1,255) was performed in G1/G2 media containing either 0.5 mg/mL rHA (group A) or 5 mg/mL HSA (group B), and GQ embryos were vitrified by day 6. Clinical data were evaluated for patients with vitrified embryos in groups A (n=67) and B (n=68).

RESULTS: Patient age was similar for groups A and B (35.6±0.5 vs. 35.7±0.4 years, respectively). The total number of vitrified day 2/3 embryos and day 5/6 blastocysts were 51 and 106 in group A and 48 and 175 in group B, respectively. By the end of March 2016, groups A and B underwent 80 (day 2/3 ET=15, day 5/6 ET=65) and 94 (day 2/3 ET=15, day 5/6 ET=79) ET cycles with vitrified/warmed embryos, respectively. All embryos survived warming. The number of embryos transferred (1.13±0.04 vs. 1.16±0.04), implantation rates (46/90 (51.1%) vs. 41/109 (37.6%)), clinical pregnancy rates per ET (44/80 (55.0%) vs. 38/94 (40.4%), and ongoing/ delivered pregnancy rates per ET (36/80 (45.0%) vs. 30/94 (31.9%)) did not differ between groups A and B, respectively. Twins occurred in 1/34 (group A) and 1/29 (group B) of live deliveries. Groups A and B had similar perinatal outcomes, including gestational age (39.4±0.2 vs. 38.7±0.4 wk) and birth weight (3195±91 vs. 3059±394 g). Birth defects occurred in 3/55 (group A) and 2/30 (group B) neonates.

CONCLUSIONS: The viability of human embryos cultured in rHA media was comparable to or slightly better than that of embryos cultured in conventional HSA media, resulting in live births after vitrified ET. Our findings demonstrate the feasibility of using defined culture media to yield GQ embryos, and subsequently, successful pregnancies. Further studies, including those focused on improving rHA media to increase blastocyst yield and with more participants, are being performed to validate the efficacy. Using rHA will help develop a standardized ART system to eliminate potential risks associated with the use of serum proteins.

References:

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PRELIMINARY EVIDENCE THAT ILOPROST PREVENTS APOTOPSIS IN CULTURED EMBRYOS. B. Schniers, A. Huang, S. Prien. *Reproductive Physiology, Texas Tech University, Lubbock, TX; †Obstetrics and Gynecology, Texas Tech University, Lubbock, TX; ‡Ob/Gyn, Texas Tech University Health Sciences Center, Lubbock, TX.

OBJECTIVE: Previous research has demonstrated that the inclusion of Iloprost, a pharmaceutical grade Prostacyclins (PGI2), in culture media can improve embryo development and pregnancy rates. While the exact mechanism is not known, Iloprost has been demonstrated to decrease apoptosis. Earlier studies have established that embryos produce survivin, an anti-apoptotic protein, and it appears to be vital to their normal development. The objective of the present study was to determine if Iloprost might stimulate this pathway as a means of enhancing embryo development.

DESIGN: Lab based culture study.

MATERIALS AND METHODS: Two to four-cell mouse embryos were harvested using standard techniques. Initially, studies were performed to determine the half-maximal inhibitory concentration (IC-50) of the survivin inhibitor YM-155 (an apoptosis-inducing agent) by exposing the embryos to varying concentrations of YM-155 for 15 hrs then following development over 5 days. Once the IC-50 was established, subsequent experiments were performed exposing embryos to one of four culture conditions: an Iloprost group, a YM-155 group, a combination group, and a control group. Two-cell stage embryos were randomly assigned to different treatment groups and were observed, again exposing the embryos to the various combinations of conditions used for 15 hrs before following development over 5 days.

RESULTS: Resulting data suggests that, unopposed, YM-155 inhibited surviving at concentrations in the nM range with an estimated IC-50 of 0.145 nM. While 54% (22/35) of the control embryos reached blastocyst, only 45% (17/33) of the embryos exposed to YM-155 reached the same stage. Further, 86% (30/35) of embryos exposed to the Iloprost reached blastocyst and 68% (28/37) of those exposed to both YM-155 and Iloprost developed to blastocyst.

CONCLUSIONS: Data from the current experiments continue to suggest that Iloprost, via survivin pathway to inhibit apoptosis, enhances embryo development. Further study to include more embryos is ongoing to confirm this observation.

References:

Supported by: Laura W. Bush Institute for Women’s Health.

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CLINICAL UTILITY OF MONOPNOCURLAR ZYGOTES OBTAINED AFTER INTRACYTOPLASMIC SPERM INJECTION (ICSI). H. Tsuji, N. Tokoro, N. Fukunaga, E. Asano, S. Kounogi, Y. Asada. 1,2,3 Asada Ladies Clinic Medical Corporation, Nagoya, Japan; 2Asada Ladies Kagihawa Clinic, Nagoya, Japan; 3Asada Institute for Reproductive Medicine, Nagoya, Japan.

OBJECTIVE: We have demonstrated that 80.7% of 1PN zygotes derived from conventional IVF (cIVF) or ICSI had a biparental chromosome and some of these developed to the blastocyst stage (Tokoro et al. ASRM 2015). However, it has also been reported that all embryos derived from monopronuclear zygotes following ICSI (1PN-ICSI) are chromosomally
abnormal and these zygotes should be discarded, though 1PN zygotes derived from cIVF (1PN-cIVF) could be used for reproductive purposes (Matheo et al. Fertil Steril. 2013; 99: 897-902). In this study, we examined whether 1PN-ICSI could develop normally.

DESIGN: This was a retrospective study in a private IVF clinic including 613 ART patients treated in 667 cycles where 817 zygotes formed 1PN after ICSI in the period January 2013 to December 2014.

MATERIALS AND METHODS: Blastocyst rates and clinical pregnancy rates after a single blastocyst embryo transfer following the culture of 1PN-ICSI zygotes were compared with data on 1PN-cIFV or normal 2PN zygotes. Furthermore, follow up information was obtained on the health status of live births derived from 1PN-ICSI zygotes. Statistically significant effects were determined at the level of P-values using the chi-square test.

RESULTS: The blastocyst rate of 1PN-ICSI zygotes was significantly lower compared to 1PN-cIFV zygotes or normal 2PN (12.4% vs. 25.8, 59.8%, P<0.05). In addition, the clinical pregnancy rate of 1PN-ICSI zygotes was significantly lower compared to 1PN-cIFV zygotes or normal 2PN (21.4% vs. 40.0, 38.6%, P<0.05). However, five healthy newborns were encountered from these successful pregnancies after embryo transfer of 1PN-ICSI blastocysts.

CONCLUSIONS: These results demonstrate that not all 1PN-ICSI zygotes are abnormal, allowing viable pregnancies and healthy live births. Continued culture of 1PN-ICSI zygotes should be carried out to assess their potential and in order to provide embryos for transfer.

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THE IMPACT OF PREINCUBATION TIME BETWEEN OOCYTES RETRIEVAL AND INTRACYTOPLASM SPERM INJECTION (ICSI) ON FERTILIZATION AND EMBRYO QUALITY BY AGE. M. Kobayashi,1 H. Watanabe2, H. Hasegawa,3 K. Tsukamoto,3 R. Suzuki,1 T. Kyoya4, S. Saito1, J. Kobayashi1, Kanagawa Ladies Clinic, Kanagawa-ken, Japan; 5Kanagawa Ladies Clinic, Kanagawa, Japan.

OBJECTIVE: It is thought to be necessary to preincubate oocytes for a few hours following oocyte retrieval before performing ICSI. The aim of this study was to examine the relationship between different preincubation periods of oocytes and patient age and the outcome of intracytoplasmic sperm injection (ICSI).

DESIGN: Oocytes retrieval was done 35h after triggering of hCG. Preincubation times were defined as time (2-9h) from oocyte retrieval to demethylation. Oocytes were classified into four groups according to the preincubation time: <4h (group A, 490 cycles), 4h-<5h (group B, 646 cycles), 5h-<6h (group C, 247 cycles) and 6h-<9h (group D, 94 cycles). We also classified the oocytes into three age groups: <35 (156 cycles), 35-<40 (385 cycles) and 40 (963 cycles).

MATERIALS AND METHODS: From January 2013 to December 2014, 1949 MII oocytes were analyzed according to fertilization (2PN, 0PN2PB, <3PN, 1PN and degeneration rate) 15-22h after ICSI and culture result (Day3 good embryo, Day5 blastocyst, Day5 good blastocyst and Day6 blastocyst rate). We used Veeck’s criteria (good embryo = 8cell-G2 or greater) and Gardner’s criteria (good embryo = 3BB or greater) for embryo evaluation. All statistical analyses were performed using chi squared analysis.

RESULTS: 2PN rate of group A (66.9%) was the lowest, it was significantly lower than group C (72.6%) (P<0.05), 0PN2PB rates of group A (10.5%), B (9.1%) were significantly higher than for group C (7.3%), D (5.7%) (P<0.05). The degeneration rate of group D (10.4%) was significantly higher than for group A (6.9%), B (7.1%) (P<0.05).

The Day 3 good embryo rate of group D (41.0%) was significantly lower than for group A (51.8%), B (49.9%) (P<0.05).

There was no difference between all age groups with respect to fertilization rate. However, in the <35 groups, Day5 blastocyst rate of group A (67.8%) was significantly higher than group C (51.9%), D (50.9%).Day5 good blastocyst rate of group A (50.7%) was significantly higher than group C (37.9%) (P<0.05). In ≥35-<40 age groups, Day3 good embryo rate of group A (53.8%) was the highest, and it was significantly higher than for group B (44.6%), C (44.2%) and D (35.2%) (P<0.05). The Day5 blastocyst rate of group A (50.7%) was the highest, and it was significantly higher than group D (40.4%) (P<0.05).

In ≥40 age group, there was no difference between the four preincubation groups.

CONCLUSIONS: It is advised that ICSI is performed within 6 hours following oocyte retrieval. Furthermore, the impact from preincubation time on clinical results is larger for younger than older patients. This may be because oocytes form aged patients has already decreased quality in their body.

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HATCH-ALL TECHNIQUE IMPROVES EMBRYO DEVELOPMENT AND PREGNANCY OUTCOME. G. A. Abdo,1 M. Goodwin,2 A. G. Abdo,3 F. I. Sharara. Virginia Center for Reproductive Medicine, Reston, VA.

OBJECTIVE: To determine the impact of laser-assisted hatching (LAH) of all embryos on blastocyst formation and pregnancy outcome compared to no laser-assisted hatching (NALH). Previous studies on the effect of AH have produced conflicting results but have only examined patient groups with advanced age or previously failed ART cycles. The current study tests the hypothesis that performing LAH in all patients will result in increased usable (transferred + cryopreserved) blastocyst formation (UF) and improvement in pregnancy rates (PR) compared to no intervention.

DESIGN: Retrospective analysis.

MATERIALS AND METHODS: Outcome of ICSI cycles performed at a private ART center between 2010 and 2016 were reviewed. All patients undergoing ICSI since March 2013 have undergone LAH on day 3 (N=233) with or without PGS (day 5 trophectoderm biopsy) followed by day 5 or 6 ET. Patients who did not undergo LAH (i.e. from Jan 2010 to March 2013) served as controls (NALH) (N=245). Usable blastocyst formation and PR between the two groups were compared.

RESULTS: There were 478 cycles in this study: 233 LAH cycles with or without PGS and 245 NALH. There were no differences in age (35.40 vs 35.22 years in LAH vs NALH, respectively, P=0.645), number of oocytes retrieved (11.73 vs 12.20 in LAH vs NALH, respectively, P=0.334), MII oocytes retrieved (8.76 vs 9.05 in LAH vs NALH, respectively, P=0.454), or number of fertilized zygotes (7.77 vs 7.59 in LAH vs NALH, respectively, P=0.612). Cycles with LAH had significantly more 5-11 vs 2.66 in LAH vs NALH respectively, P=0.017 and significantly more cryopreserved blastocysts (1.75 vs 1.01 in LAH vs NALH respectively, P=0.001). Although LAH had a significantly higher number of embryos transferred (1.92 vs 1.49 in LAH vs NALH respectively, P<0.001), there was a higher PR in LAH cycles (67.6% vs 60.4% in LAH vs NALH, respectively, P=0.105). In order to determine the effect of LAH alone without PGS, we compared a subgroup of 167 cycles with LAH alone (LAH-NO PGS) against NALH cycles. There were significantly more UBF (3.11 vs 2.66 in LAH-NO PGS vs NALH, respectively, P<0.001) and significantly more cryopreserved blastocysts (2.15 vs 1.01 in LAH-NO PGS vs NALH, respectively, P<0.001). There were no differences in age, number of retrieved oocytes, number of MII oocytes, or number of fertilized zygotes between LAH-NO PGS and NALH cycles. Cycles with LAH-NO PGS had a higher PR (66.7% vs 60.4% in LAH-NO PGS vs NALH, respectively, P=0.198) despite a higher number of ET in group NALH vs LAH - NO PGS (1.92 vs 1.59 NALH vs LAH - NO PGS, respectively, P<0.001).

CONCLUSIONS: Embryos subjected to laser assisted hatching were more likely to form usable blastocysts than embryos without LAH. Blastocysts developing after LAH are more likely to be of higher quality and could potentially result in improved clinical outcomes.

P-675 Wednesday, October 19, 2016
SINGLE VERSUS SEQUENTIAL CULTURE MEDIUM: WHAT IS THE BETTER CHOICE TO IMPROVE ONGOING PREGNANCY RATES? A SYSTEMATIC REVIEW AND META-ANALYSIS. F. Dieamant1,2, C. G. Petersen1, A. L. Mauri1,2, L. D. Vagnini1, A. Renzi1, G. R. Oliveira-Pelegrin1, J. Ricci1, M. Cavagna1, J. A. Oliveira1,2, R. L. Baruffi1,2, J. G. Franco, Jr.,1,2 Center for Human Reproduction Prof. Franco Jr, Ribeirão Preto, Brazil;1Paulista Center for Diagnosis Research and Training, Ribeirão Preto, Brazil;2Women’s Health Reference Center Perola Byington Hospital, Sao Paulo, Brazil.

OBJECTIVE: Several factors influence the success of treatment with IVF techniques; the embryo culture, especially the composition of the culture medium, is a particularly important factor. Two hypotheses for the best composition of the culture medium are considered. One is the “back to nature” need for sequential medium” hypothesis, the culture media mimics in vivo conditions. The other is the “free choice embryo/single culture medium” hypothesis, which states that an embryo should be cultured in a constant medium that contains all the components necessary for development. Currently, there are no data available to determine which culture medium is best for embryo culture. This study aimed to evaluate whether single embryo culture medium is better than sequential medium to improve the ongoing pregnancy rates in patients undergoing IVF/ICSI cycles.
**Table 1. Single medium versus sequential medium. Ongoing pregnancy rate. Fixed effect.**

<table>
<thead>
<tr>
<th>Trial</th>
<th>Single n/N</th>
<th>Sequential n/N</th>
<th>RR</th>
<th>95%CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cleavage stage</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Campo et al., 2010</td>
<td>18/84</td>
<td>19/83</td>
<td>0.94</td>
<td>0.53, 1.64</td>
</tr>
<tr>
<td><strong>Blastocyst stage</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sepulveda et al., 2009</td>
<td>28/40</td>
<td>20/38</td>
<td>1.33</td>
<td>0.93, 1.96</td>
</tr>
<tr>
<td>Macklon et al., 2012</td>
<td>20/84</td>
<td>10/43</td>
<td>1.02</td>
<td>0.54, 2.01</td>
</tr>
<tr>
<td>Hardarson et al., 2015</td>
<td>18/41</td>
<td>16/46</td>
<td>1.26</td>
<td>0.75, 2.14</td>
</tr>
<tr>
<td><strong>Cleavage+blastocyst stages</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sfountouris et al., 2015</td>
<td>22/44</td>
<td>24/48</td>
<td>1.00</td>
<td>0.66, 1.51</td>
</tr>
<tr>
<td>Total (fixed effects)</td>
<td>106/293</td>
<td>89/258</td>
<td>1.11</td>
<td>0.89, 1.38</td>
</tr>
<tr>
<td><strong>Blastocyst stage</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Combined</td>
<td>66/165</td>
<td>46/127</td>
<td>1.23</td>
<td>0.92, 1.63</td>
</tr>
</tbody>
</table>

**DESIGN:** Meta-analysis. **MATERIALS AND METHODS:** A systematic review based on electronic searches of databases up to March 2016 was conducted, and five randomized controlled trials (RCTs) were identified as targets for data extraction and meta-analysis. The primary outcome was ongoing pregnancy rate (OPR). Dichotomous data were expressed as Relative Risk (RR) with a 95% confidence interval (CI). Study data were combined using a fixed-effects model. **RESULTS:** The ongoing pregnancy rate was reported by five studies: Embryo transfer: cleavage stage (1), blastocyst stage (3), and cleavage+blastocyst stages (1).

**REFERENCES:**


**P-677 Wednesday, October 19, 2016**

**THE IMPACT OF M-PHASE ON BLASTOCYST DEVELOPMENT: A TIME-LAPSE STUDY.** B. Huang L. Jin. Reproductive Medical Center, Tongji Hospital, Wuhan, China.

**OBJECTIVE:** To determine the key morphokinetic parameters on blastulation using a time-lapse monitoring system (TMS). **DESIGN:** Retrospective observational cohort study. **MATERIALS AND METHODS:** Patients were treated at the Reproductive Medicine Center of Tongji Hospital from 2013 to 2014. A total of 1,038 embryos were enrolled by using TMS, and all patients gave written informed consent. All patients in this study underwent routine IVF/ICSI cycles. Although not show differences between the two culture medium, it is important to highlight the small number of randomized studies/low sample size on this important topic that cause difficulties in drawing inferences from meta-analyses.

**RESULTS:**

- Embryo culture medium, whether continuous or sequential, does not improve ongoing pregnancy rates in patients undergoing IVF/ICSI cycles. Although not show differences between the two culture medium, it is important to highlight the small number of randomized studies/low sample size on this important topic that cause difficulties in drawing inferences from meta-analyses.

