

Sequential Screening

using first and second trimester markers

The American College of Obstetricians and Gynecologists recommends that **“A strategy that incorporates both first - and second-trimester screening should be offered to women who seek prenatal care in the first trimester.”**¹ Sequential Screening utilizes the best of the first and second trimester markers, resulting in screening performance that surpasses first trimester screening and second trimester quad marker screening. Furthermore, it identifies those women whose first trimester Down syndrome risk is high enough to warrant immediate discussion of prenatal diagnosis.

An early result for those with the highest risks

Sequential Screening starts with a nuchal translucency (NT) ultrasound and measurement of maternal serum PAPP-A in the first trimester. A Down syndrome risk of 1 in 40 or greater will be reported immediately to the provider. While only 1% of women will have a screen positive result in the first trimester, their pregnancies will be identified as high risk early in the screening process, which will allow them to consider earlier prenatal diagnostic options.

The remaining women will continue in the Sequential Screening pathway that requires a second trimester serum sample for final interpretation. The second sample measures AFP, uE3, hCG, and inhibin. This combination of markers maintains high detection rates, not only for Down syndrome, but also for trisomy 18 and open neural tube defects.

| Sequential Screening | | | |
|----------------------|----------------------------|-------------------------|---------------------------------------|
| | Down syndrome ² | Trisomy 18 ³ | Open neural tube defects ⁴ |
| Detection Rate* | 89% | 88% | 83% |
| Screen Positive* | 3% | 0.8% | 3% |

*Actual Down syndrome detection and screen positive rates will depend on maternal and gestational age distribution.

| Comparing Screening Methods for Down syndrome | | | | | |
|---|--------------------|------------------------|-------------------|-------------------|-------------------------|
| | Quad Marker Screen | First Trimester Screen | Sequential Screen | Integrated Screen | Serum Integrated Screen |
| Detection Rate | 81% | 84% | 89% | 90% | 85% |
| Screen Positive | 5% | 5% | 3% | 3% | 3% |

Keep in Mind...

- Almost all women screened (99%) will have their results reported after the second trimester sample is analyzed.
- Women who are screen positive in the first trimester are not eligible for second trimester screening.
- Sequential Screening is dependent upon careful timing of both the first and second trimester serum samples. Both samples must be sent to and analyzed by the same laboratory.
- Sequential Screening requires an NT-certified sonographer to perform the nuchal translucency measurement.

Serum Integrated Screening

If the NT measurement is not obtainable, Serum Integrated Screening is available. Serum Integrated Screening is the most effective method of screening using serum markers only^{2,5}. While Serum Integrated Screening is less effective than Sequential Screening, it has a higher detection rate and lower screen positive rate than a quad marker screen.

Reimbursement

Most insurers should cover Sequential Screening to the extent that they cover prenatal ultrasound and serum screening procedures. Patients are encouraged to check with their insurance carriers if in doubt.



Screening Requirements

Part 1 (11-13 weeks)

- Complete Part 1 of FBR Sequential Screening test requisition*
- CRL between 45 and 84 mm
- Nuchal translucency (NT) measured**
- Serum drawn for PAPP-A

Part 2 (15-21 weeks)***

- Complete Part 2 of FBR Sequential Screening test requisition*
- Serum drawn for AFP, uE3, hCG, and inhibin

* Both samples must be sent to the Foundation for Blood Research (FBR).

** NT must be measured by sonographer certified by FMF or NTQR.

*** Women who screen positive after Part 1 will not need to complete Part 2.

If you would like us to provide Sequential Screening to your patients:

Part 1

- Fetal CRL must be between 45 and 84 mm as determined by Dartmouth-Hitchcock sonographers.
- The first serum sample is drawn following the NT measurement.
- If NT cannot be measured accurately, then we will take the responsibility of rescheduling the ultrasound or ordering a Serum Integrated Screen.
- One percent of women will be screen positive after Part 1. These results will be called to your office and your patient by a Dartmouth-Hitchcock genetic counselor. For all other patients, you will receive a letter confirming receipt of the first sample along with a lab slip to use for the second serum sample.

- Patients referred because of increased risk, e.g. advanced maternal age or family history, will be offered genetic counseling by Dartmouth-Hitchcock counselors.

Part 2

- Patients may have their blood drawn at the Dartmouth-Hitchcock sites in Lebanon, Manchester, or Nashua. If blood is drawn elsewhere, that facility will need to make arrangements to have the sample sent to the Foundation for Blood Research (FBR).
- Results are available approximately 3-5 days after receipt of the second sample.
- Screen positive results will be called to your office and your patient by a Dartmouth-Hitchcock genetic counselor.
- Screen negative results will be faxed to your office from FBR. You will need to inform your patients of these results.

¹ ACOG Committee on Practice Bulletins. ACOG Practice Bulletin No. 77: screening for fetal chromosomal abnormalities. *Obstet Gynecol* 2007;109(1):217-27.

² Wald NJ, Rodeck C, Hackshaw AK, Walters J, Chitty L, Mackinson AM. First and second trimester antenatal screening for Down's syndrome: the results of the Serum, Urine and Ultrasound Screening Study (SURUSS). *J Med Screen* 2003;10(2):56-104.

³ Palomaki GE, Neveux LM, Knight GJ, Haddow JE. Maternal serum-integrated screening for trisomy 18 using both first- and second-trimester markers. *Prenat Diagn* 2003;23(3):243-7.

⁴ Wald NJ, Cuckle H, Brock JH, Peto R, Polani PE, Woodford FP. Maternal serum alpha-fetoprotein measurement in antenatal screening for anencephaly and spina bifida in early pregnancy. Report of U.K. collaborative study on alpha-fetoprotein in relation to neural-tube defects. *Lancet* 1977;1(8026):1323-32.

⁵ Knight GJ, Palomaki GE, Neveux LM, et al. Integrated serum screening for Down syndrome in primary obstetric practice. *Prenat Diagn* 2005;25(12):1162-7.

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For more information:

Lebanon: (603) 653-6025 | Manchester: (603) 695-2902 | Nashua: (603) 577-4324

Refer a patient:

Download referral forms and lab requisition: www.dhmc.org/goto/referralforms

When making a referral, fax a completed referral and lab requisition form to
Lebanon: (603) 653-3545 | Manchester: (603) 623-7216 | Nashua: (603) 577-3497



*Prepared in collaboration with the Foundation for
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