

Fecundability trends among sperm donors as a measure of donor performance

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Objective: To examine fecundability trends among sperm donors.

Design: Retrospective analysis.

Setting: University-based sperm bank and donor insemination program.

Patient(s): Sperm donors and recipients.

Intervention(s): A group of recipients underwent IUI with cryopreserved donor sperm. Fecundability was calculated for 20 sperm donors over 800 insemination cycles.

Main Outcome Measure(s): Average fecundability per donor was compared for the first 40 cycles of a donor's use and for those donors within a group of more fertile recipients. Sperm parameters, recipient ages, and number of unique recipients for each donor were analyzed.

Result(s): Average donor fecundability is constant; however, individual donors demonstrated differences among their fecundabilities (overall mean, 0.09; range, 0.01–0.26). These differences persisted for donors among a group of more fertile recipients (overall mean, 0.12; range, 0.02–0.35). A donor's fecundability at 15 cycles is predictive of his future performance.

Conclusion(s): Differences in fecundability exist among sperm donors which cannot be discerned through routine semen parameters. Sperm donor fecundability should be analyzed periodically, and directors of sperm banks should consider discontinuing use of a donor whose outcome is substandard. (*Fertil Steril*® 1999;71:891–5. ©1999 by American Society for Reproductive Medicine.)

Key Words: Sperm bank, fecundability, fecundity, andrology, donor insemination, intrauterine insemination

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Insemination with donor sperm is used frequently as a reproductive option. National data from a survey of sperm banks over a decade ago estimated that 30,000 pregnancies annually resulted from donor IUI (1). The reported pregnancy rates (PRs) per cycle with cryopreserved donor sperm range from 9%–13% (2–4), averaging approximately half the PRs of natural cycles. Cryopreservation decreases sperm viability and motility by as much as 50% (5, 6), subsequently lowering the success rate of donor insemination programs (7).

The costs of donor screening and selection are significant. At the Oregon Health Sciences University sperm donor program, only 20% of men initially evaluated are accepted as donors (8). This is similar to a 70%–87% drop out or failed screening seen in other studies (9, 10). Approximately a \$5,000 investment is accrued from screening and cryostorage for each donor

before a sample is released into the general population. Because of the expense and effort involved in recruiting donors and maintaining a sperm bank, it is difficult to discard donors without just cause.

However, to improve outcomes, it is desirable to remove poorly performing donors. Currently, there are no national guidelines or minimum performance standards for sperm donors. There are also no reliable tests to predict a donor's fecundity before use in a recipient population. Multiple studies have attempted to use sperm parameters for prognostic purposes; however, these parameters alone have been unable to consistently predict an individual donor's fecundability (11–13). Some studies suggest that sperm morphology is an important variable (4, 14), whereas other studies have found this parameter to have no prognostic value (15).

Evaluation is made more difficult by the confounding effect of the recipient's fecundity. Prior studies have demonstrated a decreasing PR per cycle for recipients who have failed to achieve a pregnancy after multiple inseminations and for women ≥ 35 years (2, 16, 17). Maximizing the number of female recipients exposed to an ejaculate has been identified as the only way to minimize this confounding factor (18). McGowan et al. (4) suggested dropping donors who had not produced a pregnancy by 12 cycles, thereby eliminating most low fertility donors, with only a small chance of discarding a good donor (4). However, because maternal age or other infertility factors may adversely impact selected donors, a trial of 12 cycles may be too strict. In this study, an attempt was made to evaluate donors from the perspective of a sperm bank with limited recipient knowledge. Given a large recipient pool, fecundability trends among sperm donors were analyzed to determine practical points at which a donor declares himself as superior, average, or poor and may be maintained or discontinued.

