

Test Specific Guidelines

Prenatal Aneuploidy FISH Testing

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Introduction

Prenatal aneuploidy FISH testing is addressed by this guideline.

Procedures Addressed

The inclusion of any procedure code in this table is provided for informational purposes and is not a guarantee of coverage nor an indication that prior authorization is required.

<u>Procedures addressed by this guideline</u>	<u>Procedure codes</u>
<u>FISH Analysis for Aneuploidy</u>	<u>88271</u> <u>88274</u> <u>88275</u>

What Is a Chromosome Abnormality?

Definition

A chromosome abnormality is any difference in the structure, arrangement, or amount of genetic material packaged into the chromosomes.

Humans typically have 23 pairs of chromosomes. Each chromosome has a characteristic appearance that should be the same in each person. Chromosome abnormalities can lead to a variety of developmental and reproductive disorders. Common chromosome abnormalities include Down syndrome (trisomy 21), trisomy 18, trisomy 13, Turner syndrome, and Klinefelter syndrome. Chromosome abnormalities occur in approximately 1 in 150 live births. A higher percentage of pregnancies are affected but lost during pregnancy.

“Existing studies examining IUFD [intrauterine fetal demise] in the setting of Down syndrome reported fetal loss rates of 5% to 16%, compared to 0.6% among all pregnancies. Other studies reported combined miscarriage and IUFD rates for fetuses with Down syndrome after amniocentesis or chorionic villus sampling that are even higher, ranging from 12% to 54%.”¹ In a 2016 study, the overall rate of IUFD was 7.4% for fetuses with Down syndrome.¹

The risk of having a child with an extra chromosome, notably Down syndrome, increases as a woman gets older.² However, many babies with Down syndrome are born to women under 35, and the risk of having a child with other types of chromosome abnormalities, such as Turner syndrome, is not related to maternal age. Therefore, prenatal screening for Down syndrome and certain other chromosome abnormalities is now routinely offered to all pregnant women. Prenatal diagnostic testing via amniocentesis or chorionic villus sampling (CVS) is also an option for any woman.³

Test Information

Introduction

Fluorescence in situ hybridization (FISH) can be used to assess how many copies of a chromosome or smaller piece of DNA is in a cell.

FISH uses fluorescent probes that bind only to certain regions of a chromosome.

After binding, these fluorescent signals can be viewed by microscopy and counted in a sample of cells to determine if the appropriate number of copies is present.

Because chromosomes come in pairs, most normal cells will have two fluorescent signals for each probe.

FISH analysis of prenatal samples (amniocentesis and CVS) is widely available for the chromosomes that are most commonly involved in prenatal chromosome abnormalities: 13, 18, 21, X, and Y.³

FISH does not require dividing cells like conventional karyotyping. Therefore, results are generally available much more quickly (often within 2 days of the procedure) than for standard chromosome analysis (which usually takes at least 7 days).

While FISH results have been shown to be highly accurate, most experts recommend that no irreversible decisions be made unless the FISH results are either confirmed by traditional metaphase chromosome analysis or chromosomal microarray or the abnormal result fits with the remainder of the clinical findings (e.g., ultrasound anomalies are consistent with the particular chromosome abnormality).³

Guidelines and Evidence

Introduction

The following section includes relevant guidelines and evidence pertaining to prenatal aneuploidy FISH testing.

American College of Obstetricians and Gynecologists

The American College of Obstetricians and Gynecologists (ACOG, 2016) issued prenatal diagnosis guidelines and recommended:³

"All pregnant women should be offered prenatal assessment for aneuploidy by screening or diagnostic testing regardless of maternal age or other risk factors."

ACOG recommended the following in regards to FISH testing:³

"When structural abnormalities are detected by prenatal ultrasound examination, chromosomal microarray will identify clinically significant chromosomal abnormalities in approximately 6% of the fetuses that have a normal karyotype. For this reason, chromosomal microarray analysis should be recommended as the primary test (replacing conventional karyotype) for patients undergoing prenatal diagnosis for the indication of a fetal structural abnormality detected by ultra- sound examination. If a structural abnormality is strongly suggestive of a particular aneuploidy in the fetus (e.g., duodenal atresia or an atrioventricular heart defect, which are characteristic of trisomy 21), karyotype with or without FISH may be offered before chromosomal microarray analysis."

"An abnormal FISH result should not be considered diagnostic. Therefore, clinical decision making based on information from FISH should include at least one of the following additional results: confirmatory traditional metaphase chromosome analysis or chromosomal microarray, or consistent clinical information (such as abnormal ultrasonographic findings or a positive screening test result for Down syndrome or trisomy 18)."

Criteria

Introduction

Requests for prenatal aneuploidy FISH testing are reviewed using the following criteria.

Testing with aneuploidy FISH is allowed once per pregnancy when at least one of the following indicates an increased risk for a chromosome abnormality:

Screening result suggests aneuploidy

Advanced maternal age

One major or at least two minor fetal structural defects found on ultrasound

Previous fetus or child with aneuploidy

Parent of this pregnancy has a structural chromosome abnormality (e.g., translocation, inversion) involving chromosome 21, 13, 18, X, or Y

Parent of this pregnancy has an extra chromosome (e.g., Down syndrome, XXX syndrome, Klinefelter syndrome)

Billing and Reimbursement Considerations

FISH testing (procedures codes defined in this policy) is presumed to be performed for prenatal diagnosis when:

88271 is billed on the same date of service as procedure code 88235 (Tissue culture for non-neoplastic disorders; amniotic fluid or chorionic villus cells), and 88271 is billed with 5 or more units

When FISH testing is performed for prenatal diagnosis, it will be coverable when:

The age of the person having the procedure is 34 years or older at date of service, or

An ICD code is present that indicates an increased risk of chromosome abnormality as defined in the Increased Risk for Chromosome Abnormality ICD Codes table.

Table: Increased Risk for Chromosome Abnormality ICD Codes

<u>ICD code(s)</u>	<u>Description</u>
<u>O02.X</u>	<u>Other abnormal products of conception</u>
<u>O09.5</u>	<u>Supervision of elderly primigravida and multigravida</u>
<u>O28.X</u>	<u>Abnormal findings on antenatal screening of mother</u>
<u>O35.0</u>	<u>Maternal care for (suspected) central nervous system malformation in fetus</u>
<u>O35.1</u>	<u>Maternal care for (suspected) chromosomal abnormality in fetus</u>
<u>O35.2</u>	<u>Maternal care for (suspected) hereditary disease in fetus</u>
<u>R93.8</u>	<u>Abnormal findings on diagnostic imaging of body structures</u>
<u>Q00.0-Q99.9</u>	<u>Chromosomal abnormalities, not elsewhere classified</u>
<u>Z82.79</u>	<u>Fam hx of congen malform, deformations and chromsomi abnlit</u>

References

Introduction

This guideline cites the following references

Sparks TN, Griffin E, Page J, et al. Down syndrome: perinatal mortality risk with each additional week of expectant management. *Prenat Diagn.* 2016;36(4):368-74.

Allen EG, Freeman SB, Druschel C, et al. Maternal age and risk for trisomy 21 assessed by the origin of chromosome nondisjunction: a report from the Atlanta and National Down Syndrome Projects. *Hum Genet.* 2009;125(1):41-52.

ACOG Practice Bulletin No. 162. Prenatal diagnostic testing for genetic disorders. *Obstet Gynecol.* 2016 May;127(5):976-978.