

Communiqué

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Maternal Serum Quad Screening: Review of Laboratory Testing and Clinical Application

Multiple marker serum screening has become a standard tool in obstetrical care to identify pregnancies that may have an increased risk for certain birth defects, including open neural tube defects, trisomy 21 (Down syndrome), and trisomy 18 (Edwards syndrome). These screens are performed by measuring analytes in maternal serum that are produced by the baby and the placenta. The analyte values derived from the assay, along with maternal demographic information (eg, age, gestation, diabetic status, and race) are used in a complicated mathematical model to derive a risk estimate (ie, the calculated risk). The laboratory establishes a specific cutoff for each condition, which classifies the result 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 rather indicates that further evaluation should be considered.

Screening vs Diagnostic Testing

A screen is utilized to test a specific population (in this case pregnant women) to identify individuals who may be at an increased risk for a specific abnormality. Diagnostic testing involves testing a particular individual to rule in/out a specific diagnosis. Effective screening tests should be useful to evaluate large populations and reliably identify a subset of individuals at high risk who are candidates for diagnostic testing. An effective screening program must meet the following requirements:

- Disorder - well defined
- Prevalence - known
- Natural history - medically important with effective remedy
- Financial - cost-effective
- Facilities - available or easily installed
- Test performance
 - simple and safe
 - distributions of test values in affected and unaffected individuals known and extent of overlap is small
 - cutoff level defined
- Ethical - procedures following a positive result are acceptable to laboratories, government agencies, public health departments, and patients



Gina exhibits the classic features of Down syndrome including:

- flat facial profile with depressed nasal bridge
- upward slant to the eyes
- tongue may appear large in relationship to size of mouth
- epicanthal folds
- short neck
- shortened long bones of the arms

The Quad Screen

In the early years of maternal serum screening, alpha-fetoprotein (AFP) was the only analyte studied for early detection of fetal abnormalities. As science and technology marched forward, additional analytes were added and multiple marker maternal serum screens were introduced. Today, second trimester multiple marker maternal serum screens are available with up to 4 markers studied. There are several versions of the 4-marker maternal serum screen available in the market today, utilizing different analyte combinations.

Mayo Medical Laboratories (MML) offers [Alpha-Fetoprotein \(AFP\), Four Marker Screen, Maternal Serum #81149](#), commonly called the “quad screen.” This assay tests for levels of AFP, total beta-human chorionic gonadotropin (total beta-hCG), unconjugated estriol (uE3), and free alpha-human chorionic gonadotropin (free alpha-hCG). This test provides a risk assessment for the pregnancy for Down syndrome, trisomy 18, and neural tube defects.

Some studies have shown a relationship between serum screening results and adverse pregnancy outcomes. However, according to the American College of Medical Genetics: “... routine maternal serum AFP screening prior to amniocentesis for the sole purpose of screening for such pregnancy complications is not recommended because there is no consensus on the methods for surveillance should an abnormal result be detected. The sensitivity or specificity of predicting adverse perinatal outcomes using antenatal electronic fetal monitor testing, serial ultrasound studies for measuring growth or umbilical-cord blood flow or biophysical profile is not known in cases of unexplained elevated maternal serum AFPs, nor has the effectiveness of such monitoring been demonstrated.”¹

Down Syndrome

Down syndrome has an incidence of 1 in 800 live births. Every pregnant woman has a risk of having a child with Down syndrome; however, the risk of a Down syndrome pregnancy increases with increasing maternal age. Down syndrome is the result of an extra copy of chromosome 21 (trisomy 21). (See Karyotype 1.) The clinical features include characteristic facial features, mental retardation, hypotonia, as well as heart and other birth defects. According to the National Institutes of Health (NIH), Down syndrome is one of the most common causes of mental retardation in industrialized countries. A recent report indicated that the average life span for Down syndrome patients has nearly doubled to 49 years.²

Trisomy 18

Trisomy 18 has an incidence of 1 in 2400 pregnancies through the second trimester. There are a high percentage of spontaneous terminations, which reduces the incidence of a live birth to 1 in 8000 pregnancies. This disorder is the result of



