Gamete Donation: Medical and Genetic Implications

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The US fertility industry is one of the least regulated among developed nations. No records exist for the number of children born from sperm donation or for the number of children born from each donor. In April, we discussed the emotional implications on the offspring. This article focuses on both potential and reported medical implications.

The mission of the Donor Sibling Registry (DSR) is to educate, connect, and support all persons associated with gamete donation. The DSR has >30,000 members and has facilitated mutual consent contact between >8500 donor-conceived persons and their half-siblings and/or their genetic parents.

Since its establishment in 2000, the DSR has counseled many donor recipients whose children have an inherited and previously undisclosed disease. Some parents find that their donor did not disclose a hereditary disorder or that their sperm bank did not disclose that offspring of the donor they used had been diagnosed with a hereditary disorder. Others have even found out that their sperm bank has amended information on the donor's medical form (*Johnson v California Cryobank*).[1]

Medical Implications

The consequences of nondisclosure can be devastating. Over the years, many cases were publicly discussed in professional and lay publications. Between 2009 and 2011 alone the following cases were reported:

- London Women's Clinic used chromosomally abnormal donor sperm to treat 11 women, including a couple who had to destroy 22 embryos created over a year of treatment
- A child conceived using gametes from anonymous sperm and ova donors was diagnosed with spinal muscular atrophy type 1
- New England Cryogenic was sued by a woman claiming that her children inherited genetic disorders. Other families who used this donor also reported issues
- A Pacific Reproductive Services donor passed along hypertrophic cardiomyopathy, a fatal heart disease, to 9 of his 22 known offspring. One child consequently died
- At least 9 children (California Cryobank/Nordic Cryobank) that have been conceived via an anonymous donor have been born with the inheritable disease neurofibromatosis type 1.

The frequency and severity of these health issues are of significant concern because donors can father in excess of 50 to 100 children. The largest known half-sibling group in the DSR is approaching 130 children.

Sperm banks have estimated that only 20% to 40% of women report their live births to them, meaning there is no accurate accounting of all children born from any one donor. When a donor illness is reported, it is impossible to notify all relevant families, because for the most part they are not known. To complicate matters, 21% to 27% of our surveyed donors reported donating to >1 fertility clinic.[2] Some sperm banks refuse to give donors their donor numbers, making it practically impossible for them to make mutual consent contact and share important medical information with biologic offspring.

Donors can father in excess of 50 or even 100 children. Therefore, a donor with an undisclosed hereditary disorder can easily pass on a disease to many children.

Many US clinics and sperm banks refuse to update donor or offspring medical information. Of those who accept updates, some refuse to share the information with families.

Our research on 164 sperm donors revealed that 84% of them have never been contacted by their clinics or sperm banks for medical updates, although 23% reported feeling that they or close family members had medical/genetic issues that would be important to share with recipient families.[2] In addition, 94% of surveyed sperm donors said that they would have accepted an offer for genetic testing had it been offered by their sperm bank.[2]

The few following quotes from parents of donor-conceived children or from donors illustrate the impact of the lack of regulation in the industry:

1. "Our daughter is 6 years old and has been diagnosed with a hereditary bone disease called MHE [multiple hereditary exostoses]. There is no history in our family"
2. "At the age of 3, my daughter developed a very rare disease, Rasmussen's encephalitis, which caused seizures and significant brain damage"
3. "My father and grandmother both died of multiple myeloma, a nasty cancer. Many members of my family suffer from depression" [former sperm donor]
4. "My husband was a medical student and was an occasional sperm donor….He died of pancreatic cancer in 2002"
5. "I would like to contact other offspring. Both my children have autism, and we have no history in my family of any disabilities."

Our own research on 155 egg donors showed that only 2.6% of them had been contacted by their fertility clinics after donation to update information that might impact the donor-conceived offspring, although 31% of them reported that they or close family members had medical/genetic issues that would be important to share with recipient families.[3]

Survey respondents reported developing breast cancer, being diagnosed with hemochromatosis, or giving birth to a child who was a carrier for cystic fibrosis. Even more surprising, >33% of the egg donors who reported a new medical problem in themselves or a close family member did not attempt to contact their fertility clinic.[3] Overwhelmingly, the reason reported was lack of education about the value of providing such information, and a lack of encouragement by the fertility clinic to do so.

Two of our most recent reports on donors and offspring experiences have just been published.[4,5]

Donor Screening in the United States

Oversight from the US Food and Drug Administration has so far been directed at the prevention of infectious diseases, including sexually transmitted diseases (STDs). Little attention has been paid to genetic disease transmission. Genetic testing varies significantly by clinic.

