BOSTONIVF
at The Women's Hospital

Karyotyping for Infertility

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Genetic karyotyping—also known as chromosome analysis—is testing that can reveal certain genetic abnormalities. It can be used to confirm or diagnose a genetic disorder or disease. Or, the testing may reveal that a couple is at risk for having a child with a genetic or chromosomal disorder. Your doctor may recommend genetic karyotyping if:

- You've been unable to conceive for more than a year.
- You've experienced two or more consecutive miscarriages.
- You've experienced a stillborn birth.
- The male partner has no sperm in his semen or an extremely low sperm count. (Also known as azoospermia or severe oligozoospermia.)
- The female partner has been diagnosed with primary ovarian dysfunction. (Also known as POI, primary ovarian insufficiency, or POF, premature ovarian failure.)

Genetic karyotyping may be required before receiving assisted reproductive technology, including IUI or IVF. This is especially true for those considering IVF with ICSI, which increases the risk of passing on male infertility and some genetic disorders.

How the Test Is Done

For infertile couples, the test is usually done via a blood draw, from both the male and female partner. The blood samples are then processed in a lab.

Cells from the blood sample are placed in a special container to encourage them to grow. Once the cells reach a particular stage of growth, the cells are stained and studied under a microscope.

The lab technician evaluates the cells' size and shape. They also take a photograph of the cells and count the number of chromosomes in the cells. The specialized photograph enables the chromosome arrangements to be evaluated.

Genetic testing may find the cause for your infertility or repeated losses. Knowing why you can't get pregnant, or why you keep miscarrying, may help your doctor recommend the best treatment options.

Another reason to do genetic testing before fertility treatment is to avoid passing on a genetic birth defect to a future child. Some genetic mutations can cause infertility when it's present in one parent, but, when both parents carry the mutation, they can pass onto their child a more significant genetic condition.

For example, *CFTR* gene mutation is associated with some kinds of male infertility. It is also associated with a serious condition, cystic fibrosis. If just the father has a CFTR gene mutation, there is a risk of passing on male infertility to his child. If both the father and mother are carriers of a CFTR gene mutation, there is a 1 in 4 chance they will have a child with cystic fibrosis.

With IVF-ICSI, a single sperm is chosen and injected directly into the egg. The odds of a genetically "weaker" sperm fertilizing an egg is much higher in this situation. This raises the risk of passing on some genetic problems.

Possible Results From Testing

What is your doctor looking for when they do karyotype or DNA analysis testing for fertility or recurrent miscarriage? Here are some (but not all) possibilities:

Klinefelter syndrome: This is a disorder that affects the sex chromosomes, X and Y. Normally, people have just two sex chromosomes. If they are XX, they are genetic female. If they are XY, they are genetically male. With Klinefelter syndrome, the person has XXY sex chromosomes. One of the possible effects of this is male infertility.

Y Chromosome Micro-deletions: This is another disorder caused by problems with the sex chromosomes. A male with Y-chromosome microdeletions has the typical XY chromosomes, but the Y-chromosome is missing some genes. This can cause infertility.

Balanced translocation: Translocations can occur in both men and women and may lead to infertility or recurrent miscarriage. A balanced translocation is when "pieces of" chromosomes switch places. So, they aren't missing genes (like with the Y-chromosome microdeletions) and they don't have "extra" genes they shouldn't (like with Klinefelter syndrome.) But, the genes aren't where they should be. Kind of like if you had all your socks and silverware at home, but someone put your socks in your silverware drawer in your kitchen, and put your silverware in your bedroom dresser.
Sometimes balanced translocations don't cause any health problems, but other times, they do. Recurrent miscarriage is a possible outcome.

Kallmann syndrome: Kallmann syndrome is a rare genetic disorder that occurs in both men and women and can lead to infertility. People with this disorder typically don't go through puberty as they should. The good news is that fertility treatment is usually successful.

CFTR gene mutation: Full cystic fibrosis requires both parents to pass on the gene to their child. However, some men who carry the cystic fibrosis gene will experience fertility problems, even though they don't present with the full disease.

Risk of passing on a genetic condition: Sometimes genetic testing for fertility can be used to determine the potential for passing on a genetic condition to your child. Your doctor may be looking for a particular risk or condition based on your family history, or a more general screening may be used.

Options for a High Genetic Risk

Your options will depend on what genetic risk you're facing. In some cases, the diagnosis of a genetic problem or risk may confirm or help make a specific infertility diagnosis, increase your risk of miscarriage or stillbirth, increase your risk of having a child with a specific genetic disorder, and increase your risk of passing on male or female infertility to your child

A genetic counselor should review your results with you. Generally speaking, your options may include any of the following:

- **Add preimplantation genetic diagnosis (PGD) to your IVF treatment**. With PGD, a developing embryo has one cell removed to test for genetic mutations. (Removing this cell doesn't harm the embryo.) The healthiest looking embryos can then be transferred. Those with genetic defects—many of which may have never survived anyway—are discarded. PGD may reduce the risk of early miscarriage and may reduce the risk of certain genetic defects. But even with PGD, a pregnancy and child isn't guaranteed to be 100% genetically healthy. You may still miscarry even with PGD. Some are ethically or religiously opposed to PGD testing.
- **Choose to forgo IVF-ICSI**. Usually, when egg and sperm are put together, only the healthiest sperm manage to penetrate and fertilize an egg. Natural selection eliminates the weaker sperm, which may also be genetically flawed sperm. With IVF with ICSI, sperm are directly injected into an egg. Natural selection can't take place. This may increase the risk of passing on genetic mutations. You may decide not to take the risk and avoid IVF-ICSI. Instead, you may try regular IVF (even though it may have a lower success rate for you), discontinue treatment, or choose a sperm or embryo donor instead.
- **Go on with treatment**, disregarding the increased risk of passing a genetic condition or male infertility to your child. Being *at risk* for passing down a condition is not a guarantee you *will*. Speak to a genetic counselor so you can make an informed decision.
- **Choose to use a sperm donor, egg donor, or embryo donor.** Of course, even donor gametes can carry genetic defects. Donors are usually screened, but no choice is risk free. If you're choosing an egg or sperm donor, it's important the donor is tested for the genetic disease you're at risk for passing down.
- **Pursue adoption or a childfree life.** After receiving genetic testing results, some couples decide to adopt. Others decide to stop trying to have a child and live a childfree life.

Emotional Considerations

Receiving the results of a genetic karyotyping can be emotional and difficult. Sometimes, the results can help you make choices about your treatment. Other times, there's not much that can be done with the information. This can cause emotional distress, without any real cause.

It's important you understand what information genetic counseling will give you and whether you can even act on it *before* you go through testing. Before you agree to testing, ask to speak with a genetic counselor.

They can explain the pros and cons of testing and help you decide if testing makes sense for you and your partner. Also, be sure there will be a genetic counselor available to discuss any results.