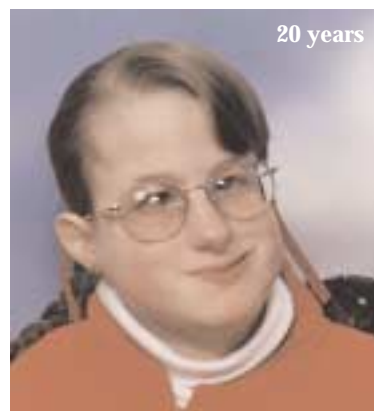
3 months



4 months



5 years



20 years

Shown at several ages, Stacy exhibits the classic features of Edwards syndrome (trisomy 18) including:

- low-set, underdeveloped ears
- small eyes, nose, and mouth
- radial aplasia
- clenched fists with the index finger overlapping the 3rd and 4th digits
- underdeveloped thumbs
- strabismus
- narrow bifrontal diameter
- epicanthal folds

While most infants with Edwards syndrome die within the first year, some survive longer. Stacy, shown here at 20 years of age, has been cytogenetically studied and confirmed trisomy 18. Stacy has never had tissue studies performed to rule out mosaicism.

an extra copy of chromosome 18 (trisomy 18). (See Karyotype 2.) The risk of a trisomy 18 pregnancy increases with increasing maternal age. The clinical features of trisomy 18 include severe mental retardation, birth defects, and a significantly decreased life span. While only 5% survive beyond the first year of life, there are documented cases of trisomy 18 patients living into their 30s.

Neural Tube Defects

Neural tube defects have an incidence of 1-2 in 1000 live births. More than 30% of pregnancies affected by neural tube

defects will result in miscarriage or stillbirth.³

Neural tube defects are the result of incomplete development of the neural tube, which becomes the brain and spinal cord during fetal development. Spina bifida (an open or closed defect along the spine), anencephaly (an open defect involving the absence of a major portion of the brain, skull, and scalp), and encephalocele (generally a closed defect involving a congenital gap in the skull with herniation of brain substance) are neural tube defects, with spina bifida and anencephaly accounting for approximately 90% of neural tube cases. Neural tube defects form early, between the 17th and 30th day after conception.³

The following factors increase an individual's risk for having a pregnancy affected by a neural tube defect:

- **Folic acid deficiency:** folic acid deficiency has been identified as a risk factor for neural tube defects; folic acid supplementation is now recommended prior to conception.
- **Geographic variance:** in the United States, incidence is higher in the South than the North, and also in the East compared with the West.
- **Racial variance:** Caucasians are at the highest risk, followed by Hispanics, with African Americans having the lowest risk.
- **History of maternal disease or exposures:** insulin dependent diabetes mellitus (IDDM), seizures, and other medications are associated with increased risk.
- **Family history:** recurrence risks vary because the neural tube defect may be a component of a genetic disorder or may be due to multifactorial inheritance.

Risk Assessment

A large amount of information is required to provide a risk assessment via maternal serum screening. The quality of the interpretation is affected by the accuracy of this information. The major informational components involved in maternal serum screening are:

- Maternal age, specifically date of birth (for Down syndrome and trisomy 18)
- Gestational age
- Analyte values
- Additional factors that influence analyte values
 - number of fetuses
 - maternal weight
 - diabetic status
 - race
 - in vitro fertilization (IVF) pregnancy

The **calculated screen risks** for Down syndrome and trisomy 18 are derived using a complicated mathematical model that incorporates maternal age-related risk, analyte values, gestational age, and other variables including the patient's race, weight, and diabetic status.

Maternal Age

Every pregnancy involves the risk of having a child with a birth defect. In general, the risk is very low, approximately 3-5% chance of having a child with a birth defect. However, the risk of certain birth defects increase with a woman's age, specifically the risk of Down syndrome, trisomy 18, and other more rare chromosomal problems. For example, during the second trimester of pregnancy, a 25-year-old woman has a risk of approximately 1/1100 of carrying a fetus with Down syndrome. The same risk for a 40-year-old woman is approximately 1/100. It should be noted that maternal age is not a factor in risk assessment for neural tube defects.

The reported **maternal age-related risk** reflects the risk of carrying a fetus with Down syndrome based solely on the age of the mother.

Gestational Age

Gestational age refers to the number of completed weeks in a pregnancy. The range of normal values for each of the analytes measured varies by week of pregnancy. Thus, it is important to accurately determine the gestation of the fetus on the specimen collection date.

