Overview

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

Testing Algorithm
Sequential maternal screening is a 2-step test, with first- and second-trimester components. It requires a nuchal translucency (NT) 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 in Special Instructions:

- 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
No

Specimen

Specimen Type
Serum

Advisory Information
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 form in Special Instructions.

Specimen Required

Container/Tube:

Preferred: Red top

Acceptable: Serum gel

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 (CRL) range of 31 to 80 mm.

2. Centrifuge and aliquot serum within 2 hours of collection.

Forms

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

Specimen Minimum Volume

0.5 mL

Reject Due To

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Specimen Stability Information

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Clinical and 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 which 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.

SEQA / Sequential Maternal Screening, Part 1, Serum 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 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 result 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 sample is tested for AFP, unconjugated estriol (uE3), human chorionic gonadotropin (hCG), 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 (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 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.

Down Syndrome (trisomy 21):

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 (PAPP-A), alpha-fetoprotein
(AFP), unconjugated estriol (uE3), human chorionic gonadotropin (hCG), 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:

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 (NTD) 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
2. Prenatal Diagnostic Testing for Genetic Disorders. ACOG Practice Bulletin No. 163. American College of

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

Day(s) and Time(s) Test Performed
Monday through Friday; 8 a.m.-4:30 p.m.

Analytic Time
1 day

Maximum Laboratory Time

Document generated September 2, 2020 at 6:56pm CDT
Test Definition: SEQA
Sequential Maternal Screen, Part 1

3 days

Specimen Retention Time
9 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
84163

LOINC® Information

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