Donor screening for STDs includes HIV, human T-lymphotropic virus, hepatitis B and C, syphilis, gonorrhea, chlamydia, and cytomegalovirus. Some fertility clinics and sperm banks also test for cystic fibrosis, sickle-cell disease, Tay-Sachs disease, Canavan disease, Gaucher disease, Niemann-Pick disease, and beta thalassemia.

The DSR recommends that all donors be tested for a larger scope of tests, possibly including karyotyping, cystic fibrosis, Tay-Sachs disease, fragile X syndrome, hemochromatosis (for *HFE* mutation), *BRCA1* and *2* mutations, celiac disease, polyposis conditions caused by *APC* gene mutations, hereditary nonpolyposis colorectal cancer, glycogen-storage diseases, such as Fabry disease and Niemann-Pick disease, polycystic disease, Huntington disease, melanoma (*CDKN2A* mutation), myopia, and Marfan syndrome (for donors taller than 6 ft 2 in).

In addition, the DSR recommends more thorough physical examinations, face-to-face medical history intakes, and full psychologic screening. Among our surveyed donor offspring who wished to make contact with their donors, 74% listed learning more about their medical background as a reason for the desired contact.[6]

Recommendations for Fertility Clinics

- Adequately counsel prospective donors before they begin donation, including the legal, ethical, moral, and mental health implications for themselves, recipients, and offspring. They must also be educated about their legal and ethical responsibilities to be honest as a donor
- Require donors to regularly update their family medical history and have this information available to all families who have used this donor
- Track all recipients, donors, and births, and report all live births from each donor
- Limit the number of births conceived from any one donor; the DSR lists 32 sibling groups of between 15 and 129 children, and 91 groups of >10 half siblings
- Counsel parents on openness, full disclosure, and the importance of using open donors; emphasize the importance of having information about genetic, ancestral, and medical backgrounds
- Encourage all donors and recipient parents to register with the DSR to be able to share and update medical information with one another.

As we hear more frequently from families who have been formed using donor conception, we think that the industry should respond accordingly as it moves forward, and consider updating

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FDA Approves...

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cases of toxoplasmosis reinfection or relapse has not been established.

The *T gondii* parasite is largely associated with cats, but it can be found in a wide array of animal and bird species worldwide.

Combination Therapy Cuts Mother-to-Child HIV Transmission

A new study from the National Institutes of Health (NIH) has shown conclusively that adding 1 or 2 drugs to zidovudine (Retrovir) reduces mother-to-child HIV transmission (www.nih.gov/news/health/mar2011/nichd-02.htm).

"Our results showed conclusively that the 2- and 3-drug regimens are superior to the standard treatment with zidovudine," said lead investigator Karin Nielson-Saines, MD, Clinical Professor of Pediatrics, University of California, LA.

According to the NIH, approximately 20% of Americans with HIV are unaware that they carry the virus, and many of the women delivering the 100 to 200 neonates born with HIV annually are not tested early in pregnancy or are not treated during pregnancy. When HIV is not diagnosed until a woman is in labor, the infant is given prophylactic zidovudine therapy.

The investigators reviewed 1684 infants born to mothers whose HIV infection was not diagnosed until they went into labor. The infants were randomized to standard 6-week therapy with zidovudine, 6 weeks of zidovudine plus 3 doses of nevirapine (Viramune) during the first week of life, or 6 weeks of zidovudine plus 2 weeks of lamivudine (Epivir) and nelfinavir (Viracept). HIV transmission was reduced by more than 50% with the 2- and 3-drug regimens: the proportions of infants infected with HIV at 3 months were 4.9% with zidovudine alone; 2.2% with zidovudine plus nevirapine; and 2.5% with zidovudine, nevirapine, and nelfinavir.

IVF Yields Poorer Obstetric Outcomes than Spontaneous Conception

Babies born through in vitro fertilization (IVF) have inferior obstetric outcomes compared with their non-IVF counterparts, regardless of whether they are born through IVF with single embryo transfer (SET), elective SET (eSET), nonelective SET (non-eSET), or double embryo transfer (DET), a Swedish study showed (Sazonova A, et al. *Hum Reprod*. 2011;26:442-450).

The researchers compared outcomes for all IVF (N = 13,544) and non-IVF (N = 587,009) children born in Sweden between 2002 and 2006, examining the main outcomes of preterm birth (born <28 weeks, <32 weeks, or <37 weeks of gestation), low birth weight (LBW), and very low birth weight (VLBW).

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and reevaluating the methodologies that are now known to be insufficient in safeguarding the health of all involved. ■

References

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