A variety of different methods including last menstrual period (LMP), ultrasound dating, and physical examination are used to establish the gestational age. Ultrasound gestation is generally the most accurate form of dating, with first trimester ultrasound gestational dating providing more accurate dating than second trimester ultrasound. Utilization of LMP dating is not always accurate because of variations in monthly menstrual cycles and poor patient recollection of their LMP. Studies have shown that the normal range of analyte values in pregnancies dated by ultrasound exhibit less variance than those dated by LMP.³ Different data sets are used in the risk calculation depending upon the method of dating. In general, ultrasound dating allows for a higher detection rate (percent of all affected cases that are picked up by the screen) and lower initial positive rate.

When providing gestational information to MML, the most accurate form of gestational dating available should be provided, as only 1 gestational date can be used in the risk calculation. **Ultrasound dating is the preferred method.** Both the date of the ultrasound procedure and the gestation on the date the ultrasound was performed are needed (not on the serum collection date-if different). Alternatively, an expected date of delivery (EDD) determined by the ultrasound may be provided. When an EDD is provided, you must indicate whether this is based upon ultrasound dating or LMP. Our laboratory computer system will calculate the gestation on the specimen collection date. If multiple forms of dating are provided, the laboratory will preferentially use dating in the

following order:

1. Ultrasound (or EDD by ultrasound)
2. LMP
3. EDD determined by LMP
4. Physical exam

Analytes Values in Maternal Serum

MML's quad screen (#81149) measures free AFP, uE3, total beta-hCG, and free alpha-hCG in the maternal serum. The analyte values are converted to a multiple of median (MoM) to account for the normal variation in analyte values at various gestations. The MoM is obtained by dividing the patient's serum analyte concentration (at a particular gestational age) by the population median concentration at the same gestation age.

Maternal Serum Alpha-fetoprotein (MSAFP)

AFP is a fetal protein that is initially produced in the fetal yolk sac and liver. The gastrointestinal tract also produces a small amount. By the end of the first trimester, nearly all of the AFP is produced by the fetal liver. The concentration of AFP peaks in fetal serum between 10 and 13 weeks. Fetal AFP diffuses across the placental barrier into the maternal circulation. A small amount is also transported from the amniotic cavity. The AFP concentration in maternal serum rises throughout pregnancy, from the normal nonpregnancy level of 0.20 ng/mL to about 250 ng/mL at 32 weeks gestation.

MSAFP levels (MoM) are higher in pregnancies affected with an open neural tube defect and, on average, lower in pregnancies affected with Down syndrome and trisomy 18.

MSAFP is the only marker used in the risk assessment for neural tube defect; it detects approximately 75-80% of fetuses with open spina bifida and 95% of fetuses with anencephaly.¹

MSAFP testing in the early 1980s was capable of detecting 25-30% of Down syndrome cases. By the late 1980s, MSAFP testing was being combined with other markers and the detection rate increased to approximately 60%. Today's multiple marker serum screen is capable of detecting up to 70% of Down syndrome and up to 80% of trisomy 18 cases.

Estriol

Unconjugated estriol (uE3) is produced in the placenta and the concentration of uE3 in maternal serum increases throughout pregnancy. Levels of uE3 are typically lower in pregnancies affected with Down syndrome and trisomy 18.

Human Chorionic Gonadotropin (hCG) (total beta-hCG and free alpha-hCG)

Human chorionic gonadotropin, another glycoprotein produced in the placenta, consists of an alpha subunit and a

beta subunit. The concentration and proportion of free subunits and intact molecules varies throughout pregnancy. Total beta-hCG levels rise from implantation to about 8 weeks of gestation, plateau from 8-12 weeks, decrease from 12-18 weeks, and then plateau until term. Free alpha levels rise as pregnancy proceeds. Both free alpha- and total beta-hCG are, on average, higher in pregnancies affected with Down syndrome, but lower in pregnancies affected with trisomy 18.

Table 1 summarizes the serum analyte trends for Down syndrome, trisomy 18, and neural tube defects.

Analyte	Trisomy 21	Trisomy 18	NTD
AFP	↓	↓	↑
Estriol	↓	↓	↔
Total beta and free alpha HCG	↑	↓	↔

Table 1. Congenital Disorders and Analyte Levels

Additional Factors That Affect Analyte Values

Analyte levels change according to stage of pregnancy. The differences at varying gestational ages are standardized by calculating a MoM as previously described. There are also other factors that alter the analyte value and unless corrected for, may alter the detection rate and initial positive rate.

