Should all oocyte donors receive prophylactic antibiotics for retrieval?

In a retrospective study comparing 526 oocyte donors who received prophylactic antibiotics for oocyte retrieval with a comparable group of 625 who did not, the incidence of infection after retrieval was reduced from 0.4% to 0 in the group receiving antibiotics. Donors take risks but have no medical indication for the procedures that they undergo; our data suggest that prophylactic antibiotics at retrieval should be considered to minimize the risk of infection. (Fertil Steril® 2010;94:2935–7. ©2010 by American Society for Reproductive Medicine.)

**Key Words:** Oocyte, egg, donation, donor, antibiotics, prophylaxis, complications, prevention, IVF, ART, retrieval, trans-vaginal

Since its introduction in the early 1980s, oocyte donation has become an increasingly common part of infertility services. In the United States, in 2006, healthy donors participated in 10,984 assisted reproductive technology (ART) cycles (1). This participation has almost tripled since 1996 (2) and shows no sign of decreasing. As participation increases, small percentages of risk translate into larger numbers of complications.

We have previously reported on the serious complications experienced among egg donors, which include ovarian hyperstimulation syndrome, ovarian torsion, bleeding, ovarian cyst rupture, and infection (3). When we recruit young, healthy women to be donors, we owe them both informed consent about the risks they might encounter and our best efforts to minimize those risks. We specifically address the risk of infection and the possibility that prophylactic antibiotics could reduce that risk for oocyte donors.

Pelvic infection is a rare yet potentially serious complication of transvaginal oocyte retrieval (TVOR) in patients participating in ART. The incidence of pelvic infection after this procedure ranges from 0 (4) to 1.3% (5), and the severity of infection ranges from a minor infection with pyrexia, leukocytosis, and abdominal pain, to a major medical event such as pelvic abscess formation or sepsis (6).

Several mechanisms for the etiology of pelvic infection after TVOR have been proposed. The first is direct inoculation of vaginal flora into the ovary or peritoneal cavity at the time of needle puncture through a nonsterile vaginal wall. Infection could also occur by reactivation of chronically infected ovaries in patients with a history of pelvic inflammatory disease (PID) or by inadvertent bowel puncture during TVOR. Because the bacterial agents cultured from abscesses resulting from TVOR are often common vaginal flora, bacterial contamination from the transvaginal route is considered the most common etiology (7). This theory is supported by past observations of postoperative ovarian abscesses developing in premenopausal women after vaginal hysterectomy in the years before antibiotic prophylaxis was routinely employed (8). Finally, a study of oocyte retrieval via a transabdominal route reported no infectious complications (9).

Although complication and infection rates of TVOR have been well documented for infertile women undergoing in vitro fertilization (IVF), few data are available for the unique population of women participating in oocyte donation. Unlike some of their IVF counterparts, donors are, by definition, young and healthy and are generally excluded from participation in oocyte donation if they have a history of endometriosis, PID, ruptured appendicitis, or other potential source of increased risk for infection after retrieval. We would therefore expect oocyte donors to have a low incidence of pelvic infections, which has been shown (3, 10, 11).

Our goal, however, is to reduce the risk of donor complications as far as possible. We previously reported two cases of pelvic infection in oocyte donors. After these occurrences, we administered intravenous antibiotics perioperatively for all oocyte donors. It is our intention to compare the incidence of pelvic infection before and after implementation of prophylactic antibiotics, and to ask whether it may be appropriate to add antibiotic prophylaxis to all protocols for donor egg retrieval.

This study consists of a retrospective historical analysis of all completed oocyte donation cycles at the New York Presbyterian Hospital-Weill Cornell Medical School between April 1, 1991, and June 30, 2009. Institutional review board approval was obtained. All donors were evaluated according to the American College of Obstetricians and Gynecologists guidelines for donor egg retrieval.
Society for Reproductive Medicine guidelines and in accordance with U.S. Food and Drug Administration (FDA) mandates. Screening and stimulation protocols were consistent with those described in our previous study (3).

In all donors, the vulva and vagina had a povidone-iodine or (in cases of allergy) PHisoHex solution applied at the time of TVOR. The vagina was then thoroughly rinsed and irrigated with normal saline until clear. Before August 1, 2003, donors did not receive prophylactic antibiotics. After August 1, 2003, all donors received either 2 g of cefoxitin or, if penicillin allergic, 900 mg of clindamycin IV intraoperatively at the time of TVOR.

