

CONNECTICUT FERTILITY ASSOCIATES



CONSENT FOR PREIMPLANTATION GENETIC DIAGNOSIS (PGD) OF ANEUPLOIDY

PURPOSE

Pre-implantation genetic diagnosis (PGD) is used in conjunction with in vitro fertilization (IVF) to identify, select and transfer into the uterus only those embryos which do not have recognizable chromosomal abnormality.

BACKGROUND

Chromosomes are structures found in the center or nucleus of cells. A human typically has 46 chromosomes or 23 pairs. We receive 23 chromosomes from the sperm and 23 from the egg. Chromosomes are made of genes, which contain the information that instructs the body how to function. Having extra or missing chromosome(s) (*aneuploidy*) can result in lack of implantation of an embryo, pregnancy loss, and other conditions such as infertility and Down's syndrome.

PGD of aneuploidy is most often used in patients undergoing in-vitro fertilization (IVF) who are 38 years old or older. Patients in this age group are at increased risk of miscarriage or birth defects. PGD may reduce these risks. PGD of aneuploidy may also assist the embryologists to select embryos more likely to result in a pregnancy. PGD of aneuploidy may also be used for patients of all ages who have unexplained failure to conceive despite several IVF cycles. Other patients who may benefit are patients with a history of miscarriages, especially when testing reveals no clear explanation. Patients who have had an aneuploid pregnancy in the past may also want to consider PGD of aneuploidy.

PROCEDURE : BIOPSY OF BLASTOMERES

A blastomere is a cell from an embryo. To test the blastomere, an opening is made in the covering of the embryo during its third day of development when the embryo has 4 to 10 cells. A blastomere is removed via aspiration with a pipette. The embryo is placed in an incubator while the cell is analyzed.

ANALYSIS

The biopsied cells are analyzed using a technique called fluorescence in-situ hybridization (FISH). This technique uses probes, small pieces of DNA that are a match for the chromosomes we want to analyze, to count the chromosomes present. These probes are different colors. The probes are applied to the biopsied cell and attach to the chromosomes. Under a microscope, we then count the number of chromosomes of each type (color) that are in that cell. The geneticist can tell normal cells from cells with aneuploidy. Testing of the cells destroys them because they must be glued to a glass slide and repeatedly heated and cooled. Therefore, the cells cannot be used for another purpose or returned to the embryo. The slides are kept for future reference. This analysis is accomplished in one day.

LIMITATIONS

We are unable to study all of the chromosomes via PGD, and we are also unable to study the structure of the chromosomes. Because of these limits, prenatal testing after the IVF cycle with PGD is strongly advised in order to confirm the diagnosis and review the number and structure of all the chromosomes. This prenatal testing may be done in the first trimester via chorionic villus sampling (CVS) or during the second trimester via amniocentesis. CVS is a procedure done in the late first trimester that takes cells from the placenta and analyzes them for chromosomal abnormalities. Amniocentesis is a procedure usually done between 16 and 20 weeks of pregnancy that takes fluid from around the baby and analyzes the baby's cells in the fluid for chromosomal abnormalities.

THE RISK OF EMBRYO BIOPSY

The risk of damage to an embryo during removal of the cell(s) is less than 1%. If an embryo is damaged by the procedure it will stop growing and will not be suitable for transfer into the uterus. The future fetus will

CONNECTICUT FERTILITY ASSOCIATES



CONSENT FOR PREIMPLANTATION GENETIC DIAGNOSIS (PGD) OF ANEUPLOIDY

be complete even if one or two cells are removed from the embryo. The procedure merely delays cell division for a few hours, after which the embryo continues its development.

It is unknown whether biopsied embryos implant less than embryos that have not been biopsied. Embryo biopsy may lower implantation rates slightly, but selection of chromosomally normal embryos via PGD of aneuploidy may increase implantation rates. The implantation rate is the probability that the individual embryo will result in a pregnancy.

MISDIAGNOSIS

The accuracy of PGD of aneuploidy is approximately 90%. This means that the chance of the diagnosis being wrong is 7-10%. One type of misdiagnosis is a false negative result, where a problem is not detected. Another is a false positive result, where you are told there is a problem when there is not. There is also the possibility that the testing will not work and not give a result. A **mosaicism** can also occur. A mosaicism means that the same embryo has cells with different chromosomal make-up. Typically, all cells of the embryo have the same chromosomal make-up as they originate from the same fertilized egg. However, it is possible for cells of the same embryo to have differing numbers of chromosomes. A mosaicism can result in a specific type of false negative or false positive result. For example, if we analyze a cell that has normal chromosomal content, but another cell in the same embryo has an extra chromosome, we would erroneously diagnose that embryo as being chromosomally normal. Due to the chance of misdiagnosis, as well as the presence of types of aneuploidy for which we do not test, we recommend prenatal testing by CVS or amniocentesis. CVS and amniocentesis offer higher accuracy and lower misdiagnosis rates than PGD, in addition to more information.