Number of Fetuses

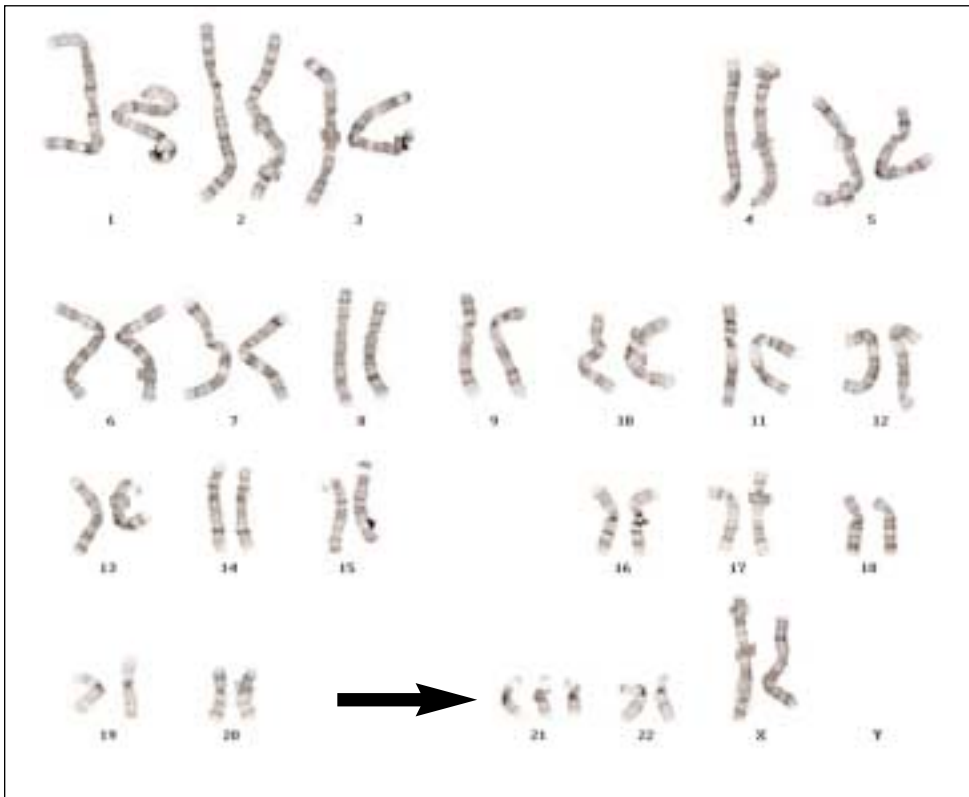
The analytes measured in the quad screen are produced by the fetus and/or the placenta. When multiple fetuses are present, an increased amount of all the analytes are typically present in the maternal serum. When a twin gestation is known, the MoM value for each marker is adjusted by dividing it by the corresponding MoM in unaffected twin pregnancies. Using this method, twin gestations can be classified as either screen positive or screen negative. It is not possible to determine the analyte contribution from each fetus. Given the rarity of data available in twin pregnancies where only 1 fetus is affected with Down syndrome, we are unable to calculate an actual numerical risk in twin gestations. Additionally, we are unable to provide an interpretation for multiple gestations exceeding 2 fetuses.

Weight

The concentration of analytes circulating in the maternal serum varies with a woman's weight. Heavier women have a larger blood volume, which dilutes the analyte concentration. Maternal weights are used to mathematically adjust analyte values for differences in maternal blood volumes.