Between April 1, 1991, and June 30, 2009, 1,151 stimulation cycles with oocyte retrieval were completed at our center. There were 526 cycles completed before implementation of prophylactic antibiotics in August 2003 (group 1), and 625 completed after this date (group 2). Groups 1 and 2 were similar in age, number of oocytes retrieved, and peak estrogen levels (see Table 1). Screening for both groups was similar and specifically excluded prospective donors with a history of endometriosis, PID, or major pelvic infections. Fisher’s exact test was used to compare the infection rate between group 1 and group 2. A 95% confidence interval (CI) for the difference in the infection proportions between group 1 and group 2 was calculated to assess the precision of the obtained estimate.

Two donors were hospitalized for pelvic infections in group 1, resulting in an infection rate of 0.4% for this group. Both donors presented with fevers above 39°C and lower abdominal pain and were without ultrasound evidence of tubo-ovarian abscesses. Both were hospitalized and treated aggressively with broad spectrum IV antibiotics, and both defervesced within 24 hours of initiation of treatment, remained afebrile throughout treatment, and had no sequelae of the treated infection. Blood cultures failed to identify an organism in either donor.

There were no infections reported in group 2 patients (out of 625 cycles). Therefore, the rate of pelvic infections dropped from 0.4% in group 1 to 0 in group 2 with the institution of prophylactic antibiotics (difference = 0.4%; 95% CI for difference = –0.3%, 1.1%; P = .21).

Though TVOR is considered a relatively safe procedure, it is not without the risk of complications. Women undergoing TVOR for treatment of infertility accept this risk in the hope that they will achieve a pregnancy. On the other hand, women participating in oocyte donation subject themselves to an invasive procedure without a medical indication. It has been argued that donors should, therefore, be considered ethically more similar to research subjects than to patients (12, 13). Specifically, the principle of beneficence should be applied; we are particularly responsible to do no harm and minimize risks in such populations. Thus, even though the infection rate in our patients before August 2003 was only 0.4%, it should be our goal to either minimize or eliminate infection as a potential complication of oocyte donation.

Many steps are taken in our program to minimize the risk of complication among oocyte donors. We screen and eliminate potential donors with conditions associated with increased risk of infection. At retrieval, the vulva and vagina are cleansed with povidone-iodine or PHisoHex solution. In addition, every effort is made to puncture the vaginal wall as few times as possible (preferably once for each ovary) during the oocyte collection. Finally, we now administer prophylactic intravenous antibiotics to all participants intraoperatively. This has led to a series of 625 cycles without a single infection.

Considering the rarity of infection as a complication among oocyte donors in general, it could be argued that the observed difference in infection rates is coincidental. Although the difference in the infection rate between the two groups in our study was not statistically significant (P = .21), the 95% CI for the difference (–0.3%, 1.1%) was consistent with a reduction in infection risk for patients receiving prophylactic antibiotics (i.e., most of the CI favors larger differences with the use of prophylactic antibiotics).

The sample size required for statistical significance cannot be determined accurately because the incidence in the treatment group was zero. Assuming a near-zero value of 0.001 in the treatment group for calculation, a Fisher’s exact test with a .05 two-sided significance level will have 80% power to detect the difference between a group 1 proportion of 0.004 (0.4%) and a group 2 proportion of 0.001 (0.1%) when the sample size in each group is 4,700 oocyte donors. Thus, it is possible, but unlikely, that a properly powered prospective randomized study will be undertaken in the future.

This scenario parallels a prior controversy about the effectiveness of antibiotic prophylaxis (AP) to prevent endocarditis after dental procedures. In that clinical scenario, as in this one, the incidence of infection is extremely low, and no prospective clinical trial has been powered to prove the effectiveness of AP. However, observation that endocarditis occurred without prophylaxis—and that AP was effective in preventing it—led to the current recommendation that AP be given to patients with vascular prostheses who are undergoing dental procedures, despite the absence of evidence-based clinical trials (14–16).

There is currently no standard of care in terms of AP before TVOR. Although many physicians advocate the use of antibiotics for women with a history of endometriosis or PID, patients without these factors are often untreated. In this unique subpopulation of healthy young women who are oocyte donors, we believe the benefit of minimizing the incidence of pelvic infection outweighs the risk of allergy, discomfort, or bacterial resistance resulting from antibiotic use. In oocyte donors undergoing TVOR—among whom pelvic infection rates ideally should be zero—our data suggest that antibiotics reduced the infection rate. We raise the possibility that prophylactic antibiotics should be included in all oocyte donor retrieval protocols.

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<td><strong>Demographics of groups 1 and 2.</strong></td>
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