Overview

Useful For

First-trimester prenatal screening for trisomy 21 (Down syndrome) and trisomy 18 (Edwards syndrome)

Testing Algorithm

Sequential maternal screening is a 2-step test, with first- and second-trimester components. It requires a nuchal translucency measurement and blood collection in the first trimester. If the result from part 1 indicates a risk for Down syndrome that is higher than the screen cutoff, the screen is completed, and a report is issued. If the results from part 1 are negative, an additional blood collection in the second trimester is required (see SEQB / Sequential Maternal Screening, Part 2, Serum). If the second specimen is not received for sequential screening, the results are uninterpretable and no maternal risk will be provided.

The following are available:

-Sequential Maternal Serum Screening Testing Process

-Prenatal Aneuploidy Screening and Diagnostic Testing Options Algorithm

Special Instructions

- NT/CRL Data for First Trimester/Sequential Maternal Screening
- First Trimester/Sequential Maternal Screening Patient Information
- Sequential Maternal Serum Screening Testing Process
- Prenatal Aneuploidy Screening and Diagnostic Testing Options
- Maternal Screening: Sonographer Approval Process

Method Name

Immunoenzymatic Assay

NY State Available

Yes

Specimen

Specimen Type

Serum

Ordering Guidance

When part 1 is negative, part 2 must be completed in order to receive an interpretable result. If collecting a second-trimester specimen is expected to be difficult, order first-trimester screening instead (see 1STT1 / First Trimester

Maternal Screen, Serum).

If a stand-alone neural tube defect risk assessment is desired, order MAFP1 / Alpha-Fetoprotein (AFP), Single Marker Screen, Maternal, Serum.

Additional Testing Requirements

Sequential maternal screening is a 2-part test that includes a first-trimester sample (SEQA / Sequential Maternal Screening, Part 1, Serum) and a second-trimester sample (SEQB / Sequential Maternal Screening, Part 2, Serum).

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 in Special Instructions. Complete the NT/CRL Data for First Trimester/Sequential Maternal Screening.

Specimen Required

Container/Tube:

Preferred: Serum gel

Acceptable: Red top

Submission Container/Tube: Plastic vial

Specimen Volume: 1 mL

Collection Instructions:

1. The ultrasound and blood draw must be completed within a gestational window of 10 weeks, 0 days and 13 weeks, 6 days, which corresponds to a crown-rump length range of 31 to 80 mm.

2. Centrifuge and aliquot serum into plastic vial within 2 hours of collection.

Forms

First Trimester/Sequential Maternal Screening Patient Information (T593) is required.

Reject Due To

Gross hemolysis	Reject
Gross lipemia	OK

Gross icterus	OK

Specimen Minimum Volume

0.5 mL

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum	Refrigerated (preferred)	14 days	
	Frozen	90 days	
	Ambient	7 days	

Clinical & Interpretive

Clinical Information

Maternal serum screening is used to identify pregnancies that may have an increased risk for certain birth defects, such as trisomy 21 (Down syndrome), neural tube defects (NTD) and trisomy 18. Various options for maternal serum screening are available and include: first trimester, second trimester, and cross-trimester. Sequential screening is a type of cross-trimester screening that has an improved detection rate as compared to either first- or second-trimester screening. Sequential screening combines biochemical and ultrasound markers (nuchal translucency: NT) measured in both trimesters of the pregnancy.

This test involves an ultrasound and a blood draw. The ultrasound measurement, referred to as the NT measurement, is difficult to perform accurately. Therefore, NT data is accepted only from NT-certified sonographers. Along with the NT measurement, a maternal serum specimen is collected to measure pregnancy-associated plasma protein A (PAPP-A). The results of the ultrasound measurement and blood work, along with the maternal age and demographic information, are used to calculate trisomy 21 (Down syndrome) and trisomy 18 risk estimates.

