

Lab Updates

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 **UMassMemorial**

Laboratories

Second Trimester Maternal Serum Alpha-Fetoprotein (MSAFP) Screening for Open Neural Tube Defects (ONTD)

ONTD's are congenital structural abnormalities of the brain (Anencephaly) and vertebral column (spina bifida) that occur either as an isolated malformation, along with other malformations, or as part of a genetic syndrome. They result from a failure in the closure of the developing fetal nervous system within the first month of pregnancy. The cause of non-syndromic ONTD's is not known. Scientists believe that genetic, environmental and nutritional components all play an important role. ONTD's occur in 1-2 per 1000 pregnancies and are the second most common major congenital anomaly worldwide. Anencephaly accounts for one half of all cases of ONTD and is incompatible with life. With treatment, 80-90% of infants with Spina Bifida survive with varying degrees of disability. Most importantly, ONTD's are among the few birth defects for which primary prevention is possible (ACOG Practice bulletin 44:203).

MSAFP test screening is clinically useful for identifying a fetus' risk for ONTD's. The opening in the fetal neural tube allows AFP in the fetal circulation to leak across the defect causing higher than normal levels of AFP in maternal serum and amniotic fluid (AF). Women carrying fetuses with closed neural tube defects generally have a serum and AF AFP level within the normal limits.

Many other conditions are known to be associated with increased maternal serum AFP including but not limited to: Multiple gestations, Incorrect gestational dating, Miscarriage risk, Stillbirth, Intrauterine growth retardation (IUGR), Fetal complications. The etiology of increased maternal serum AFP in pregnancies destined to manifest these conditions is undefined.

UMass Memorial Labs offers first trimester (MSFIRST) for Down syndrome (DS) and Trisomy -18 (T-18) and second trimester (QUAD) and Combined first and second trimester (Sequential and Integrated) tests for ONTD, DS and T-18.

Second trimester Maternal Screen ONTD test (MSAFP) is recommended as a follow up for first trimester screen test (MSFIRST). This is because MSFIRST screens for DS and T-18 only. Screening for ONTD is included in 2nd trimester Integrated (MSSINT2), Sequential (MSSEQ2) and QUAD (MSQ) maternal screen tests, thus if one of these aforementioned 2nd trimester screens is performed the MSAFP screening test is unnecessary. This second trimester MSAFP test does not screen for DS or T-18.

- Second trimester MSAFP maternal serum test is performed between 15 w 0 d – 22 w 6 d of pregnancy. The best time to screen is between 16 w – 18 w of pregnancy.



Results will be reported as “Normal” or “Abnormal” along with “Pre-Test” and “Post-Test” risk estimates. The ONTD “Pre-test” risk estimate is based on the background of ONTD prevalence. There is currently no accurate data available on the current prevalence of ONTD's. Currently we set the background prevalence of spina bifida and anencephaly as 1 in 1000 live births. Please note that women who take folic acid immediately prior to pregnancy will have a reduced “Pre-test risk” (up to 70%).

The ONTD “Post-test” risk estimate is derived from a mathematical model that is dependent upon maternal demographic information (age, weight, gestational age, diabetic state, IVF pregnancy, previous pregnancy with ONTD, and race) together with the serum AFP result (Cut off 2.5 MoM).

Error in the estimates of gestational age is the most common reason for a false positive result. A test result initially based upon the last menstrual period (LMP) will be adjusted only if subsequent ultrasound estimation of gestational age is substantially different (> or = 10 days) from menstrual dating. Prenatal lab screening is not diagnostic; the intent of these screening tests is to enable



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pregnant women to make informed decisions regarding the pregnancy and be better prepared in the event of the birth of an affected infant.

Effective February 13, 2012, UMass Laboratories will begin to perform 2nd trimester MSAFP only screening (Mnemonic: MSAFP). After this date we will no longer be sending specimens for ONTD screening to a reference laboratory. There are no changes in specimen collection requirements, One full Gold/SST tube (Serum only). The specimen must be accompanied by a completed requisition. The ONTD screening test will be performed daily, Monday through Friday, with a turn-around time of one to five days.

