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Of Men (and Pigs and Goats) in Mice?

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Traditionally, infertility was viewed as a "woman's problem" or as the "woman's fault." However, in recent decades, research has generally determined 40% of infertility is attributable to men, 40% is attributable to women, 10% is attributable to a combination of the man and the woman, and the remaining 10% is of an unknown origin. Because of its traditional basis in women and the complexity of women's reproductive systems, much of the scientific and social research has focused on deciphering and correcting or overcoming female reproductive malfunction. Even though an equal percentage of men and women have reproductive malfunction, research has been slow to discover breakthroughs in testis function and subsequent treatment, despite intracytoplasmic sperm injection (ICSI). But even ICSI only solves the pressing problem for the present generation. It is not known whether men who use ICSI or other assistive reproductive technologies (ART) produce offspring, specifically boys, with similar reproductive malfunctions or assistive reproductive needs. Despite calls from bioethicists, doctors, sociologists, and psychologists to determine whether we are consciously creating a generation of reproductively challenged offspring, such information may never be known. Children of people who use ART, including ICSI, are not followed prospectively to determine whether similar reproductive challenges arise in subsequent generations or for any other medical, social, or psychological reason.

In the absence of this knowledge, the still-nascent field of ART is eager to better and comprehensively unravel the working of testis function. However, to do so and be successful, an in vitro model was the elusive ideal, until now.

Honaramooz et al[1] recently reported in the August 15, 2002, issue of *Nature* complete spermatogenesis in newborn mouse, pig, and goat testis tissue after being grafted into castrated immunodeficient mouse hosts. The sperm generated from fresh, refrigerated, and cryopreserved grafts, for each species, were viable and able to fertilize mouse oocytes. The authors note 4 immediate uses for this procedure. First, they suggest testis tissue preservation as superior to sperm preservation because of the possibility for limitless male gametes. More specifically, the authors suggest this technique may benefit cancer patients who once relied on autologous germ cell transplantation by reducing or

eliminating the risk of transmitting tumor cells because fresh gametes are produced. Next, the increased propagation of endangered species and valuable livestock might also result by facilitating sperm production from immature males. And finally, having a mouse host provides the once elusive in vitro model essential for future research on testis function and germ cell development.

While helping cancer patients protect their fertility, preserving endangered species, and escalating the reproductive capacity of certain livestock are admirable endeavors, the true value of this breakthrough lies in the increased potential for a better understanding of testis function and germ cell development. Such research will hopefully lead to remedies and treatments for infertility in men, with no possibility of its arising in subsequent generations. At least then, part of the debate about tracking deformities and malfunctions in ART offspring will be silenced, guarding the children's future and their privacy.

Footnotes

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References

1 Honaramooz A, Snedaker A, Boiani M, Schöler H, Dobrinski I, Schlatt S. Sperm from neonatal mammalian testes grafted in mice. *Nature*. 2002;418:778 -781.[Medline]