



CAROLINA CONCEPTIONS

CAROLINA CONCEPTIONS CONSENT TO PERFORM PREIMPLANTATION GENETIC DIAGNOSIS (PGD) FOR THE INDICATION OF INFERTILITY OR RECURRENT PREGNANCY LOSS, TESTING 9 CHROMOSOMES

PURPOSE

The purpose of this procedure is to select and transfer into the uterus embryos that do not have recognizable chromosomal abnormalities.

BACKGROUND

Chromosomes are structures found in the center (nucleus) of cells. A human typically has 46 chromosomes, in 23 pairs. An embryo receives 23 chromosomes from the sperm and 23 from the egg. Chromosomes are made of genes, which contain the information that instructs the body's cells how to function. Having extra or missing chromosome(s) (called aneuploidy) can result in infertility, Down's syndrome, failure of an embryo to implant, and pregnancy loss.

PGD of aneuploidy is offered to patients undergoing in-vitro fertilization (IVF) who are 35 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. The procedure may also benefit 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

The entire procedure consists of five different steps, usually performed by different experts and laboratories. (i) The first part is producing embryos by In Vitro Fertilization (IVF). This part will take place at Carolina Conceptions. (ii) The second part is embryo biopsy in order to remove and analyze one cell from the embryo. This is done by Carolina Conceptions. (iii) The processing of the cell, in this case called cell fixation, is performed by [Carolina Conceptions](#) (iv) the analysis of the cell is performed by Reprogenetics. (v) The final step, the transfer of the embryos to the female patient, is done by the physicians at [Carolina Conceptions](#).

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ABSTENTION FROM INTERCOURSE. *It is critical that Patients refrain from sexual intercourse for a period of time beginning fifteen (15) days prior to the date that the Patient's eggs are retrieved, and ending not before the date the Patient receives conclusive results of a pregnancy test performed by the Patient's physician. Abstention from intercourse is required because sperm can survive up to fifteen (15) days in vivo. As such, it is possible that sperm from intercourse may result in fertilization and implantation of an embryo, in addition to, or instead of, fertilization and implantation that results from IVF. This would negate the results of PGD testing.*

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BIOPSY AND FIXATION OF BLASTOMERES

A blastomere is a cell from an embryo. To test the blastomere, an embryologist from Carolina Conceptions makes an opening in the covering of the embryo on the third day of development when the embryo has 5 to 10 cells, and removes a blastomere via aspiration with a pipette. The embryo is returned to an incubator and the cell that was removed from the embryo is fixed to a glass slide and sent to Reprogenetics for analysis. Please read and sign the consent form for embryo biopsy and fixation given to you by Carolina Conceptions which will explain the risks of this procedure.

CELL TRANSPORT

After the cells have been biopsied and fixed Carolina Conceptions sends the slides to Reprogenetics for analysis using same-day or next-morning delivery couriers.

ANALYSIS

This test analyzes chromosomes X, Y, 13, 15, 16, 17, 18, 21, and 22. These chromosomes are responsible for about 70% of pregnancy losses and the most common chromosome abnormalities affecting live births. The fixed cells are analyzed by Reprogenetics using a technique called *fluorescence in-situ hybridization* or FISH. This technique uses probes, small pieces of DNA that are a match for the chromosomes to be analyzed, to count the chromosomes present. These probes are attached to molecules that are like microscopic colors. The probes are applied to the biopsied cell and attach to the chromosomes. Under a microscope, the number of chromosomes, identified by color, are counted and the geneticist can distinguish normal cells from cells with aneuploidy. The cells must be glued to a glass slide and repeatedly heated and cooled in order to test them, and they are destroyed in the process. Therefore, the cells cannot be used for another purpose or returned to the embryo. This analysis is accomplished in one day, and the slides are kept for future reference.

LIMITATIONS

Reprogenetics is unable to study all of the chromosomes, or look at the structure of the chromosomes via PGD. Because of these limitations, 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. Prenatal testing may be performed in the first trimester of pregnancy via chorionic villous sampling (CVS) or during the second trimester via amniocentesis. CVS is a procedure carried out in the late first trimester that takes cells from the placenta and analyzes them for chromosomal abnormalities. Amniocentesis is usually carried out between 15 and 20 weeks of pregnancy; a sample of the fluid that surrounds the baby is taken, and cells from the baby that are found in the fluid are analyzed for chromosomal abnormalities.

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RISKS

THE RISK OF EMBRYO BIOPSY

PGD does not guarantee the birth of a normal baby. It is unknown whether biopsied embryos are less likely to implant than embryos that have not been biopsied. Embryo biopsy may lower implantation rates slightly in the absence of a test result, but selection of chromosomally normal embryos via PGD of aneuploidy may more than compensate for any negative effect of embryo biopsy, and it will increase the probability that the embryos transferred will implant.

If an embryo is damaged by the procedure it will stop growing and will not be suitable for transfer into the uterus. The risk of damaging an embryo during removal of the cell(s) is less than 1%. The future fetus will be complete even if one or two cells are removed from the embryo. The procedure may delay cell division for a few hours, after which the embryo continues its development. As of December 2005, more than 2000 babies have been born from IVF with PGD, with no reported increase of congenital abnormalities above the general population rate. The rate of malformations in the general population is 3-5%. This procedure, however, has not yet been performed sufficiently to rule out any detrimental effect. Thus we strongly recommended that you have prenatal testing by chorionic villus sampling or amniocentesis.