If the result from part 1 indicates a risk for Down syndrome that is higher than the screen cutoff, the screen is completed, and a report is issued. In that event, the patient is typically offered counseling and diagnostic testing. When the part 1 screen is completed, NTD risk is not provided. For a stand-alone NTD-risk assessment, order MAFP1 / Alpha-Fetoprotein (AFP), Single Marker Screen, Maternal, Serum.

If the risk from the first trimester is below the established cutoff, an additional serum specimen is collected in the second trimester for SEQB / Sequential Maternal Screen, Part 2, Serum. The blood specimen is tested for AFP, unconjugated estriol , human chorionic gonadotropin , and inhibin A. The information from both trimesters is combined and a report is issued. If results are positive, the patient is typically offered counseling and diagnostic testing.

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 and trisomy 18 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.

PAPP-A:

PAPP-A is a 187-kDa protein comprised of 4 subunits: 2 PAPP-A subunits and 2 pro-major basic protein 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 fourteenth week of gestation are associated with an increased risk for Down syndrome and trisomy 18.

Reference Values

An interpretive report will be provided.

Interpretation

Maternal screens provide an estimation of risk, not a diagnosis. A negative result indicates that the estimated risk falls below the screen cutoff. A positive result indicates that the estimated risk exceeds the screen cutoff.

Trisomy 21 (Down Syndrome):

First-trimester results are negative when the calculated risk is below 1/50 (2%). If part 1 is negative, submit an additional specimen in the second trimester (order SEQB / Sequential Maternal Screening, Part 2, Serum).

Second-trimester results are negative when the calculated risk is below 1/270 (0.37%). Negative results mean that the risk is less than the established cutoff; they do not guarantee the absence of Down syndrome.

Results are positive when the risk is greater than the established cutoff (ie, > or =1/50 in the first trimester and > or =1/270 in the second trimester). Positive results are not diagnostic.

When both sequential maternal screening parts 1 and 2 are performed with a screen cutoff of 1/270, the combination of maternal age, nuchal translucency (NT), pregnancy-associated plasma protein A , alpha-fetoprotein , unconjugated estriol , human chorionic gonadotropin , and inhibin A has an overall detection rate of approximately 90% with a false-positive rate of approximately 3% to 4%. In practice, both the detection rate and false-positive rate vary with maternal age.

Trisomy 18 (Edwards Syndrome):

In part 1, trisomy 18 results are only reported if the Down syndrome risk is positive.

In part 2, the screen cutoff for trisomy 18 is 1/100 (1%). Risks that are greater or equal to 1% are screen-positive; positive results are not diagnostic. Risks less than 1% are screen-negative; negative results do not guarantee the absence of trisomy 18.

Use caution when revising trisomy 18 positive results with earlier dating. Babies with trisomy 18 tend to be small, which can lead to underestimation of gestational age and an increased chance of missing a true-positive.

When sequential maternal screening parts 1 and 2 are performed, the overall detection rate is approximately 90% with a false-positive rate of approximately 0.1% using a screen cutoff of 1/100.

Neural Tube Defect:

Risk assessment for neural tube defects is only available after completion of part 2 of the sequential maternal screen. See SEQB / Sequential Maternal Screening, Part 2, Serum for details.

Follow-up:

Verify that all information used in the risk calculation is correct (maternal date of birth, gestational dating, etc). If any information is erroneous, contact the laboratory for a revision.

Screen-negative results typically do not warrant further evaluation.

If the results are positive, the patient is typically offered counseling, ultrasound, diagnostic testing, and possibly, referral to genetics counseling or a high-risk clinic.

Cautions

Nuchal translucency (NT) measurements must be obtained from NT-certified sonographers. NT-measurement quality indicators will be monitored on a regular basis. Sonographers will be contacted if there is ongoing deviation in the quality indicators.

Incorrect or incomplete information may significantly alter results.

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.

In twin pregnancies, the risk for Down syndrome is approximated, using twin-adjusted medians. In cases where one twin has demised, results may be unreliable.

Results are not available for triplets or higher-multiple pregnancies.

