Preimplantation Genetic Diagnosis

Xpert Fertility Care

What is Preimplantation Genetic Diagnosis?

Preimplantation genetic diagnosis or PGD is a technology that allows genetic testing of an embryo prior to implantation and before pregnancy occurs. This technology is used in conjunction with in vitro fertilization (IVF), and allows only embryos diagnosed as free of a specific genetic disease to be transferred into a woman for pregnancy. The testing is performed by removing a single cell from a 3-day old embryo and having the cell genetically screened for a specific disease.

Who Might Consider PGD?

Any couple who has a significantly increased risk of having a child with an inherited genetic disorder is a candidate. However, in order to perform PGD, the genetic disorder must be "testable." In other words, a DNA test must already exist or be possible to create that can identify the specific mutation or gene alteration which causes the disease in the family. In certain conditions where the exact gene location has not been found, PGD testing can be done by "linkage," or tracking the disease through the family. The PGD genetic counselor can tell you if you are a candidate for this technology.

Examples of situations when PGD could be considered include couples who have a 25% risk of having a child with a recessive genetic disease such as cystic fibrosis, spinal muscle atrophy or sickle cell anemia. Other examples include families who have a 50% risk to have a child with a dominant genetic disease such as Huntington's disease or 25% risk for a sex-linked disease such as hemophilia or Duchenne muscular dystrophy.

Figure 1. Embryo biopsy. A small hole is drilled in the shell surrounding the embryo, allowing a cell to be removed for genetic testing.

How is PGD performed?

The woman is given daily medicine by injection to stimulate the ovaries to produce many eggs. After roughly two weeks of fertility medications, the eggs are removed and fertilized by sperm in the laboratory. This is called in vitro fertilization, a safe technology used to help infertile couples achieve pregnancies for more than 20 years. After fertilization, the early embryo divides for several days in the laboratory. When it has approximately 8 cells, it is ready for biopsy and testing. The very early embryo is made up of identical cells called blastomeres. Any one of them can be removed while allowing the remaining embryo to continue to grow in the fertility laboratory. Once a single cell is removed, it is labeled and transported to the genetic laboratory where it undergoes testing for the genetic disease. The genetics laboratory contacts the fertility lab where the embryos are growing and instructs the fertility center which embryos are diagnosed as free of the specific genetic disease. The fertility doctor transfers those embryos into the woman and approximately 9 days later a pregnancy test is performed to determine if she is pregnant.

Is a Pregnancy Guaranteed?

No. Even with IVF without PGD testing, the pregnancy rate is no greater than 50%. Many factors are involved in determining the odds for pregnancy including a woman's age, pre-pregnancy hormone levels and other tests, past pregnancy history, the genetic condition being tested as well as other factors. In addition, there is a chance that the embryos might not grow after the biopsy or that the laboratory cannot successfully perform testing on all the embryos. These specific issues will be carefully discussed with you during one of your IVF-PGD consultations.

Is it Possible I May Become Pregnant With Twins or Triplets?

Yes. This is always a possibility with IVF. You and your fertility doctor will discuss the odds that this may happen. You will have an opportunity to decide how many embryos to transfer based on these odds and your personal family views and situation.

Figure 2. Embryo biopsies are performed by an Embryologist working with micromanipulators on an inverted microscope.

How Many PGD Tests Have Been Performed?

PGD has been performed on thousands of embryos worldwide for a variety of genetic diseases. The first PGD case was performed in 1988 at Hammersmith Hospital in London. An international consortium has been following outcomes of PGD cases since 1997. As of May 2001, this consortium has documented more than 1,500 completed PGD cycles, which have resulted in over 300 clinical pregnancies.

Are There Alternatives to PGD?

Yes. If you are at increased risk to have a child with a specific testable genetic disease, an alternative is to achieve a pregnancy spontaneously and have genetic testing performed during your pregnancy. This is called prenatal diagnosis and can be performed by one of two different tests: a chorionic villus sampling (CVS), performed at 10–12 weeks of pregnancy or an amniocentesis, performed after 15 weeks of pregnancy. Depending on the genetic condition, the results of these tests may take 1–6 weeks. Unfortunately, if the fetus is found to have the genetic disease, the options are limited to interrupting the pregnancy or continuing the pregnancy.

What Are The Benefits of PGD?

One of the benefits of PGD is that only embryos diagnosed as free of the specific genetic disease are transferred into the woman for pregnancy. Therefore, the chances that a prenatal test would detect a fetus with the disease after PGD is performed are substantially reduced. In most cases,

this enables the family to avoid the decision of whether or not to end the pregnancy once it is established.

Another advantage of PGD is that it eliminates the need for an adult who is 'at risk' for a serious adult-onset genetic disease to undergo testing that would determine if he/she has the gene and will eventually develop the condition. If these couples want to have biological children free of the disease but do not want to know if the parent has the gene, PGD is an option. Only embryos that are free of the gene are implanted and the results of the embryo genetic testing are not disclosed to the couple. This type of PGD is called "non-disclosing" PGD. Examples of diseases for which a family might be at risk include: Huntington's disease, hereditary ataxia and other adult onset testable diseases.

What Are the Drawbacks of PGD?

There are several. First, it does not always result in a pregnancy, as the statistics for pregnancy rates following PGD are slightly lower than with IVF alone. Second, PGD is significantly more expensive than conceiving a pregnancy the usual way and undergoing prenatal testing. Third, this technology is still considered experimental.

Figure 3. A 2-day old human embryo with 8 cells.

What Is The Reliability of PGD?

There is a small error rate with PGD due to the complexity of testing a single cell in the laboratory. PGD is approximately 96–98% accurate and depends in part on the specific disease being tested. It must be stressed that this technology is still considered experimental. For this reason, prenatal testing by chorionic villus sampling or amniocentesis is required by the PGD laboratory to confirm their diagnosis. PGD can only detect a specific genetic disease in an embryo. It cannot detect many genetic disorders at a time and cannot guarantee that the fetus will not have an unrelated birth defect.

Is There Any Risk Of Causing A Birth Defect Through PGD?

In the PGD cases performed to date, the rate of birth defects remains in the same range as the general population (3–5%). This is the same rate of birth defects detected in babies NOT undergoing PGD. Again, the number of births studied to date is limited. Since the cell is taken from the embryo at a stage where all cells are equal and not yet committed to become a
particular tissue or body part, this risk should be low. In addition, the rate of birth defects to women undergoing IVF has been studied extensively and most studies suggest that this risk is not increased. However, results from long-term follow-up studies are needed to effectively evaluate the risks.

How Do I Learn More About PGD?

The decision of whether or not to have preimplantation genetic testing is important and complex. For this reason, our program is organized into several different steps. After the completion of each step, you may decide if you wish to proceed to the next level.

Step One: Call and talk to one of the PGD genetic counselors.

They will give you general information and determine whether or not the laboratory is able to perform PGD given your specific genetic situation. You may be asked to send medical records and gather more family information.

Step Two: Arrange a PGD consultation with the genetic counselor.

During the hour session, you will discuss many aspects of the PGD process including general timeline, options, accuracy issues, consent forms and other issues.

Step Three: Have a conference call with the genetic testing lab director.

Your genetic counselor will help to arrange this call.

Step Four: Arrange for an appointment at the fertility center.

An appointment will be made at the fertility center. At your appointment, the fertility specialist will discuss and prescribe pre-testing work-up including blood tests and other necessary tests to ensure the process is as successful as possible.

Step Five: Begin IVF

The IVF medication plan is established and the process begins.