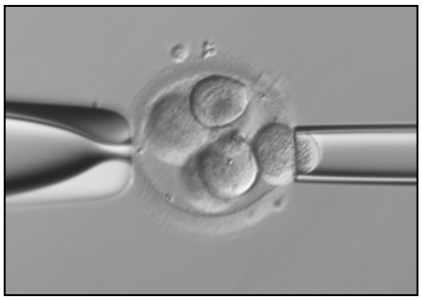
Preimplantation Genetic Diagnosis



Preimplantation genetic diagnosis, or PGD, is the genetic testing of embryos produced through in vitro fertilization (IVF). PGD enables physicians to identify embryos carrying specific genetic alterations that can cause disease, and transfer those without the specific genetic alterations into a woman's uterus to start a pregnancy. PGD allows couples at risk of having children with serious genetic disorders to increase their chances of having a child without the disorder.

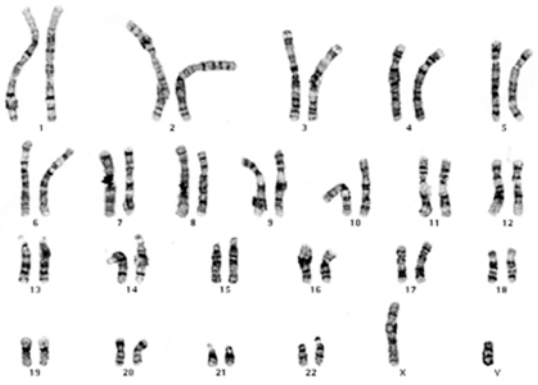
More than 1,000 babies have been born worldwide using this technique since it was introduced over a decade ago. PGD has been used to diagnose chromosome abnormalities as well as single gene disorders such as cystic fibrosis, Tay Sachs disease, Marfan syndrome, muscular dystrophy, sickle cell and Fanconi anemias, and thalassemia. More controversial is the use of PGD to test for the sex of the embryo, or for late onset disorders such as Alzheimer disease, or for genetic susceptibility to diseases like hereditary breast cancer.

Chromosome Abnormalities: Translocations and Aneuploidy

Human cells normally contain 46 chromosomes, 23 from a mother's egg and 23 from a father's sperm.

A **chromosomal translocation** occurs when a piece of one chromosome is mistakenly attached to a different chromosome. Reciprocal translocations occur when two different chromosome swap segments; sometimes two whole chromosomes will fuse to become one. Both types of translocations can affect fertility and pregnancy outcomes.

The term **aneuploidy** refers to the occurrence of one or more extra or missing chromosomes. This can lead to infertility, pregnancy loss, birth defects, genetic syndromes, and/or mental retardation.



A karyotype showing the "normal" chromosome content of a male.

As in all IVF, eggs removed from the mother are fertilized in the laboratory. Two to four days after fertilization, the embryo consists of approximately eight cells. Typically, one to two cells are removed by biopsy and subjected to genetic tests. Alternatively, genetic tests can be performed on cells (called polar body cells) that are cast off by the egg as it matures during fertilization. PGD uses two basic techniques to analyze genetic material from the embryo: (1) chromosomal analysis to assess the number or structure of chromosomes present in the cells, and (2) DNA analysis to detect specific gene mutations. The embryos determined to contain the desired genetic characteristics are transferred into a woman's uterus to start a pregnancy.

Because only one or two cells are available for genetic testing, PGD can be challenging. Although techniques continue to improve, inconclusive genetic test results can lead to

misdiagnosis. Likewise, because only one cell typically is tested, a test cannot be repeated and verified. Because misdiagnosis is possible, PGD often is confirmed by subsequent prenatal diagnosis with either chorionic villi sampling or amniocentesis. As science and technology advance, new techniques are being developed to decrease the error rate and increase the number of diseases and conditions that can be tested for. PGD has been used to test for more than 100 different genetic conditions to date.

Also, as with IVF generally, there is no certainty that a pregnancy will occur after the embryo is transferred into a woman's uterus.

The impact of embryo biopsy on the embryo and subsequent fetus and child is not well known. There have been no definitive studies of whether the biopsy procedure hinders implantation of the embryo into the uterus to initiate pregnancy, nor have follow up studies of the health of babies born from PGD been conducted. Any potential long-term effects on people born from biopsied embryos have not yet been researched.

Genetic Testing in PGD

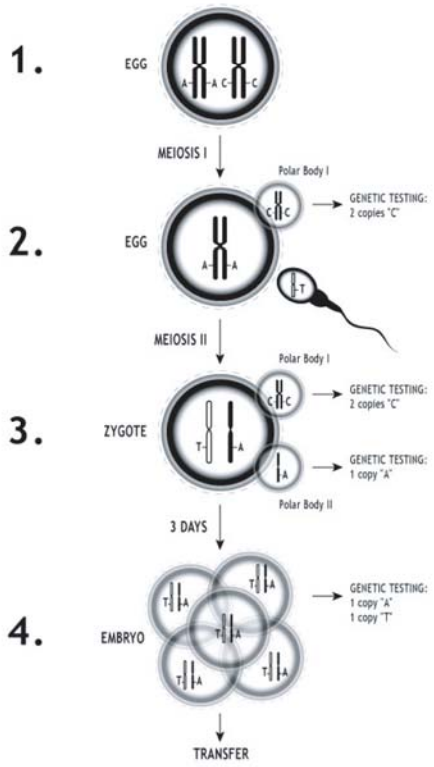
1. Eggs are harvested from a woman in preparation for IVF.

2. During fertilization, the egg matures and casts off the first of two polar body cells. Polar body cells do not become part of the embryo.

3. A second polar body cell is cast off some time later. One or both of these polar body cells can be removed by biopsy and subjected to genetic tests.

4. At two to four days after fertilization, one or two of the cells from an eight-cell embryo also can be removed by biopsy and subjected to genetic tests.

Embryos containing the desired genetic characteristics are transferred into a woman's uterus to start a pregnancy.



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