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

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. Prenatal Diagnostic Testing for Genetic Disorders. ACOG Practice Bulletin No. 163. American College of Obstetricians and Gynecologists. Obstet Gynecol. 2016 May;127(5):979-981. doi: 10.1097/AOG.0000000000001439

3. Wald NJ, Rodeck C, Hackshaw AK, et al: SURUSS in Perspective. Semin Perinatol. 2005 Aug;29(4):225-235

4. Palomaki GE, Steinort K, Knight GJ, et al: Comparing three screening strategies for combining first- and second-trimester Down syndrome markers. Obstet Gynecol. 2006 Feb;107(2 Pt 1):367-375

5. Palomaki GE, Neveux LM, Knight GJ, et al: Maternal serum-integrated screening for trisomy 18 using both first- and

second-trimester markers. Prenat Diagn. 2003 Mar;23(3):243-247

6. Yarbrough ML, Stout M, Gronowski AM: Pregnancy and its disorders. In: Rifai N, Horvath AR, Wittwer CT, eds. Tietz Textbook of Clinical Chemistry and Molecular Diagnostics. 6th ed.. Elsevier; 2018:1655-1696

Performance

Method Description

This test includes measuring the nuchal translucency (NT) and pregnancy-associated plasma protein A (PAPP-A). The NT and PAPP-A are compared to median values for a given gestational age and a multiple-of-the-median (MoM) is calculated for each. The MoM results are entered into a multivariate algorithm that includes the mother's age to derive risk factors for Down syndrome and trisomy 18. If the calculated risks exceed the screen cutoff, the results are reported and the screen is ended. If the results from the first part of screening fall below the screen cutoff, the results are held until the second sample is analyzed. PAPP-A is performed on the Beckman Access using an automated immunoenzymatic assay with paramagnetic separation and chemiluminescent detection.(Package insert: PAPP-A, Beckman-Coulter Access, 2019)

PDF Report

No

Specimen Retention Time

9 months

Performing Laboratory Location

Rochester

Fees & Codes

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 US Food and Drug Administration.

CPT Code Information

84163

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
SEQA	Sequential Maternal Screen, Part 1	49086-2

Result ID	Reporting Name	LOINC®
29473	Additional Comments	48767-8
29474	Recommended Follow Up	80615-8
29487	General Test Information	62364-5
29470	Down Syndrome Maternal Age Risk	49090-4
29471	Trisomy 18 Screen Risk Estimate	43994-3
DIAB1	Insulin Dependent Diabetes	33248-6
RACE_	Patient Race	32624-9
IVF1	IVF	47224-1
SNDT1	Scan Date	34970-4
CRL1A	CRL	11957-8
NT1	NT	33069-6
FET1	Number of Fetuses	11878-6
CRL2A	CRL Twin	11957-8
NTTB1	NT Twin	33069-6
CHOR1	Chorions	92568-5
29451	Recalculated Maternal Serum Screen	43995-0
29452	Specimen Collection Date	33882-2
29453	Maternal Date of Birth	21112-8
29890	Calculated Age at EDD	43993-5
29454	Maternal Weight	29463-7
29455	Maternal Weight	29463-7
29891	GA on Collection by U/S Scan	11888-5
29468	PAPP-A	48407-1
29469	Down Syndrome Screen Risk Estimate	43995-0
29472	Interpretation	49586-1
601802	Results Summary	50679-0
601799	PAPP-A MoM	76348-2
601800	NT MoM	49035-9
601801	NT Twin MoM	49035-9
SMKN2	Current cigarette smoking status	72166-2
PRNTA	Prev Pregnancy w/ Neural Tube Defect	53827-2
PTNTA	Patient or father of baby has a NTD	53827-2
INTL2	Initial or repeat testing	86955-2
SONOM	Sonographer Name	49088-8
SNCD1	Sonographer Code	No LOINC Needed
SONO1	Sonographer Reviewer ID	49089-6
DRPH2	Physician Phone Number	68340-9

PRHIX	Prev Down (T21) / Trisomy Pregnancy	53826-4