**REFERENCES:**

GROWTH FACTORS IGF-I AND IGF-II IN HUMAN EMBRYO CO-CULTURE WITH AUTOLOGOUS GRANULOSA CELL CLUSTERS COMPARED TO REGULAR EMBRYO CULTURE IN IVF. A. Vithoulkas,a M. J. Levanuski,b V. Goudas,c,a K. Illmensee,a Genesys Fertility Center, Patras, Greece; Embryology, Westchester Fertility and Reproductive Endocrinology, White Plains, NY; Advanced Fertility Center of Texas, Houston, TX.

OBJECTIVE: To investigate and compare the presence of IGF-I and IGF-II in human embryo culture with and without autologous granulosa cell supplementation.

DESIGN: Randomized prospective comparative study.

MATERIALS AND METHODS: 19 IVF couples agreed to participate in this study. For autologous comparison, half of the MI-oocytes from the same patient were assigned randomly either to co-culture (group I) or to regular culture (group II), treated for ICSI and cultured in microdrops of Irvine Continuous Single Culture Medium with 15% SSC. As control, autologous granulosa cell clusters were cultured alone (group C). On day 3, 50μl of supernatants from group I, II and control group C were collected and stored frozen. Supernatants were analyzed for IGF-I and IGF-II with growth factor-specific magnetic bead panels by Lab Supplies Inc., Athens, Greece.

RESULTS: IGF-I was not detectable in group II, although it was detected in considerable levels in group I and in the control group C. The difference in concentration of IGF-I between groups I and C was not statistically significant (table 1). IGF-II was detected in all groups (see Table 1). However, IGF-II concentration in group II was at significantly higher levels when compared to group I and group C (p < 0.05 and < 0.04 respectively, two-tailed unpaired t-tests).

CONCLUSIONS: We identified IGF-I both in co-culture and control supernatants but not in regular IVF culture, confirming that IGF-I is secreted from granulosa cells. We now propose that IGF-I is another essential growth factor for embryo culture. Investigators have in the past shown an anti-apoptotic effect of IGF-I on cell growth and morphology when added separately in embryo culture media without co-culture. Separately, we noted that IGF-II is present in samples from all groups, but excessively higher in samples from regular IVF culture, thus suggesting that granulosa cells regulate the level of IGF-II in the co-culture. We have previously documented that granulosa-cell supplementation to human embryo culture improves embryo development, due to beneficial contribution of growth factors (Ref. 1). Supplementation of embryo culture with granulosa cell clusters is therefore recommended for IVF.

Table 1. Mean Concentration (pg/mL) of IGF-I and IGF-II in the three groups.

<table>
<thead>
<tr>
<th>Growth Factor</th>
<th>Group I</th>
<th>Group II</th>
<th>Group C</th>
</tr>
</thead>
<tbody>
<tr>
<td>IGF-I</td>
<td>11</td>
<td>0</td>
<td>26.5</td>
</tr>
<tr>
<td>IGF-II</td>
<td>13.3</td>
<td>66</td>
<td>24.3</td>
</tr>
</tbody>
</table>

References:
1. A. Vithoulkas, M. Levanuski, V.T. Goudas, K. Illmensee Growth factors associated with embryo co-culture and autologous granulosa cell clusters compared to regular embryo culture in IVF. Fertil Steril, 102, 3 suppl, e218, 2014

Supported by: Ferring Hellas.


OBJECTIVE: Environmental stressors encountered in the IVF laboratory can negatively impact embryo development. Introduction of benchtop incubators and use of single-step uninterrupted culture methods aim to reduce harmful environmental deviations and improve system stability. However, exposure and the subsequent increase in media osmolality could be induced from culture in the non-humidified environment present in many benchtop incubators, which could be amplified due to extended culture time with no media refreshment; especially in laboratories who culture embryos for up to 7 days. This study examines the impact of extended culture times in a non-humidified benchtop incubator on media osmolality.

DESIGN: Basic research study.

MATERIALS AND METHODS: Microdrops of media (25μl) were prepared in a sterile airflow hood at room temperature by pipetting 12.5μl of media onto the surface of a 35mm dish, covering with 3.5ml of unwashed mineral oil (Ovoil, Vitrolife), removing the media and adding 25ul of fresh media. Dishes were made every 24 hours over 7 consecutive days (168h) and placed into a 37°C non-humidified benchtop incubator (G185, K-systems). Identical dishes were prepared and cultured in a 37°C humidified box incubator (MCO-18AC, Sanyo). At the end of 7 days, all dishes were removed and osmolality measured using a vapor pressure osmometer (Wescor). Positive controls included media directly out of the bottle (con) and microdrops under oil for 10min (con drops). The resulting 16 treatments were measured 3 times. Data are presented as the mean ±SEM and analyzed using ANOVA and Tukey analysis, p<0.05.

RESULTS: Mean osmolality of con and con drops were 263±1.0 and 265±2.1 mOsm, respectively. These values did not significantly differ. Osmolality of microdrops following 1-7 days of culture in a dry incubator increased over time, differing significantly from con after 24h and differing from con drops and humidified incubator drops after 72h. Osmolality in a humidified incubator remained unchanged and similar to con and control drops at all time points examined.

CONCLUSIONS: Uninterrupted culture for up to 7 days in a non-humidified incubator resulted in an increase in media osmolality over time, while osmolality of microdrops in a humidified incubator remained unchanged. These findings may vary based on volume of media and oil overlay used. Care must be taken when implementing use of dry-culture incubators or uninterrupted culture within the IVF laboratory to avoid creation of damaging culture conditions.

Table 1. Osmolality (mOsm) of media over time

<table>
<thead>
<tr>
<th>Osmolality (mOsm) of media over time</th>
<th>24h</th>
<th>48h</th>
<th>72h</th>
<th>96h</th>
<th>120h</th>
<th>144h</th>
<th>168h</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dry</td>
<td>270.3±2.4&lt;sup&gt;a&lt;/sup&gt;</td>
<td>271.7±1.6&lt;sup&gt;b&lt;/sup&gt;</td>
<td>277.7±1.8&lt;sup&gt;c&lt;/sup&gt;</td>
<td>282.7±1.2&lt;sup&gt;a&lt;/sup&gt;</td>
<td>283.3±1.3&lt;sup&gt;b&lt;/sup&gt;</td>
<td>288.7±0.9&lt;sup&gt;c&lt;/sup&gt;</td>
<td>300.7±2.3&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Humidified</td>
<td>267.3±1.9&lt;sup&gt;a&lt;/sup&gt;</td>
<td>265.3±1.2&lt;sup&gt;b&lt;/sup&gt;</td>
<td>266±1.2&lt;sup&gt;c&lt;/sup&gt;</td>
<td>266.7±0.9&lt;sup&gt;a&lt;/sup&gt;</td>
<td>266.7±0.9&lt;sup&gt;b&lt;/sup&gt;</td>
<td>268±1.0&lt;sup&gt;c&lt;/sup&gt;</td>
<td>269.3±2.4&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

Different superscripts within a time point indicate statistically significant differences, p<0.05.
RESULTS: Embryos with implantation had a shorter time from fertilization to 9 cell formation compared to embryos without implantation, which trended towards significance (66.4 vs. 73.3h, p=0.081). When data was analyzed from time of PN fading, we observed the same results. When controlled for differences in patient age, AMH, and peak estradiol levels, we found a trend in delayed appearance of the blastocele in embryos that failed implantation (99 vs. 94h, p=0.075). No statistical difference was observed in time to PN fading or fertilization in embryos that failed to implant. Clinical factors favoring implantation included maternal factors of decreased oocyte age and increased ovarian reserve, consistent with previous reports. Much larger numbers will be forthcoming and needed to determine if morphokinetic parameters can aid embryo selection within subsets of age and ovarian reserve.

P-681 Wednesday, October 19, 2016


OBJECTIVE: To determine if single medium embryo culture is equivalent to a sequential one regarding embryo quality, pregnancy rate, abortion and ongoing pregnancy. Analyze the presence of cytoplasmic pitting, its relationship to the medium used and its impact on ICSI results.

DESIGN: Observational prospective study.

MATERIALS AND METHODS: 194 cycles of patients younger than 40 years-old with fresh embryo transfer were included. The sequential media used were G1 and G2 (Vitrolife), and single medium CSC (Irvine) without renewal on day 3. The presence of cytoplasmic pitting was identified on day 3 of culture. In order to analyze its impact on the results, only the transfers of two embryos with or without pitting were studied, including 44 patients. Comparisons between groups were performed using Pearson’s chi-squared tests or Fisher’s exact tests. Logistic regression models were adjusted for clinical pregnancy tests. Logistic regression models were adjusted for clinical pregnancy and ongoing pregnancy according to the exploratory variables: culture medium, pitting, low ovarian response, male factor, day of transfer and number of embryos transferred.

RESULTS: Multivariate analysis for clinical pregnancy suggests a favorable trend toward sequential media (p=0.047). A significant association between the presence of pitting and single medium culture was found (CSC 34.3% vs. G1/G2 2.23%; p<0.001). This morphological feature was beneficial in terms of blastulation, pregnancy and implantation rates; however, it is not significant for abortion or ongoing pregnancy.

CONCLUSIONS: According to the exploratory variables, it is suggested that the embryo culture in G1/G2 sequential media increases the probability of achieving a clinical pregnancy when compared to single medium CSC without renewal on day 3. The results of this observational study show a beneficial effect of the presence of pitting on day 3 on the blastulation and pregnancy rates, which should be further examined in order to be confirmed.

Results according to the presence or absence of cytoplasmic pitting

<table>
<thead>
<tr>
<th>Variable</th>
<th>Presence of cytoplasmic pitting</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beta subunit positive</td>
<td>Yes: 72.7% (16/22) No: 27.2% (6/22)</td>
<td>0.006</td>
</tr>
<tr>
<td>Clinical pregnancy</td>
<td>Yes: 53.63% (14/26) No: 27.2% (5/22)</td>
<td>0.01</td>
</tr>
<tr>
<td>Implantation rate</td>
<td>Yes: 54.5% (20/44) No: 18.18% (8/94)</td>
<td>0.01</td>
</tr>
<tr>
<td>Abortions</td>
<td>Yes: 0.00% (0/20) No: 12.5% (1/8)</td>
<td>0.633</td>
</tr>
<tr>
<td>Ongoing pregnancy</td>
<td>Yes: 45.4% (10/22) No: 22.73% (5/22)</td>
<td>0.203</td>
</tr>
</tbody>
</table>

STEM CELLS

P-683 Wednesday, October 19, 2016

SPONTANEOUS SINGLE-COPY LOSS OF TP53 IN HUMAN EMBRYONIC STEM CELLS MARKedly INCREASES CELL PROLIFERATION AND SURVIVAL. H. Amir, K. Sabatini, D. Chhabra, R. Morey, L. C. Laurent. Obstetric and Gynecology, The Tel Aviv Sourasky Medical Center, Tel Aviv, Israel; Department of Reproductive Medicine, UCSD, San Diego, CA.

OBJECTIVE: In a prior study, we identified a common region of single-copy deletion of chr17p13.1 that arose in several subcultures of WA09 human embryonic stem cells (hESCs) during extended passage. The aim of the current study was to characterize the phenotype of hESCs carrying a single-copy deletion of chr17p13.1, and identified TP53 as a gene that contributes significantly to the phenotype conferred by this mutation.

DESIGN: Laboratory study using hESCs.

MATERIALS AND METHODS: Four single-cell clones were sub-cultured from a WA09 hESC culture that was mosaic for a single-copy deletion of chr17p13.1: two mutant clones, which carried the deletion; and two wildtype (WT) clones. Each characterized for the following parameters: cell proliferation using MTT assay, cell cycle using EDU incorporation, clonogenicity by low density plating, and apoptosis using Annexin V-PI staining. Differentiation was determined using embryoid body (EB) and teratoma assays. To confirm the effects of TP53 deletion in the hESC carrying chr17p13.1 loss, we...
knocked-down TP53 in two WT hESC lines. RNA sequencing was performed to study the effect of this deletion on gene expression.

RESULTS: The proliferation rate of the mutant was significantly higher than WT clones. Higher fraction of cells in S phase in the mutant compared with WT clones was detected. The mutant displayed a ~2-fold higher cloning efficiency compared to WT clones. The mutant hESC underwent 2 fold less apoptosis upon staurosporine treatment. All four clones differentiate toward all three germ layers. However, mutant EBs displayed abnormal morphology, lower attachment and higher OCT-4 expression than WT EBs. Knockdown of TP53 in WT cells mimicked the chr17p13.1 deletion phenotype. Gene expression results indicate lower activity of TP53 pathway in the mutant compared to WT clones.

CONCLUSIONS: Our results indicate that a single-copy deletion of chr17p13.1 in hESCs has important phenotypic effects, and suggest that TP53 is the key driver gene in this mutation. These findings highlight the need not only to monitor the genomic stability of hESCs, but also investigate the phenotypic effects of identified genomic changes on cellular behavior, in order to ensure the safety of these cells for cell transplantation.

P-684 Wednesday, October 19, 2016

OBJECTIVE: To review the clinical experience of gamete donors participating in a paid program for procuring oocytes for stem cell research and to survey participants’ attitudes about their experience.

DESIGN: Retrospective longitudinal review and survey.

MATERIALS AND METHODS: All women who participated in the oocyte donor program for stem cell research at Columbia University between 10/2008 - 4/2016 were included. A total of 109 participants, median age 26 years (yrs) (IQR 24-28), initiated a cycle. Most were Caucasian (54.7%), identified as Christian (69.5%), were nulliparous (92.8%), had not previously donated oocytes (71.7%), and held a college degree or higher (79.5%). Median anti-mullerian hormone level and antral follicle count was 2.6 ng/mL (IQR 1.9-3.3) and 20 (IQR 12-22) respectively. Cycle outcomes including days of stimulation, peak estradiol (E2), # oocytes retrieved, and complication rates were analyzed. Skin biopsy at time of retrieval was performed to harvest fibroblast cells. Phone call survey addressing participant experience was attempted for each woman that completed a cycle.

RESULTS: Of the 109 participants, 16 (14.7%) were cancelled due to poor stimulation and the remaining 93 underwent retrieval. Median days of stimulation was 10 (IQR 10-10), peak E2 was 2149 pg/mL (IQR 1347-3607), and # oocytes retrieved was 20 (IQR 14-26). Complication rate, including minor complications, was low (8%). 693/ (6.5%) women returned for office evaluation of complaints related to ovarian hyperstimulation with no need for medical intervention or hospitalization. One woman had an infected skin biopsy; another was sent to the hospital for evaluation of pain and underwent laparoscopy with no resultant torsion/injury noted.

Survey response rate was 47/93 (50.5%). Most respondents would report again/recommend the program to a friend (89.4%), found the experience rewarding (91.5%), and had no regrets about donating (97.9%). Women reported that their primary incentive to donate was: financial (34.1%), for advancement of science (8.5%), to help others (17.0%), or both for financial reasons and to help others (40.4%). 2/46 (4.3%) reported a complaint in regard to skin biopsy (one infection, one scar). Despite extensive consents, most, but not all, recalled that they had donated for research (39/46; 84.8%); of these, 19/46 (41.3%) recalled that their oocytes were being used specifically for stem cell research. In overall experience rating (1: worst - 10: best), women reported a favorable experience with a median score of 9 (IQR 8-10).

CONCLUSIONS: A successful donor oocyte program for research can be achieved using paid participants with a good gamete yield and minimal complications. Participants largely found donating oocytes for research to be rewarding, were incentivized primarily by money/desire to help others, and reported an overall favorable experience. Despite concerted efforts to provide informed consent prior to participation, donors retained only a partial understanding of the nature of the research.

P-685 Wednesday, October 19, 2016
DERIVATION OF INTEGRATION-FREE iPSCS FROM HUMAN MURAL GRANULOSA CELLS. B. Cai, Y. Xu, C. Zhou. Reproductive Medical Center, The First Affiliated Hospital, Sun Yat-sen University, Guangzhou, China.

OBJECTIVE: Induced pluripotent stem cells (iPSCs) provide a unique opportunity for disease modelling, drug screening, and regenerative medicine. But the donor cells’ type needs to be expanded and the safety reprogramming method needs to be optimized. The aim of this study was to establish the integration-free iPSC reprogramming system using human mural granulosa cells as the donor cell, and compared its granulosa cell-like (GC-like) cells differentiation potential with fibroblast-derived iPSCs.

DESIGN: Granulosa cells were collected and transduced with integration-free Sendai viral vectors, the resulting iPSC clones were subjected to determine their pluripotency characteristics. Then established mural granulosa cell (mGC)-iPS lines were differentiated into GC-like cells, compared with fibroblast-derived hiPSCs regarding the differentiating efficiency.

MATERIALS AND METHODS: Human mural granulosa cells were collected from egg follicles retrieved from women undergoing infertility treatment. After short-term culture, the granulosa cells were infected with Sendai viral vectors, mGC-iPSCs were subjected to further determine their pluripotency characteristics. For differentiation of hiPSCs to granulosa cells, we used two step approaches comprising in vitro treatments with cocktails of growth factors for 12days. Expression of granulosa cell markers were analyzed. Using this system, the GC-like differentiation efficiency was compared between mGC-iPSCs and fibroblast-iPSCs.

RESULTS: mGC-iPSCs were successfully generated and shown to resemble human embryonic stem cells (hESCs) in many respects, including morphological traits, growth requirements, gene and marker expression profiles, and in vitro and in vivo developmental propensities. We also confirmed the absence of the Sendai reprogramming vectors by RT-PCR. The differentiated GC-like cells expressed the granulosa cell-specific marker FOXL2, CYP19A1, AMH, AMHR2, and FSHR. However, they did not express the LHR. These GC-like cells were also capable of producing AMH and aromatizing testosterone to estradiol, suggesting that they were biologically functional. Flow cytometry showed that the percentage of AMH2-, FSHR-, and CYP19A1-positive cells increased, and mGC-iPSCs group have a higher percentage numbers than fibroblast-iPSCs group, indicating the higher differentiation efficiency.