MATERIALS AND METHODS

The sperm donors at Oregon Health Sciences University underwent standardized screening per protocol, which included physical examination, review of medical and family history, and infectious disease screening. History of prior pregnancies was not necessary for participation in the donor program. All met minimum semen criteria by high-quality phase contrast optics on wet preparations (magnification $\times 400$) (19) defined as $>70\%$ normal morphology, sperm count $>60 \times 10^6/\text{mL}$, and post-thaw motility $>25\%$, and all had evidence of $>50\%$ recovery after freezing. Specimens were frozen in a 6%–7% buffered glycerol, 10% egg yolk-based cryoprotectant. Before May 1, 1995, specimens for use in IUIs were prepared with use of a two-centrifugation sperm wash-resuspension protocol. After that date, preparation was changed to a three-layer Percoll density gradient based on higher recovery of motile sperm (20).

Women requested donor insemination for varied reasons, such as azoospermic partners or no male partner, and indications were not quantified or further evaluated. Women receiving inseminations at Oregon Health Sciences University underwent baseline evaluations. Those with possible tubal disease suggested by a history of chlamydia infection, pelvic inflammatory disease, or prior ectopic pregnancy were screened with hysterosalpingography. They needed at least one patent tube to receive donor insemination. Women who were oligoovulatory or anovulatory received either clomiphene citrate or gonadotropins to achieve ovulation. Inseminations occurred the day of or the day after a positive LH surge as determined by commercially available urinary LH kits.

From February 1990 to July 1996, 20 sperm donors were used for 1,434 insemination cycles. The first 40 cycles for each donor were analyzed. Pregnancy was determined by a

positive urine or serum hCG. Fecundability was calculated by dividing the number of pregnancies by the number of insemination cycles. This was done for each cycle, over 40 cycles, so that for a given donor the fecundability calculation varied as pregnancies accrued. There was no restriction on the number of insemination cycles per recipient. One-way analysis of variance (ANOVA) was used to compare fecundability among donors. Multiple regression analysis was used to compare sperm parameters in relation to donor fecundability. This study was designed as a retrospective review of sperm donor results, performed for quality control purposes of the andrology laboratory, and institutional review board approval was not sought.

RESULTS

Two hundred ninety-four recipients participated in the 800 donor insemination cycles. Women received an average of 2.6 inseminations (range, 1–19), and 77% used only one donor. The average age of the recipient was 34.1. There were 77 pregnancies in 800 IUIs (fecundability, 0.096), with 74% live births, 22.1% spontaneous abortions, 2.6% unknown pregnancy outcomes, and 1.3% ectopic pregnancies. For 4.5% of the cycles, two inseminations were performed in the same cycle per patient request. The average PR for these cycles was lower (0.06) than the rate when one insemination was used (0.10), although this was not statistically significant ($P = .36$, χ^2). These were counted as one insemination cycle for the purposes of calculating the donor's fecundability.

Pregnancies were reported for all 20 donors. The occurrence of a donor's first reported pregnancy varied from the first cycle to as late as the 34th cycle. Donors were selected and used by an average of 18.7 different women (range, 12–25) in 40 cycles. There were no trends in fecundability based on the number of unique recipients (Table 1).

A minimum of 20×10^6 motile sperm was used in 91% of the inseminations. Post-thaw sperm parameters analyzed included volume, motility, morphology, and morphologically normal, motile sperm. Statistically significant differences were noted when comparing the means for each sperm parameter among donors ($P < .0001$, one-way ANOVA). However, these differences were not necessarily predictive of outcome.

For each cycle, sperm parameters were compared with the donor's calculated fecundability and the pregnancy outcome of that cycle. Volume, motility, and morphology were not significant predictors of fecundability ($P < .44$, $P < .14$, $P < .07$, respectively, multiple regression analysis) or pregnancy ($P < .21$, $P < .66$, $P < .55$, respectively, multiple regression analysis) in a given insemination cycle. However, the percentage of postthaw, morphologically normal, motile sperm directly correlated with fecundability ($P < .0001$, multiple regression analysis).

