Maternal Serum Screening

The American College of Obstetricians and Gynecologists (ACOG), American College of Medical Genetics and Genomics (ACMG), and Society for Maternal-Fetal Medicine (SMFM) recommend offering both screening and diagnostic testing for chromosomal abnormalities and neural tube defects (NTD) to all pregnant women.\(^1,2,3\) Screening options include maternal serum screening (MSS), cell-free DNA (cfDNA) screening, and ultrasound. Testing is optional; women may decline screening, as well as prenatal diagnosis. High-risk results merit prompt, appropriate follow-up with critical clinical decisions based on diagnostic rather than screening test results. Refer to the ARUP Consult Prenatal Screening and Diagnosis for Chromosomal Abnormalities and Neural Tube Defects topic for additional details.

Disease Overview

Incidence

- Open neural tube defects (ONTD): 1/1,400 pregnancies\(^4\)
- Trisomy 21 (T21): 1/660 births\(^5\)
- Trisomy 18 (T18): 1/3,300 births\(^5\)

Background

ONTD: pretest risk is independent of maternal age

- Most common ONTDs include:
  - Spina bifida: variable presentation which includes some degree of paralysis of lower limbs, loss of bowel and bladder control, ventriculomegaly
  - Anencephaly: incompatible with life

T21: pretest risk increases with maternal age

- Caused by an extra chromosome 21 in all cells
- Clinical features include hypotonia, characteristic facial features, developmental delays/intellectual disability, and short stature

T18: pretest risk increases with maternal age

- Caused by an extra chromosome 18 in all cells
- Clinical features include intrauterine growth restriction, multiple congenital anomalies, and intellectual disability
- High risk for pre- and postnatal mortality

Test Description

MSS uses biochemical markers present in maternal blood to identify pregnancies with a higher risk for ONTDs, T21, and T18. Some of the panel tests require NT measurements obtained by certified sonographers to be provided to the laboratory. Gestational age windows for test components are specific. Please refer to the ARUP First and Second Trimester Screening Options table for more information.

Tests to Consider

Maternal Serum Screen, First Trimester, hCG, PAPP-A, NT 3000145
Method: Quantitative Chemiluminescent Immunoassay

- First-trimester screening test for T21 and T18
- Does not include alpha fetoprotein (AFP) for ONTD screening
- Requires nuchal translucency (NT) measurement performed by an ultrasonographer certified by the Fetal Medicine Foundation (FMF) or the Nuchal Translucency Quality Review (NTQR)

Maternal Screening, Sequential, Specimen #1, hCG, PAPP-A, NT 3000146
Method: Quantitative Chemiluminescent Immunoassay

- First-trimester screening test for T21 and T18
- Requires NT measurement performed by an ultrasonographer certified by the FMF or NTQR
- Risks provided in both first and second trimesters

Maternal Screening, Sequential, Specimen #2, Alpha Fetoprotein, hCG, Estriol, and Inhibin A 3000148
Method: Quantitative Chemiluminescent Immunoassay

- Second-trimester screening test for T21, T18, and ONTD
- Requires a previously submitted first-trimester specimen, Maternal Screening, Sequential, Specimen #1, hCG, PAPP-A, NT (3000146)
- Requires NT measurement performed by an ultrasonographer certified by the FMF or NTQR
- Risks provided in both first and second trimesters

Maternal Serum Screening, Integrated, Specimen #1, PAPP-A, NT 3000147
Method: Quantitative Chemiluminescent Immunoassay

- First-trimester screening test for T21, T18, and ONTD
- Risks determined using a combination of first- and second-trimester serum markers,
Test Interpretation

Results

NOTE: The cut-off values were selected based on a ≤5% false-positive rate

<table>
<thead>
<tr>
<th>Disorder(s)</th>
<th>Result</th>
<th>Posttest Risk Cutoff</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal Serum Screen, First Trimester Only (3000145)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>First Trimester</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T21</td>
<td>Screen positive</td>
<td>≥1/230</td>
</tr>
<tr>
<td></td>
<td>Screen negative</td>
<td>&lt;1/230</td>
</tr>
<tr>
<td>T18</td>
<td>Screen positive</td>
<td>≥1/100</td>
</tr>
<tr>
<td></td>
<td>Screen negative</td>
<td>&lt;1/100</td>
</tr>
<tr>
<td>Maternal Serum Screen, Sequential (3000146 [first trimester] and 3000148 [second trimester])</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>First Trimester</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T21</td>
<td>Screen positive</td>
<td>≥1/25</td>
</tr>
<tr>
<td>T18</td>
<td>Screen negative</td>
<td>&lt;1/25</td>
</tr>
<tr>
<td><strong>Second Trimester</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T21</td>
<td>Screen positive</td>
<td>≥1/110</td>
</tr>
<tr>
<td></td>
<td>Screen negative</td>
<td>&lt;1/110</td>
</tr>
<tr>
<td>T18</td>
<td>Screen positive</td>
<td>≥1/100</td>
</tr>
<tr>
<td></td>
<td>Screen negative</td>
<td>&lt;1/100</td>
</tr>
<tr>
<td>ONTDs</td>
<td>Screen positive</td>
<td>≥1/250 and/or AFP ≥2.5 MoM</td>
</tr>
</tbody>
</table>

Other measurements that may indicate areas of increased risk include:
- uE3 of ≤0.14 MoM: congenital steroid sulfatase deficiency or Smith-Lemli-Optiz syndrome
- hCG of ≥3.5 MoM: poor fetal outcome