CONCLUSIONS: These findings provide a safety means of generating hiPSCs from human mural granulosa cells, and observed mGC-derived iPSCs revealed a higher GC-like cells differentiation efficiency than fibroblast-derived hiPSCs. This system may not only enables modeling of infertility-associated disease, but also provides safety GC-like cells efficiently for possible cell therapy of infertility-associated disease, such as POF.

References:

Supported by: 1. National Natural Science Foundation of China (31401269); 2. Science and Technology Foundation of Guangdong Province (2014A020211012)

HEALTH DISPARITIES

P-686 Wednesday, October 19, 2016
RACIAL DIFFERENCES IN RISK AND COMPONENTS OF METABOLIC SYNDROME IN WOMEN WITH PCOS: A MULTI-NATIONAL STUDY. J. L. Chan, a S. Kat, a E. Vanky, a E. Stener-Victorin, b L. Morin-Papunen, a aMac, 1, l Sundstrom, 1, z J. Mellembakken, b aA. Dokras. a aOBGYN, Univ of Pennsylvania, Philadelphia, PA; b Kar Clinic, Nagar, India; c Children’s and Women’s Health, Trondheim, Norway; d Karolinska Institutet, Stockholm, Sweden; e OBGYN, Univ of Oulu, Oulu, Finland; f Gynecology, Univ of Sao Paulo Medical School, Sao Paulo, Brazil; g Women and Children’s Health, Uppsala Univ, Uppsala, Sweden; h OBGYN, Oslo Univ Hospital, Oslo, Norway.

OBJECTIVE: To compare the prevalence of metabolic syndrome (MetSyn) and clustering of its components in women with PCOS in the United States, India, Brazil, Finland, Norway and Sweden.


Supported by: 1. National Natural Science Foundation of China (31401269); 2. Science and Technology Foundation of Guangdong Province (2014A020211012)

HEALTH DISPARITIES
RESULTS: The data reflect 6,947,063 total ART cycles utilizing both fresh and previously cryopreserved embryos from autologous oocytes. Metabolic syndrome (3/5 criteria present) 28.3% 52.0%a 29.6% 29.6% 27.7% 40.4% b 15.2%b

Prevalence of MetSyn and its components in women with PCOS; a p < 0.001, b p < 0.05

<table>
<thead>
<tr>
<th>Country</th>
<th>U.S. White (referent)</th>
<th>U.S. Black</th>
<th>India</th>
<th>Brazil</th>
<th>Finland</th>
<th>Norway</th>
<th>Sweden</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>184</td>
<td>100</td>
<td>220</td>
<td>233</td>
<td>94</td>
<td>344</td>
<td>165</td>
</tr>
<tr>
<td>Mean age years (SD)</td>
<td>29.0 (5.0)</td>
<td>29.4 (5.2)</td>
<td>25.5 (3.2)a</td>
<td>27.3 (4.6)b</td>
<td>33.5 (7.0)b</td>
<td>28.6 (5.0)</td>
<td>33.7 (6.8)b</td>
</tr>
<tr>
<td>Mean FG score (SD)</td>
<td>11.1 (7.7)</td>
<td>11.0 (7.0)</td>
<td>15.6 (6.5)a</td>
<td>11.6 (6.2)</td>
<td>7.8 (5.1)b</td>
<td>5.9 (6.4)b</td>
<td>9.8 (6.7)</td>
</tr>
<tr>
<td>Women with Oligo/anovulation</td>
<td>90.8%</td>
<td>85.8%</td>
<td>89.5%</td>
<td>89.7%</td>
<td>94.4%</td>
<td>96.3%</td>
<td>91.4%</td>
</tr>
<tr>
<td>Metabolic syndrome (3/5 criteria present)</td>
<td>28.3%</td>
<td>52.0%a</td>
<td>29.6%</td>
<td>29.6%</td>
<td>27.7%</td>
<td>40.4%b</td>
<td>15.2%b</td>
</tr>
<tr>
<td>BMI criterion (&gt;30kg/m²)</td>
<td>47.3%</td>
<td>74.0%</td>
<td>37.3%b</td>
<td>42.1%</td>
<td>47.9%</td>
<td>51.5%</td>
<td>33.9%b</td>
</tr>
<tr>
<td>TG criterion (&gt;150 mg/dL)</td>
<td>20.7%</td>
<td>10.0%b</td>
<td>26.8%</td>
<td>26.6%</td>
<td>11.7%</td>
<td>22.7%</td>
<td>12.7%b</td>
</tr>
<tr>
<td>BP criterion (Systolic BP &gt;130 mmHg or Diastolic BP &gt;85 mmHg or use of anti-hypertensive medication)</td>
<td>36.4%</td>
<td>59.0%a</td>
<td>16.8%a</td>
<td>35.2%</td>
<td>36.2%</td>
<td>49.4%b</td>
<td>21.8%b</td>
</tr>
<tr>
<td>Fasting glucose criterion (&gt;100 mg/dL or pre-existing diabetes mellitus)</td>
<td>12.0%</td>
<td>22.0%b</td>
<td>28.6%a</td>
<td>17.6%</td>
<td>17.0%</td>
<td>24.4%b</td>
<td>8.5%</td>
</tr>
<tr>
<td>HDL criterion (&lt;=50 mg/dL)</td>
<td>41.9%</td>
<td>72.0%a</td>
<td>97.3%a</td>
<td>59.2%a</td>
<td>43.6%</td>
<td>59.3%a</td>
<td>26.1%b</td>
</tr>
</tbody>
</table>

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Women 20-50 years with PCOS (Rotterdam criteria) were included. Age, blood pressure (BP), body mass index (BMI), high-density lipoprotein (HDL-C), triglyceride (TG), and fasting glucose were recorded. MetSyn was defined by NCEP-ATPIII criteria. Comparison of each group with U.S. White women (reference group) were performed using ranksum or chi-square tests.

RESULTS: In the 1797 women included, the median age was 28 years and 46% met all 3 Rotterdam criteria for PCOS. Brazilian women had the highest mean total testosterone levels (86.4 ng/dL, p < 0.001) and Indian women had the highest mean FG score (15.6, p < 0.001). Finnish women had the highest prevalence of polycystic-appearing ovaries (100%, p < 0.001). Complete data for all 5 criteria of MetSyn was available in 1340 subjects (Table). US Black women had the highest (52%) and Swedish women the lowest prevalence of MetSyn (15.2%) compared to the US White group. The age-adjusted Odds Ratio for Metsyn was 2.8 (95% CI 1.7-4.6) in Blacks, 1.7 (95% CI 1.2-2.5) in Norwegians and 0.5 (95% CI 0.3-0.8) in Swedes compared to US White women. Significantly more Black women met the BMI and BP criteria and interestingly, fewer met the TG criteria, compared with other groups. The increased prevalence of MetSyn in Norwegian women was associated with significant abnormalities in BP, glucose and low HDL-C. Although the prevalence of MetSyn in Indian women was similar to the US White group, they demonstrated different clustering with a significantly higher % of glucose abnormalities and had the highest prevalence of low HDL-C criterion (97.3%, p < 0.001).

CONCLUSIONS: Despite a unifying diagnosis of PCOS in young women, we report significant differences in the prevalence of MetSyn and clustering of its components amongst different races. Our data highlights the need to perform a complete metabolic screen to identify preventive and therapeutic targets for metabolic risk based on race. These findings may reflect contributions from both genetic and environmental factors.
Doctors should be able to help transgender people have children; OR for “Support”

<table>
<thead>
<tr>
<th>Demographics</th>
<th>In Support:</th>
<th>Opposed:</th>
<th>Adjusted OR (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age: 18-29y</td>
<td>174 (85.3)</td>
<td>11 (5.4)</td>
<td>1.00 (ref)</td>
</tr>
<tr>
<td>Age: 45-59y</td>
<td>188 (68.9)</td>
<td>36 (13.2)</td>
<td>0.46 (0.22-0.99)</td>
</tr>
<tr>
<td>Political Party: Democrat</td>
<td>304 (86.1)</td>
<td>12 (3.4)</td>
<td>1.00 (ref)</td>
</tr>
<tr>
<td>Political Party: Republican</td>
<td>82 (55.4)</td>
<td>31 (21.0)</td>
<td>0.09 (0.04-0.20)</td>
</tr>
<tr>
<td>Heterosexual</td>
<td>543 (74.0)</td>
<td>81 (11.0)</td>
<td>1.00 (ref)</td>
</tr>
<tr>
<td>Sexual Minority</td>
<td>122 (88.8)</td>
<td>4 (2.9)</td>
<td>3.61 (1.27-10.22)</td>
</tr>
<tr>
<td>Married/Civil</td>
<td>300 (69.8)</td>
<td>51 (11.8)</td>
<td>1.00 (ref)</td>
</tr>
<tr>
<td>Union</td>
<td>90 (84.1)</td>
<td>5 (4.7)</td>
<td>3.14 (1.19-8.27)</td>
</tr>
<tr>
<td>Parent: No</td>
<td>366 (82.0)</td>
<td>29 (6.5)</td>
<td>1.00 (ref)</td>
</tr>
<tr>
<td>Parent: Yes</td>
<td>299 (70.0)</td>
<td>56 (13.1)</td>
<td>0.44 (0.26-0.72)</td>
</tr>
</tbody>
</table>

Democrats, and non-parents (Table). Interestingly, respondents who did not know a gay person (OR=0.20, CI=0.09-0.42) or only knew a gay person without children (OR=0.29, CI=0.17-0.50) were more often opposed than those who knew a gay parent. No differences in gender, geography, education, or household income were seen. Of the 9.7% of respondents opposed, the most common reasons were that “children could be negatively affected” (63.1%) and “it’s not natural” (46.4%). Fewer respondents supported doctors helping transgender minors preserve gametes prior to their gender transition (60.5%) or helping a transgender man who kept his uterus carry a pregnancy (60.1%). Fewer respondents supported doctors helping transgender minors preserve gametes prior to their gender transition (60.5%) or helping a transgender man who kept his uterus carry a pregnancy (60.1%).

CONCLUSIONS: The majority of respondents who support assisted and third-party reproduction also support such interventions to help transgender people have biological children. This study offers new insights to potential obstacles facing transgender individuals seeking to parent.

P-689 Wednesday, October 19, 2016

RACIAL DISPARITIES IN ELECTIVE SINGLE EMBRYO TRANSFER (eSET) UTILIZATION IN THE UNITED STATES: A NATIONAL STUDY.

T. C. Ploidy, S. L. Mumford, K. Kim, V. L. Baker, A. Christie, A. K. Styer. NICHD, NIH, Rockville, MD; Division of REI, Department of Obstetrics and Gynecology, Stanford University, Stanford, CA; Contraception Discovery and Development Branch, NIH, Rockville, MD; Massachusetts General Hospital/Harvard Medical Sch, Boston, MA.

OBJECTIVE: The evolving practice of eSET has provided the means to reduce the likelihood of multiple pregnancies and its attendant complications of pregnancy. However, the use of eSET in the United States (U.S.) is inconsistent and it is unclear if there are racial differences in eSET utilization. The objective of this study is to evaluate utilization of eSET among racial groups in the United States.

DESIGN: Cohort study from the Society for Assisted Reproductive Technology Clinic Online Reporting System, 2004-2013.

MATERIALS AND METHODS: Fresh autologous cycles among women ages 18-37 years using partner’s semen and who underwent an eSET (defined as a single embryo transfer with concurrent embryo cryopreservation) were assessed. All gestational carriers, preimplantation genetic screening/diagnosis, research cycles and cycles that did not report patients’ race were excluded. Race categories included Caucasian, Asian, African-American, Hispanic and multi-race. Modified Poisson regression with robust error variance was used to evaluate factors associated with eSET. Results are reported as adjusted relative risk (ARR) and 95% confidence intervals (CIs).

RESULTS: A total of 19,733 cycles were classified as eSET. In 2004 and 2005, eSET was utilized at a significantly lower rate in African-American women compared to Caucasian women (2004: ARR 0.37, 95% CI 0.15-0.93; 2005: ARR 0.46, 95% CI 0.23-0.93). This trend was observed over time as the rate of eSET continued to increase for all races. Body mass index (BMI), infertility diagnosis, day of embryo transfer and year of treatment were associated with eSET utilization in each racial group. These associations were similar among each racial group. Among women 35-37 years old, black women were less likely to undergo eSET compared to Caucasian women (ARR 0.56, 95% CI 0.32-0.97).

CONCLUSIONS: Although eSET utilization has increased since 2004, racial differences in this practice exist. The lower utilization of eSET in African-American women compared to Caucasian women may be related to specific demographic characteristics and warrants further investigation as a potential area of disparity in assisted reproductive technology.

Supported by: This research was supported, in part, by the Intramural Research Program of NICHD.

P-690 Wednesday, October 19, 2016

LESBIAN, GAY, BISEXUAL, TRANSGENDER (LGBT) CONTENT ON REPRODUCTIVE ENDOCRINOLOGY AND INFERTILITY CLINIC WEBSITES.

H. Y. Wu, B. C. Monseur, O. Yin, J. H. Selter, B. D. Lau, M. S. Christianson. Gynecology and Obstetrics, Johns Hopkins University School of Medicine, Baltimore, MD; Surgery, Johns Hopkins University School of Medicine, Baltimore, MD; Gynecology and Obstetrics, Johns Hopkins University School of Medicine, Lutherville, MD.

OBJECTIVE: To assess geographical distribution and practice characteristics of fertility clinics that are specifically inclusive of the lesbian, gay, bisexual, and transgender (LGBT) population.

DESIGN: Cross-sectional analysis.

MATERIALS AND METHODS: Society for Assisted Reproductive Technology (SART) member clinics were identified from the SART database. Websites were analyzed in January-March 2016. Clinic characteristics collected included state, size (number of cycles per year), private- or university-based, and location in a state with mandated insurance coverage for reproductive services. Websites were surveyed for contextual keywords including: gay, lesbian, bisexual, homosexual, LGBT/LGBTQ, same sex, orientation, trans/transgender. Home page cues inclusive of the LGBT population were also noted. The proportion of clinic websites with LGBT content was categorized by region. Chi-squared test was used to determine regional differences in proportion of websites with LGBT content. Logistic regression was performed to determine the association between inclusion of LGBT content and variables of interest.

RESULTS: Of 379 websites analyzed, 201 (53%) contained LGBT content with at least one keyword or home page cue. Clinics with the highest proportion of LGBT website content were in the West (60/92, 65%), Northeast (59/201, 57%) and Pacific (3/4, 75%), while the lowest was in the Midwest (2/74, 3%) and South (50/126, 39%). These regional differences were statistically significant (p<0.001). 68% of websites with LGBT content used home page cues, and 69% used ≥3 content markers. Most frequently used terms included lesbian (72%), LGBT/LGBTQ (69%), gay (68%), and same sex (68%), while less used terms included trans/transgender (32%), bisexual (15%), and homosexual (6%). Practice type was not associated with a clinic website having LGBT content. Clinics in states with mandated insurance for reproductive services were 1.7 times more likely to have LGBT website content (OR 1.68, 95% CI 1.12, 2.55, p=0.013). Also, increasing clinic size was significantly associated with a website having LGBT content (p<0.001).

CONCLUSIONS: While just over half of SART member fertility clinics included LGBT content on their websites, those in the Midwest and South were significantly less likely to do so. Predictive factors for having LGBT website content included location in Northeastern and Western regions, location in states with mandated insurance coverage for reproductive services, and increasing clinic size. Further studies are needed to evaluate if inclusion of LGBT content on clinic websites impacts use of reproductive services by the LGBT patient population.

P-691 Wednesday, October 19, 2016

IMPACT OF RACE ON OVOCYTE DONATION.

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OBJECTIVE: Several publications have reported racial disparities in the live birth rate following fresh autologous in-vitro fertilization (IVF) cycles. This disparity has been hypothesized to stem from differences in ovarian reserve to uterine factors such as fibroids. Less is known about the impact of race on oocyte donation outcomes. The objective of this study was to compare ovarian reserve, ovarian
RESULTS: 492 oocyte donors were included: 410 White (83.3%), 18 Black (3.7%), 36 Asian (7.3%) and 28 Hispanic (5.7%). Demographics were compared between groups (Table 1). Asian donors had a higher mean AMH compared to White donors, while Hispanic donors had a lower day 3 FSH compared to White donors. Ovarian responsiveness as measured by peak estradiol was not different between groups. In addition, there were no significant differences in cancellation rates between groups. There were no significant differences in the mean number of oocytes retrieved: 19.7 (SD 7.2) in Black donors, 17.6 (SD 7.1) in Asian donors and 18.0 (SD 9.2) in Hispanic donors. % Cycles Canceled: 7.8% in White donors, 5.6% in Asian donors, 10.7% in Hispanic donors and 0.0% in Black donors.

CONCLUSIONS: There were no differences in ovarian responsiveness or number of oocytes retrieved from oocyte donors retrieved from different racial groups. This information can be used clinically to reassure donor oocyte recipients regarding overall excellent prognosis with oocyte donation cycles.

Table 1: Group Characteristics (N=492)

<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>Oocyte Donation</th>
<th>Sperm Donation</th>
<th>Embryo Donation</th>
<th>Gestational Carrier</th>
<th>Multiple Third-Party</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Hispanic White</td>
<td>43.1%</td>
<td>29.9%</td>
<td>33.9%</td>
<td>33.6%</td>
<td>48.4%</td>
</tr>
<tr>
<td>Non-Hispanic Black</td>
<td>32.0%</td>
<td>22.1%</td>
<td>27.7%</td>
<td>25.4%</td>
<td>41.9%</td>
</tr>
<tr>
<td>Asian/Pacific Island</td>
<td>42.3%</td>
<td>24.3%</td>
<td>37.0%</td>
<td>33.3%</td>
<td>46.9%</td>
</tr>
<tr>
<td>Hispanic</td>
<td>41.6%</td>
<td>31.5%</td>
<td>36.0%</td>
<td>33.0%</td>
<td>48.1%</td>
</tr>
<tr>
<td>Other</td>
<td>43.5%</td>
<td>24.2%</td>
<td>36.0%</td>
<td>35.1%</td>
<td>49.3%</td>
</tr>
</tbody>
</table>

Supported by: Intramural funds from The Center for Human Reproduction and grants from The Foundation for Reproductive Medicine.