It is surprising that, from 2 to 40 cycles, mean fecund-

TABLE 1

Fecundability and number of unique recipients per donor after 15 and 40 cycles of IUI.

Donor No.	Fecundability after 15 cycles	No. of recipients after 15 cycles	Fecundability after 40 cycles	No. of recipients after 40 cycles	Fecundability with "more fertile" recipients	No. of cycles with "more fertile" recipients
1	0.00	7	0.05	14	0.08	13
2	0.00	10	0.05	16	0.04	24
3	0.00	9	0.05	20	0.00	22
4	0.00	7	0.05	19	0.00	13
5	0.00	7	0.10	24	0.14	22
6	0.07	10	0.03	17	0.04	26
7	0.07	10	0.13	21	0.12	17
8	0.07	8	0.10	19	0.11	27
9	0.07	9	0.03	16	0.05	19
10	0.07	7	0.08	17	0.17	6
11	0.07	7	0.05	18	0.13	16
12	0.13	8	0.15	18	0.11	27
13	0.13	10	0.10	19	0.25	16
14	0.13	8	0.18	22	0.21	24
15	0.13	10	0.13	25	0.08	25
16	0.13	8	0.08	22	0.17	12
17	0.13	7	0.13	15	0.17	24
18	0.27	7	0.13	12	0.16	19
19	0.27	10	0.13	19	0.18	17
20	0.27	10	0.23	20	0.31	13

Note: Donor fecundability with "more fertile" recipients is shown in comparison with fecundability with the general recipient pool (see text). Number of unique recipients after 40 cycles demonstrated no significant relation to donor fecundability (regression analysis, $P < .21$).

ability of the 20 donors was constant (simple linear regression, $P = .88$, range from .062 to .10, mean .094). However, donors demonstrated statistically significant differences among their mean fecundabilities (overall mean 0.09; range of means, 0.01–0.26, $P < .0001$, one-way ANOVA) (Fig. 1). As determined by regression analysis, a donor's performance at 15 cycles was predictive of his performance at 30 and 40 cycles (Fig. 2, $P < .0005$).

To judge an individual donor's ability to achieve pregnancy, his mean fecundability was plotted with the other donors. A normal distribution of fecundability among donors was observed ($P = .113$, Shapiro-Wilk W test for normalcy, data not shown). This curve was divided into quartiles for further analysis. An individual donor did not have a constant fecundability but showed variation. After the first 15 cycles, 80% of the donors showed relative consistency in their ability to achieve a pregnancy, remaining within two adjacent quartiles. The other 20% demonstrated more variation, moving among three or four quartiles over time. Figure 2 depicts the donors' fecundabilities after 15, 30, and 40 cycles, showing the relative consistency in performance over time. After 15 cycles, the mean fecundability for the lowest quartile of donors was zero, compared with 0.13 for the remaining quartiles. Four of the five donors in the lowest quartile after 15 cycles were still in the lowest quartile after 40 cycles. Two other donors showed a decline in their fecundability after 30 and 40 cycles.

