

Overview

Useful For

Prenatal screening for Down syndrome and trisomy 18

Testing Algorithm

See [Prenatal Aneuploidy Screening and Diagnostic Testing Options](#) in Special Instructions.

Special Instructions

- [NT/CRL Data for First Trimester/Sequential Maternal Screening](#)
- [First Trimester/Sequential Maternal Screening Patient Information](#)
- [Prenatal Aneuploidy Screening and Diagnostic Testing Options](#)
- [Maternal Screening: Sonographer Approval Process](#)

Method Name

Immunoenzymatic Assay

NY State Available

Yes

Specimen

Specimen Type

Serum

Advisory Information

This test **does not** screen for neural tube defects. If risk assessment for neural tube defects is desired, collect specimen between 15 weeks, 0 days and 22 weeks, 6 days for an AFP single marker screen, MAFP1 / Alpha-Fetoprotein (AFP), Single Marker Screen, Maternal, Serum.

QUAD screening (QUAD1 / Quad Screen [Second Trimester] Maternal, Serum) is **not** recommended following first-trimester screening.

Necessary Information

Approval to send specimen for first-trimester screening is required and may take up to 5 business days to complete. Nuchal translucency (NT) measurements are only accepted from NT-certified sonographers. **Do not send specimen to Mayo Clinic Laboratories if the sonographer is not NT-certified or before completing the application process.** See [Maternal Screening: Sonographer Approval Process](#) link or complete the [NT/CRL Data for First Trimester/Sequential Maternal Screening](#) form in Special Instructions.

Specimen Required

Collection Container/Tube:

Preferred: Red top

Acceptable: Serum gel

Submission Container/Tube: Plastic vial

Specimen Volume: 1 mL

Collection Instructions: Centrifuge and aliquot within 2 hours of collection

Additional Information:

1. Blood draw and ultrasound must be completed between 10 weeks, 0 days and 13 weeks, 6 days, which corresponds to a crown-rump length (CRL) range of 31 to 80 mm.

2. Initial or repeat testing is determined in the laboratory at the time of report and will be reported accordingly. To be considered a repeat test for the patient, the testing must be within the same pregnancy and trimester, with interpretable results for the same test and both tests are performed at Mayo Clinic.

Forms

[First Trimester/Sequential Maternal Screening Patient Information \(T593\)](#) is required; see Special Instructions.

Specimen Minimum Volume

0.75 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	OK

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum	Refrigerated (preferred)	7 days	
	Frozen	90 days	

Clinical and Interpretive

Clinical Information

Multiple marker serum screening has become a standard tool used in obstetric care to identify pregnancies that may have an increased risk for certain birth defects such as Down syndrome (trisomy 21) and trisomy 18 (Edward syndrome). Since early 2000s first-trimester screening has been established as an alternative option of equal or better performance when compared to second-trimester screening programs.

The first-trimester screen is performed by measuring analytes human chorionic gonadotropin (hCG) and pregnancy-associated plasma protein A (PAPP-A) in maternal serum that are produced by the fetus and the placenta. Additionally, the nuchal translucency (NT) measurement, a sonographic marker shown to be effective in screening fetuses for Down syndrome and trisomy 18, is included in the risk calculation. A mathematical model is used to calculate a risk estimate by combining serum concentrations to hCG and PAPP-A, NT measurement, and maternal demographic information. The laboratory establishes a specific cutoff for each condition, which classifies each screen as either screen-positive or screen-negative. A screen-positive result indicates that the value obtained exceeds the established cutoff. A positive screen does not provide a diagnosis, but indicates that further evaluation should be considered.

Human Chorionic Gonadotropin (Total Beta-hCG)

hCG is synthesized by placental cells starting very early in pregnancy and serves to maintain the corpus luteum and, hence, progesterone production during the first trimester. Thereafter, the concentration of hCG begins to fall as the placenta begins to produce steroid hormones and the role of the corpus luteum in maintaining pregnancy diminishes. Increased total hCG levels are associated with an increased risk for Down syndrome. Low levels of hCG are associated with an increased risk for trisomy 18.