P-693 Wednesday, October 19, 2016

EFFECT OF RACE AND ETHNICITY ON LIVE BIRTH RATES IN THIRD-PARTY ART CYCLES IN THE U.S. A. Shapiro, D. H. Barad, S. Darmon, D. Albertini, N. Gleicher, V. A. Kushnir, Rutgers New Jersey Medical School, New York, NJ; Center for Human Reproduction, New York, NY; Albert Einstein College of Medicine, Bronx, NY; University of Kansas Medical Center, Kansas City, KS; Rockefeller University, New York, NY.

OBJECTIVE: To examine live birth rates for third-party Assisted Reproductive Technology (ART) performed in the United States.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: We compared the ethnic and racial demographics of the entire birth cohort in the USA between 2005 and 2013 (National Vital Statistics Report Vol 64, No. 1, 01/15/15) to ART data reported to the Society for Assisted Reproductive Technology (SART) over the same time period. ART data were stratified as routine ART or third-party ART (including all donor oocyte, sperm, embryonic, and gestational carrier cycles). ART data are de-identified and represent more than 90% of all ART cycles performed in the US.

RESULTS: As the table demonstrates, overall fertility rates are relatively high for Hispanic and Black women while utilization of both routine and third-party ART among these groups are relatively low. Conversely White and Asian women have relatively low fertility rates and relatively high utilization of both routine and third-party ART. Routine ART results in the highest live birth rates among White and Hispanic women and relatively low live birth rates among Asian and especially Black women. Third-party ART results in improved live birth rates for all groups; however, Black women still experience the lowest live birth rates.
<table>
<thead>
<tr>
<th>Age at First Birth, 2013</th>
<th>White</th>
<th>Asian</th>
<th>Black</th>
<th>Hispanic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean female age</td>
<td>35.4 +/- 4.7</td>
<td>36.0 +/- 4.5</td>
<td>36.3 +/- 4.9</td>
<td>35.8 +/- 4.9</td>
</tr>
<tr>
<td>Live Birth Rate 1,000 women aged 15-44</td>
<td>31.2%</td>
<td>25.8%</td>
<td>22.5%</td>
<td>29.3%</td>
</tr>
<tr>
<td>Third-Party ART Cycles</td>
<td>67%</td>
<td>9%</td>
<td>6%</td>
<td>6%</td>
</tr>
<tr>
<td>Mean female age</td>
<td>40.6 +/- 5.5</td>
<td>41.8 +/- 5.6</td>
<td>42.1 +/- 5.4</td>
<td>40.6 +/- 5.9</td>
</tr>
<tr>
<td>Live birth rate</td>
<td>40.5%</td>
<td>40.1%</td>
<td>30.2%</td>
<td>39.7%</td>
</tr>
</tbody>
</table>

CONCLUSIONS: These data imply that utilization of ART reflects fertility rates among different ethnic and racial groups. Those with highest fertility rates utilize ART the least. Whether this is related to lower demand or disparity in access to ART by Hispanic and Black women, remains to be determined. More research is needed to identify lower demand or disparity in access to ART by Hispanic and Black women, influenced by cultural norms. When creating educational interventions, and treatment seeking, among this population in order to appropriately modify risk behavior and support; and 3) Infertility does not require a medical resolution, possible need for internet-based, anonymous resources for information about due to gender-related stigma and shame, which speaks to the context of their family and culture, 13 Latino undergraduate students (ages 19-22) at a midwestern university in the U.S. were recruited to participate in a focus group.

RESULTS: Three major themes were identified: 1) Infertility is not considered when looking towards the future. This refers also to desire to postpone childbearing, which speaks to the importance of providing information on the age boundaries of fertility; 2) Infertility is not talked about due to gender-related stigma and shame, which speaks to the possible need for internet-based, anonymous resources for information and support; and 3) Infertility does not require a medical resolution, which suggests the need to understand how causal factors are perceived among this population in order to appropriately modify risk behavior and treatment seeking.

CONCLUSIONS: College students have the opportunity to make lifestyle modifications that can optimize fertility, but intention to change behavior is contingent on accurate fertility knowledge, which is often influenced by cultural norms. When creating educational interventions, it is important to take into account the cultural lens through which infertility is understood.

Supported by: The Office of Institutional Diversity at Ball State University provided financial support for this research.

P.695 Wednesday, October 19, 2016
REligious ATTendance and Ethical Views on Various Treatments for Infertility Among Reproductive-Aged U.S. Women. S. C. Collinsa E. Chan. "Department of Obstetrics, Gynecology, and Reproductive Sciences, Yale University School of Medicine, New Haven, CT; "Department of Sociology, Yale University, New Haven, CT.

OBJECTIVE: Religions play a central role in shaping the ethical values of their adherents. To enable clinicians to better meet the needs of their religious patients, we sought to determine the relationship between religious attendance and ethical concerns that women have about specific treatments for infertility.

DESIGN: Cross-sectional survey.

MATERIALS AND METHODS: Data were obtained from the National Survey of Fertility Barriers (Wave 1, 2004-2007), a US-wide random-digit-dialing telephone survey of 4794 women, aged 25-52. Multiple logistic regression was performed to determine the relationship between religious attendance and ethical concerns about the following treatments for infertility: intrauterine insemination (IUI), in vitro fertilization (IVF), donor sperm IUI, donor egg IVF, true surrogacy, gestational carrier, and fertility treatments which increase the chance of twins. The regression model adjusted for race, age, income, educational level, religious affiliation, history of infertility, nulligravidity, nulliparity, marital status, urban vs. rural, and geographic region.

RESULTS: The infertility treatments with the highest rates of ethical concerns were true surrogacy (56.2%), fertility treatments which increase the chance of twins (53.1%), and gestational carriers (50.5%). Concerns about ethical concerns with IUI were uncommon (13.4%). Women who regularly attend religious services were more likely to have serious ethical concerns with IVF (adjusted odds ratio (aOR) 1.73 [95% confidence interval (CI) 1.06 - 2.83]), donor sperm IUI (aOR 2.27 [CI 1.51 - 3.39]), donor egg IVF (aOR 1.59 [CI 1.12 - 2.26]), true surrogacy (aOR 2.30 [CI 1.64 - 3.22]), and the use of a gestational carrier (aOR 2.38 [CI 1.65 - 3.45]), when compared to women who do not regularly attend religious services. There was no significant association between regular religious attendance and serious ethical concerns with IUI, but only with lesser ethical concerns about IUI (aOR 1.54 [CI 1.08 - 2.18]). There were no significant associations between regular religious attendance and either serious or lesser ethical concerns with fertility treatments that increase the chance of twins.

CONCLUSIONS: Regular attendees of religious services are more likely to have serious ethical concerns about IVF and third-party reproductive technologies, but are only more likely to have lesser concerns about IUI. Despite being one of the most ethically concerning fertility practices across the population, treatments which increase the rate of twins are not more ethically concerning to women who attend religious services. These findings can help clinicians to counsel religious patients with sensitivity to their cultural preferences in fertility healthcare.
significant difference in AMH, AFC and basal FSH among the groups as shown in table 1. In logistic regression analysis, ovarian reserve correlated significantly with ethnic group even after adjusting for age, smoking, BMI (AOR 1.59, 95% CI 1.29 - 1.99, P < 0.01). In comparison to white women, further adjusting for number of embryos transferred, odds of clinical pregnancy and live birth were reduced for Asians (AOR 0.40; 95% CI 0.36-0.44), Hispanics (AOR 0.40; 95% CI 0.36-0.44). Black race was an independent risk factor for reduced live birth rate (AOR 0.41; 95% CI, 0.12 - 0.99).

CONCLUSIONS: Our study showed significant difference in ovarian reserve and IVF outcomes between different ethnic groups. In multivariate regression analysis, these differences persisted even after controlling for potential confounding factors. Further research with larger representative dataset is warranted to confirm these findings.

References:

GENETIC COUNSELING

P-697 Wednesday, October 19, 2016

BECKWITH-WIEDEMANN SYNDROME IN IVF: NEED FOR IMPROVEMENT IN PREGNATAL DIAGNOSIS.
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OBJECTIVE: Beckwith-Wiedemann Syndrome (BWS) is an overgrowth disorder that affects at least 1 in 11,000 children who are at increased risk for neonatal hypoglycemia and cancer. BWS may be suspected during routine fetal ultrasound due to omphalocele, renal anomalies, or placentomegaly or with elevated serum alpha-fetoprotein (AFP) in the second trimester screen. Prenatal diagnosis is important for early intervention and management. Children conceived via assisted reproductive technology have a 3-9 fold higher risk of BWS than the general population. We investigated the rate of prenatal diagnosis of BWS in pregnancies conceived via in vitro fertilization (IVF) compared to natural conceptions (NC).

DESIGN: Case-control study.

MATERIALS AND METHODS: A retrospective review of the BWS patient registry of the Children's Hospital of Philadelphia was performed. Thirty-three patients with loss of methylation at the IC2 locus were identified, 15 NC and 15 IVF patients. Alpha fetoprotein (AFP) measurement was available for 15 IVF patients and 15 NC patients. Alpha fetoprotein (AFP) measurement was available for 6 NC and 7 IVF patients. Rates of prenatal diagnosis between the IVF and NC groups were compared using a chi-squared analysis.

RESULTS: Results are shown in the table. Abnormalities such as omphalocele, placentomegaly, renal anomalies, and macroglossia were noted in 40% NC and 60% IVF patients. Other nonspecific abnormalities including large for gestational age (LGA) and polyhydramnios were also noted.

CONCLUSIONS: Despite close surveillance and a trend toward a higher rate of abnormal ultrasound findings in the IVF group, the rate of prenatal diagnosis of BWS was the same in IVF and NC. Screening AFP may be emerging as an early screening tool for detection of BWS, however with its decreasing use secondary to non-invasive prenatal testing, we are at increased risk of missing cases of BWS. Additionally, special attention to the tongue, palate, and to growth parameters in IVF conceptions could improve rates of prenatal diagnosis of BWS.

Supported by: K08CA193915 and St Baldwin’s Foundation.

P-698 Wednesday, October 19, 2016


OBJECTIVE: The Fragile X mental retardation 1 (FMR1) gene premutation (CGG repeats 55-200) has been associated with primary ovarian insufficiency (POI). There is still controversy regarding the significance of CGG repeats below the premutation range to reproductive potential. The objective of this study was to determine whether the number of CGG repeats within the normal range (<45) is predictive of a patient’s fertility potential.

DESIGN: Retrospective analysis.

MATERIALS AND METHODS: Our study included women who underwent both fragile X and ovarian reserve testing between June 2013 and July 2015. CGG repeats on allele 1 (CGG1) and allele 2 (CGG2), respectively, as well as anti-mullerian hormone levels (AMH) were recorded. Patients with CGG repeats ≥45 and AMH<10 were excluded from the study. Based on a preliminary Classification and Regression tree analysis (CART), the cohort was divided by age: <33 and ≥33. Using multivariable regression models, we analyzed the correlation between AMH and CGG1, CGG2 and age for each age group.

RESULTS: A total of 1674 patients were included in the study. In the younger women (<33, n=559), regression analysis demonstrated a significant positive linear relationship between AMH and CGG1 levels (p=0.04) and also a significant negative linear relationship between AMH and age (p=0.001). Among the older group of women (≥33, n=1115), no statistically significant relationship was obtained between AMH and CGG1 or CGG2 levels. Only age had a significant negative linear relationship (p=0.0001). The correlation of AMH with age for the older group was stronger than for the younger group.

CONCLUSIONS: 1. The number of CGG repeats does not predict diminished ovarian reserve below the threshold of 45.
2. Of interest is the observation of a higher AMH with increasing repeats in patients less than 33 years of age; the significance of this observation is that to be determined.

P-699 Wednesday, October 19, 2016

THE WEIGHT OF THE INTERCHROMOSOMAL EFFECT IN RECIPROCAL TRANSLATION CARRIERS. T. Escudero,1,2, L. Ribustello,1,3, E. M. Armenti,1,4 E. Liu,1,5 J. Grifo,1,6 J. Hitkari,1,7 R. Schmidt,8 B. R. Witt,1,9 M. Doyle,1,10 A. Nasserip,7 S. Munne,6 Reprogenetics, Livingston, NJ; 2NYU Fertility Center, New York, NY; 3Olive Fertility Centre, Vancouver, BC, Canada; 4NOVA IVF, Mountain View, CA; 5Greenwich Fertility Center, Greenwich, CT; 6CT Fertility, Bridgeport, CT; 7The Valley Hospital Fertility Center, Paramus, NJ.

OBJECTIVE: To determine if the presence of a reciprocal translocation in a carrier increases the proportion of aneuploid chromosomes unrelated to the translocation in the blastocyst created from gametes of such carrier.

DESIGN: Retrospective.

MATERIALS AND METHODS: 6861 blastocyst from 12790 PGS cases with an average age of 35.4 (PGS group) yo (years old), were compared to 1,184 blastocyst from 199 PGD cases of reciprocal translocations with an average age of 33.4 (PGD group). The aneuploidy results from the PGS cases were compared with the aneuploidy results from the PGD cases excluding the results from the chromosomes involved in the translocations. These two groups were further divided in two subgroups by age of the female patient: below 35 yo, and 35 yo and above. The statistical analysis used was chi-square test.

RESULTS: The significant results are summarized in table I. The majority of the chromosomes does not show change in rate of aneuploidy when
IMPLANTATION GENETIC TESTING.

A. P. Hutchinson,
N. Pereira, D. P. Lilienthal, S. Coveney, J. P. Lekovich, R. Elias,
Z. Rosenwaks. The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: Although the relationship between FMR1 premutation status and decreased ovarian reserve and responsiveness has been well established, there is scarce data regarding any association between premutation status and embryo development. We investigate the impact of FMR1 pre-mutation status on blastocyst development in patients undergoing intracytoplasmic sperm injection (ICSI) and pre-implantation genetic diagnosis (PGD) for the same premutation.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: All patients <40 years undergoing ICSI with PGD at blastocyst-stage between 2005 and 2013 for FMR1 premutation status were included in the study. Patients undergoing ICSI with pre-implantation genetic diagnosis or screening (PGD/S) for single-gene disorders or history of recurrent pregnancy loss were considered as controls. The baseline demographics and ovarian stimulation parameters of the two groups were compared. Blastocyst development, calculated per metaphase II (MII) oocyte
retrieved and per 2-pronuclear (2-PN) embryo after ICSI, was also compared between the two groups. Odds ratio (OR) for blastocyst development in the FMR1 and control groups were calculated. A similar sub-analysis was carried out for the former group with age-matched controls. Spearman’s correlation was used to evaluate the correlation between the number of FMR1 CGG repeats and blastocyst development.

RESULTS: 1625 patients met inclusion criteria: 69 (4.25%) patients in the FMR1 group 1556 (95.75%) in the control group. Patients in the FMR1 group were younger compared to controls [33 (31-36.3) vs. 38 (34-41) years; P<0.01]. Ovarian responsiveness of the former group was decreased in comparison to the latter as evident by higher gonadotropin doses (4162.5 vs. 3000 IU; P<0.01), lower peak estradiol level (1070.5 vs. 1825 pg/ml; P<0.01), and lesser MII oocytes retrieved (6 vs. 11; P<0.01). The blastocyst development rate in the FMR1 group was comparable to controls [1/6) 16.6% vs. (2/11) 18.9% per MII oocyte and (1/5) 20% vs. (2/9) 22.2% per 2-PN embryo]. Comparison of the FMR1 group with age-matched controls revealed similar trends in decreased ovarian responsiveness. In contrast, blastocyst development was lower in the FMR1 group: (1/6) 16.6% vs. (4/12) 33.3% per MII oocyte and (1/5) 20% vs. 40.0% per 2-PN embryo. This represented a 0.40 (95% CI 0.21-0.78) and 0.38 times (95% CI 0.19-0.71) lower odds of blastocyst development. There was also a significant inverse correlation between the number of FMR1 CGG repeats and blastocyst development per MII oocyte (r=-0.51; P=0.04).

CONCLUSIONS: Our study suggests lower rates of blastocyst development per MII oocyte and 2-PN embryo in patients with FMR1 pre-mutation status compared to age-matched controls undergoing ICSI with PGD/S. Furthermore, there is significant inverse correlation between the number of FMR1 CGG repeats and blastocyst development.

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PREIMPLANTATION GENETIC SCREENING (PGS) APPEARS UNABLE TO CORRECTLY DETERMINE PLOIDY OF EMBRYOS FROM A SINGLE TROPHOECTODERM BIOPSY (TEB). N. Gleicher,a,b A. Vidal,vi V. A. Kushner,vii D. H. Barad,a,b C. Hudson,vi Q. Wang,iv L. Zhang,iv D. Albertini.v Center for Human Reproduction, New York, NY; viRockefeller University, New York, NY; viiWake Forest School of Medicine, Winston-Salem, NC; a,bAlbert Einstein College of Medicine, Bronx, NY; viiiFertility Center of Las Vegas, Las Vegas, NV; ixUniversity of Kansas Medical Center, Kansas City, KS.

OBJECTIVE: To determine inter-laboratory and intra-embryo variability between repeat embryo biopsies at blastocyst stage in preimplantation genetic screening (PGS).

DESIGN: Cohort study.

MATERIALS AND METHODS: This study involved dissection of 11 embryos from 2 infertile couples who were found to have no euploid embryos in their respective IVF cycles. To assess PGS in defining embryo ploidy, we retrieved and per 2-pronuclear (2-PN) embryo after ICSI, was also compared between multiple TEBs and inner cell mass biopsies. Although patients who carry the BRCA mutation are known to have accelerated age-related decline in ovarian reserve and oocyte yield was demonstrated in BRCA 1 carriers. Despite this, all patients had oocytes retrieved and blastocysts available for biopsy. Patients who carry the BRCA mutation are known to have an altered DNA repair mechanism, their embryos did not demonstrate increased aneuploidy. Given the low incidence of the mutation, multi-center studies on BRCA mutation carriers who utilize PGS are needed to corroborate these preliminary findings.