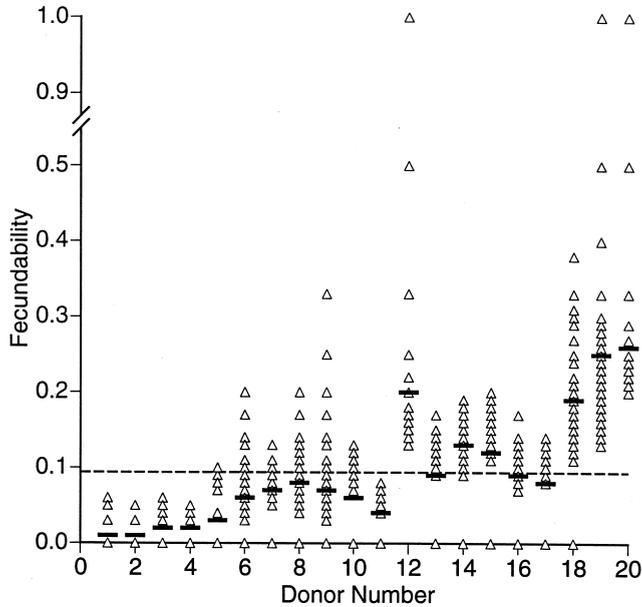
The same data analysis was performed for the cycles in which the recipient was <35 years of age and had had fewer than 7 donor insemination cycles. There were 47 pregnancies in 388 cycles with these "more fertile" recipients, for an average fecundability of 0.12. A broader range of donor fecundability was seen (Table 1) (overall mean, 0.12; range of means, 0.02–0.35, $P < .0001$, one-way ANOVA). However, donors whose fecundabilities were in the lowest quartile after 15 cycles in the general recipient pool fared no better in this subgroup of more fertile recipients. Within the subgroup, the mean fecundability for the 5 donors who had been in the lowest quartile after 15 cycles was 0.05 in 94 cycles. The mean fecundability for the 15 other donors was 0.15 in 288 cycles. Table 1 shows donors' fecundabilities in the general recipient pool and in the group of "more fertile" donors.

DISCUSSION

All parties involved in the process of artificial insemination with donor sperm are interested in achieving the highest possible PRs. When looking at a population of donors in a sperm bank, it would be desirable to use only those donors whose fecundability is at worst, average, and at best, superior. This necessitates periodic review of performances of individual donors, and removal of those donors whose pregnancy record is substandard.

FIGURE 1

Fecundability from 40 insemination cycles is represented for donors 1–20. Equivalent data points are superimposed. The mean fecundability for each donor's first 40 cycles is calculated and represented as a *bar*. Differences among mean fecundabilities is statistically significant (one-way ANOVA, $P < .0001$; range, 0.01–0.26). The mean fecundability of all donors is shown as a *broken line* (mean of means 0.094). Fecundabilities for donors 1–4 never rise above the mean.



Tracking outcomes for donors in a sperm bank is challenging. Not only are there time delays in receiving reports of pregnancies when inseminations are performed in the same location as a sperm bank, but for those banks who receive orders via mail, fax, or internet, and ship specimens across the country, follow-up is much more formidable. Sperm banks may send postcards to be returned weeks later when a positive or negative outcome has been determined, or individuals may make phone calls or send E-mail to physicians' offices months after the specimens have been shipped in an attempt to track outcomes. Overall, gathering results can be time-consuming and inconsistent. However, it is imperative that the data continue to be collected and analyzed. The onus lies on physicians' offices performing inseminations to inform sperm banks of their pregnancy outcomes. Until a better screening strategy that can predict a donor's potential success with IUI is developed, we are left with clinical end points, such as pregnancy, as our only means by which to judge donors.