Diabetic Status

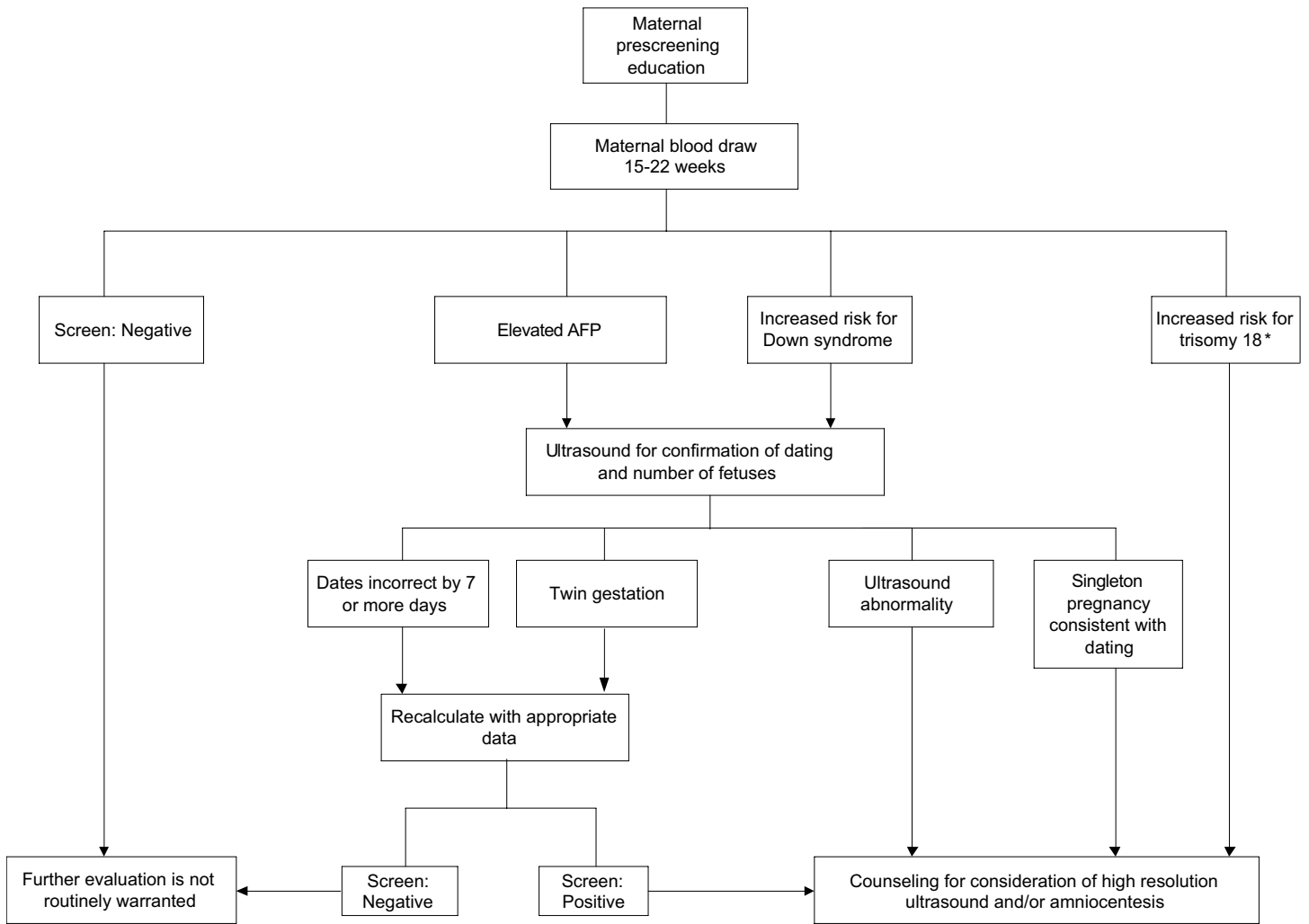
On average, the concentrations of MSAFP, uE3, and free alpha-hCG are lower in women with IDDM. Mothers who have IDDM have a 10-fold higher risk of having a child with a



Karyotype 1. Down syndrome-trisomy 21



Karyotype 2. Edward syndrome-trisomy 18



*Many pregnancies affected with trisomy 18 are small for gestational age. Recalculations that lower the gestational age may decrease the detection rate for trisomy 18.

Figure 1. Maternal Serum Screening Protocol

neural tube defect. The MSAFP levels are lower for IDDM mothers than for Caucasians in general. Given this combination of an increased risk for neural tube defects and a lower level of MSAFP in women with IDDM, measures must be taken to ensure the same detection rate is achieved. Some laboratories use a lower screening cutoff value. Others, MML included, adjust the MoM to account for this factor, thereby maintaining a consistent cutoff for MSAFP.