RESULTS: Only 2/11 (18.2%) embryos demonstrated identical assessments between two PGS laboratories. On second PGS, 4/11 (36.4%) of pre-implantation genetic screening (PGS) (via trophectoderm biopsy of blastocysts) for both BRCA and chromosome copy number. Student’s t-test, chi-square and linear regression were used.

CONCLUSIONS: Though based on a relative small sample size, findings presented here are highly concerning, and question the biological basis of PGS based on unacceptably high inter-laboratory and intra-embryo variability in biopsy results. Excessive intra-embryo variability between multiple TEBs and inner cell mass biopsies was recently also report by Izraeli and his investigators (Orivieto et al., Reproductive Endocrinology, 2016). While differences in diagnostic platforms between PGS laboratories may contribute to inter-laboratory variability, they cannot explain intra-embryo variability. Combined, data presented here suggest a much higher prevalence of mosaicism in trophectoderm (TE) than has been so far appreciated. Thus, it seems likely that a single TEB cannot reliably determine embryo ploidy. Relying on a single TEB will lead to a large number of false-positive diagnoses and the discarding of many biologically normal embryos. High mosaicism in TE should not surprise since the TE is where mosaic embryos segregate abnormal cell lines. False-positive diagnoses are especially harmful to poor prognosis patients who produce few embryos.

Supported by: Intramural funds from The Center for Human Reproduction and grants from The Foundation for Reproductive Medicine.
P-705 Wednesday, October 19, 2016

GENOME-WIDE DNA METHYLATION ANALYSIS OF SPERM DNA FROM SMOKING MALES SUFFERING FROM IDIOPATHIC INFERTILITY. M. M. Laqan,a J. Walter,a Y. A. Alkahled,a S. Tierling,b M. E. Hammadeh,a bObstetrics & Gynecology, Saarland University, Germany, Homburg, Germany; 3Genetik/Epigenetik, Saarland University, Germany, Saarbruecken, Germany.

OBJECTIVE: To identify if there is any connection between smoking and alterations in DNA methylation of sperm DNA obtained from smoking sub-fertile, smoking fertile and non-smoking fertile male.

DESIGN: Human semen samples were collected during the period between August 2014 to May 2015 from males who developed idiopathic infertility.

MATERIALS AND METHODS: Infinium 450K BeadChip arrays were used to identify genomic regions that show smoking-related differences in sperm DNA methylation patterns between sub-fertile and fertile males from couples that have idiopathic infertility and underwent intracytoplasmic sperm injection.

RESULTS: In this study 13 CpG dinucleotides have been found to be significantly and consistently different in a smoking-related manner (between 35.62% and 67.39%, fdr-adj.p < 0.1) in the DNA methylation level in sperm samples of 3 subfertile smokers compared to 3 non-smoking subfertile males. Only 5 of those (DNA methylation difference between 35.62% and 49.16%) do not overlap common annotated SNPs, all 5 CpGs were found to be directly linked to the genes KCNJ5, COL4A1, MAGI1, RP11-281J9.2 and DEFB128. Currently, these results are under validation through local bisulfite sequencing and are planned to be tested on a larger sample cohort.

CONCLUSIONS: The present study identified 5 consistently altered CpG dinucleotides in sperm, which may represent novel candidates linked to smoking-related idiopathic infertility. If detectable in a larger sample cohort these CpG sites might serve as a future prognostic tool for smoking-related infertility.

 Supported by: Department of Obstetrics and Gynecology, University of Saarland.

P-706 Wednesday, October 19, 2016


OBJECTIVE: Duchenne/Becker Muscular Dystrophy (DMD/BMD) is an X-linked recessive disorder associated with progressive limb muscle weakness, atrophy, and cardiac disease in affected males. Approximately two-thirds of diagnosed cases have a carrier mother. Due to the size of the DMD gene, population-based genetic carrier screening for DMD/BMD was previously cost-prohibitive. However, recent advances in genetic testing make carrier screening for DMD/BMD feasible.

DESIGN: Retrospective review.

MATERIALS AND METHODS: Performed chart review of all samples tested for DMD/BMD via genetic carrier screening on next generation sequencing, qPCR, and multiplex ligation-dependent probe amplification, at a single reference laboratory. Identified carriers of a DMD mutation had additional chart review to determine if they chose to pursue preimplantation genetic diagnosis (PGD) for DMD/BMD at the same reference laboratory. PGD test development was performed using Illumina CytoSNP-12b microarrays with an informatics technique. PGD for embryo samples included or excluded direct mutation analysis based on mutation type.

RESULTS: Of 30,232 patients screened for DMD/BMD, 55 (0.18%) were identified to be carriers of a pathogenic or likely pathogenic DMD variant. Of these patients, 3 elected to proceed with PGD test development for DMD/BMD. Maternal age range was 25-42 years. Patient 1, 2, or 3 of the DMD gene. Given the size of the deletion, direct mutation analysis could not reliably be performed on embryo biopsy samples. PGD test development using homolog phasing was not possible because clinical testing of the patient’s mother revealed the DMD variant was de novo in origin. Thus, PGD test development could not be completed. Patient 2 had a family history of an unspecified muscular dystrophy in her father. Genetic carrier screening identified a likely pathogenic point mutation in the DMD gene. PGD test development for the variant was successful, and the patient is planning her first IVF cycle. Patient 3 presented to an IVF clinic due to unexplained infertility and pursued genetic carrier screening prior to her IVF cycle. Family history of DMD/BMD was negative, but she was found to carry a point mutation in the DMD gene. PGD test development was successful, and the couple’s first IVF cycle produced 11 embryos, 6 of which were chromosomally normal and unaffected with the maternal DMD mutation.

CONCLUSIONS: Previously, routine carrier testing for DMD/BMD was unavailable. As such, many at risk women had multiple children before learning of their carrier status for DMD, often following the diagnosis in a child. Due to recent advances in expanded carrier screening, women now have the option to screen for DMD/BMD prior to or during pregnancy, affording many opportunities for reproductive decision-making, including diagnostic testing in pregnancy, PGD, or alternative family planning methods.

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PATERNAL AGE DOES NOT IMPACT ANEUPLOIDY RATES AS DETERMINED BY COMPREHENSIVE CHROMOSOME SCREENING (CCS) IN DONOR OOCYTE CYCLES. J. Horne,a J. M. Franasiak,b C. R. Juneau,b S. J. Morin,b E. J. Forman,b N. R. Treff,b R. T. Scott,b aRutgers, Robert Wood Johnson, Basking Ridge, NJ; bReproductive Medicine Associates of New Jersey, Basking Ridge, NJ; cRMANJ, Rutgers-RWJ, Basking Ridge, NJ.

OBJECTIVE: Aneuploidy is a common cause of IVF failure and miscarriage in the infertility population. There is a strong and clear correlation between embryonic aneuploidy rates and oocyte age. The correlation between paternal age and aneuploidy rate has been suggested but is limited by small sample size and largely utilized FISH as the aneuploidy screening tool. The objective of this study was to determine the contribution of paternal age to aneuploidy as determined by comprehensive chromosome screening (CCS) in a donor oocyte model.

DESIGN: Retrospective cohort.

MATERIALS AND METHODS: Patients from a single institution who underwent fresh donor oocyte cycles with CCS from 2011 to March of 2016 were included. Patients who used donor sperm were excluded. Oocyte donors underwent routine ovarian stimulation and oocyte retrieval. After extended culture, trophectoderm biopsy was performed and CCS analysis was carried out using validated 24 chromosome platforms. A simple linear regression was performed correlating embryonic aneuploidy rate with paternal age utilized for insemination and ANOVA used to compare groups. A p-value <0.05 was considered significant.

RESULTS: There were 201 cases which met criteria for inclusion. Mean donor age was 26.1 (range 21-31). Mean paternal age was 42.6 (23-62). Mean cohort aneuploidy rate was 18.6% (range 0-75%). The median number of embryos evaluated was 8 (range 1-34). No correlation was found between the rate of aneuploidy in the donor population and paternal age (p=0.49). When analyzing data based upon SART age groups there was no difference between groups (p=0.81). The results are summarized in Table 1. When further breakdown of paternal age was <40 (n=67), 40-44 (n=64), 45-50 (n=52), and >50 (n=18) there was still no difference seen (p=0.90).

CONCLUSIONS: Paternal age does not have a significant effect on the rate of aneuploidy when oocyte factors are held constant in a donor oocyte model. It is important to note that this screening platform does not detect duplications and deletions to genetic counseling for advanced paternal age may still be warranted. However, additional counseling regarding whole chromosome aneuploidy screening based solely on paternal age is not necessary.

<table>
<thead>
<tr>
<th>Paternal Age Range</th>
<th>Number of Cases</th>
<th>Aneuploidy Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;35</td>
<td>23</td>
<td>19.4</td>
</tr>
<tr>
<td>35-37</td>
<td>23</td>
<td>21.7</td>
</tr>
<tr>
<td>38-40</td>
<td>35</td>
<td>17.8</td>
</tr>
<tr>
<td>&gt;42</td>
<td>92</td>
<td>17.5</td>
</tr>
</tbody>
</table>

Comparison of paternal age by SART age group and aneuploidy rate (p=0.81).
CLINICAL UTILITY OF EXPANDED CARRIER SCREENING: REPRODUCTIVE BEHAVIORS OF AT-RISK COUPLES.  
K. K. Wong, a K. Ready, a C. Lieber, a J. D. Goldberg, b I. S. Haque, a G. A. Lazarin, a C. Ghiossi, a  
Counsil, South San Francisco, CA; bCounsil, Inc., South San Francisco, CA; aCalifornia State University, Long Beach, CA.

OBJECTIVE: Survey at-risk carrier couples to learn about their reproductive decisions.

DESIGN: Expanded carrier screening panels analyze dozens or hundreds of recessive disease genes for couples planning to have children, but literature on the clinical utility of screening conditions beyond professional guidelines is scarce. We surveyed at-risk carrier couples for this purpose.

MATERIALS AND METHODS: Patients used an expanded carrier screening via Counsil laboratory for up to 110 genes. At-risk carrier couples were those in which both partners were carriers for the same autosomal recessive diseases. We invited 537 consecutive at-risk carrier couples who received their results between 4/2014 - 8/2015 to participate via email, SMS text message, and paper survey in an IRB-approved study.

RESULTS: Of 537 eligible participants, 76 completed the study; 12 that reported a family history were excluded from analysis. 45 (70%) were not pregnant at time of screening.

Of the 45 participants that were not pregnant, 62% indicated they would choose IVF with PGD, prenatal diagnosis, gamete donation, adoption, or no reproduction. 29% indicated that they were not planning to alter reproductive plans, indicating perceived severity as a major reason. The remainder did not indicate clear plans.

Of the 19 participants that were pregnant, 42% (8) elected prenatal diagnosis. Beyond that, 2 reported interest in testing, but miscarried before the procedure could be done. 9 did not consider the condition sufficiently severe to consider pregnancy termination. Of 8 pregnancies that underwent prenatal diagnosis, 5 were unaffected and 3 were affected. 2 of the affected pregnancies was terminated and 1 was continued.

The Fisher’s Exact test revealed the association between the severity of the disease and clinical utility was significant (p=0.000145), whereas the association between pregnancy status and clinical utility was not (p=0.088).

CONCLUSIONS: Most at-risk couples altered reproductive planning, demonstrating clinical utility of this information. Perceived severity of the condition factored into decision making with milder diseases less likely to change planning.

P-709  Wednesday, October 19, 2016

DO PATIENTS PURSUING PREIMPLANTATION GENETIC DIAGNOSIS (PGD) FOR MONOGENIC DISORDERS HAVE AN INCREASED RISK OFANEUPLOIDY COMPARED TO AGE-MATCHED CONTROLS?  
NYU Fertility Center, New York, NY.

OBJECTIVE: Patients with diminished ovarian reserve (DOR) have higher rates of embryonic aneuploidy following pre-implantation genetic screening (PGS). 1 We investigated whether patients predisposed to DOR, including Fragile X pre-mutation carriers, may have an increased risk of aneuploidy following PGD/PGS compared to age-matched controls undergoing PGD:

DESIGN: Nested Case-Control Study.

MATERIALS AND METHODS: All patients undergoing their first cycle of IVF, trophectoderm biopsy, and PGD with concurrent 24-chromosome aneuploidy screening (PGS) from 2011-2014 were identified. Patients were excluded if they underwent cleavage-stage biopsy, PGD for human leukocyte antigen typing, PGD for translocation, or family balancing. All patients pursuing PGS-alone during the same period were identified; age-matched controls meeting the above criteria were selected using a random number generator in a 2:1 ratio (Excel). Baseline demographics and controlled ovarian hyperstimulation (COH) cycle parameters were collected. A sub-analysis was performed on patients at risk for DOR (Fragile X pre-mutations carriers). Statistical analyses were performed using student’s T-test and Fischer’s exact test (p<0.05).

RESULTS: 108 patients underwent PGD/PGS, and 72 patients (n=503) biopsied blastocysts met criteria for analysis. 1061 PGS cycles were performed during this period, and 144 age-matched controls (n=952 biopsied blastocysts) were identified. Results are summarized in Table 1. By design there was no difference in age between groups. There were no differences in ovarian reserve testing (day 2 follicle stimulating hormone [FSH]) or COH cycle parameters. Patients with SGD undergoing concurrent aneuploidy screening had significantly lower euploidy rates compared to controls (47.7% vs. 54.8%, p=0.01). In Fragile X pre-mutation carriers undergoing PGD (n=8) with aneuploidy screening, the percentage of euploid embryos was lower compared to those with SGD not associated with DOR (45% vs. 48%), but this was not statistically significant.

CONCLUSIONS: Patients with SGD have a decreased percentage of euploid embryos compared to age-matched controls. Future studies are needed to investigate the relationship between single gene disorders and aneuploidy, particularly in patients with conditions predisposing to DOR. This data will help providers counsel patients with single gene disorders regarding their risk of aneuploidy.

References:  
blastocysts), was calculated at 50%, comparable to IVF cycles using young fertile oocyte donors. A total of 16 FETs have been performed to date with 7 live deliveries (44%) and one patient accounting for 5 negative FET outcomes indicating a potential uterine abnormality.

CONCLUSIONS: Individuals with BRCA1 and BRCA2 mutations are known to have a compromised DNA damage signaling pathway. Nevertheless embryo development and blastocyst quality appeared not to be impacted by these germline mutations even though it is well known that BRCA proteins are expressed during the preimplantation stage. Ongoing follow-up of upcoming FETs in this population group is required in order to determine any post-implantation impact.

P-711 Wednesday, October 19, 2016

CHROMOSOMAL MICROARRAY ANALYSIS OF MISCARRIAGE PRODUCTS IN RECURRENT PREGNANCY LOSS. D. Bar-Avin Dayan, S. Rienstein, H. Yonath, E. Guetta, E. Pras, H. Carp, D. Seidman. 1Department of Obstetrics and Gynecology, Sheba Medical Center, Ramat Gan, Israel; 2Institute of Genetics, Sheba Medical Center, Ramat Gan, Israel.

OBJECTIVE: Our objective was to determine the incidence of chromosomal aberrations detected by a newly introduced chromosomal microarray (CMA) technology based test, in aborted fetal and placental tissue from women with unexplained recurrent pregnancy loss (RPL).

DESIGN: Retrospective analysis.

MATERIALS AND METHODS: We reviewed the results of all consecutive cases of CMA and 30 cases of conventional karyotype, performed on DNA from aborted fetal and placental tissue, for women with RPL, or for those who underwent termination of pregnancy (TOP) for medical indications, at a tertiary university affiliated referral center, since June 2014. Additional data was collected from patient electronic charts at the gynecologic department. The data was analyzed separately for three groups: CMA results for miscarriage tissue of women with idiopathic RPL (RPL-CMA); CMA results for miscarriage tissue of women with idiopathic RPL (RPL-CMA); and karyotype test (KT) for miscarriage tissue of women with idiopathic RPL (RPL-KT). The incidence of genetic findings, and the type of chromosomal aberrations found was compared between the groups. No power analysis was calculated as the study is based on a convenience sample. A difference was considered to be significant at p<0.05.

RESULTS: The outcome of genetic testing of miscarriage tissue from women with RPL was studied by CMA test in 52 cases and conventional KT in 30 additional women. Results were obtained for 43 further CMA samples from patients who underwent TOP for medical indications. There was no significant difference between the groups with regard to maternal age and BMI. The mean gestational age was significantly higher in the TOP group. Chromosomal aberrations were detected by CMA analysis in 28.8% of the RPL cases and 38.5% of the TOP cases (p=0.5). Chromosomal aberrations were detected by KT in 10.0% of the RPL-KT group (p=0.05), failure to obtain a genetic result was significantly (p=0.0002) more common in the RPL-KT group (36.7%) than in the RPL-CMA group (3.8%). In the RPL-CMA group, there was a higher rate of chromosomal aberrations in the primary aborter women than in the secondary aborters, and there was a higher rate of chromosomal aberrations in the ≥40 years old group than in the younger group (not statistically significant). The most prevalent chromosomal aberrations were trisomy (80%) in the RPL-CMA group, and other genomic duplications or deletions (66.7%) in the TOP-CMA group (statistically significant).

CONCLUSIONS: Chromosomal analysis using conventional karyotyping of gestational products from women with RPL is known to be prone to technical failure. We showed that CMA has a significantly higher success rate in detecting chromosomal aberrations. We conclude that CMA is a valuable new tool for identification of chromosomal aberrations in miscarriage products. The higher yield of detection achieved with CMA may greatly benefit women undergoing consultation for RPL.

P-712 Wednesday, October 19, 2016

MATERNAL WHOLE EXOME SEQUENCING REVEALS CANDIDATE PATHWAYS FOR EMBRYONIC ANEUPLOIDY RISK. D. Marin, C. Bohrer, Y. Zhang, Y. Zhan, R. T. Scott, J. Xing, N. Treff, RMANJ, Rutgers-RWJ, Basking Ridge, NJ; 2Foundation for Embryonic Competence, Basking Ridge, NJ; 3Department of Genetics, Rutgers, the State University of New Jersey, Piscataway, NJ.

