Specialists In Reproductive Medicine & Surgery, P.A.

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Excellence, Experience & Ethics

Patient Consent for Embryo Biopsy With Preimplantation Genetic Testing
Assisted Reproductive Technologies

Introduction:

Preimplantation Genetic Testing (PGT) involves the removal of a few cells from an embryo to test for chromosome or specific genetic abnormalities before the embryo is transferred to the uterus. The goal is to reduce the risk of miscarriage, improve live birth rates, and avoid passing on genetic diseases.

Definitions:

AH (Assisted Hatching):

A technique where a small hole is made in the embryo's outer shell (zona pellucida) to perform an embryo biopsy. AH is also performed to assist in the implantation of the embryo.

Aneuploidy:

Abnormal chromosome number, including extra chromosomes (trisomy), missing chromosomes (monosomy), and extra sets of chromosomes (polyploidy).

Euploid:

An embryo is described as euploid (normal) when 46 normal chromosomes are present (e.g., Male: 46,XY and Female: 46,XX)

Mosaicism:

A condition where a person has two or more different sets of DNA in their body.

PGT-A:

Testing for chromosome number and sex.

PGT-M:

Testing for single-gene disorders (e.g., cystic fibrosis, muscular dystrophy, and some cancers).

PGT-SR:

Testing for chromosome rearrangements, such as translocations and inversions.

Translocation:

A rearrangement where a piece of one chromosome is switched with a piece of another.

Trophectoderm:

Cells that form a sphere around the embryo eventually form the placenta and membranes.

ZP (Zona Pellucida):

The outer protective layer of the early embryo.

Genetic Consultation:

Your clinician will discuss the advantages and disadvantages of using PGT. If your case is complex,

you may be referred to a certified Genetic Counselor. You may also request to speak with a Genetic Counselor at any time.

Indications:

There are several circumstances when PGT should be considered:

- In women 35 or older.
- Both partners carry the same genetic mutation.
- When a woman is carrying an X-linked disease (e.g., Fragile X syndrome, Muscular Dystrophy).
- History of recurrent loss when other options have failed.
- Known balanced chromosome translocations.
- Inherited dominant diseases that could lead to significant illness or premature death.
- Sex selection.

Ethical Concerns:

SRMS will not perform PGT-P (Polygenic testing). This testing ***attempts*** to identify embryos with specific physical and intellectual characteristics, such as height and eye color. The test also claims to identify embryos with slightly lower disease rates, such as diabetes or heart disease. This test does **not** account for the frequent environmental influences on gene expression. It is also inaccurate in non-white patients or when lifestyle changes reduce an underlying genetic risk. ***This is a non-standard, unvalidated, and experimental form of genetic testing.*** It is not condoned by any national medical society in the U.S. and will not be performed at SRMS.

SRMS also will not knowingly transfer embryos with serious known diseases. For example, SRMS will not transfer an embryo known to carry dwarfism, even if requested by parents who both have the condition. In medicine, the motto is "to do no harm," and this procedure would intentionally cause harm to an individual who never had a say in the decision.

Procedure:

- The eggs are fertilized on "Day 0" (retrieval day).
- On Days 5-7, healthy blastocysts are biopsied using a laser, first performing Assisted Hatching (AH), and then removing about <10 trophectoderm cells. Not all blastocysts are healthy enough to tolerate a biopsy.
- Embryos are then vitrified (rapid cryopreservation) and stored.
- Each biopsy is carefully labeled and sent for analysis.
- Results take about 2-3 weeks.

There are occasional circumstances where there is a request to biopsy the embryo ***after*** cryopreservation. The process is similar to what was outlined above, except that the embryos are warmed, AH is performed, cells are removed for analysis, and the embryo is then refrozen.

Transportation:

The specimens will be sent to the genetics lab for analysis. On very rare occasions, specimens may be

lost or delayed, resulting in the death of the biopsied cells. SRMS will not be responsible for transportation errors beyond its control.

