Male sex preselection through sperm isolation*

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After the publication of data by Ericsson and co-workers¹ describing the recovery of fractions rich in Y sperm (up to 85%) after layering of washed sperm over columns of bovine serum albumin, clinical trials were started using the three-step, three-layer technique. We present the results to date and discuss the apparently negative effects of combining this technique with the use of clomiphene citrate.

MATERIALS AND METHODS

In 1976, couples were gradually attracted for the clinical study so that we could evaluate the results of insemination with albumin-separated sperm, including fertile women of childbearing age who had previously delivered only female infants (26 patients had 59 previous children, 57 females and 2 males [one deceased, one adopted out]). The patients were informed of the uncertainties: (1) whether the 85% Y sperm would translate into the same proportion of male infants and (2) whether insemination (as proposed) high in the cervix of only a few million spermatozoa would result in pregnancy in a reasonable length of time. Additionally, the paucity of human data on the integrity of the offspring was discussed. As the study progressed, more reassuring data appeared in the literature.

The separation technique used¹ starts by dilution of the ejaculate by an equal volume of Tyrode's solution. The diluted specimen is divided into 0.5 ml aliquots of washed sperm, which are then layered over a 7.5% solution of salt-poor human serum albumin (hSA) (Cutter Laboratories, Berkeley, CA) for 1 hour in an 8 x 75-mm glass column. The initial sperm layer is then removed by pipette, the albumin centrifuged at 2800 to 3200 RPM for 10 minutes, and the sperm "disk" resuspended in Tyrode's solution. The sperm disk is then layered over a two-layer hSA column, 12.5% at the top and 20% at the bottom. At 1 hour, the sperm layer is removed, and after another half hour the 12.5% layer is removed. The 20% hSA is then centrifuged for 10 minutes and the sperm disk resuspended in 0.25 ml of Tyrode's solution, which is then inseminated high in the cervix.

Results are given for the author's personal patients and total results are given, reported from all centers* using albumin separation.

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RESULTS

It was first observed during 1980 that patients given Clomid (Merrell-National Laboratories, Cincinnati, OH) for irregular or infrequent ovulation delivered a high proportion of females. Six Clomid patients delivered one male and six females (including one set of dizygotic female twins). Results are given separately for Clomid-induced and non-Clomid-induced pregnancies.

As of October 1981, 66 patients have been inseminated in our office. Twenty-two patients have discontinued therapy after an average of three inseminations. Of the remaining 44 patients, 30 have conceived (68%). Twenty-four conceived in three cycles or less (80%). There were three abortions (10%). Five patients are still pregnant. Of the 20 patients who delivered, 13 had males and 7 had females (there were two sets of female twins, one after Clomid treatment). Of the 15 non-Clomid-treated women who delivered, 12 had males and 3 had females. This is statistically significant only when compared with deliveries after Clomid treatment (Table 1).

Total results from all centers using three-step, three-layer separation are as follows: Fifty-three patients delivered 39 males and 16 females (two sets of female twins), a male birth ratio of 73.5%. Excluding Clomid deliveries, 46 patients delivered 38 males and 9 females (one set of female twins), a male birth ratio of 82.6%. This is statistically significant (Table 2).

Two-step, two-layer separation, which yields approximately 70% Y sperm, has produced a male birth ratio of 73.5%. Excluding Clomid deliveries, 46 patients delivered 38 males and 9 females (one set of female twins), a male birth ratio of 82.6%. This is statistically significant (Table 2).

DISCUSSION

These are the first statistically significant results reported from insemination with albumin-separated sperm in the human. Much larger numbers will be available in a few years because of increasing exposure of the results to date. The following data have encouraged the authors to view albumin separation as likely to have a favorable effect on the population of spermatozoa for insemination.

In 1972 teratogenic studies by Ericsson et al. had shown no observed increase in congenital abnormalities in rabbits pregnant by insemination with albumin-separated sperm, when compared with controls, pregnant by the same male. In 1976 Glaub et al. reported better motility in separated human sperm following short-term freezing. In 1980 Wall et al. confirmed improved motility of spermatozoa in rabbits and bulls after albumin separation and increased fertility, as measured by the numbers of cleaved ova.

In 1979 a field trial by Ericsson et al. with cattle inseminated with separated sperm showed increased numbers of bull calves and fewer abortions, as compared with controls, pregnant by the same bulls.

Support for an effect by Clomid on the sex ratio was given by James in late 1980. His review of the literature on Clomid and Pergonal (Serono Laboratories, Inc., Braintree, MA) yielded 590 deliveries where the sex of the infant was mentioned, 266 males and 324 females (a 43.5%:56.5% ratio). A recent review of 335 Clomid births from our office showed 156 males and 179 females (a 46.6%:53.4% ratio).

The question of a "preselected" population has been brought up regarding the group of patients under discussion. Our experience, and that of the other centers participating in this study, shows that couples coming for male sex preselection have had only girls. It is not known that this would change the "risk" in either direction for their next offspring. Reference is made to a paper by Bernstein, which discusses the possible effects on the incidence of siblings of the same sex, based on research from family records traced from Who's Who in America, Mormon records, and several other sources.

DISCUSSION

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ADDENDUM

Since this paper was originally submitted, an additional four patients have delivered three males and one female. This makes a total for our office of 24 deliveries, 16 males and 10 females (with two sets of female twins), a 67% male birth ratio. Non-Clomid deliveries number 20, 15 males and 6 females (with one set of female twins), a 75% male birth ratio.

As of April 1982, all centers report 91 deliveries, 68 males and 25 females (two sets of female twins), a 75% male birth ratio. Non-Clomid deliveries number 84, 66 males and 19 females, a 79% male birth ratio.

SUMMARY

Results are presented of deliveries after albumin separation for male sex preselection. Currently, 91 deliveries have been reported, with 68 males and 25 females (two sets of dizygotic female twins), a 75% male birth ratio. Excluding Clomid deliveries, 84 patients delivered 66 males and 19 females, a 79% male birth ratio.

Three-step, three-layer separation, to markedly enhance the chance for a male child, appears to be a practical and effective method for male sex preselection. For the time being, the use of Clomid in patients desiring male sex preselection appears to be contraindicated.

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REFERENCES