

Pre-Implantation Genetic Diagnosis for Sex Selection

William E. Gibbons, MD

Women and men differ in that there are two X chromosomes in women and both an X and Y chromosome in men. Each of the gametes, i.e. eggs in women and sperm in men, provide a sex chromosome for the developing embryo at the time of fertilization. All of the sex chromosomes in eggs are X chromosomes. The sperm contain either an X or a Y chromosome. Therefore, the sex of the offspring is determined by male's contribution to the embryo.

The sex of the embryo can be determined prior to implantation by different methods.

They include:

1. Sperm sorting to separate X and Y bearing sperm.
2. Determination of the genetic sex of the embryo by embryo biopsy, and then,
 - a. Fluorescent in situ hybridization of the separate chromosomes
 - b. Polymerase chain reaction (PCR) of genes on the Y chromosome

Sperm Sorting:

Using a technique that was 'perfected' by the US Department of Agriculture for use in the cattle industry to separate bull sperm, one 'company' in the US has been licensed to perform this technique. Sperm are separated within a cell sorter, one by one, on the basis of the minute difference in their DNA content. The female 'X' chromosome is larger and therefore has a larger amount of DNA than Y sperm. This represents a few percent difference in the total DNA of a sperm.

The process is not perfect and is superior for the separation of female/X sperm. From the standard 50:50 ratio of female to male sperm, the separation will shift the ratio to 88:12 (or 7/8 sperm will be X bearing). For producing male offspring and sorting for male sperm the ratio shifts from 50:50 to ~67:33 or 2 of 3 sperm will be Y bearing and this is the ratio of the offspring born using this technique.

Determination of the genetic sex by DNA analysis of the embryo:

To perform an analysis of an embryo to evaluate its genetic make-up, the embryo is generally cultured for three days after egg retrieval. One of the cells of the developing embryo are biopsied and evaluated. The limitations include: 1) the testing probes may not attach to the specific DNA tested (occurs about 8% of the time). 2) the single cell biopsied and tested does not represent the rest of the embryo. This is called mosaicism. It is not uncommon. However, since the majority of human embryos are abnormal and will not implant, a mosaic embryo would rarely be viable. 3) Contamination of cells other than the biopsied cell from the embryo is tested. This would not be the case with fluorescent in situ hybridization since the cell being studied is visible, but is possible with the PCR technique. There are procedures to prevent contamination.

Fluorescent in situ hybridization (FISH)

It is possible to produce probes that will attach to a specific chromosome or set of chromosomes. By attaching a fluorescent dye to the probe under UV light, the probe will fluoresce making the chromosome visible. This allows the number of the specific chromosomes to be counted. Except for the X and Y chromosomes there should be two of each of the 22 autosomes (or non-sex) chromosomes.

PCR amplification of a DNA sequence on the Y chromosome

By constructing primers that will attach to either side of a specific sequence of a gene unique to the Y chromosome, this segment of the gene can be amplified a million times within the PCR cycle process to make this segment visible and identifiable. Thus, making the determination of whether there is or is not a Y chromosome present. This technique will say if there is a Y chromosome or not. It can not, routinely, tell how many copies of the Y chromosome are present, i.e. if there is an extra Y chromosome, XYY or XYYY such as is possible with FISH.

Pre-Implantation Genetic Diagnosis for Sex Determination: The American Society of Reproductive Medicine.

In October of 1999, in Vol 72 of the Journal Fertility and Sterility, pages 595-98, the Ethics Committee of the American Society of Reproductive Medicine which included our internationally-respected, John Robertson, published their comments concerning, "Sex selection and preimplantation genetic diagnosis." They evaluated the spectrum of associations of PGD with Advanced Assisted Reproduction which is shown in their table below.

Embryo sex identification by preimplantation genetic diagnosis for nonmedical reasons.

- (a) Patient is undergoing IVF and PGD.
Patient learns sex identification of embryo as *part of*, or as a *by-product of*, PGD done for other medical reasons.
 - (b) Patient is undergoing IVF and PGD.
Patient requests that sex identification be *added to* PGD being done for other medical reasons.
 - (c) Patient is undergoing IVF, but PGD is not necessary to treatment.
Patient *requests PGD* solely for the purpose of sex identification.
 - (d) Patient is not undergoing either IVF or PGD (for the treatment of infertility or any other medical reason).
Patient *requests IVF and PGD* solely for the purpose of sex identification.
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They spell out the arguments for sex selection and PGD, making two primary appeals. The first is the right to reproductive choice with sex selection being an extension of this right. The second is the good that is possible to be achieved through any technique or medical process. Above all this applies to the effort to prevent the transmission of lethal

genetic diseases for which PGD was designed. “There are also perceived individual and social goods such as gender balance or distribution in a family with more than one child, parental companionship with a child of one’s own gender, and preferred order among one’s children.” It is argued that it is the less of two evils, i.e. sex determination by prenatal diagnosis/amniocentesis and sex-selected abortion.

Arguments against include: the potential for inherent gender discrimination, inappropriate control over nonessential characteristics, unnecessary medical burdens/costs for parents, and inappropriate use of limited medical resources as well as psychological harm to offspring by increasing the pressure of expectation, marital conflict over the decision process, and adverse societal effects. It crosses into the lively national debate concerning the right to life and the right to choose.

The recommendations of the Ethics Committee are the following:

1. PDG used for sex selection for prevention of serious genetic disease is ethically acceptable.
2. Patients undergoing IVF already for other medical reasons as in (a) through (c) of the table above holds some risk of gender bias, harm to individuals and society, and inappropriateness in the use of medical resources and should not be encouraged.
3. The initiation of IVF with PGD solely for sex selection holds an even greater risk and should be discouraged.
4. Ethical caution regarding PGD for sex selection calls for the study of the consequences of this practice. Such study should include cross-cultural as well as intracultural patterns, assessment of competing claims for medical resources, and reasonable efforts to discern changes in the level of social responsibility and respect for future generations.