The MoM value for each marker is adjusted by dividing it by the corresponding MoM in unaffected diabetic pregnancies. Adjusting the MoMs in this way allows for differences in levels of the markers between diabetic and nondiabetic women. A pseudo-risk is then calculated as if the pregnancy were a nondiabetic singleton gestation. The pseudo-risk is compared with the risk cutoff to classify the result as screen positive or screen negative. The pseudo-risk is not the woman's true risk of having a pregnancy with Down syndrome. Neither the true risk nor the detection rate can be calculated, because the distributions of the serum markers are not known in diabetic pregnancies where the fetus is affected with Down syndrome. However, the pseudo-risk yields an initial-positive rate that is similar to that in singleton nondiabetic pregnancies.

Race

Normal variations in MSAFP levels are race dependent. On average, black mothers have MSAFP concentrations 9% higher than nonblack mothers. This difference is adjusted for in the calculation of MoM values and allows for similar detection rates and initial positive rates between blacks and nonblacks.

Blacks have the highest MSAFP levels and the lowest risk for neural tube defects; followed by Asians, who have lower levels of MSAFP and a comparatively increased risk for neural tube defects; while Caucasians have the lowest MSAFP levels and the highest risk for neural tube defects. Other racial differences have not been fully documented and therefore are not currently adjusted. These are grouped together in a nonblack category.

Assisted Reproduction (in vitro fertilization)

Studies have shown that marker levels are altered in pregnancies conceived by IVF.⁴ Specifically, hCG levels are higher and uE3 levels are lower, which increases the initial positive rate for Down syndrome. The laboratory should be informed if a donor egg was used, along with the donor's birth date (to account for the donor's maternal age).

Timing of Testing

Alpha-Fetoprotein (AFP), Four Marker Screen, Maternal Serum #81149 can be performed to screen for Down syndrome

and trisomy 18 between 14 and 22 weeks' gestation. Screening for neural tube defects is available between 15 and 22 weeks; however, the detection rate for neural tube defects is greatest between 16-18 weeks. To maximize screening utility, we recommend specimen collection after 15 weeks' gestation.

Laboratory Established Cutoff Values

Cutoff values are used to determine which pregnancies are at a risk that is high enough to warrant further testing. An important factor in establishing cutoff values is the risk of the follow-up diagnostic procedure typically offered to determine whether a screen positive result is truly an affected pregnancy. Amniocentesis is the most common diagnostic procedure used in the second trimester and has a procedural-related miscarriage risk of approximately 0.5% (1/200). The goal of maternal serum screening is to identify as many high-risk pregnancies as possible, while minimizing the number of invasive procedures and their associated risks (eg, miscarriage) to unaffected pregnancies. For Down syndrome, the cutoff used is a second trimester risk greater than or equal to 1/270. For trisomy 18 the cutoff is 1/100 and for neural tube defects the cutoff is 2.50 MoM.

Interpretation

Down Syndrome and Trisomy 18

Screen Negative - a screen negative result indicates that the calculated screen risk is below the established cutoff of 1/270 for Down syndrome and 1/100 for trisomy 18. A negative screen does not guarantee the absence of trisomy 18 or Down syndrome. The detection rates for Down syndrome are 63% by LMP dating and 70% by ultrasound dating. The detection rate for trisomy 18 is up to 80%.

Screen Positive - a screen positive result indicates that the calculated screen risk exceeds the established cutoff of 1/270 for Down syndrome or 1/100 for trisomy 18. A screen positive result does not provide a diagnosis of trisomy 18 or 21, but indicates that further evaluation should be considered. At the 1/100 risk level, 99 of the pregnancies would be expected to be unaffected. Other explanations for a screen positive result include incorrect gestational dating, normal variation, and other chromosome abnormalities.

Neural Tube Defects

Screen Negative - a screen negative result indicates that the calculated MSAFP MoM falls below the established cutoff of 2.50 MoMs. A negative screen does not guarantee the absence of neural tube defects. Using 2.50 MoM as a cutoff, the detection rate for open neural tube defects is approximately 75-80%.

Screen Positive - a screen positive result indicates that the calculated MSAFP MoM is ≥ 2.50 MoM and may indicate an increased risk for open neural tube defects. The actual risk

depends on the level of MSAFP and the individual's pretest risk of having a child with neural tube defects based on family history, geographical location, and preconception and prenatal use of folate. A screen positive result does not infer a definitive diagnosis of a neural tube defect, but indicates that further evaluation should be considered. Other explanations for an elevated MSAFP include incorrect gestational dating, normal variation, multiple gestation, structural abnormalities of the placenta, abdominal wall defects, chromosome abnormalities, and recent maternal-placental bleeding. Unexplained elevations of MSAFP have also been associated with fetal demise, fetal growth restriction, preeclampsia, and risk of premature delivery.

