Test Specific Guidelines

Prenatal Maternal Serum Screening

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Introduction

Prenatal maternal serum screening is addressed by this guideline.

Procedures Addressed

The inclusion of any procedure code in this table is provided for informational purposes and is not a guarantee of coverage nor an indication that prior authorization is required.

Procedures covered by this guideline	Procedure codes
Prenatal Maternal Serum Screening, Two Markers	81508
Prenatal Maternal Serum Screening, Three Markers, First Trimester	81509
Prenatal Maternal Serum Screening, Three Markers, Second Trimester	81510
Prenatal Maternal Serum Screening, Four Markers	81511
Prenatal Maternal Serum Screening, Five Markers	81512

What Is Prenatal Maternal Serum Screening?

Definition

Approximately 3% of pregnancies have a birth defect.[1] Down syndrome and neural tube defects (NTDs) are among the most common serious birth defects. Down syndrome affects about 1 in 700 live births.[2] Spina bifida is the most common type of NTD and about 1,400 babies are born with spina bifida each year in the United States.[3] Some factors predict an increased risk for Down syndrome and NTDs, such as maternal age, family history, and maternal diabetes or seizure disorder. However, there are no recognizable risk factors to explain the vast majority of babies born with these birth defects.[4,5] As a result, prenatal screening to identify affected pregnancies is routinely offered to all pregnant women.[5,6]

While not the focus of maternal serum screening programs, other birth defects (such as abdominal wall and heart defects) and general risks for poor pregnancy outcome may also be identified.

Test Information

Introduction

Prenatal maternal serum screening relies on maternal serum markers (PAPP-A, HCG, unconjugated estriol, inhibin, and AFP), and sometimes nuchal translucency ultrasound data (ACOG recommended technique when available)[6] to predict the risk for fetal Down syndrome, open NTDs, and other rarer birth defects such as trisomy 18.

Typical marker patterns for these birth defects are seen in the first and second trimesters. Measurements are provided as multiples of the median (MoM), which compare results to normal population medians. Therefore, values are higher or lower relative to 1.0. Risk assessment algorithms evaluate several factors, so pregnancies may be at-risk without each marker being abnormal.

AFP measured at 15-20 weeks gestation is the only maternal serum marker used to assess for the risk of open NTDs.

Screening results are generally reported as "screen positive" for Down syndrome or trisomy 18 if the predicted risk exceeds a laboratory-determined risk cut-off (often about 1 in 270 for Down syndrome and 1 in 100 for trisomy 18). A pregnancy is screen-positive for neural tube defect if the maternal serum AFP (MSAFP) exceeds a cut-off, which is usually 2.5 MoM.[4] However, different MoM calculations or cut-offs may be used for those with recognized risk factors or multiple gestations.[7]

Guidelines and Evidence

Introduction

The following section includes relevant guidelines and evidence pertaining to prenatal maternal serum screening.

American College of Medical Genetics and Genomics and American Academy of Family Physicians

The American College of Medical Genetics and Genomics (ACMG, 2009)[7] and the American Academy of Family Physicians (AAFP, 2020)[5] published prenatal screening statements similar to American College of Obstetricians and Gynecologists' recommendations stated below.

American College of Obstetricians and Gynecologists

Practice guidelines from the American College of Obstetricians and Gynecologists (ACOG, 2020) addressed prenatal screening for chromosome abnormalities and recommended:[6]

"Prenatal genetic screening...and diagnostic testing options...should be discussed and offered to all pregnant women regardless of maternal age or risk of chromosomal abnormality." [evidence level A: "good and consistent scientific evidence"]

Prenatal cell-free DNA screening (not prenatal maternal serum screening) "…is the most sensitive and specific screening test for the common fetal aneuploidies." [evidence level A: "good and consistent scientific evidence"]. However, "…there is not one screening test that performs optimally in all clinical scenarios."

