

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 pregnancies⁴
- Trisomy 21 (T21): 1/660 births⁵
- Trisomy 18 (T18): 1/3,300 births⁵

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

Disorder(s) ^a	Result	Posttest Risk Cutoff
Maternal Serum Screen, First Trimester Only (3000145)		
First Trimester		
T21	Screen positive	≥1/230
	Screen negative	<1/230
T18	Screen positive	≥1/100
	Screen negative	<1/100
Maternal Serum Screen, Sequential (3000146 [first trimester] and 3000148 [second trimester])		
First Trimester		
T21 T18	Screen positive	≥1/25
	Screen negative	<1/25
Second Trimester		
T21	Screen positive	≥1/110
	Screen negative	<1/110
T18	Screen positive	≥1/100
	Screen negative	<1/100
ONTDs ^b	Screen positive	≥1/250 and/or AFP ≥2.5 MoM

^aOther 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

^bCutoffs 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

with or without first-trimester NT measurement

- Risks provided after testing is completed for second-trimester specimen, Maternal Serum Screening, Integrated, Specimen #2, Alpha Fetoprotein, hCG, Estriol, and Inhibin A (3000149)

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.



Disorder(s) ^a	Result	Posttest Risk Cutoff
--------------------------	--------	----------------------

	Screen negative	<1/250 and AFP <2.5 MoM
--	-----------------	-------------------------

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

Second Trimester

T21	Screen positive	$\geq 1/110$
	Screen negative	<1/110
T18	Screen positive	$\geq 1/100$
	Screen negative	<1/100
ONTDs	Screen positive	$\geq 1/250$ and/or AFP ≥ 2.5 MoM
	Screen negative	<1/250 and AFP <2.5 MoM

Maternal Serum Screen, Quad (3000143)

Second Trimester

T21	Screen positive	$\geq 1/150$
	Screen negative	<1/150
T18	Screen positive	$\geq 1/100$
	Screen negative	<1/100
ONTDs ^b	Screen positive	$\geq 1/250$ and/or AFP ≥ 2.5 MoM
	Screen negative	<1/250 and AFP <2.5 MoM

Maternal Serum Screen, Alpha Fetoprotein (3000144)

Second Trimester

ONTDs ^b	Screen positive	$\geq 1/250$ and/or AFP ≥ 2.5 MoM
--------------------	-----------------	--

^aOther measurements that may indicate areas of increased risk include:

- uE3 of ≤ 0.14 MoM: congenital steroid sulfatase deficiency or Smith-Lemli-Optiz syndrome
- hGC of ≥ 3.5 MoM: poor fetal outcome

^bCutoffs for ONTDs vary as follows:

- Diabetic: $\geq 1/250$ and/or AFP ≥ 1.90 MoM
- Twins: $\geq 1/103$ and/or AFP ≥ 4.50 MoM
- Twin and diabetic: $\geq 1/103$ and/or AFP ≥ 2.94 MoM

MoM, multiple of median



Disorder(s) ^a	Result	Posttest Risk Cutoff
	Screen negative	<1/250 and AFP <2.5 MoM

^aOther measurements that may indicate areas of increased risk include:

- uE3 of ≤ 0.14 MoM: congenital steroid sulfatase deficiency or Smith-Lemli-Optiz syndrome
- hGC of ≥ 3.5 MoM: poor fetal outcome

^bCutoffs for ONTDs vary as follows:

- Diabetic: $\geq 1/250$ and/or AFP ≥ 1.90 MoM
- Twins: $\geq 1/103$ and/or AFP ≥ 4.50 MoM
- Twin and diabetic: $\geq 1/103$ 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

1. The American College of Obstetricians and Gynecologists (ACOG). [Practice Bulletin No. 226: Screening for fetal chromosomal abnormalities](#). [Published Oct 2020]
2. Driscoll DA, Gross SJ; Professional Practice Guidelines Committee. [Screening for fetal aneuploidy and neural tube defects](#). Genet Med. 2009;11(11):818-821.
3. Gregg AR, Skotko BG, Benkendorf JL, et al. [Noninvasive prenatal screening for fetal aneuploidy, 2016 update: a position statement of the American College of Medical Genetics and Genomics](#). Genet Med. 2016;18(10):1056-1065.
4. Palomaki GE, Bupp C, Gregg AR, et al. [Laboratory screening and diagnosis of open neural tube defects, 2019 revision: a technical standard of the American College of Medical Genetics and Genomics \(ACMG\)](#). Genet Med. 2020;22(3):462-474.
5. Jones KL, Jones MC, Del Campo, M. Smith's Recognizable Patterns of Human Malformation. 7th ed. Elsevier Saunders; 2013:7-13.

Additional Resources

Allred SK, Takwoingi Y, Guo B, et al. [First trimester ultrasound tests alone or in combination with first trimester serum tests for Down's syndrome screening](#). Cochrane Database Syst Rev. 2017;3(3):CD012600.

Audibert F, Gagnon A, Genetics Committee of the Society of Obstetricians and Gynaecologists of Canada, et al. [Prenatal screening for and diagnosis of aneuploidy in twin pregnancies](#). J Obstet Gynaecol Can. 2011;33(7):754-767.

Gagnon A, Wilson RD, Society of Obstetricians and Gynaecologists of Canada Genetics Committee. [Obstetrical complications associated with abnormal maternal serum markers analytes](#). J Obstet Gynaecol Can. 2008;30(10):918-932.

Malone FD, Canick JA, Ball RH, et al. [First-trimester or second-trimester screening, or both, for Down's syndrome](#). N Engl J Med. 2005;353(19):2001-2011.

Palomaki GE, Lee JE, Canick JA, et al. [Technical standards and guidelines: prenatal screening for Down syndrome that includes first-trimester biochemistry and/or ultrasound measurements](#). Genet Med. 2009;11(9):669-681. Erratum in: Genet Med. 2009;11(12):873.

Wald NJ, Rodeck C, Hackshaw AK, et al. [SURUSS in perspective](#). BJOG. 2004;111(6):521-531.

Wald NJ, Rodeck C, Hackshaw AK, et al. [First and second trimester antenatal screening for Down's syndrome: the results of the Serum, Urine and Ultrasound Screening Study \(SURUSS\)](#) [published correction appears in J Med Screen. 2006;13(1):51-52]. J Med Screen. 2003;10(2):56-104.



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

ARUP Laboratories is a nonprofit enterprise of the University of Utah and its Department of Pathology. 500 Chipeta Way, Salt Lake City, UT 84108
(800) 522-2787 | (801) 583-2787 | aruplab.com | arupconsult.com
Content Review March 2021 | Last Update May 2021

