# Unit 1: Paper Summary PGD

## Preimplantation Genetic Testing: a Practice Committee Opinion

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Preimplantation genetic testing is a procedure in which a single cell from an early stage embryo is removed and tested for genetic abnormalities. Embryos that test genetically normal can then be implanted into the uterus and hopefully develop into a healthy pregnancy. As the long term effects of this procedure have not been completely determined, it is advised that this procedure only be used with couples who are at risk for transmitting a known genetic mutation or who have chromosomal structural abnormalities. This article reviews instances where preimplantation testing is appropriate, the techniques used, and the statistical outcomes.

Preimplantation Genetic Diagnosis (PGD)

PGD is used to determine if an embryo carries a specific and known mutation. For example, PGD may be requested if one patient undergoing in vitro fertilization is known to carry an identifiable genetic mutation such as in Huntington's disease. In naturally occurring pregnancies where both parents are carriers, the risk of transmitting a dominant disease (like Huntington's) is 50% and for recessive genes, 25%. Some couples may have chromosomal abnormalities such as Down syndrome, caused by three copies of chromosome 21.

Polymerase chain reaction (PCR) can be used to identify known mutations. In this technique, a small section of the DNA known to contain the mutation is repeatedly copied creating a larger amount of the genetic material (gene). Then the DNA sequence can be analyzed. In the case of abnormal chromosomes, a technique called Fluorescent In Situ Hybridization (FISH) can be performed. In this technique a DNA probe is made that is labeled with fluorescent dye. The DNA in the probe is the same sequence as the gene thought to be defective on the chromosomes. If the DNA probe is applied to the DNA of the cell under certain conditions, the probe will bind to any matching base pair sequence on the chromosome. The chromosome will then be labeled fluorescently. This can be used to examine if there are the wrong number of chromosomes, or if the sequence is abnormal it can identify an abnormal chromosome.

Any couple seeking to undergo PGD must be made aware of the general risks involved in the procedure. Some examples:

- Risks of in vitro fertilization
- The risks to the embryo
- Some embryos may be misidentified as abnormal and discarded
- Some abnormal embryos might not be detected
- There will be fewer embryos to attempt to implant and this might result in a smaller chance of becoming pregnant

Preimplantation Genetic Screening (PGS)

PGS is used to determine whether an embryo has developed aneuploidy, or an abnormal number of chromosomes. Aneuploidy can develop even if the parents have normal chromosomes. It is the cause of most early pregnancy failures, as embryos with the wrong number of chromosomes fail to develop. An exception to this rule is a "trisomy" (three) of chromosome 21, which results in Down Syndrome. Aneuploidy can be detected using FISH, as described in the previous section. Aneuploidy is more likely to occur at certain chromosomes, so generally only these are analyzed. Another technique, called Comparative Genome Hybridization can be used to examine all the chromosomes at once. DNA from one cell of the embryo being tested and one cell from a normal control embryo are amplified using fluorescent molecules. Two different colors are used, one for the tested embryo and one for the control embryo. If the DNA has the same amount of color after amplification, the embryo is most likely normal. If they have different levels the test embryo probably is aneuploid.

The authors indicate PGS to be appropriate in the following situations:

*Maternal advanced age*: In older women (defined here as older than 37), where nondisjunction events during egg development are more likely to occur. Nondisjunction means the chromosomes do not separate properly during meiosis and an egg receives either two copies or no copies of a chromosome instead of the normal single copy. A pregnancy from one of these eggs would be aneuploid and is unlikely to survive to term. If it survives, the baby could have serious developmental and health problems.

*Recurrent pregnancy loss*: If a woman has repeatedly miscarried and these miscarriages are known to be the result of aneuploidy and not some other factor, PGS is an option to increase the chance of a successful pregnancy.

*Repeated implantation failure*: If a woman has failed to become pregnant following multiple IVF implantation procedures, PGS is an option to increase the chance of a successful pregnancy.

Parents considering PGS should consider the following

- All the risks previously described in PGD
- PGS has not been shown statistically to increase the rate of live births
- Aneuploidy can develop from nondisjunction during mitosis in the embryo itself. In this case some of the cells would be normal and some abnormal. If a normal cell happens to be selected from an abnormal embryo for testing, you may implant a nonviable embryo. Also, depending on how many cells are abnormal, an embryo may be able to survive and "correct" the problem. Therefore, an embryo identified as abnormal may actually be viable.