Pregnancy-Associated Plasma Protein A (PAPP-A)

PAPP-A is a 187 kDA protein comprised of 4 subunits: 2 PAPP-A subunits and 2 pro-major basic protein (proMBP) subunits. PAPP-A is a metalloproteinase that cleaves insulin-like growth factor-binding protein-4 (IGFBP-4), dramatically reducing IGFBP-4 affinity for IGF1 and IGF2, thereby regulating the availability of these growth factors at the tissue level. PAPP-A is highly expressed in first-trimester trophoblasts, participating in regulation of fetal growth. Levels in maternal serum increase throughout pregnancy. Low PAPP-A levels before the 14th week of gestation are associated with an increased risk for Down syndrome and trisomy 18.

Nuchal Translucency (NT)

The NT measurement, an ultrasound marker, is obtained by measuring the fluid-filled space within the nuchal region (back of the neck) of the fetus. While fetal NT measurements obtained by ultrasonography increase in normal pregnancies with advancing gestational age, Down syndrome fetuses have larger NT measurements than gestational age-matched normal fetuses. Increased fetal NT measurements can therefore serve as an indicator of an increased risk for Down syndrome and trisomy 18.

Reference Values

DOWN SYNDROME

Calculated screen risks $<1/230$ are reported as screen negative.

Risks $>$ or $=1/230$ are reported as screen positive.

TRISOMY 18

Calculated screen risks $<1/100$ are reported as screen negative.

Risks $>$ or $=1/100$ are reported as screen positive. A numeric risk for trisomy 18 risk is provided with positive results on non-diabetic, non-twin pregnancies.

An interpretive report will be provided.

Interpretation

Screen-Negative:

A screen-negative result indicates that the calculated risk is below the established cutoff of $1/230$ for Down syndrome and $1/100$ for trisomy 18. A negative screen does not guarantee the absence of trisomy 18 or Down syndrome. Screen-negative results typically do not warrant further evaluation.

Screen-Positive:

When a Down syndrome risk cutoff of $1/230$ is used for follow-up, the first trimester maternal screen has an overall detection rate of approximately 85% with a false-positive rate of 5%. In practice, both the detection rate and false-

positive rate increase with age, thus detection and positive rates will vary depending on the age distribution of the screening population.

Cautions

Upon receiving maternal serum screening results, all information used in the risk calculation should be reviewed for accuracy (eg, maternal date of birth, demographics, sonographic information). If any information is incorrect, the laboratory should be contacted for a recalculation of the estimated risks.

A screen-negative result does not guarantee the absence of fetal defects. A screen-positive result does not provide a diagnosis but indicates that further diagnostic testing should be considered (an unaffected fetus may have screen-positive result for unknown reasons). In fact, given the low prevalence of Down syndrome, the majority of women with a positive screen will not have a Down syndrome fetus.

Each center offering maternal serum screening to patients should establish a standard screening protocol that provides pre- and post-screening education and appropriate follow-up for screen-positive results.

Variables Affecting Marker Levels:

-All serum marker multiple of medians are adjusted for maternal weight (to account for dilution effects in heavier mothers). The estimated risk calculations and screen results are dependent on accurate information for gestation, maternal age, and weight. Inaccurate information can lead to significant alterations in the estimated risk.

-In twin pregnancies, the risk for Down syndrome is calculated using twin-adjusted medians. Risks for triplets and higher multiples cannot be calculated.

-Nuchal translucency (NT) measurements must be obtained from a trained and certified sonographer. NT quality indicators are monitored by the performing laboratory on a regular basis. Institutions will be contacted if there is ongoing deviation in the quality indicators.