THE RISKS OF FIXATION

After embryo biopsy, the biopsied cell is glued (fixed) to a glass slide and an acid solution removes all but the center of the cell (the nucleus), which contains the chromosomes to be studied. After this process, the cells are no longer viable in any way and can only be used for analysis. A fraction of cells may not yield a test result: some cells may not contain a nucleus, a cell may be lost during the fixation process, or may have suboptimal fixation rendering it inadequate for analysis. Embryos without a result from the analysis may still be transferred, but the advantages of PGD may not apply.

THE RISK OF TRANSPORT

Once the cells are fixed a third party transports the cells to Reprogenetics for analysis using same day or next morning delivery services. Weather and air travel conditions may delay the receipt of samples. ***Rarely samples do not arrive at Reprogenetics or are damaged during transport.***

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THE RISKS OF THE PGD ANALYSIS

The risk of a clinical misdiagnosis resulting in a fetus or baby with chromosome abnormalities after a PGD procedure is less than 1%. This risk seems lower than that found without PGD or in natural conceptions in women of advanced maternal age. 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.

NO EMBRYOS FOR FREEZING

If the majority of your embryos that are tested are found to be abnormal, you may only have a few embryos for transfer, and none left for freezing. This is common.

NO NORMAL EMBRYOS

The test may find that none of the embryos are normal, and there may be no embryo transfer procedure. The likelihood that this will happen is dependent on your age.

NO DIAGNOSIS AND PARTIAL DIAGNOSIS

Some embryos will have no diagnosis, due to the absence of a nucleus, or to the fixation process. Embryos without a result can still be transferred, but all the possible advantages of PGD will not apply. In addition, sometimes the analysis may not be clear for one of the chromosomes being tested. This embryo could be transferred, but the possible advantages of PGD may not apply.

Because of the possibility of misdiagnosis, your pregnancy should be carefully monitored. Between 10 to 18 weeks, we strongly recommend prenatal testing by chorionic villous sampling (CVS) or amniocentesis. The fetus should also be monitored with ultrasound examination to check its growth and development. There is no guarantee that a child will be normal after IVF with PGD.

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POSSIBLE BENEFITS:

In the majority of cases, aneuploid embryos are indistinguishable morphologically and developmentally from chromosomally normal ones. Thus, without genetic testing, an embryologist cannot differentiate normal embryos from aneuploid embryos and you could have aneuploid embryos transferred. Most chromosomally abnormal embryos either do not implant or spontaneously abort shortly after implantation. The probability of conceiving a healthy child may increase after PGD. PGD of aneuploidy has been reported to double implantation rates in some studies. The test may reduce pregnancy loss and increase the chance of delivering a healthy baby. PGD will not cause you any physical discomfort other than that experienced during a regular IVF cycle.

ALTERNATIVES

Alternatives to PGD during pregnancy include standard prenatal testing for abnormalities (chorionic villous sampling, amniocentesis, ultrasound examination). You are not obliged to undergo PGD even if your physician recommends it. You should have prenatal testing when you become pregnant. The risks, benefits and alternatives of this testing should be discussed thoroughly with your genetic counselor, obstetrician or the person performing/ordering the tests. If you wish to be referred to a genetic counselor, please let us know. ***Although these tests may serve as alternatives to PGD, PGD is not a substitute for routine prenatal testing.***

COSTS

Fees for PGD are in addition to the cost of the IVF cycle. The Finance Department of **Carolina Conceptions** will advise you of the fees. If the PGD procedure is paid for but not performed, your payment will be refunded less the cancellation fee. You are also responsible for any additional medical costs incurred as a result of complications or other medical care required as a result of receiving PGD. Insurance cover for all or any part of this total procedure may not be available, and you are personally responsible for payment of such costs, including hospital and laboratory charges, and the physician's professional fees.

CONFIDENTIALITY:

Confidentiality of your records will be maintained in accordance with applicable state and federal laws at all times.

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GENETIC CONSULTATION BEFORE PGD:

It is recommended that you have a consultation with a genetic counselor that specializes in PGD before undergoing PGD. ***This can be arranged through Carolina Conceptions***

SPECIMEN RETENTION:

The cells to be tested will be destroyed during the process of the analysis. This will usually occur within 5 days of the biopsy. ***DNA from these cells will be retained for a minimum of one year.***

FOLLOW-UP

Prenatal testing during pregnancy can be carried out via chorionic villous sampling (CVS) or amniocentesis. Your obstetrician, or someone he or she refers you to, can perform these tests. If prenatal diagnostic testing is not performed, cord blood at the time of the delivery should be analyzed for chromosomes. If a pregnancy loss occurs, we request that chromosome studies be performed on the products of conception. All results from genetic testing of the pregnancy or the child up to the age of one year will be forwarded to the PGD Program Coordinator at Reprogenetics. This information will remain confidential and will be used to monitor outcomes of the PGD program.

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We 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 wish to proceed with PGD for aneuploidy.

We also understand that undergoing PGD for aneuploidy *does not eliminate* the need for standard prenatal testing such as chorionic villous sampling or amniocentesis. The need for these tests *remains the same* whether or not PGD for aneuploidy is performed. We understand that if we have questions about CVS or amniocentesis we may ask our obstetrician or we may request a referral to a genetic counselor.

We have been given an opportunity to ask questions about the PGD procedure and the contents of this consent form. If we think of additional questions, we may contact our physician, genetic counselor or nurse.

Female Partner's Signature _____ Date _____

Male Partner's Signature _____ Date _____

Witness' Signature _____ Date _____

You may request a copy of this form for your records.