Laboratory Testing:

Testing includes all 24 chromosomes (22 pairs of chromosomes plus X & Y). The actual testing method is beyond the scope of this consent. Specific probes will need to be created when screening for mutations and translocations, so the analysis techniques with these patients differ slightly.

Reporting:

The following is reported:

PGT Procedure	Chromosome Number	Sex	Specific Mutations	Unbalanced Chromosomes
PGT-A	☒	☒		
PGT-M			☒	
PGT-SR				☒
Common Wording	46,XX, 46,XY Extra/Missing Partial Deletions	Male, Female	Absent, Carrier, Affected	Balanced, Unbalanced

A few important points:

- It is routine for PGT-A to be combined with PGT-M and PGT-SR.
- Around 10% of the biopsies may return with "no result." These embryos may still be viable.
- SRMS believes that mixed test results, sometimes described as "mosaic," are completely unreliable. SRMS requests that the testing organization not report such results.

PGT-A Complete (Optional):

SRMS currently utilizes CooperGenomics as the genetic testing laboratory. They offer **PGT-A Complete**, which provides the following:

1. Chromosome number and sex of the embryo (normal PGT-A).
2. Determining if any extra chromosomes came from the egg or the sperm.
3. Confirming that the biopsy came from the patient and partner. Those who use donor eggs or sperm usually cannot have this test, as cheek swabs are used to confirm parentage. Anecdotal evidence suggests perhaps 1/250 – 1/1,000 biopsies do not entirely match the parents.

SRMS will discuss this additional testing option. The additional information may be beneficial for some patients. Extra laboratory charges will apply.

Potential Benefits:

Genetically intact embryos tend to implant more frequently, miscarry less often, and result in slightly higher delivery rates compared to untested embryos. The testing is extraordinarily helpful when identifying specific genetic mutations and translocations, significantly improving the chance of having a healthy child. Tens of thousands of babies have been successfully delivered in the U.S. using PGT.

Potential Risks:

As with every medical procedure and test, there are some potential downsides:

- **False Positive:** Where the embryo is reported as abnormal, but it is normal. This occurs in **≤18%** of the biopsies. There are rare occasions where "abnormal" embryos may be transferred in the hope that they are normal.
- **False Negative:** Where an embryo is reported as normal, but it is not: **≤1-3%.**
- **All Abnormal:** About 1/3rd of the patients utilizing PGT will not have normal/desired embryos. The older the female patient, the more likely this outcome is to occur.
- While the testing doesn't change the normality of the embryo, being able to focus on the most normal embryos will decrease the number of failed embryo transfer procedures.
- **Embryo Destruction:** It is estimated that **≤1%** of the biopsied embryos will not survive the procedure.
- The testing will not identify fetal malformations, birth defects, cerebral palsy, or intellectual defects, which occur in about 3-5% of all pregnancies.
- Specific diagnoses may be missed with PGT-A
    - Translocations/inversions
    - Microdeletions/duplications
    - Extra sets of chromosomes (e.g., triploidy or tetraploidy)
    - True mosaicism (more than one cell line)

It is important to use the PGT results as a guide and not assume that the reported results are always accurate. Even genetically intact, seemingly healthy embryos will fail to implant or be miscarried.

Alternatives:

There are other options besides testing the embryos before transfer. One can conceive and then test.

1. Noninvasive testing near 10-11 weeks' gestational age
2. Chorionic villus sampling performed at 11 weeks' gestational age
3. Genetic amniocentesis is commonly performed at 16+ weeks' gestational age.

If the gestation is found to be abnormal, the pregnancy can be terminated. Because of Florida's current abortion laws, you will have to travel to another state for the procedure.

Another option for those patients carrying genetic diseases or translocations would be to consider adoption, donor eggs, donor sperm, or donor embryos.

Discussion:

Once results are available, your clinician will meet with you to discuss each embryo. You will decide whether to keep or discard them. Normal embryos are not discarded at SRMS.