OBJECTIVE: Advanced maternal age is strongly associated with increased embryonic aneuploidy, yet age alone poorly predictive of an individual patient’s risk. This study investigates the maternal exome in order to identify and develop genetic markers that may predict risk of producing aneuploid embryos.

DESIGN: Extreme phenotype whole exome sequencing.

MATERIALS AND METHODS: DNA samples were obtained from patients who underwent IVF and comprehensive chromosome screening (CCS). 236 patients were identified as young with higher than average embryonic aneuploidy rates (Group A) and 229 as older with lower than average aneuploidy rates (Group B). Whole exome sequencing was performed using the Ion AmpliSeq Exome kit on an Ion Proton. TVC software (Ion Torrent) was used to identify variants which were then annotated with ANNOVAR. Since it is unlikely that a single variant accounts for genetic aneuploidy risk, GeneGO MetaCore software was used for pathway specific enrichment analysis. The ExAC database was used to compare pathway variant frequencies in the general population (16,685 individuals).

RESULTS: 6134 stop gain and loss, and non-synonymous gene variants were obtained from patients who underwent IVF and comprehensive chromosome screening (CCS). 236 patients were identified as young with higher than average embryonic aneuploidy rates, accounting for 1244 genes, whereas 1424 were present in the group of older patients with low aneuploidy rates accounting for 1070 genes. Pathway analysis performed revealed five significantly enriched pathways for each group (p<0.05) relevant to oocyte development or cell cycle regulation (Table 1). Frequencies of all variants involved in each pathway for either group were significantly higher than frequencies observed in the general population (p<0.05) except for one pathway in group B.

CONCLUSIONS: Our analysis shows candidate pathways fundamental for determining the embryonic ploidy status. These findings suggest that gene variants found in group A might modify the pathways resulting in higher than average embryonic aneuploidy rates in younger patients, whereas the effect of variants found in group B might be protective of embryonic euploidy. Given that recent publications have indicated an association between mutations in the BRCA1 gene and diminished ovarian reserve, it is also of interest that the BRCA1 DNA repair pathway was the most enriched in both study groups.

Supported by: MERCK SERONO Grant for Fertility Innovation.

Enriched pathways and added allele variant frequencies. *Frequencies not significantly different.

<table>
<thead>
<tr>
<th>Enriched pathways in group A</th>
<th>Allele frequencies Group A</th>
<th>Allele frequencies general population</th>
<th>Enriched pathways in group B</th>
<th>Allele frequencies Group B</th>
<th>Allele frequencies general population</th>
</tr>
</thead>
<tbody>
<tr>
<td>DNA damage Role of Brca1 and Brca2 in DNA repair</td>
<td>0.0107</td>
<td>0.0333</td>
<td>DNA damage Role of Brca1 and Brca2 in DNA repair</td>
<td>0.0677</td>
<td>0.0184</td>
</tr>
</tbody>
</table>
(-80%)
| Ovarian cancer (main signaling cascades) | 0.0593 | 0.150 | Cell cycle Regulation of G1/S transition (part 1)* | 0.0284 | 0.0092 |
| DNA damage ATM/ATR regulation of G1/S checkpoint | 0.0551 | 0.0123 | DNA damage ATM/ATR regulation of G1/S checkpoint | 0.0240 | 0.0058 |
| Cell cycle Role of Nek in cell cycle regulation | 0.0127 | 0.0010 | Ovarian cancer (main signaling cascades) | 0.0415 | 0.0098 |
| DNA damage ATM / ATR regulation of G2 / M checkpoint | 0.0508 | 0.0128 | DNA damage ATM / ATR regulation of G2 / M checkpoint | 0.0197 | 0.0041 |
ACUPUNCTURE AND CLINOMPHÈNE FOR INFERTILITY IN THE POLYCYSTIC OVARY SYNDROME: A MULTICENTRE RONDOMIZED CONTROLLED TRIAL. X. Wu,1,6 E. Stener-Victorin,1 J. Liu,2 T. Wu,2 E. Ng,2 R. S. Legro,2,6 H. Zhang.1 1Department of Obstetrics and Gynecology, Heilongjiang University of Chinese Medicine, Harbin, China; 2Department of Physiology and Pharmacology, Karolinska Institutet, Stockholm, Sweden; 3Centre for Evidence-Based Chinese Medicine, Beijing University of Chinese Medicine, Beijing, China; 4Chinese Clinical Trial Registry, Chinese Ethics Committee of Registering Clinical Trials, Chengdu, China; 5Department of Obstetrics and Gynecology, The University of Hong Kong, Hong Kong, China; 6Department of Obstetrics and Gynecology, Penn State University College of Medicine, Hershey, PA; 7Department of Biostatistics, Yale School of Public Health, New Haven, CT.

OBJECTIVE: To evaluate efficacy of live birth with acupuncture alone or combined with clomiphene to induce ovulation in infertile women with polycystic ovary syndrome (PCOS).

DESIGN: A double-blinded (clomiphene) and single blind (patients to type of acupuncture), multi-center (N=21 sites), 2x2 factorial trial.

MATERIALS AND METHODS: 1000 women with PCOS were randomly assigned in a 1:1:1:1 ratio, to receive acupuncture (active or control twice a week for 30 min per treatment) and medication (clomiphene or placebo for 5 days per cycle) for up to four cycles. The primary outcome measure was live birth, and ovulation was determined by weekly serum progesterone levels.

RESULTS: The live birth rates were significantly higher in the groups treated with clomiphene and acupuncture vs. placebo and acupuncture (P<0.015) with no interaction between type of acupuncture and medication: active acupuncture plus clomiphene group (69 of 250 women [27.6%]), control acupuncture plus clomiphene group (66 of 250 [26.4%]) active acupuncture plus placebo (31 of 250 [12.4%]) and control acupuncture plus placebo group (39 of 250 [15.6%]). Ovulation rates were similarly higher in the two clomiphene arms compared to placebo arms. The rate of twin pregnancies was significantly higher in women who ovulated and were treated with control acupuncture and clomiphene than those treated with active acupuncture and placebo (6 of 223 [2.7%] vs. 0 of 161 [0.0%], P<0.05). Clomiphene was associated with more dysmenorrhea and less abnormal vaginal bleeding, and active acupuncture was associated with more bruising and diarrhea.

CONCLUSIONS: Clomiphene was twice as effective at achieving live birth than placebo with no effect of acupuncture alone or in combination. These findings do not support acupuncture as an infertility treatment in women with PCOS. [ClinicalTrials.gov number, NCT01573858].

References:


ALLOGENEIC TRANSPLANTATION OF OVARIAN TISSUE WITH SOLE USE OF NOVEL IMMUNOMODULATOR, PREIMPLANTATION FACTOR (PIF), RESTORED OVARIAN FUNCTION IN BABOONS. M. Feichtinger,1,2 E. R. Barnea,1,2 A. Nyachae1, M. Brannstrom,3 S. Kim,2,6 Department of Obstetrics and Gynecology, Medical University of Vienna, Vienna, Austria; 4Wunschbaby Institut Feichtinger, Vienna, Austria; 5BioIncept LLC, Cherry Hill, NJ; 6SIEP – Society for the Investigation of Early Pregnancy, Cherry Hill, NJ; 7Institute of Primate Research (IPR), Karen, Nairobi, Kenya; 8University of Gothenburg, Gothenburg, Sweden; 9University of Kansas, Kansas City, KS; 10American-Sino Women’s and Children’s Hospital, Shanghai, China.

OBJECTIVE: Although allo-transplantation of ovarian tissue can be a useful option for women with premature ovarian failure, immune rejection has been a big barrier for clinical application. PIF is an endogenous immunomodulator that regulates transplant acceptance. The study objectives are to a) evaluate the feasibility of ovarian allo-transplantation for restoration of ovarian function and b) assess the efficacy of syntetic PIF as sole immune acceptance regimen.

DESIGN: Experimental animal study on non-human primates (Papio anubis).

MATERIALS AND METHODS: After obtaining IACUC approval two female olive baboons with regular cycles were prepared for allogeneic orthotopic ovarian transplantation. PIF was administered (10mg, twice a day, subcutaneously) as a sole agent to prevent immune rejection starting from one day before surgery. The animals underwent bilateral oophorectomy followed by transplantation of prepared ovarian cortex from the other animal. Postoperatively, animals were monitored for clinical and biochemical signs of graft rejection and return of ovarian function (perineal swelling followed by menstruation). Blood samples were obtained weekly for surveillance of rejection and of endocrine function.

RESULTS: Post operatively, there were no clinical signs of rejection (vital signs, weight, urine output and skin change). Laboratory parameters (ALT, AST, BUN, creatinine) did not indicate organ rejection at any stage of the experiment. Histology of ovarian tissue before grafting showed multiple follicles. Serum FSH, E2 and progesterone levels showed ovarian failure after grafting. Seven months after transplantation, one animal restored ovarian function (evidenced by perineal swelling and return of menstruation).

CONCLUSIONS: Organ rejection was prevented by a novel immunomodulator PIF (without side effects) after allogeneic ovarian transplantation in baboons. In addition, our study showed the clinical feasibility of ovarian allo-transplantation. Importantly, the study showed the PIF effectiveness for restoration of ovarian function and fertility.

Supported by: This study was funded by the Medical Scientific Fund of the Mayor of Vienna (Nr: 14063), the Wunschbaby Institut Feichtinger, by an unrestricted grant from BioIncept and by private funds of M.F. and S.S.K.

FIRST LIVE BIRTH USING HUMAN OOCYTES RECONSTITUTED BY SPINDLE NUCLEAR TRANSFER FOR MITOCHONDRIAL DNA MUTATION CAUSING LEIGH SYNDROME. J. Zhang.1 H. Liu.1 S. Luo,1 A. Chavez-Badiola,1 Z. Liu,1 m. yang,1 S. Munne,1 M. Konstantinidis,1 D. Wells,1 T. Huang,1 New Hope Fertility Center, New York, NY; 2Division of Human Genetics, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH; 3New Hope Fertility Center, Guadalajara, Mexico; 4Reprogenetics, Livingston, NJ; 5Reprogenetics, Oxford, United Kingdom; 6Human Genetics, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH.

OBJECTIVE: Mutations in mitochondrial (mt) DNA are maternally inherited and can cause fatal or debilitating disorders without effective treatment.1,2 The severity of clinical symptoms is often associated with the mtDNA mutation load in heteroplasmy.3 Experimental nuclear transfer in metaphase II (MI) spindle oocytes or in pronuclear (PN) zygotes, also called mitochondrial replacement therapy, has been shown to be a novel technology in minimizing mutated mtDNA transmission from oocytes to pre-implantation embryos.3 Here we report the first live birth of a boy following spindle nuclear transfer (SNT).

DESIGN: Translational research.

Supported by: National Public Welfare Projects for Chinese Medicine of China (201107005, 200808702), the National Key Discipline of Chinese Medicine in Gynecology during the year of 2009-2016, the Heilongjiang Province Foundation for Outstanding Youths (JC200804), the Intervention for Polycystic Ovary Syndrome Based on Traditional Chinese Medicine Theory—‘TianGui Disorder’ (2011TD006), and the National Clinical Trial Base in Chinese Medicine Special Projects (JDZX2012036, 2015B009) during the year of 2009-2016 in First Affiliated Hospital, Heilongjiang University of Chinese Medicine. Heilongjiang Province “Longjiang Scholar” Program (Xiao-Ke Wu, Richard S. Legro and Elisabet Stener-Victorin) and
MATERIALS AND METHODS: The patient is a 36-year-old woman with 24.5% mtDNA displaying 8993T>G mutation in subunit 6 of ATPase gene known to cause Leigh syndrome. She had 4 pregnancy losses and 2 deceased children at age 8 months and 6 years from Leigh syndrome as confirmed by >95% mutation load. She was seeking conception of a healthy baby and elected to have SNT over PN transfer for religious reasons. Under IRB-approved protocol with proper consent, the patient’s spindle nuclei were isolated and transferred into the perivitelline space of enucleated donor oocytes. The micro-manipulated complexes were then subjected to 1.4 kV/cm DC voltage for cell membrane fusion. The reconstituted oocytes were fertilized by intracytoplasmic sperm injection (ICSI). The developed blastocysts were biopsied for preimplantation genetic screening (PGS) by array comparative genetic hybridization and whole quantitative genomic mtDNA analysis by Next Generation Sequencing.

RESULTS: Five MII oocytes with birefringent spindles were subjected to meiotic SNT. The 5 oocytes were successfully reconstituted and fertilized normally by ICSI. Four out of 5 fertilized oocytes developed into blastocysts. PGS showed that one blastocyst was euploid (46XY), while 3 embryos were aneuploid. The average transmission rate of maternal mtDNA in the biopsied euploid blastocyst was 5.10 ± 1.11% and the heteroplasmy level for 8993T>G was 7.53%. Transfer of the euploid embryo resulted in an uneventful pregnancy with delivery of a healthy boy at 37 weeks of gestation. The average level of transmitted mother’s mtDNA in several neonatal tissues including buccal epithelium, hair follicles, circumcision foreskin, urine precipitate, placenta, amnion, umbilical blood, and umbilical cord was less than 1.60 ± 0.92%. The baby is currently 3 months old and doing well.

CONCLUSIONS: Human oocytes reconstituted by SNT are capable of producing a healthy live birth. SNT may provide a novel treatment option in minimizing pathogenic mtDNA transmission from mothers to their babies.

References:

O-268 Wednesday, October 19, 2016 12:02 PM
FIRST US-BASED PHASE 3 STUDY OF ULTRAPELIC ACTETE (UPA) FOR SYMPTOMATIC UTERINE FIBROIDS (UF): RESULTS OF VENUS-I. J. Simon, W. H. Cathiero, J. Segars, R. Blakeley, A. Chan, V. Snikueni, A. Al-Hendy. Women’s Health and Research Consultants, Washington, DC; Uniformed Services University of the Health Sciences, Bethesda, MD; Johns Hopkins University School of Medicine, Baltimore, MD; Allergan plc, Jersey City, NJ; Augusta University, Augusta, GA.

OBJECTIVE: To assess the efficacy and safety of UPA vs placebo in achieving amenorrhea and improving activity score.

SUBJECTS AND METHODS: Ultrapelicate Phase 3, prospective, randomized, double-blind study (VENUS-I; NCT02147197).

MATERIALS AND METHODS: Eligible women (18-50 years) were premenopausal (FSH ≤ 20 mIU/mL with cyclic (≥ 22 days but ≤ 35 days) excessive uterine bleeding ≥ 4 of the last 6 menstrual cycles, menstrual blood loss ≥ 80 mL by the alkaline hematin method over first 8 days of menses, ≥ 1 discrete UF of any size and location observable by transvaginal ultrasound ≥ 20 mm in diameter). Patients were randomized 1:1:1 to UPA 10 mg, UPA 5 mg, or placebo once daily for 12 weeks, with a 12-week drug-free follow-up. Amenorrhea was defined as no bleeding (spotting permitted) for ≥ 35 consecutive days before end of treatment (EOT)/Day 84. Activity score was assessed by the revised activity subscale of the UF symptom health related quality of life questionnaire. Safety was assessed via adverse events (AEs) and endometrial biopsies.

RESULTS: Of 157 patients randomized (48 UPA 10 mg, 53 UPA 5 mg, 56 placebo), 69% were Black. Significantly more patients achieved amenorrhea for ≥ 35 consecutive days before EOT/Day 84 with UPA 10 mg (58.3%; p < 0.0001) and UPA 5 mg (47.2%; p < 0.0001) vs placebo (1.8%). The hazard ratio (HR) versus placebo for achieving amenorrhea at any time was significant with UPA 10 mg (49.1%, p < 0.0001) and UPA 5 mg (35.5, p < 0.0001). Least squares mean change in activity score was significantly greater with UPA 10 mg (59.0; p < 0.0001) and UPA 5 mg (52.1; p < 0.0001) vs placebo (21.2). Most common AEs (≥ 5%) for UPA and placebo were hypertension (n = 6 [5/6 reported hypertension at baseline] vs n = 0), blood creatinine phosphokinase increased (5 vs 0), hot flush (5 vs 0), acne (3 vs 1), and nausea (2 vs 1). No treatment-related serious AEs or deaths were reported. No patients discontinued UPA due to AEs. No malignancies or endometrial atypical hyperplasia were reported.

CONCLUSIONS: In this US-based study, UPA was superior to placebo in rate of and time to amenorrhea. UPA also significantly improved patients’ activity scores and was well tolerated.

Supported by: Supported by Allergan plc

FREEZE-ALL VERSUS FRESH EMBRYO TRANSFER IN IVF/ICSI, A RANDOMISED CONTROLLED TRIAL (NCT02471573). L. T. Vuong, V. Q. Dang, T. M. Ho, B. G. Huynh, D. T. Ha, T. D. Pham, L. K. Nguyen, R. J. Norman, B. W. Mol, OB/GYN, University of Medicine and Pharmacy at Ho Chi Minh, Ho Chi Minh City, Viet Nam; Research Center for Genetics and Reproductive Health, School of Medicine, Vietnam National University Ho Chi Minh City, Ho Chi Minh, Viet Nam; IVFMD, My Duc hospital, Ho Chi Minh, Viet Nam; Intensive Care Unit, national hospital of can tho, can tho, Viet Nam; Robinson Research Institute, University of Adelaide, Trammere, Australia; Obstetrics & Gynaecology, The University of Adelaide, North Adelaide, Australia.

OBJECTIVE: A growing body of evidence suggests that in women undergoing IVF/ICSI frozen embryo-transfer (ET) is superior to fresh ET. However, this hypothesis is not tested in large randomized controlled clinical trials (RCT). We performed a RCT comparing the effectiveness of frozen versus fresh ET in infertile women undergoing IVF/ICSI.

DESIGN: RCT in My Duc Hospital, Viet Nam.