Cutoffs for ONTDs vary as follows:
- Diabetic: ≥1/250 and/or AFP ≥1.90 MoM
- Twins: ≥1/103 and/or AFP ≥4.50 MoM
- Twin and diabetic: ≥1/103 and/or AFP ≥2.94 MoM

MoM, multiple of median

Maternal Serum Screening, Integrated, Specimen #2, Alpha Fetoprotein, hCG, Estriol, and Inhibin A (3000149)
Method: Quantitative Chemiluminescent Immunoassay
- Second-trimester screening test for T21, T18, and ONTD
- Requires a previously submitted first-trimester specimen, Maternal Serum Screening, Integrated, Specimen #1, PAPP-A, NT (3000147)
- Risks are determined after second-trimester specimen is received, using a combination of first- and second-trimester serum markers with or without first-trimester NT measurement

Maternal Serum Screen, Alpha Fetoprotein, hCG, Estriol, and Inhibin A (Quad) 3000143
Method: Quantitative Chemiluminescent Immunoassay
Second-trimester screening test for T21, T18, and ONTD
See Related Tests for screening test (2007537) and diagnostic tests.
<table>
<thead>
<tr>
<th>Disorder(s) (^a)</th>
<th>Result</th>
<th>Posttest Risk Cutoff</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screen negative</td>
<td>&gt;1/250 and AFP &gt;2.5 MoM</td>
<td></td>
</tr>
</tbody>
</table>

Maternal Serum Screen, Integrated (3000147 [first trimester] and 3000149 [second trimester])

### Second Trimester

<table>
<thead>
<tr>
<th>T21</th>
<th>Screen positive</th>
<th>≥1/110</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screen negative</td>
<td>&lt;1/110</td>
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</tr>
<tr>
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<td>Screen positive</td>
<td>≥1/250 and/or AFP ≥2.5 MoM</td>
</tr>
<tr>
<td>Screen negative</td>
<td>&lt;1/250 and AFP &lt;2.5 MoM</td>
<td></td>
</tr>
</tbody>
</table>

Maternal Serum Screen, Quad (3000143)

### Second Trimester

<table>
<thead>
<tr>
<th>T21</th>
<th>Screen positive</th>
<th>≥1/150</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screen negative</td>
<td>&lt;1/150</td>
<td></td>
</tr>
<tr>
<td>T18</td>
<td>Screen positive</td>
<td>≥1/100</td>
</tr>
<tr>
<td>Screen negative</td>
<td>&lt;1/100</td>
<td></td>
</tr>
<tr>
<td>ONTDs(^b)</td>
<td>Screen positive</td>
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</tr>
<tr>
<td>Screen negative</td>
<td>&lt;1/250 and AFP &lt;2.5 MoM</td>
<td></td>
</tr>
</tbody>
</table>

Maternal Serum Screen, Alpha Fetoprotein (3000144)

### Second Trimester

| ONTDs\(^b\) | Screen positive | ≥1/250 and/or AFP ≥2.5 MoM |

\(^a\)Other measurements that may indicate areas of increased risk include:
- uE3 of ≤0.14 MoM: congenital steroid sulfatase deficiency or Smith-Lemli-Opitz syndrome
- hCG of ≥3.5 MoM: poor fetal outcome

\(^b\)Cutoffs for ONTDs vary as follows:
- Diabetic: ≥1/250 and/or AFP ≥1.90 MoM
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- Twin and diabetic: ≥1/103 and/or AFP ≥2.94 MoM

MoM, multiple of median
### Disorder(s)

<table>
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</thead>
<tbody>
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<td>Screen negative</td>
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*aOther measurements that may indicate areas of increased risk include:
- uE3 of ≤0.14 MoM: congenital steroid sulfatase deficiency or Smith-Lemli-Opitz syndrome
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*bCutoffs for ONTDs vary as follows:
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- Twin and diabetic: ≥1/103 and/or AFP ≥2.94 MoM

MoM, multiple of median

### Limitations

- For test specific sensitivity, see Supplemental Resources.
- False positives may occur with incorrect gestational age, multiple gestation pregnancies, fetal demise, placental abnormalities, fetal ventral wall defects, fetal conditions not targeted by MSS, or due to other fetal and maternal biological factors.

### References


### Additional Resources


Related Information

Prenatal Screening and Diagnosis for Chromosomal Abnormalities and Neural Tube Defects

Related Tests

**Non-Invasive Prenatal Testing for Fetal Aneuploidy 2007537**
*Method*: Targeted sequencing with SNPs

**Chromosome Analysis, Chorionic Villus 2002291**
*Method*: Giemsa Band

**Chromosome Analysis, Amniotic Fluid 2002293**
*Method*: Giemsa Band

**Cytogenomic SNP Microarray - Fetal 2002366**
*Method*: Genomic Microarray (Oligo-SNP Array)

**Chromosome Analysis, Amniotic Fluid, with Reflex to Genomic Microarray 2008367**
*Method*: Giemsa Band/Genomic Microarray (Oligo-SNP Array)

**Chromosome FISH, Amniotic Fluid with Reflex to Chromosome Analysis or Genomic Microarray 2011130**
*Method*: Fluorescence in situ Hybridization (FISH)

**Chromosome FISH, Chorionic Villus with Reflex to Chromosome Analysis or Genomic Microarray 2011131**
*Method*: Fluorescence in situ Hybridization (FISH)

**Alpha Fetoprotein (Amniotic Fluid) with Reflex to Acetylcholinesterase and Fetal Hemoglobin 3000142**
*Method*: Quantitative-Chemiluminescent Immunoassay/Electrophoresis