If most of your embryos are found to be abnormal, you may only have a few embryos for transfer. It is possible that none of your embryos will be found to be normal. Embryo transfer will then not be performed.

The risks involved in microsurgery of the embryos (the procedure used to obtain cells for PGD) are uncertain. Animal and human studies suggest that the microsurgery needed to remove the cells does not affect the fetus's development. This procedure, however, has been performed only in a limited number of studies on human embryos, so the negative effects, if any, are unknown. In animal studies, there have been no apparent problems. The major known risk is that the procedure will not be successful. There is also the possibility of obtaining a false positive or false negative result. The other risks include genetic and developmental damage during the procedure. Because of these possibilities, your pregnancy should be carefully monitored. Between 10 to 18 weeks, we strongly recommend that you have chorionic villus sampling or an amniocentesis performed. These tests will provide a genetic analysis of the fetus. The fetus should also be monitored with ultrasound to check its growth and development. It is not possible to guarantee you that a normal pregnancy will result from this procedure. Again, the purpose of the procedure is simply to attempt to decrease the risk of certain types of aneuploidy that you may be at risk for.

POSSIBLE BENEFITS

PGD may reduce the miscarriage rate and the chance of having a child with aneuploidy by allowing the identification of chromosomally normal embryos for transfer. PGD may also increase the implantation rate. This benefit increases when more embryos are analyzed. If there are fewer than 6 embryos, there may not be any increase in implantation rate. When a patient produces fewer than 6 embryos, it may be appropriate to cancel the PGD. This decision should be discussed with your physician prior to the cycle start. PGD may increase the likelihood that you become pregnant with a healthy fetus. PGD will not cause you any physical discomfort other than what is experienced during a regular IVF cycle.

ALTERNATIVES

Alternatives to PGD include standard prenatal testing for abnormalities once pregnant (chorionic villus sampling, amniocentesis, blood tests for Down's Syndrome, and/or advanced ultrasound). You are not obligated to undergo PGD even if your physician recommends it. You should undergo recommended

CONNECTICUT FERTILITY ASSOCIATES



CONSENT FOR PREIMPLANTATION GENETIC DIAGNOSIS (PGD) OF ANEUPLOIDY

prenatal testing that is based on your age and medical history. The risks, benefits, and alternatives of this testing should be discussed thoroughly with your physician. You may also discuss your options with a genetics counselor. If you desire referral to a genetics counselor in your area please inform us.

COSTS

Fees for PGD are in addition to the cost of the IVF cycle. The Finance Department personnel will advise you of the fees. If the PGD procedure is paid for but not performed, your payment will be refunded. You can change your mind and not have PGD performed at any time prior to the procedure.

FOLLOW-UP

Testing of a resulting pregnancy can be done via chorionic villus sampling (CVS) or amniocentesis. Your obstetrician, or someone he or she refers you to, can perform these tests locally. If prenatal diagnostic testing is not performed, chromosome analyses should be performed on cord blood at the time of delivery. We request that all results from genetic testing of the pregnancy or the child be forwarded to us. This information will remain confidential and will be used to monitor outcomes of our PGD program.

We (I) have read the entire consent form, or it has been read to us. We understand that PGD has benefits and risks, some of which may be unknown at this time.

We (I) want to proceed with PGD for aneuploid pregnancy in the past may also want to consider PGD of aneuploidy.

We (I) also understand that undergoing PGD for aneuploidy does not eliminate the need for standard prenatal testing such as chorionic villus sampling or amniocentesis; or prenatal care. The need for these tests remains the same whether or not PGD for aneuploidy is performed.

We (I) also understand that if we have questions about CVS or amniocentesis we may ask our obstetrician or we may request a referral to a genetics counselor.

We (I) have been encouraged to ask questions until they have been answered to my satisfaction. Any further questions can be addressed to Connecticut Fertility Associates or to its Medical Director, Dr. Michael B. Doyle; at 203-373-1200, or 203-855-1200, or 203-799-1200.

Signature of Patient Date Signature of Witness Date

Signature of Partner Date Signature of Witness Date

This consent has been read by and discussed with the patient and her partner, where applicable.

Signature of CFA Physician Date