MATERIALS AND METHODS: We studied infertile couples undergoing their first or second IVF/ICSI cycle. Women with PCOS were excluded. All participants were treated with a gonadotropin-releasing antagonist protocol. Couples were eligible if at day 3 at least 1 high quality embryo was present. After informed consent, couples were randomised to a freeze-all or fresh ET strategy. In the freeze-all group, all grade 1 and 2 embryos were cryopreserved and then thawed on the day of ET in the following manipulated cycle. In the fresh ET group, a maximum of two fresh embryos were transferred in the stimulated cycle. The primary endpoint was ongoing pregnancy. Analysis was by intention-to-treat. We planned a marker analysis for endometrial thickness and serum progesterone.

RESULTS: Baseline characteristics were comparable. The primary endpoint ongoing pregnancy occurred in 36.3% versus 34.5% (RR 1.05 (0.87, 1.27)). Pregnancy rates, clinical outcomes and rates of treatment complications or adverse events were also comparable (see table). There was no significant interaction between both endometrial thickness (p = 0.101) and progesterone (p = 0.109) and the treatment effect.

CONCLUSIONS: In non-PCOS infertile couples undergoing IVF/ICSI, a freeze-all ET strategy did not improve the ongoing pregnancy rate as compared to a fresh ET strategy.

Supported by: Research Center for Genetics and Reproductive Health, School of Medicine, Vietnam National University, Ho Chi Minh City, Vietnam

<table>
<thead>
<tr>
<th>Patients (%)</th>
<th>Freeze-all (n=391)</th>
<th>Fresh ET (n=391)</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary outcome</td>
<td>Ongoing pregnancy rate</td>
<td>142 (36.3)</td>
<td>135 (34.5)</td>
</tr>
<tr>
<td>Multiple pregnancy rate</td>
<td>42 (10.7)</td>
<td>43 (11.0)</td>
<td>0.97 (0.65, 1.46)</td>
</tr>
<tr>
<td>Treatment complications</td>
<td>Moderate/severe OHSS</td>
<td>3 (0.8)</td>
<td>4 (1.0)</td>
</tr>
<tr>
<td>Ectopic pregnancy</td>
<td>6 (1.5)</td>
<td>12 (3.1)</td>
<td>0.50 (0.19, 1.32)</td>
</tr>
<tr>
<td>Delivery at &lt;24 weeks</td>
<td>1 (0.3)</td>
<td>3 (0.8)</td>
<td>0.33 (0.03, 3.19)</td>
</tr>
</tbody>
</table>
RELIABLE DETECTION OF SEGMENTAL ANEUPLOIDY IDENTIFIED BY NEXT GENERATION SEQUENCING (NGS).  C. R. Juneau, a K. Scott, b S. Neal, a S. J. Morin, a Y. Zhan, b R. S. Zimmerman, b N. Treff, a J. M. Franasiak, a R. T. Scott a aRMANJ, BR, NJ; bFEC, BR, NJ.

OBJECTIVE: Improved resolution in NGS provides an opportunity to go beyond screening for whole chromosome aneuploidy and also detect segmental aneuploidy. De novo segmental aneuploidy, or dup/dels, represents a new class of findings in PGS. With any novel finding, the first step is to validate the analytical result. Initial reports found the frequency of dup/dels ranges from as low as 3.9% to as high as 70%. Such variability makes the possibility of inaccurate results a major concern. The next step is to characterize the nature of the biologic error identified so clinical implications might be understood. This study seeks to confirm the reliability of the analytical result and to determine the nature of the biologic error involved in embryonic dup/dels.

DESIGN: Prospective blinded observational.

MATERIALS AND METHODS: All IVF patients who utilized NGS as part of a RCT were reviewed. All blastocysts demonstrating a segmental aneuploidy ≥ 5 MB and a concurrent whole chromosome aneuploidy in a separate chromosome were included as these embryos were not suitable for transfer. Each embryo was biopsied at 4 additional sites - 3 from the trophectoderm (TE) and 1 from the inner cell mass. Results were classified into 1 of 4 categories: 1) subsequent biopsies all contained the same error as the original confirming the result and indicating an error in meiosis, 2) subsequent biopsies demonstrated reciprocal errors indicating a mitotic error, 3) segmental aneuploidy confirmed in ≥ 1 rebiopsy, or 4) the subsequent biopsies did not demonstrate the original dup/del.

RESULTS: 32 embryos from the original RCT met criteria for inclusion. A true dup/del error was confirmed in 28 (88%) of those embryos. 9 of the segmental abnormalities were meiotic and found in all subsequent biopsies, and 19 embryos demonstrated mitotic error. In 4 embryos, the dup/del found in the original biopsy could not be confirmed in subsequent biopsies. The source of this discrepancy cannot be resolved with these data, but likely represents a mix of analytical error and low level mosaics where subsequent biopsies did not contain cells impacted by the dup/del.

CONCLUSIONS: A true biologic error was confirmed in 88% of blastocysts which had dup/dels on the embryos’ initial TE biopsy. Given the high prevalence of mitotic errors and limited sampling, this represents a very high level of diagnostic accuracy. Patients should be counseled that detection of segmental aneuploidy in a TE biopsy evaluated by NGS likely represents true biologic error when making decisions about the suitability of embryos for transfer.

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Supported by: Foundation for Embryonic Competence
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<td>Al-Hendy, A.</td>
<td>NIH, Grant recipient; Bayer, Paid consultant; Allergan, Paid consultant; Repros, Grant recipient Abb-vie, Grant recipient</td>
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<tr>
<td>Alper, M. M.</td>
<td>EMD Serono, Honoraria; Good Start Genetics, Advisory Board; Ferring, Honoraria; Reprosource, Advisor-Board; Finox, Grant recipient</td>
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<tr>
<td>Anderson, R. E.</td>
<td>Ovation Fertility, Direct stockholder</td>
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<tr>
<td>Apter, D.</td>
<td>Bayer, Grant recipient; Merck, Grant recipient; Exelitis, Grant recipient; Bayer, Merck and Exelitis, Speakers bureau; GSK, Grant recipient</td>
<td></td>
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<tr>
<td>Archer, D. F.</td>
<td>AbbVie, Paid consultant; AbbVie, Grant recipient; TherapeuticsMD, Paid consultant; TherapeuticsMD, Grant recipient; Bayer Healthcare, Paid consultant; Bayer Healthcare, Grant recipient; Agile Pharmaceuticals, Paid consultant; Exelitis/CHEMO France, Paid consultant; Endoecutis, Paid consultant; Endoecutis, Grant recipient; TEVA/HR Pharma, Paid consultant</td>
<td>Barnea, E. R. BiolIncept, LLC, Company officer Barharn, K. Bayer, Paid consultant; SPD, Paid consultant Barrett, C. B. Reprosource Fertility Diagnostics, Paid consultant Barriere, P. Genevriër France, Honoraria; Merck Serono France, Paid consultant; MSD France, Paid consultant; HRA Pharma, Paid consultant; Ferring France, Honoraria Progyny, Inc., Company officer Allergan, Grant recipient Auxogyn, Direct stockholder; Ivigen, Direct stockholder</td>
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<tr>
<td>Armenti, E. M.</td>
<td>Pfizer, Direct stockholder; GE, Direct stockholder</td>
<td>Bartasi, G. Allergan, Grant recipient Bedaiwy, M. A. Bayer, Paid consultant; SPD, Paid consultant Behr, B. Reprosource Fertility Diagnostics, Paid consultant</td>
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<tr>
<td>Arrach, N.</td>
<td>Progenesis, Company officer</td>
<td>Bendikson, K. Theralogix, Paid consultant&lt;br&gt;Bedaiwy, M. A. Bayer, Paid consultant; SPD, Paid consultant Behr, B. Reprosource Fertility Diagnostics, Paid consultant</td>
</tr>
<tr>
<td>Arunajadai, S.</td>
<td>Celmatix Inc, Full-time company employee</td>
<td>Bergh, C. M. MedSoftware, Company officer Bergh, P. A. MedSoftware, Direct stockholder Berkeley, A. S. Merck, Direct stockholder; Pfizer, Direct stockholder; Glaxo, Direct stockholder; Becton, Dickenson, Full-time company employee; Bristol Myers, Direct stockholder Berliss, M. Recombine, Paid consultant</td>
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<td>Azziz, R.</td>
<td>GlobalPET, Direct stockholder; Kindex Pharmaceuticals, Paid consultant; JDS Therapeutics, Honoraria</td>
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<td>Babigumira, J. B.</td>
<td>Androvia Life Sciences, Paid consultant; Genentech Inc, Paid consultant</td>
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<tr>
<td>Name</td>
<td>Company/Position</td>
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<td>Berro, R.</td>
<td>Celmatix Inc, Full-time company employee</td>
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<td>Berwald, T.</td>
<td>Illumina, Direct stockholder</td>
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<td>Bjugstad, K. B.</td>
<td>Aytu BioScience, Full-time company employee</td>
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<td>Blakesley, R. E.</td>
<td>Allergan, Full-time company employee</td>
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<td>Blazek, J.</td>
<td>Genesis Genetics, Full-time company employee</td>
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<td>Bocca, S.</td>
<td>Merck-Organon, Speakers bureau Grant</td>
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<tr>
<td>Boekelheide, K.</td>
<td>Boehringer Ingelheim, Grant recipient; Boehringer Ingelheim, Paid consultant; Zafgen, Paid consultant; Semma Therapeutics, Direct stockholder; Serviers, Paid consultant</td>
<td></td>
</tr>
<tr>
<td>Bonafede, M.</td>
<td>Truven Health Analytics, An IBM Company, Full-time employee of Truven Health Analytics, An IBM Company which received a research contract to conduct this study with and on behalf of AbbVie, Inc.</td>
<td></td>
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<tr>
<td>Bradford, A.</td>
<td>UpToDate, Royalties</td>
<td></td>
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<tr>
<td>Bradford, C.</td>
<td>Bayer Pharma AG, Principal investigator; scientific advisor; Boston Scientific, Scientific advisory member; Smith Nephew, Speakers bureau; Smith Nephew, Scientific advisory panel; Gynesonic, Data safety and monitoring committee member</td>
<td></td>
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<tr>
<td>Brannigan, R. E.</td>
<td>Abbvie, Inc., A grant in support of Northwestern University’s Andrology fellowship was provided to Northwestern University, Feinberg School of Medicine. I am the Director of the Andrology Fellowship; The American Urological Association/ The Journal of Urology, I am an Assistant Editor for The Journal of Urology</td>
<td></td>
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<tr>
<td>Breton, B.</td>
<td>Good Start Genetics, Full-time company employee</td>
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<td>Bristow, S. L.</td>
<td>Recombine, Full-time company employee; Recombine, Stock options</td>
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<tr>
<td>Broekmans, F. J.</td>
<td>Member of the external advisory board for Ferring BV; The Netherlands, Paid consultant; Member of the external advisory board for Merck Serono, The Netherlands, Paid consultant; Consultancy work for Gedeon Richter, Belgium, Paid consultant; Educational activities for Ferring BV, The Netherlands, Honoraria; Strategic cooperation with Roche on automated AMH assay development, Honoraria; Research cooperation with Ansh Labs, USA, Honoraria</td>
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<td>Burkart Sadusky, A.</td>
<td>Omeros Corporation, Direct stockholder</td>
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<td>Bush, M.</td>
<td>Natera, Direct stockholder; Natera, Paid consultant</td>
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<td>Cabey, R. E.</td>
<td>Reprogenetics, Full-time company employee</td>
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<td>Cameron, E.</td>
<td>Genesis Genetics, a Cooper Surgical company employee; Cooper Surgical, Direct stockholder</td>
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<td>Cardona, C.</td>
<td>Androvia LifeSciences LLC, Full-time company employee; Androvia LifeSciences LLC, Direct stockholder</td>
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<td>Carlsson, I. B.</td>
<td>Recombine, Full-time company employee; Recombine, Stock options</td>
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<td>Carrell, D. T.</td>
<td>Episona, Inc, Direct stockholder; Nanone, Inc, Direct stockholder</td>
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<td>Casper, R.</td>
<td>OvaScience, Inspection-LifeBank, Circadian-Zirclight, TRIO Fertility, Direct stockholder; AbbVie, Allergan, Bayer, EMD-Serono, Ferring, Merck, OvaScience, Pfizer., Paid consultant; TRIO Fertility, Circadian-Zirclight, Inspection-Lifebank, Company officer; Up-to-date, Teva, Royalties; Fertility and Sterility, Editorial editor</td>
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<td>Castelli-Haley, J.</td>
<td>AbbVie, Full-time company employee; AbbVie, Direct stockholder</td>
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<tr>
<td>Cataldo, N. A.</td>
<td>CenseoHealth, Independent</td>
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<tr>
<td>Catherino, W. H.</td>
<td>Abbvie, Paid consultant; Actavis, Paid consultant; Medical College of Wisconsin, Honoraria; Recombine, Full-time company employee; Bayer, Grant recipient</td>
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<tr>
<td>Cedars, M.</td>
<td>Ferring Pharmaceutical, Research support - investigator - initiated</td>
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<td>Celia, G. F.</td>
<td>Good Start Genetics, Paid consultant</td>
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<td>Chan, A.</td>
<td>Allergan, Full-time company employee</td>
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<td>Chang, C.-C.</td>
<td>MyEggBank, Direct stockholder; Reproductive Biology Associates, Full-time company employee</td>
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<td>Chason, R.</td>
<td>Theralogix, Direct stockholder</td>
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<tr>
<td>Chen, S. H.</td>
<td>OvaScience, Paid consultant; Hologic, Speakers bureau; Optum, Paid consultant; Recombine, Paid consultant</td>
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<td>Chin, W.</td>
<td>EMD Serono, Full-time company employee</td>
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<td>Cho, S.-H.</td>
<td>SK Chemicals Co., Ltd., Contracted researcher of SKI2670 Clinical Trial</td>
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<tr>
<td>Choe, S.</td>
<td>SK Chemicals Co., Ltd., Contracted researcher of SKI2670 Clinical Trial</td>
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<tr>
<td>Cholkeri-Singh, A.</td>
<td>DySIS Medical, Speakers bureau; Hologic, Inc, Speakers Bureau, Advisory Board Member; Smith &amp; Nephew, Paid consultant; Bayer, Speakers Bureau, Advisory Board Member</td>
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<tr>
<td>Chwalisz, K.</td>
<td>AbbVie Inc., Full-time company employee; AbbVie Inc., Direct stockholder</td>
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</table>
Clementi, C. Celmatix Inc, Full-time company employee
Coddington, C. PG, Merck, AbbVie, Stock; AbbVie Endometriosis Advisory Board, Advisory Board
Cohen, J. Reprogenetics LLC, Paid consultant; Althea Science INC, Company officer; Life Global Inc., Grant recipient
Cohen, L. Philips Ultrasound, Speakers bureau
Commander, S. B. CombiMatrix, Full-time company employee
Conrad, D. PierianDx, Grant recipient
Considine, R. Eli Lilly Research Labs, Paid consultant; Merck Research Labs, Paid consultant
Copperman, A. B. EMD Serono, Speakers bureau; Merck, Speakers bureau; Ferring, Speakers bureau
D’Agostino, R. Sanofi, Paid consultant; GSK, Paid consultant; Edwards Lifesciences, Paid consultant; Sandoz, Paid consultant; Cardiovyl, Paid consultant
DeGeyter, C. Ferring, Grant recipient
Demko, Z. Natera, Inc., Direct stockholder
D’Hooghe, T. M. Merck Serono, Ferring, Roche, Grant recipient; Astellas, Actavis, Bayer, Proteomika, Cartagienia, Paid consultant; Zentech, Technical support; Merck Serono, I have joined Merck Serono as Vice-President Global Medical Affairs Fertility since October 1st 2015, but continue my academic work as Professor of Reproductive Medicine and Biology at KU Leuven (University of Leuven), involved in both teaching and research.
Diamond, M. P. NICHD, AbbVie, EMD Serono, Baxter, Grant recipient; Teijin Pharmaceuticals, Auxogyn, Paid consultant; Advanced Reproductive Care, Board of Directors and Stockholder
Dokras, A. JDS Pharmaceuticals, Paid consultant
Domar, A. D. TriDea, Company officer; FertiCalm, Company officer; Merck, Speakers bureau; Ferring, Paid consultant; Merck, Paid consultant; UptoDate, Paid consultant
Doody, K. Merck Pharmaceutical, Paid consultant; Ferring Pharmaceutical, Paid consultant; Finox Pharmaceutical, Paid consultant; Serono Pharmaceutical, Speakers bureau; Good Start Genetics, Paid consultant
Feinberg, R. F.  Ferring, Medical Practice Participating in Clinical Trial; Finox, Medical Practice Participating in Clinical Trial

Fields, R. A.  Fairfax EggBank, Full-time company employee

Foidart, J.-M.  MITHRA Pharmaceuticals, Actavis (Women’s Healthcare Division), Paid consultant; IMCYSE (Biotech specialized in immune diseases), Charterman SAB

Forman, E. J.  Ferring Pharmaceuticals, Speakers bureau

Foster, S.  Recombine, Full-time company employee; Recombine, Stock options

Fraser, I. S.  Bayer Pharmaceuticals, Speakers bureau; Merck/MSD, Speakers bureau; Vifor Pharma, Speakers bureau

Fujiwara, T.  Ferring Pharmaceutical, Grant recipient; Merck Serono Co., Ltd., Grant recipient; Mochida Pharmaceutical, Grant recipient

Gallagher, C.  abbvie, Paid consultant

Garrison, L. P.  Androvia Life Sciences, Paid consultant

Gemzell-Danielsson, K.  Bayer AG, MSD/Merck, HRA Pharma, ExelGyn, Gedeon Richter, Actavis, Honoraria; Bayer, Grant recipient

Ghim, J.-L.  SK Chemical Co., Ltd., Contracted research for SK12670 clinical trial

Ghioossi, C.  Counsyl Inc., Paid consultant; Counsyl Inc., Stipend for 4-week student internship

Ginsburg, E. S.  Serono, Grant recipient

Giudice, L.  ASRM, Company officer; Merck, Pfizer, Direct stockholder; Abbvie Pharmaceutical, Paid consultant; NextGen Jane, Scientific Advisory Board member; Juniper Pharmaceuticals, Advisory Board Members

Gleicher, N.  Fertility Nutraceuticals, LLC, Direct stockholder; Generation Medical Associates, PLLC, Direct stockholder; Fertility Nutraceuticals, LLC, Receive patent licensing fees; Generation Medical Associates, PLLC, Patent licensed; U.S. Patents, NG holds patents that claim therapeutic benefits from androgen supplementation in women with LFOR and hypoandrogenism; U.S. Patents, NG is a co-inventor on a number of FMR1 gene-related U.S. patents and still pending patent applications, which claim diagnostic benefits; U.S. Patents, NG is a co-inventor on three pending AMH-related patent applications.