Recommended Follow-up

Upon receiving maternal serum screening results, all information used in the risk calculation (eg, maternal date of birth, gestational dating, etc) should be reviewed for accuracy by the referring laboratory and clinical staff. If any information is incorrect, MML should be contacted for a recalculation of the estimated risks.

Screen negative results typically do not warrant further evaluation. However, if gestational age differs by more than 7 days, MML should be contacted for a recalculation of estimated risks.

Ultrasound is recommended to confirm dates for neural tube defect or trisomy 21 screen positive results. (Many pregnancies affected with trisomy 18 are small for gestational age. Recalculations that lower the gestational age may decrease the detection rate for trisomy 18). If ultrasound yields new dates that differ by at least 7 days, a recalculation should be considered. If dates are confirmed, high-resolution ultrasound and amniocentesis are typically offered.

Each center offering maternal serum screening to patients should establish a standard testing protocol that includes prescreening and postscreening education, as well as appropriate follow-up for screen positive results. Figure 1. Maternal Serum Screening Protocol is an example of such a protocol.

MML Service

Proper interpretation of maternal serum screening tests relies in large part on the expertise of the laboratory staff. Mayo has an experienced laboratory staff, including board-certified genetic counselors. The genetic counselors work directly with the laboratory to review and ensure the accuracy of patient information provided for maternal serum screening. The counselors work with referring laboratories and physician's offices to resolve any questions or problems. They also serve as patient advocates by providing education and recommendations for follow-up through the patient's referring health care providers.

All positive and unusual results are reviewed by the genetic counselors and called to the ordering physician's office. The genetic counselors and laboratory staff are also available to assist in the interpretation of results and recalculations.

Summary

Maternal serum screening continues to be an important tool in obstetrical care. Maternal serum screening does not provide an absolute positive diagnosis or guarantee a healthy fetus. Rather, the laboratory results must be interpreted within the context of each patient's clinical and personal history. Ongoing education is necessary for providers and patients as new testing strategies and potential applications unfold. Patients should be counseled in a nondirective manner about the benefits and limitations prior to screening. Those with positive screens should receive appropriate counseling to discuss the significance of the results and the available testing options. MML offers the combined services of laboratory staff and genetic counselors to offer comprehensive maternal serum screening and support for our clients.

Please contact a Mayo laboratory genetic counselor or laboratory director at 1-800-533-1710, should you have questions about maternal serum quad screening.

Our thanks to the following individuals and organizations for providing the patient photos:
Jackie Rotondi, Sheila Hebein, and the National Association for Down Syndrome, located at www.nads.org
Barb Vanherreweghe and the Support Organization For Trisomy 18, 13, and Related Disorders (SOFT), located at www.trisomy.org

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Alpha Mannosidase Reference Value Change

As a result of ongoing evaluation of reference ranges, the reference values will change for [Alpha Mannosidase, Leukocytes #8772](#).

New Reference Values

1.04-2.68 U/10¹⁰ cells

Previous Reference Values

1.50-3.33 U/10¹⁰ cells

Arsenic Fractionation Method and Reference Value Changes

Recently a new extraction procedure was implemented for separation of inorganic and organic arsenic. This has resulted in an improved sensitivity and detection limit for [Arsenic Fractionation, Urine #80375](#). As a result, the reference values have been adjusted.

New Method

Liquid-Liquid Extraction/Inductively Coupled Plasma-Mass Spectrometry (ICP-MS)

Previous Method

Chromatographic Separation/Inductively Coupled Plasma-Mass Spectrometry (ICP-MS)

New Reference Values

Inorganic (nondietary) arsenic:

<25 µg/specimen

>25 µg/specimen are considered toxic concentrations.

The reference value is for a 24-hour collection.

Specimens collected for other than a 24-hour time period are reported in units of µg/L, for which reference values are not established.

Organic arsenic: All results are normal (reported as µg/specimen)

Previous Reference Values

Inorganic (nondietary) arsenic:

<25 µg/specimen

>26 µg/specimen are considered toxic concentrations.