Fees:

Fees will be charged for AH, biopsy, cryopreservation of the embryos, and specimen shipping. The genetics lab bills separately. There are instances where the genetics laboratory may request blood from each partner and occasionally from other family members to develop a custom probe for genetic testing. PGT-A Complete costs extra. A detailed price list will be provided.

PGT testing is rarely covered by insurance because they claim the procedure is experimental, despite its clinical use for over 30 years. SRMS can provide a summary of the charges if you would like to try submitting the bills to obtain reimbursement from insurance.

Confirmatory Testing:

Let your Obstetrician-Gynecologist, their support staff, or Maternal-Fetal Medicine know that PGT was used to achieve your pregnancy. This may modify their recommendations to you.

Remember, PGT testing is not perfect. Standardized prenatal testing, including noninvasive testing, CVS, or genetic amniocentesis, can confirm that the pregnancy is normal and should be strongly considered.

Emotional Impact:

Waiting for and receiving the results can be stressful. You may experience emotional stress when reviewing the testing results. "No result" outcomes can be frustrating. Deciding to discard abnormal embryos can be a difficult decision. A Mental Health Professional can help you work out the issues and will be provided upon request.

Embryo Disposition:

Your normal and abnormal embryos will remain cryopreserved. SRMS will keep your abnormal embryos frozen, just in case future testing could find a normal embryo. When you have completed your family, you will meet with SRMS to discuss the final disposition decisions regarding all your remaining embryos.

Required Reporting (CDC/SART):

Your cycle data will be shared, as required by law, with the Centers for Disease Control (CDC), which works with the Society for Assisted Reproductive Technology (SART). This data is confidential and will not be shared without your consent.

No Guarantee:

The practice of medicine is not an exact science. Even with normal PGT embryos, **there is no guarantee that the procedures will result in a successful and healthy pregnancy and delivery.**

Disclaimer of Responsibility:

By signing below, you acknowledge and agree that SRMS cannot and will not be held responsible for the performance, internal interpretation, or accuracy of testing conducted by the preimplantation genetic testing (PGT) laboratory itself. Any errors or omissions that occur in the PGT lab are beyond the control of SRMS.

Legal Concerns:

By signing below you agree to indemnify SRMS for any attorney's fees, court costs, damages, judgments, or any other losses or expenses incurred by SRMS, or for which SRMS, may be

responsible with respect to any 'third party" claim, legal action or defense thereto, arising out of the PGT procedures herein contemplated, including, but not limited to any claim or legal action brought by the child or children resulting from the PGT procedures.

It is understood that PGT has benefits and risks, some of which may be unknown at this time. It is again understood that PGT testing does not eliminate the need for standard prenatal testing.

In Summary:

By signing below, you acknowledge that you understand that you may elect not to continue with the PGT procedures at any time and that this decision will not affect your future medical care at SRMS. Likewise, you acknowledge that your acceptance and continued participation in the program are at the sole discretion of the ART team.

You have read the above materials and understand the potential complications associated with PGT. You have also had the opportunity to ask questions and to inquire about the risks and benefits of the PGT procedure. Your questions have been answered to your satisfaction, and you understand the information provided.

You have read and understand this consent. This consent will be adequate for all PGT procedures performed at SRMS.

You have had your questions answered and agree to the following procedures (check all that apply):

_____ PGT-A (chromosome number and sex)

_____ PGT-A Complete (chromosome number, sex, parental origin of extra chromosomes, and confirmation of parental DNA in the sample)

_____ PGT-M (mutation analysis for specific diseases)

Specific Disease Being Screened: _____

_____ PGT-SR (translocations and inversions)

_____	_____	___/___/___
Patient's Signature	Patient's Name (print)	Date
_____	_____	___/___/___
Partner's Signature	Partner's Name (print)	Date
_____	_____	___/___/___
IVF Coordinator Signature	IVF Coordinator Name (print)	Date