"…patients should have one prenatal screening approach [for fetal chromosomal abnormalities] and should not have multiple screening tests performed simultaneously." [evidence level A: "good and consistent scientific evidence "].

Several other level A and B recommendations are made about test effectiveness, choice, individual counseling, and follow-up.

While the ACOG guideline focused primarily on screening for fetal chromosomal abnormalities, they included this recommendation about open NTD screening: "All patients should be offered a second-trimester ultrasound for fetal structural defects…(with or without second-trimester maternal serum alpha-fetoprotein)."[6]

A 2017 ACOG practice guideline more directly addressed NTD screening and stated:[4]

"As a screening test, an elevated level of MSAFP is not diagnostic of an open NTD because it also can be explained by inaccurate gestational dating and can be found in association with other conditions, such as multiple gestation, fetal abdominal wall defects, fetal nephrosis, fetal demise, and placental conditions that increase risk of adverse events later in pregnancy."

"MSAFP is not usually increased with closed NTDs, which limits the value of MSAFP screening."

"With advances in ultrasonography and expansion of its use, MSAFP is less important for detection of NTDs when high-quality, second-trimester fetal anatomy ultrasonography is routinely used. In these cases, the value of MSAFP lies more in its screening for other abnormalities and placental complications."

Criteria

Introduction

Requests for prenatal maternal serum screening are reviewed using the following criteria.

Screening for aneuploidy by ONE of the following methods is covered one time per pregnancy:

First trimester screening – Total or free beta-HCG and PAPP-A levels performed on a maternal serum sample performed in conjunction with an ultrasound measurement of fetal nuchal translucency (NT) If this option is chosen, maternal serum AFP evaluation in the second trimester as a screening test for NTDs is typically medically necessary.**

Second trimester screening – human chorionic gonadotropin (hCG), alpha-fetoprotein (AFP), unconjugated estriol (uE3), and dimeric inhibin-A (DIA) performed on a maternal serum sample

Integrated, step-wise sequential, or contingent sequential screening – combines results of first and second trimester screening in various testing algorithms.

****Limits on prenatal ultrasonography will depend on the insurer's ultrasound coverage policy and are outside the scope of this program.**

Other Considerations

Maternal serum screening for aneuploidy and non-invasive prenatal screening (prenatal cell-free DNA screening) should not be performed concurrently.

If non-invasive prenatal screening (prenatal cell-free DNA screening) has been successfully performed in the current pregnancy, other aneuploidy screening (by first or second trimester screening or integrated, step-wise sequential, or contingent sequential screening) is not indicated. Maternal serum screening for neural tube defects (AFP-only) is indicated.

References

Introduction

This guideline cites the following references.

March of Dimes. Quick Reference: Fact Sheets: Birth Defects. Available at: https://www.marchofdimes.org/complications/birth-defects-and-health-conditions.aspx

March of Dimes. Quick Reference: Fact Sheets: Down syndrome. Available at: https://www.marchofdimes.org/complications/down-syndrome.aspx

March of Dimes. Quick Reference: Fact Sheets: Neural Tube Defects. Available at:https://www.marchofdimes.org/complications/spina-bifida.aspx https://www.marchofdimes.org/complications/spina-bifida.aspx

ACOG Committee on Practice Bulletins. ACOG Practice Bulletin No.187: neural tube defects.*Obstet Gynecol.* 2017 Dec;130(6):e279-e280.

LeFevre NM, Sundermeyer RL. Fetal Aneuploidy: Screening and Diagnostic Testing. *Am Fam Physician*. 2020 Apr 15;101(8):481-488.

ACOG Committee on Practice Bulletins. ACOG Practice Bulletin No. 226: screening for fetal chromosome conditions. *Obstet Gynecol.* 2020 Oct;136(4):e48-e69.

Driscoll DA, Gross SJ; Professional Practice Guidelines Committee. Screening for fetal aneuploidy and neural tube defects. *Genet Med.* 2009 Nov;11(11):818-21.