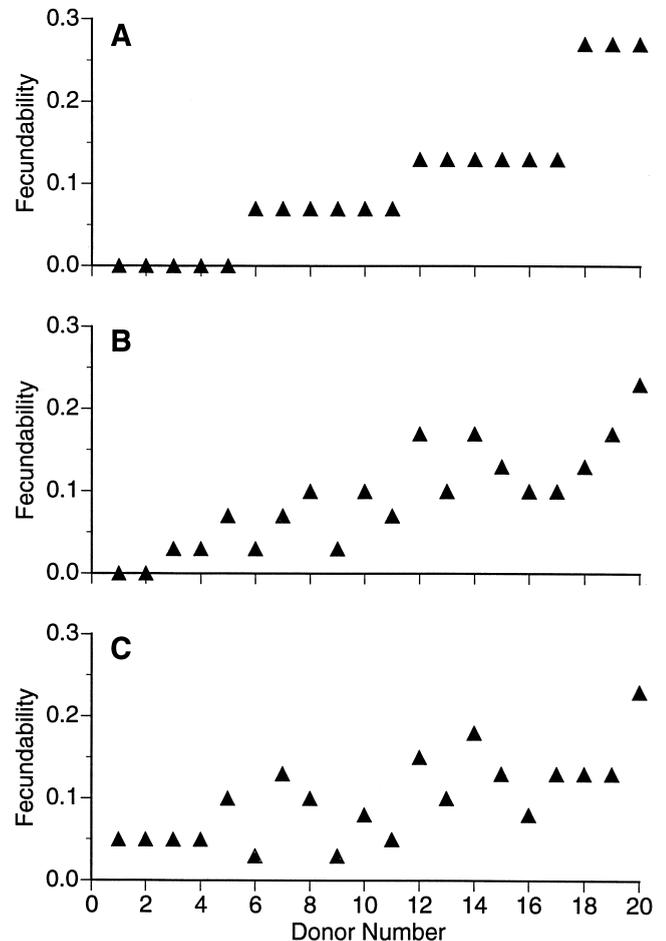
This study was designed to determine practical, clinical methods a sperm bank could use to assess its donors, given limited or no recipient knowledge. To fairly judge a donor's performance, insemination in the presence of ovulation with a patent fallopian tube are minimally necessary criteria. We

attempted to control for these factors in our basic medical screening of women before their participation in donor IUI. It is possible that confounding recipient factors, such as undiagnosed tubal disease or the use of ovarian stimulants, may have impacted outcomes in our study; however, we do not believe this to be the case. We also did not take into account prior gravidity and parity of the recipients or parenting records of the donors. We made assumptions that, based on a large sample size and prior studies (17, 21), that there would be a random distribution of recipient factors among donors.

We attempted to determine the earliest point at which a donor's fecundability was firmly established. In our group of 20 donors, those donors who failed to produce a pregnancy after 15 cycles remained relatively poor performers over the

FIGURE 2

Fecundability for donors 1–20 is shown after 15 cycles (A), 30 cycles (B), and 40 cycles (C). Four donors (donors 1–4) with the lowest fecundability after 15 cycles continued to demonstrate low fecundability after 30 and 40 cycles. Two donors (donors 6 and 9) demonstrated a drop in their fecundability after 30 and 40 cycles.



next 25 cycles. This trend persisted regardless of the age of the recipient or the number of recipients. This cannot be used as a single method of assessment, however, because donors demonstrated variability.

We propose the following suggestions managers of sperm banks could use for tracking donor performance. Calculate donor fecundability every 15 cycles and consider discarding 5%–25% of donors whose performance falls in the lowest quartile. By 15 cycles, donors' specimens likely have been used by a minimum of 4 or 5 unique recipients. In our study, a donor had been used by 7–10 unique recipients (average, 8.45) after 15 cycles. In our program, most recipients who had not become pregnant after three or four inseminations usually chose to switch donors. This may not be true in other programs, and if a donor's outcomes are unusually biased by one recipient, this method of assessment is invalid.

Additional recommendations include using specimens from new donors for women younger than 36 and with fewer than six prior inseminations. In our study, the poorly performing donors were no more likely to achieve a pregnancy in the younger women than they were in the older women. Finally, a recipient whose fecundity is lower, by either age or multiple prior failed attempts, who chooses to continue with IUI because of limited financial options, should receive an established donor who has a proven record, not an untested donor whose fertility also could potentially be low.

Should sperm banks make donors' PRs common knowledge along with height, weight, and ethnicity? Evidence of prior fecundity is not required to become a sperm donor, nor is it practical, because a large number of donors are students (9). There is a concern that recipients would choose only the highest performing donors, exhausting their supplies sooner, and leaving only poorly performing donors in the donor pool. This is not practical in areas of limited supply. However, it may be reasonable for sperm banks to publish their average PRs, broken down by specific recipient age groups, so that a nationally common standard could be achieved in the future.

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