Preimplantation Genetic Screening and Diagnosis

Introduction

Preimplantation genetic screening and diagnosis is addressed by this guideline.

Definition

Preimplantation genetic diagnosis (PGD) and preimplantation genetic screening (PGS) are used to detect genetic conditions, chromosome abnormalities, and fetal sex during assisted reproduction with in vitro fertilization (IVF). PGD refers to embryo testing that is performed when one or both parents have a known genetic abnormality. This includes single-gene mutations and chromosome rearrangements. PGS refers to screening an embryo for aneuploidy when both parents are chromosomally normal. Genetic testing is performed on cells from the developing embryo prior to implantation. Only those embryos not affected with a genetic condition are implanted. PGD may allow at-risk couples to avoid a pregnancy affected with a genetic condition. The Society for Assisted Reproductive Technology and the American Society for Reproductive Medicine have published joint practice committee opinions to address the safety, accuracy, and overall efficacy of PGD and PGS.¹ ²

• For information on prenatal and preconception carrier screening, please refer to the guideline Genetic Testing for Carrier Status, as this testing is not addressed here.

• For information on prenatal genetic testing, please refer to the guideline Genetic Testing for Prenatal Screening and Diagnostic Testing, as this testing is not addressed here.

Terminology for preimplantation genetic testing has recently been updated, with terms for various clinical testing indications:³

• PGT-M: testing performed when the embryo is at an increased risk for a monogenic disorder

• PGT-SR: testing performed when the embryo is at increased risk for a structural chromosome rearrangement

• PGT-A: testing performed to screen an embryo for aneuploidy when both parents are chromosomally normal
Guidelines and evidence

Introduction

The following section includes relevant guidelines and evidence pertaining to PGD and/or PGS.

American College of Obstetrics and Gynecology

The American College of Obstetrics and Gynecology (ACOG, 2020) stated the following:4

- Confirmation of results from PGT-M and PGT-SR should be offered. This confirmation is completed through chorionic villus sampling or amniocentesis.
- For PGT-A, "traditional diagnostic testing or screening for aneuploidy should be offered to all patients who have had preimplantation genetic testing-aneuploidy, in accordance with recommendations for all pregnant patients."

Society for Assisted Reproductive Technology and American Society for Reproductive Medicine Practice

In a joint practice committee opinion, the Society for Assisted Reproductive Technology (SART, 2008) and the American Society for Reproductive Medicine (ASRM, 2008) stated the following:5

- "PGD is indicated for couples at risk for transmitting a specific genetic disease or abnormality to their offspring."
- "Due to the risk for conceiving a child with a genetic disease or other abnormality, counseling for couples considering PGD is required..."
- Suggested key points of genetic counseling include IVF and embryo biopsy-related risks, natural history of the tested condition, other reproductive options, limitations of preimplantation testing, and prenatal follow-up options.

In a joint practice committee opinion, the Society for Assisted Reproductive Technology (SART, 2018) and the American Society for Reproductive Medicine (ASRM, 2018) stated the following:6

- "The value of PGT-A as a universal screening test for all IVF patients has yet to be determined."
- There is currently insufficient evidence to recommend the use of PGT-A in all individuals undergoing IVF.
Criteria

Introduction

Requests for preimplantation genetic diagnosis are reviewed using the following criteria.

Criteria: General Coverage Guidance

Preimplantation genetic diagnosis may be considered when ALL of the following conditions are met:

- **Technical and clinical validity**: The test must be accurate, sensitive and specific, based on sufficient, quality scientific evidence to support the claims of the test. In the case of PGD, the mutation(s) or translocation(s) to be tested in the embryo should first be well-characterized in the parent(s) AND the embryonic test results must be demonstrated to be highly accurate.

- **Clinical utility**: Healthcare providers can use the test results to provide significantly better medical care and/or assist individuals with reproductive planning.

- **Reasonable use**: The usefulness of the test is not significantly offset by negative factors, such as expense, clinical risk, or social or ethical challenges.

AND THE FOLLOWING APPLY:

- The couple is known to be at-risk to have child with a genetic condition because of ANY of the following:
  - Both parents are known carriers of a recessive genetic condition and the specific gene mutation has been identified in each parent; OR
  - One parent is affected by or known to be a carrier of a dominant condition and the specific gene mutation has been identified; OR
  - The female contributing the egg is known to be a carrier of an X-linked condition and the specific gene mutation has been identified; OR
  - One or both parents are carriers of a structural chromosome rearrangement (e.g., translocation or inversion); OR
  - One or both parents have a known chromosome microdeletion (e.g. 22q11 deletion – DiGeorge syndrome, 7q11.23 deletion – Williams syndrome);

  AND

- The genetic condition is associated with potentially severe disability or has a lethal natural history.

**Note**: This guideline ONLY addresses the genetic testing component of PGS or PGD. Coverage of any procedures, services, or tests related to assisted reproduction is subject to any applicable plan benefit limitations.
Criteria: Special Circumstances

Sex determination

- PGD for sex (X and Y chromosome testing) is considered medically necessary only for identification of potentially affected embryos for gender-related conditions.

HLA typing

- PGD for human leukocyte antigen (HLA) typing for transplant donation is considered medically necessary only if:
  - A couple has child with a bone marrow disorder needing a stem cell transplant;
  - The only potential source of a compatible donor is an HLA-matched sibling

Chromosome abnormality screening

- PGS for de novo chromosome abnormalities is not considered medically necessary. This includes the following indications:
  - Maternal age alone
  - To improve in vitro success rates
  - For recurrent unexplained miscarriage and/or recurrent implantation failures

Variants of Unknown Significance (VUS)

- PGD for variants of unknown significance is not considered medically necessary.

References

Introduction

These references are cited in this guideline.