Test Requirements:

The blood must be sent to the Laboratory along with a completed requisition. The test requisition must be filled out completely as test interpretation is dependent upon this information (age, weight, gestational age, diabetic state, IVF pregnancy, previous pregnancy with ONTD, and race); therefore results may be delayed if information is not provided or missing.

For any questions regarding methodology and interpretations, please contact:

- Dr. Nichole Korpi-Steiner, Associate Director, Prenatal Lab Testing at 774-442-9634 or via email at Nichole.Korpi-Steiner@umassmemorial.org
- Dr. L.V. Rao, Sr. Director, Clinical Laboratory Operations at 774-442-9615 or via email at Lokinendi.Rao@umassmemorial.org
- Ms. Melissa Brown, Prenatal Lab Testing Clinical Application Specialist at 774-442-9636 or via email at Melissa.Brown2@umassmemorial.org
- Ms. Judy Barron, Manager of Automated Chemistry at 774-442-9616 or via email at Judy.Barron@umassmemorial.org
- **Genetic counselors** are available for questions through client services 508-334-2863.

Change in Reference Range for Red Cell Distribution Width (RDW) upon Revalidation

Effective January 12, 2012, reference range of Red cell distribution width (RDW) will be 12.1 - 14.6 %. The old reference range was 12.1 – 14.0 %.

Changes in Fetal Lung Maturity Testing

Fetal lung maturation is one of the last developmental processes occurring during the third trimester of pregnancy. Neonatal respiratory distress syndrome (RDS) is a major cause of morbidity and mortality among premature infants and results from insufficient amounts of pulmonary surfactant in the fetal airways. Testing for fetal lung maturity (FLM) is indicated when elective deliveries are planned before 39 weeks of gestation. Testing is unnecessary for well documented pregnancies \geq 39 weeks of gestation (lung maturity is likely) and in pregnancies $<$ 32 weeks of gestation (lung immaturity is likely).

Tests most commonly used to assess fetal lung maturity include surfactant/albumin ratio (TDx-FLM II), lecithin/sphingomyelin (L/S) ratio, lamellar body count, and detection of phosphatidylglycerol (PG). Studies have indicated that all FLM tests are better at predicting the absence rather than the presence of respiratory distress.

The surfactant/albumin ratio test is based on the principle of fluorescence polarization and it uses an automated analyzer to quantitate the competitive binding of a fluorescent dye to both surfactant and albumin in a sample of amniotic fluid. The threshold for maturity is 45 mg of surfactant per gram of albumin. **The manufacturer of TDx-FLM II test is discontinuing this assay at the end of the year 2011 and there are currently no other available tests for measuring surfactant/albumin ratio.**

The lamellar body count (LBC) is a well recognized alternative method for detecting FLM directly by measuring surfactant



production. Lamellar bodies are densely packed layers of phospholipid that represent storage for pulmonary surfactant. LBC is determined by automated hematology analyzers due to the similarity in size of lamellar bodies and platelets. Studies have indicated that LBC test is as accurate as TDx-FLM II in predicting RDS.

Effective January 9, 2012 UMass Memorial Labs will start offering LBC testing to replace TDx-FLM II assay. The test mnemonic is “LBC” and minimum volume of amniotic fluid required for the test is 2 mL. Unacceptable samples include vaginal pools containing mucous, samples

that are grossly bloody or contain meconium, and frozen samples. Test interpretation is as follows:

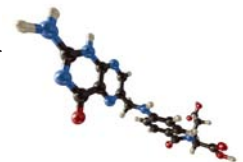
Lamellar Body Count	Interpretation
\leq 14 K particles/ μ L	Immature
15 – 59 K particles/ μ L	Intermediate
\geq 60 K particles / μ L	Mature

If you have questions, comments or suggestions, please contact:

- Dr. Hongbo Yu, Director of Hematology at 774-442-9635 or via email at Hongbo.Yu@umassmemorial.org
- Dr. M. Rabie Al-Turkmani, Associate Director Immunology and Hematology at 774-442-9663 or via email at MRabie.Alturkmani@umassmemorial.org
- Ms. Diane Connor, Manager of Hematology at 774-442-9091 or via email at Diane.Connor@umassmemorial.org