The reference value is for a 24-hour collection.

Specimens collected for other than a 24-hour time period are reported in units of µg/L, for which reference values are not established.

Organic arsenic: All results are normal (reported as µg/specimen)

Lead Test Method Change

Lead with Demographics, Blood #15070 was converted to a new platform. Previously performed utilizing flameless atomic absorption spectrometry, the test is now run utilizing inductively coupled plasma/mass spectrometry (ICP-MS). There are several major advantages for lead analysis by ICP-MS including less variation in results, greater sample throughput, less instrument downtime, and the ability to examine isotope ratios.

Bone Marrow DNA Typing Transplant Evaluation Name and Method Changes

To more accurately reflect the nature of the test, **Bone Marrow DNA Typing Transplant Evaluation, Post-Transplant #9495**, has been renamed [Chimerism Analysis #9495](#). In addition, the test has been converted to a more rapid polymerase chain reaction (PCR) method that is more sensitive, can be utilized for same sex transplants, and cuts analytic time in half (from 14 days to 7 days). The new method utilizes more markers, therefore result reports will provide more interpretive information.

New Method

PCR For Short Tandem Repeat (STR) Markers

Previous Method

Restriction Fragment Length Polymorphism by Southern Blot

Testosterone Tests Changes

As part of MML's ongoing review process, changes have been made to [Testosterone, Total, Serum #8533](#) and [Testosterone, Total and Free, Serum #8508](#). The reference value for adult women has changed. In addition, the specimen volume has been reduced for #8533. Service has also been expanded, with both tests now available Monday through Saturday.

New Reference Values

Females: ≥19 years 12-72 ng/dL

Previous Reference Value

Females: ≥19 years 20-80 ng/dL

Test #8533 ONLY

New Specimen Required

1.0 mL of serum refrigerated

Previous Specimen Required

2.5 mL of serum refrigerated



Q: Why doesn't Mayo provide a neural tube defect (NTD) risk assessment prior to 15 weeks gestation?

A: There is little published data on AFP levels in NTD pregnancies at 14 weeks. The available data indicates that the detection rate for NTDs is significantly lower prior to 15 weeks gestation. The optimal detection rate for NTD is achieved between 16-18 weeks. In the absence of evidence that the NTD screening is effective at earlier gestations, we feel it is misleading to provide a risk assessment at gestations in which the detection rate is substantially lower.

Abstracts of Interest

Thrombotic Thrombocytopenic Purpura and Hemolytic Uremic Syndrome

Michelle A. Elliott, MD, And William L. Nichols, MD

Thrombotic thrombocytopenic purpura (TTP) and hemolytic uremic syndrome (HUS) are multisystemic disorders that are characterized by thrombocytopenia, microangiopathic hemolytic anemia, and ischemic manifestations, resulting from platelet agglutination in the arterial microvasculature. Until the introduction of plasma-based therapy, TTP was associated with a mortality rate greater than 90%. Current outcomes of TTP and HUS have improved dramatically with the use of plasma exchange, which should be initiated promptly at diagnosis. Recent evidence suggests that deficiency of a specific plasma protease responsible for the physiologic degradation of von Willebrand factor plays a pathogenic role in a substantial proportion of familial and acute idiopathic cases of TTP. Although multiple triggers, such as infection, drugs, cancer, chemotherapy, bone marrow transplantation, and pregnancy, are recognized, knowledge of the pathogenesis of TTP and HUS in relationship to these disorders remains incompletely understood and continues to evolve. While uncommon, TTP and HUS are of considerable clinical importance because of their abrupt onset, fulminant clinical course, and high morbidity and mortality in the absence of early recognition and treatment.

Mayo Clinic Proceedings 2001;76:1154-1162

Meeting Calendar

Interactive Satellite Programs . . .

September 17, 2002

Advances in Wound Healing

Presenter: Steve Kavros, DPM - Moderator: Robert Kisabeth, MD

Upcoming Education Conferences . . .

Practical Spirometry

September 13-14, 2002

Holiday Inn Chicago City Centre
Chicago, Illinois

For a complete listing of all the courses offered throughout the year, contact the Mayo Reference Services Education Office at 1-800-533-1710 or 507-284-8742.

Communiqué

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