

Maternal Serum Screen, First Trimester

Overview

- About half of the families who have a child with Down syndrome (DS) or trisomy 18 (T18) have no prior family history of the condition or any other obvious risk factor, such as advanced maternal age.
- Maternal serum screening (MSS), while not diagnostic, helps identify pregnancies at increased risk for the above disorders.
- The first-trimester MSS assay evaluates a combination of ultrasound measurements and laboratory test results to estimate the risk of Down syndrome and trisomy 18.
- Nuchal translucency (NT) and crown-rump length (CRL) are measured by a specially trained ultrasonographer. These measurements, in combination with the biochemical markers pregnancy-associated plasma protein-A (PAPP-A) and total human chorionic gonadotropin (hCG), provide an 85 percent detection rate of Down syndrome with a false-positive rate of 5 percent.
- The test is valid between 11 weeks, 0 days and 13 weeks, 6 days gestation, which corresponds with a CRL of 4.2 to 8.5 cm.
- Open neural tube defects (ONTD) are not detected by this assay. ONTD screening is performed in the second trimester (ideally between 16 and 18 weeks gestation). See Maternal Serum Screen, Alpha Fetoprotein (Only) (ARUP test code 0080434).

Disease Overview

- DS is caused by an extra copy of chromosome 21. People with DS usually have moderate mental retardation, characteristic facial features, and a variety of medical problems.
- T18 is caused by an extra copy of chromosome 18. Most newborns with T18 die at birth, but approximately 5–10 percent survive at least one year. Long-term survivors have severe mental retardation and are neither ambulatory nor articulate.

Epidemiology

- DS (1:700 births) and T18 (1:6,000 births) occur regardless of race or geographical location.
- The risk of DS and T18 increases with increasing maternal age, but approximately 50 percent of mothers with affected children are under 35 years of age.

Contraindications

- For high-risk pregnancies, a diagnostic procedure (e.g., chorionic villus sampling or amniocentesis) should be considered instead of maternal serum screening. High-risk pregnancies include:
 - Women of advanced maternal age (≥ 35 years at delivery).
 - Women with a prior pregnancy affected with an ONTD, DS, or T18.
 - Women taking valproic acid or carbamazepine.
- If a cystic hygroma or a significantly increased NT (>3.5 mm) is found on ultrasound, direct fetal karyotyping is recommended.

Approximately 70 percent of first-trimester cystic hygromas are associated with a fetal aneuploidy, most commonly DS and Turner syndrome.

Additional Ordering Notes

- An ultrasound and specimen collection must occur between 11 weeks, 0 days and 13 weeks, 6 days of pregnancy. Crown-rump length (CRL) must measure between 4.2 and 8.5 cm at the time of draw and ultrasound. Although the two can be done on different days, both must be performed within the specified gestational window.
- The sonographer performing the scan must be NT-certified by the Fetal Medicine Foundation (FMF) or the Nuchal Translucency Quality Review Program (NTQR).
- CRL and NT measurements must be performed on the same calendar day. The NT should be reported to the nearest 0.1 mm, along with the date of ultrasound, gestational age, and the sonographer's name and certification number. Test reporting may be delayed if this information is not received.
- If the sonographer is not certified or is otherwise unable to obtain an NT, the serum-only integrated screen (ARUP test code 0081062) may be ordered. Please see the ARUP Laboratory Test Directory or the Maternal Serum Screening Integrated Test technical bulletin, or contact an ARUP genetic counselor for test details.
- Patient demographics are required. The Patient History for Maternal Serum Testing Form is available at http://www.aruplab.com/guides/ug/tests/iconpdf_17.pdf; forms may be ordered from ARUP Client Services using requisition number #289-1101 or GP#41130.

Interpretation

- Patient demographics and analyte/ultrasound measurements are used to calculate multiple of the median (MoM) values for each of the laboratory analytes and the NT. The pattern of the MoM values is used to calculate post-test risks for DS and T18.
- Markers used for assessment of risk include NT, PAPP-A, and total hCG.
- A DS risk of one in 230 or worse is reported as abnormal. This risk cutoff predicts a detection rate of 85 percent.
- A T18 risk of one in 100 or worse is reported as abnormal. This risk cutoff predicts a detection rate of 80 percent.

Limitations

- A screen interpreted as "normal" misses approximately 15 percent of DS cases and 20 percent of T18 cases.
- AFP is not measured in this assay; a second-trimester test for ONTD (MS AFP-only ARUP test code 0080434) may be ordered to screen for these disorders.

Follow-Up Testing

Recommended follow-up for a positive DS or T18 screen includes a targeted ultrasound examination and consideration of chorionic villus sampling (CVS) or amniocentesis for determination of fetal karyotype.

Methodology

- Chemiluminescent immunoassay.
- Calculation of post-test risks uses a multivariate log Gaussian model. Risk estimates for DS and T18 are strongly influenced by maternal age.

Related Tests

- Maternal Serum Screen, Alpha Fetoprotein (only) ([0080434](#))
- Maternal Serum Screen, Alpha Fetoprotein, hCG and Estriol ([0080108](#))
- Maternal Serum Screen, Alpha Fetoprotein, hCG, Estriol, and Inhibin A ([0080269](#))
- MSS, Integrated, Specimen #1 ([0081062](#))
- MSS, Integrated, Specimen #2 ([0081064](#))
- Maternal Screening, Sequential, Specimen #1 ([0081293](#))
- Maternal Screening, Sequential, Specimen #2 ([0081294](#))

References

1. Ashwood ER, Knight GJ. Clinical chemistry of pregnancy. In *Tietz textbook of clinical chemistry and molecular diagnostics*, 4th ed. Burtis CA, Ashwood ER, Bruns DE, eds. 2006. Philadelphia: W.B. Saunders Co., 2153–206.
2. D'Alton M, Cleary-Goldman J. First and second trimester evaluation of risk for fetal aneuploidy: the secondary outcomes of the FASTER trial. *Semin Perinatol* 2005;29:240–6.
3. Gagnon A, et al. Society of Obstetricians and Gynaecologists of Canada Genetics Committee. Obstetrical complications associated with abnormal maternal serum markers analytes. *J Obstet Gynaecol Can* 2008;30:918–49.
4. Wald NJ, et al. SURUSS in perspective. *Semin Perinatol* 2005;29:225–35.

Test Information

0081150

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For specific collection, transport, and testing information, refer to the ARUP website at www.aruplab.com.

For information on test selection, ordering, and interpretation, refer to ARUP Consult® at www.arupconsult.com.