Gold, M.  Recombine, Full-time company employee; Recombine, I have stock options.

Goldberg, J. D.  Counsyl, Inc, Full-time company employee

Goldberg-Strassler, D.  Reprogenetics, Full-time company employee

Goldfarb, J. M.  Lumara Health – no longer affiliated with teh company since 11/14, Direct stockholder; AdhereTech, Investor; Biomednics, Investor

Gore, A.  Therologix, advisory board

Graninger, D. A.  Abbvie, Speakers bureau; Shionogi, Inc., Speakers bureau

Granger, S. W.  Salimetrics, Chief Scientific Officer

Grill, E.  McGill, Honoraria; Ethicon, Paid consultant; ASRM, Content Review Committee

Grainger, D. A.  Abbvio, Speakers bureau; Shionogi, Inc., Speakers bureau

Groen, N. S.  Sangamo Biosciences, Direct stockholder

Gutmann, J.  somalogic, Paid consultant

Hall, S. J.  Semma Therapeutics, Inc., Direct stockholder

Hallam, S. E.  Good Start Genetics, Full-time company employee

Hamamah, S.  Ferring, Grant recipient

Hammond, K.  CensoHealth, Independent contractor

Han, S.  SK Chemicals Co., Ltd., Contracted researcher of SK12670 Clinical Trial

Hannam, T.  EMD Serono, Our company sells pharmaceutical products to patients; Organon, Our company sells pharmaceutical products to patients; Ferring, Our company sells pharmaceutical products to patients

Hansen, K. R.  Roche Diagnostics, Grant recipient; Ferring International Pharmascience Center US, Grant recipient

Haque, I. S.  Counsyl, Full-time company employee; Counsyl, Direct stockholder

Harada, T.  Bayer, Honoraria; Nobel Pharma Co., Paid consultant; Mochica Pharmaceutical Co., Honoraria; Takeda Pharmaceutical Co., Honoraria

Harris, E.  athenaHealth, Full-time company employee

Harton, G.  Progyny, Full-time company employee; Illuima, Paid consultant

Hayward, B.  "Temp-drop LTD". This is a start-up company which manufactures a self monitoring device which continuously measures body temperature in sleep., Medical adviser. The position is unpaid.

Hasson, J.  EMD Serono, Inc., Full-time company employee

Healey, M.  Reprogenetics Germany GmbH, Company officer; Reprogenetics GermanyGmbH, Direct stockholder

Held, K. R.  Monash IVF, Direct stockholder
Hill, G. United Healthcare Women’s Health Scientific Advisory Board, Paid consultant

Hirshfeld-Cytron, J. E. Duchesnay, Speakers bureau abbvie, Paid consultant; Lipocine, Paid consultant; Coloplast, Paid consultant; Endo, Paid consultant

Hotaling, J. StreamDx, Andro360, NanOnc, Direct stockholder

Hovanes, K. CombiMatrix, Full-time company employee

Hu, J. Intuitive Surgical, Speakers bureau; Genome Dx, Speakers bureau

Hubbard, J. EMD Serono Research & Development Institute, Full-time company employee

Humaidan, P. Merck, MSD and IBSA, Honoraria; Merck, MSD and Ferring, Grant recipient

Hunter Cohn, K. Celmatix Inc, Full-time company employee

Hurley, E. G. Theravance Biopharma (TBPH), Innoviva, Inc. (INVA), Direct stockholder

Hu-Seliger, T. Celmatix Inc., Full-time company employee

Iturriaga, A. Enlighten Health Genomics/Labcorp, Paid consultant

Jain, R. I. Former employee of AbbVie Inc., Former employee of AbbVie Inc.

Jang, J. Maria Fertility Hospital, Full-time company employee

Jasulaitis, S. Merck Pharmaceuticals, Speakers bureau

Jenkins, T. Nanonc, Direct stockholder

Jensen, J. Abbvie, Bayer Healthcare, HRA Pharma, Merck, ContraMed, MicroChips, Evofem, Paid consultant; Abbvie, Bayer, ContraMed, FHI 360, Medicines 360, Grant recipient

Jeong, H. SK chemicals, Company officer

Joergensen, N. Ferring Pharmaceutical, Ferring sponsored an investigation at my department. The investigation was unrelated to the submitted work, and within another field of andrological research

Johnson, J. Ovascience, Inc., Paid consultant

Johnson, S. SPD Development Company Ltd, Full-time company employee

Johnson, S. J. AbbVie, Paid consultant; Sanofi, Paid consultant; Alexion, Paid consultant; Astellas, Paid consultant; Takeda, Paid consultant

Kadoch, I.-J. Clinique Ovo, Clinical director; Yad-Tech, Shares holder

Kadoch, J. I. clinicine ovo, Company officer

Kalmbach, K. Celmatix Inc, Full-time company employee

Kalra, B. Ansh Labs, Full-time company employee

Kijacic, D. Natera, Full-time company employee; Natera, Direct stockholder

Kim, H. J. Maria Fertility Hospital, Full-time company employee

Kim, J. SK Chemicals Co., Ltd., Contracted researcher of SKI2670 Clinical Trial

Kim, S. M. SK Chemicals, Full-time company employee

Kitchen, J. Genesis Genetics, Full-time company employee

Klavanian, J. Genesis Genetics, a Cooper Surgical Company, Full-time company employee

Klein, N. My Egg Bank, partner in SRM, a minority owner of My Egg Bank

Knebel, S. Reprogenetics Germany, Full-time company employee

Konstantinidis, M. Reprogenetics, CooperSurgical, Full-time company employee

Kovalevsky, G. Ferring, Clinical research trial investigator; Finox, Clinical research trial investigator

Krisher, R. L. Merck Serono, Grant recipient

Kumar, A. Ava AG, Full-time company employee

Kumar, N. AnshLabs, Full-time company employee

Kushnir, V. A. US Patents, Listed as a co-inventor on a pending AMH-related patent application.

Lalioti, M. Biogen, Full-time company employee

Lamb, D. J. Cellmatix, Scientific Advisory Board- Unpaid

Lambert-Messerlian, G. Fujirebio, Grant recipient; Ansh Labs, Grant recipient; Natera Inc, Grant recipient

Laskin, C. A. Progyny, Full-time company employee

Laurel, L. GlaxoSmithKline Pharma, Advisory panel for biological Benlysta.

Laurent, L. Illumina, Inc., Full-time company employee

Laven, J. S. Ferring B.V. The Netherlands, Grant recipient; Merck Diagnostics, Switzerland, Paid consultant; Markcky Pharma GMBH, Germany, Honoraria; Metagenics INC/RFB / Women’s health, USA, Honoraria

Lawlor, D. Roche Diagnostics, Grant recipient; Medtronic, Grant recipient; Ferring, Grant recipient

Lazarin, G. A. Counsyl, Full-time company employee

Leader, B. ReproSource, Full-time company employee

Lee, W. D. Maria Fertility Hospital, Full-time company employee

Leeners, B. Ava, Member of advisory board of Ava, Research grant together with other research groups and Ava

Legro, R. S. Millendo, Paid consultant; Bayer, Paid consultant; JDS Therapeutics, Paid consultant; Euroscreen, Paid consultant; Kindex, Paid consultant
Neitzel, D. Good Start Genetics, Full-time company employee


Nelson, J. Nexgenomics, LLC, owner

Nelson, J. K. Truven Health Analytics, An IBM Company, Full-time employee of Truven Health Analytics, An IBM Company which received a research contract to conduct this study with and on behalf of AbbVie, Inc.

Nelson, S. M. Beckman Coulter, Ferring, Merck Serono, MSD, Roche, Speakers bureau; Roche Diagnostics, Grant recipient; Besins, Ferring, MSD, Merck Serono, Roche, Paid consultant

Nervi, L. Actavis, Full-time company employee

Niederberger, C. American Urological Association, Update series editor; Ferring, Grant recipient; Nexhand, Company officer

Nieman, L. HRA Pharma, Grant recipient; UpToDate, royalties

Novotny, M. Philips Healthcare, Full-time company employee

Omurtag, K. regular rate rhythm Software, Paid consultant

Oromendia, A. Celmatix, Inc., Full-time company employee

Ostermeier, G. C. Androvia LifeSciences, Full-time company employee; Androvia LifeSciences, Direct stockholder

Paduch, D. Abbvie, Speakers bureau; Bayer, Paid consultant; Abbvie, Paid consultant

Palermo, G. D. Irvine Scientific, Royalties

Palomaki, G. Ansh Laboratories, Consulting contract between employer (Women & Infants Hospital) and Ansh Laboratories

Palter, S. F. Lodestone Technology, Inc, Company officer

Paolino, N. C. Recombine, Full-time company employee

Paplomata, E. Novartis, funding of industry sponsored and investigator initiated clinical trials- funding given to the institution and not directly to the individual; Hoosier Research Network, funding of industry sponsored clinical trials- funding given to the institution and not directly to the individual; Genentech, funding of industry sponsored clinical trials- funding given to the institution and not directly to the individual; Corcept pharmaceutical, funding of industry sponsored clinical trials-

Parfitt, D.-E. Celmatix Inc., Full-time company employee

Parry, J. P. N/A, My wife and I recently have trademarked, have a provisional patent, and developed a website for the Parrisype surgical technique for which we are presenting data. Though we haven’t submitted for the full patent, our understanding of patent law is that a surgical technique patent can’t be used to prevent another doctor from performing a procedure (or charge licensing fees). (We’re doing this to avoid potential headaches from patent trolls.) We have no affiliations with or funding from any manufacturers; ASRM-SRS, I am chair of the website committee for the Society of Reproductive Surgeons and coordinate literature reviews for SRS.

Parsons, P. SPD Development Company Ltd., Full-time company employee

Patrizio, P. Counsel, scientific advisor; FertileSafe, co-founder and scientific advisor

Penrose, L. Reproductive Solutions Inc., Company officer

Penzias, A. S. OvaScience, Advisory board Member; ReproSource, Advisor

Petersdorf, K. Bayer Pharma AG, Full-time company employee; Bayer Pharma AG, Direct stockholder

Peterson, C. M. Clinical Innovations, Royalties

Petrozza, J. C. Interface Medical / Hologic, Scientific Advisory Committee; Smith and Nephew, Advisory Committee

Price, T. M. MedaCorp, Paid consultant; Gerson Lehrman Group, Paid consultant; Guidepoint, Paid consultant; Best Doctors, Paid consultant

Prien, S. Reproductive Solutions Inc, Company officer

Puig, O. Roche, Full-time company employee

Puscheck, E. E. Bayer Pharmaceuticals, Grant recipient; AbbVie Pharmaceutical Research and Development, Grant recipient; Ferring. International, Pharmacscience Center U.S., Inc, Grant recipient; Gynesonics, Grant recipient

Racowsky, C. Life Global Group, Paid consultant; UpToDate, Honoraria; World Health Organization, Paid consultant

Ramasamy, R. Lipocine, Paid consultant; Beckman, Paid consultant; Direx System, Grant recipient

Rasmussen, R. R. Health Management Resources, We own a clinic that uses their program and products.

Rassaby, L. Recombine, Full-time company employee; Recombine, Stock options
Read, K. Counsyl, Full-time company employee

Reape, K. Z. Allergan, Paid consultant; Spark Therapeutics, Inc., Full-time company employee

Reay, M. SPD Development Company Ltd, Full-time company employee

Reed, B. G. Bayer HealthCare, Full-time company employee

Ren, X. Z. Allergan, Paid consultant; Spark Therapeutics, Inc., Full-time company employee

Riche, D. M. Merck, Novo Nordisk, Speakers bureau; Novo Nordisk, Advisory Board; Arbor Pharmaceuticals, Advisory Board

Richter, K. S. EMD Serono, Paid consultant

Robinson, K. Good Start Genetics, Inc., Full-time company employee

Robinson, R. D. AbbVie, Grant recipient

Rodriguez, S. Recombine, Full-time company employee; Recombine, Direct stockholder

Rosberger, Z. Merck, Honoraria

Rosen, K. A. Bayer Pharmaceuticals Inc., Full-time company employee

Ross, R. Advagenix, Company officer

Rowan, J. P. AbbVie, Full-time company employee

Ruthazer, R. Pfizer, Paid consultant

Sakkas, D. Ferring, Grant recipient; Origio, Scientific Advisory Board; Allergan, Trial Advisory Board; INVO Biosciences, Direct stockholder

Sammel, M. D. Swiss Precision Diagnostics, Paid consultant

Sanchez, T. LuminOva, Inc., Direct stockholder

Santistevan, A. Celmatix Inc, Full-time company employee

Santoro, N. Bayer Inc, Grant recipient; Menogenix Inc, Stock Options

Saucier, J. B. Natera, Inc, Full-time company employee; Natera, Inc, Direct stockholder; Natera, Inc, option to hold stock at Natera

Schattman, G. L. Femasys, medical advisor, clinical investigator; Theralogix, Paid consultant; Ferring, Speakers bureau

Schenken, R. S. Evestra, Consultant

Schertz, J. EMD Serono Research and Development Institute, Billerica, MA, Full-time company employee

Schlegel, P. N. GNYUTES, Provider of SWL services, Company officer; Theralogix, Inc, Producer of Nutraceuticals, Paid consultant

Schmelter, T. Bayer Pharma AG, Full-time company employee; Bayer AG, Direct stockholder

Schmidt, J. Natera, Inc, Paid consultant

Schwefel, B. AbbVie, Inc, Full-time company employee; AbbVie, Inc, Direct stockholder

Scott, R. T. Foundation for Assessment & Enhancement of Embryonic Competence, Inc., Neither myself or my program get any personal benefit, Company officer; Ferring
Dr. James A. Simon has served (within the last year) or is currently serving as a consultant to or on the advisory boards of those companies listed: AbbVie, Inc. (North Chicago, IL), Actavis, PLC. (Dublin, Ireland), Agile Therapeutics (Princeton, NJ), Bayer Healthcare LLC., (Tarrytown, NY), New England Research Institute, Inc. (Watertown, MA), Novo Nordisk (Bagsvrerd, Denmark), Palatin Technologies (Cranbury, NJ), Symbio Research, Inc. (Port Jefferson, NY), TherapeuticsMD (Boca Raton, FL),. Grant recipient; Amgen Inc. (Thousand Oaks, CA), Eisai, Inc. (Woodcliff Lake, NJ), Merck (Whitehouse Station, NJ), Noven Pharmaceuticals, Inc. (New York, NY), Novo Nordisk (Bagsvrerd, Denmark), Shionogi Inc. (Florham Park, NJ), Speakers bureau; Sermonix Pharmaceuticals (Columbus, OH),. Direct stockholder Simpson, A. Androvia LifeSciences, Full-time company employee
Slayden, O. D. Bayer Pharma AG, Berlin, Grant recipient
Snabes, M. C. AbbVie, Full-time company employee
Sniukiene, V. Allergan, Full-time company employee
Soliman, A. M. AbbVie Inc., Full-time company employee; AbbVie Inc., Direct stockholder
Somers, F. Allergan plc, Full-time company employee
Spaczynski, R. Z. Polpharma Biuro Handlowe sp. z o.o., Warsaw, Poland, Speakers bureau; Ferring Pharmaceuticals Poland Sp. z o.o., Warsaw, Poland, Speakers bureau; Zentiva, A Sanofi Company, Warsaw, Poland, Speakers bureau
Sprague, M. L. Covidien, Speakers bureau
Stanczyk, F. Z. Merck & Co., Paid consultant; TherapeuticsMD, Paid consultant; Noven Pharmaceuticals, Paid consultant; Enteris Biopharma, Paid consultant; AbbVie, and, Agile Therapeutics, Paid consultant
Stein, P. Ava AG, Full-time company employee
Steinkampf, M. P. AbbVie Pharmaceuticals, Speakers bureau
Stewart, E. A. AbbVie, Allergan, Astellas, Bayer, GlaxoSmithKline, Gynesonics, Welltwise, Viteava, Paid consultant; UpToDate, Honoraria
Stimach, C. Genesis Genetics, Full-time company employee
<table>
<thead>
<tr>
<th>Name</th>
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<tr>
<td>Wells, D.</td>
<td>Reprogenetics UK, Direct stockholder; Illumina, Paid consultant; Recombine, Direct stockholder; Reprogenetics, Employee</td>
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<td>Westemeyer, M.</td>
<td>Natera, Inc., Full-time company employee; Natera, Inc., Direct stockholder</td>
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<td>Widra, E. A.</td>
<td>Counsyl, Paid consultant; Resolve, Board Member; Embryo Options, Direct stockholder; Capex MD, Board member</td>
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<td>Wilcox, J. G.</td>
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<td>Wong, K. K.</td>
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<td>Wu, H.</td>
<td>Celmatix Inc., 14 Wall Street 16D, New York, NY 10005, Full-time company employee</td>
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<td>Xia, M.</td>
<td>The people of Jiangsu Province Hospital, Direct stockholder</td>
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<td>Yang, L.</td>
<td>Bluebird Bio Inc., Direct stockholder; AbbVie Inc., Direct stockholder; Gilead Sciences, Direct</td>
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<td>Foundation for Embryonic Competence, Full-time company employee</td>
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<td>Zini, A.</td>
<td>YAD-Tech Neutraceuticals, Direct stockholder</td>
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