Clinical Reference

1. 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 Nov 10;353(19):2001-2011
2. American College of Obstetricians and Gynecologists: Practice Bulletin No. 163: Screening for Fetal Aneuploidy. *Obstet Gynecol* 2016 May;127(5):e123-137
3. Wald NJ, Rodeck C, Hackshaw AK, Rudnicka A: SURUSS in Perspective. *Semin Perinatol* 2005;29:225-235
4. Yarbrough ML, Stout M, Gronowski AM: Ch 69 Pregnancy and Its Disorders. In *Tietz Textbook of Clinical Chemistry and Molecular Diagnostics*. Sixth edition. Edited by N Rafai, AR Horvath, CT Wittwer. Elsevier, 2018, pp 1655-1696

Performance

Method Description

The first-trimester screen for Down syndrome and trisomy 18 includes pregnancy-associated plasma protein A (PAPP-A), total human chorionic gonadotropin (hCG), and nuchal translucency measurement.

The Beckman Access hCG assay is an automated 2-site, mouse monoclonal antibody-based immunoenzymatic sandwich assay with paramagnetic separation and chemiluminescent detection. Testing is performed using the Beckman Coulter Dxl.(Instruction manual: Beckman Coulter Assay Manual, Access Total BHCG 5th IS, 2018)

The Access PAPP-A assay is a 2-site immunoenzymatic sandwich assay. Testing is performed using the Beckman Coulter DxI.(Package insert: Beckman Coulter Access PAPP-A [RUO], Beckman Coulter, Inc., Fullerton, CA, 2019)

PDF Report

No

Day(s) and Time(s) Test Performed

Monday through Friday; 8 a.m.-4:30 p.m.

Analytic Time

Same day/1 day

Specimen Retention Time

12 months

Performing Laboratory Location

Rochester

Fees and Codes
Fees

- Authorized users can sign in to [Test Prices](#) for detailed fee information.
- Clients without access to Test Prices can contact [Customer Service](#) 24 hours a day, seven days a week.
- Prospective clients should contact their Regional Manager. For assistance, contact [Customer Service](#).

Test Classification

This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the U.S. Food and Drug Administration.

CPT Code Information

81508

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
1STT1	First Trimester Maternal Screen	49086-2

Result ID	Test Result Name	Result LOINC Value
26428	Recalculated Maternal Serum Screen	43995-0
601798	Results Summary	50679-0
26434	Down Syndrome Screen Risk Estimate	43995-0
26435	Down Syndrome Maternal Age Risk	49090-4
26436	Trisomy 18 Screen Risk Estimate	43994-3
26426	PAPP-A	48407-1
601515	PAPP-A MoM	76348-2



Result ID	Test Result Name	Result LOINC Value
26427	THCG	32166-1
601516	THCG MoM	32166-1
NT_	NT	49035-9
601517	NT MoM	49035-9
NT_B	NT Twin	49035-9
601518	NT Twin MoM	49035-9
26437	Interpretation	49588-7
26439	Recommended Follow Up	80615-8
26438	Additional Comments	48767-8
26411	Specimen Collection Date	33882-2
26412	Maternal Date of Birth	21112-8
26429	Calculated Age at EDD	43993-5
26413	Maternal Weight	29463-7
26880	Maternal Weight	29463-7
IDD_	Insulin dependent diabetes	44877-9
B_RCE	Patient Race	21484-1
SMKN1	Current cigarette smoking status	64234-8
DT3	Scan Date	34970-4
CRL1	CRL	11957-8
CRL2	CRL Twin	11957-8
26430	GA on Collection by U/S Scan	11888-5
NUMF	Number of Fetuses	55281-0
CHOR	Number of Chorions	92568-5
IVF	IVF	47224-1
PRHX	Prev Down (T21) / Trisomy Pregnancy	53826-4
INTL1	Initial or repeat testing	86955-2
SONON	Sonographer Name	49088-8
SONOC	Sonographer Code	No LOINC Needed
SONOD	Sonographer Reviewer ID	49089-6
DRPH1	Physician Phone Number	68340-9
10358	GENERAL TEST INFORMATION	62364-5