Changes Serum Folate Reference Range

Folate refers to all derivatives of folic acid. Folate is an essential vitamin present in a wide variety of foods such as dark leafy vegetables, citrus fruits, yeast, beans, eggs, and milk. Folate is vital to normal cell growth and DNA synthesis. A folate deficiency can lead to megaloblastic anemia and ultimately to severe neurological problems. Folate levels in both serum and red blood cells are used to assess folate status. The serum folate level is an indicator of recent folate intake. RBC folate is the best indicator of long term folate stores. A low RBC folate value can indicate a prolonged folate deficiency.



Serum folate is a relatively nonspecific test. Low serum folate levels may be seen in the absence of deficiency and normal levels may be seen in patients with macrocytic anemia, dementia, neuropsychiatric disorders, and pregnancy disorders.

The manufacturer of the Folate assay restandardized the calibrators by measuring accuracy to WHO International standard 03/178.

Effective January 9, 2012, the following changes will be made to the serum folate assay due to this restandardization.

- The new reference range is $>$ 5.9 ng/mL.
- Based on the validation studies done by UMass Lab and the manufacturer, the patient sample test results will shift upward by approx 30-45%.
- Folate Deficiency is defined values less than 4.0 ng/mL (WHO technical consultation on folate deficiency). Values between 4.0-5.9 ng/mL are considered indeterminate.

If you have questions, comments or suggestions, please contact:

- Dr. L.V. Rao, Sr. Director, Clinical Laboratory Operations at 774-442-9615 or via email at Lokinendi.Rao@umassmemorial.org
- Ms. Judy Barron, Manager of Automated Chemistry at 774-442-9616 or via email at Judy.Barron@umassmemorial.org

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Cystic Fibrosis Mutation Testing:

UMass Memorial Clinical Laboratories offers two types of Cystic Fibrosis (CF) carrier testing:

1. CF Basic Screen Panel (Mnemonic: CFIB)

This panel is intended for women with no family history of CF. This panel screens for 41 known CF mutations. When heterozygous or homozygous for D1270N is detected, an automatic reflex will invoke the CF3ADD test for three additional variants: V201M, R1070W and R74W. This reflex will provide clarification as to whether a D1270N variant, occurs by itself and is benign, or whether it is a part of a complex CFTR mutation allele [R74W+R1070W+D1270N] or [R74W+V201M+D1270N].

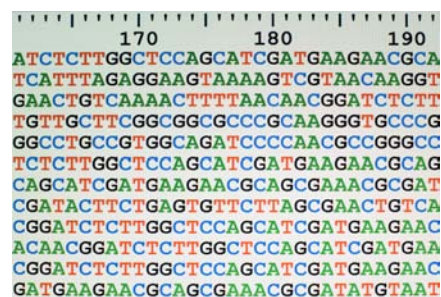
2. CF100 PLUS Panel (Mnemonic: CF100P)

This panel is intended for carrier screening for males when their partner was heterozygous for CF, individuals with family history, diagnostic testing and infertility testing. This panel screens for 124 mutations. This test was previously sent out to a reference lab (Genzyme) which offered testing for 97 mutations. CF100 plus Panel replaces the Genzyme CF analysis 97 mutations panel.

The Genzyme CF analysis 97 mutations panel (mnemonic: GENZCF) is no longer available through UMass Memorial Hospital Laboratories.

If you need help in choosing the appropriate CF test, Please contact a Genetic Counselor at 508-334-2863.

Please supply the information on patient's ethnicity, indication of testing, family history and pregnancy for both CFIB and CF100P orders. A signed consent form is required for carrier screening.



If you have questions, comments or suggestions, please contact:

- Dr. Edward Ginns at 508-856-8134 or via email at Edward.Ginns@umassmed.edu
- Dr. Marzena Galdzicka at 508-856-4384 or via email at Marzena.Galdzicka@umassmed.edu