

# Lab Updates

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March 2010

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# Changes in Quad Maternal Screen Test (QUAD)

**M**aternal serum screening is a valuable tool in prenatal management and is used to identify pregnancies at increased risk for certain birth defects and chromosomal abnormalities. Prenatal screening is not diagnostic; rather it is designed to identify those individuals with increased risk who might benefit from additional diagnostic testing.

The “Quad Marker” screen test is available during pregnancy (between 15 weeks 0 days and 22 weeks 6 days) to screen for fetal open neural tube defect (ONTD), Down syndrome (Trisomy-21) and Edwards Syndrome (Trisomy-18). The four analytes measured in the quad marker test are inhibin A (INH), unconjugated estriol (UE3), human chorionic gonadotropin (HCG) and alpha fetoprotein (AFP). The multiples of median (MoM) values are calculated for each of these analytes and these values are combined with maternal age at the time of delivery to determine the Down syndrome risk. Trisomy-18 risk is based on age, AFP, UE3 and HCG and ONTD risk assessment is based on AFP levels only. The quad marker test identifies 80% of affected pregnancies.



Photo: Kevin Vance

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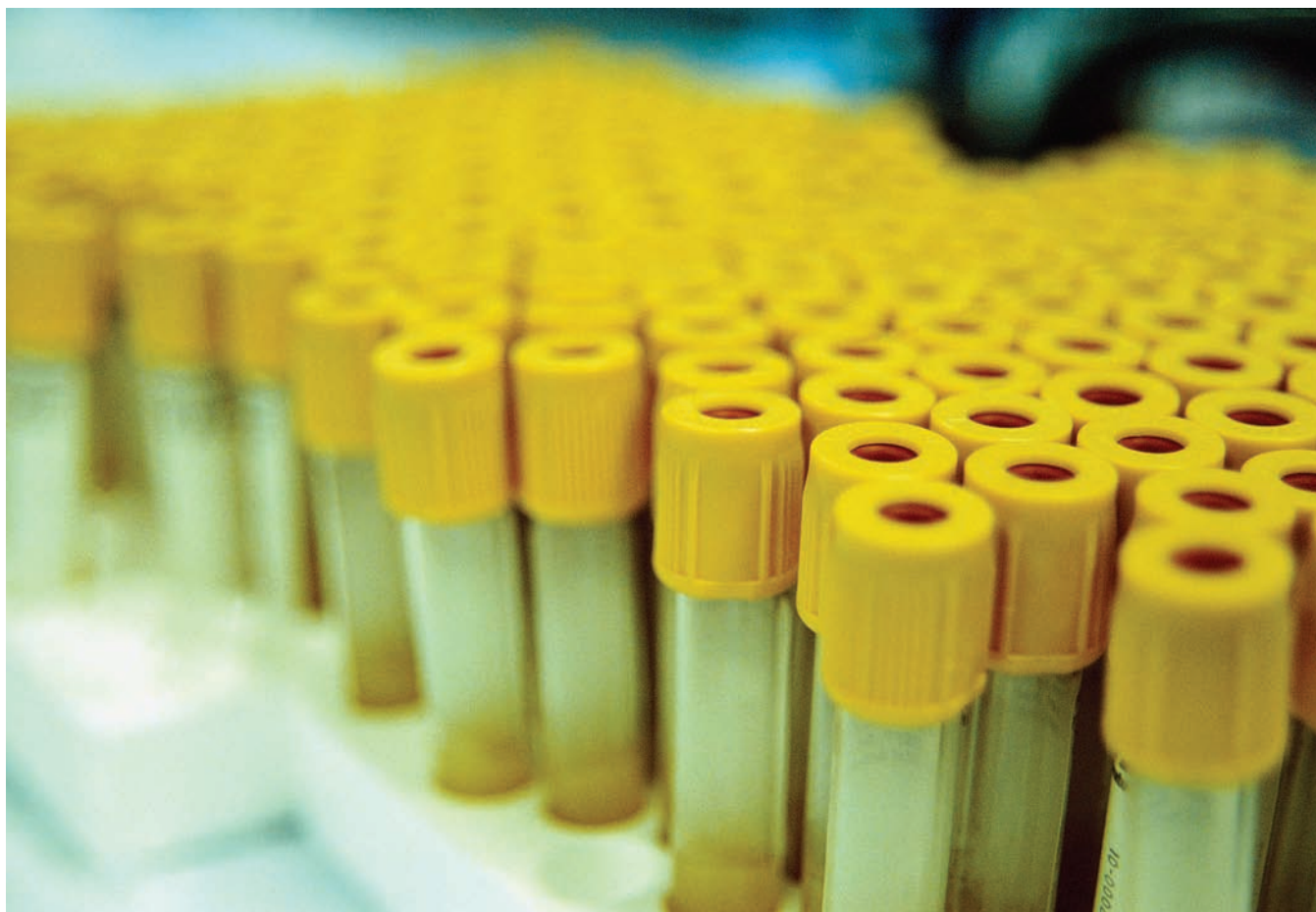
**ONTD's** are congenital structural abnormalities of the brain (Anencephaly) and vertebral column (spina bifida) that occur either as an isolated malformation, along with other malformations, or as a part of genetic syndrome. The cause of ONTD's is not known. Scientists believe that genetic, environmental 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).

**Down syndrome** is the most common cause of severe disability in children, with a live birth incidence of 1 in 700. It arises from the presence of an extra copy of chromosome 21 in the cells of the fetus. Mental retardation, characteristic features of the face and medical problems such as heart defects occur as a result of this extra chromosome 21. About 40% of pregnancies with Down syndrome will miscarry between 11 weeks and term, but 9 out of 10 affected babies who reach term will survive the first year and about one half of these individuals will reach 60 years of age.

**Trisomy-18** is a rare (birth prevalence about 1 in 7000) and usually fatal abnormality which arises from an extra copy of chromosome #18 in the cells of the fetus. The prevalence is 3–5 fold higher in the first and second trimesters than at birth because many affected fetuses die *in utero* with advancing gestation. Trisomy-18 causes severe mental retardation and birth defects. Only 10% of live borns with this condition will reach one year of age.

**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; therefore results may be delayed if information is not provided or missing. Maternal demographic information such as age, weight, gestational age, diabetic state and race is used together with the results of the four quad marker tests in a mathematical model to derive a risk estimate for each condition to identify women at increased risk of having an affected child. Results will be reported as “Normal” or “Abnormal” along with “Pre-Test” and “Post-Test” risk for each condition.





A screen “**Abnormal**” result indicates that the value obtained exceeds the established cut off. A positive result occurs when the risk for Down syndrome equals or exceeds 1 in 150 and/or when results for Trisomy-18 risk equals or exceeds 1 in 100. For ONTD the AFP MoM cut off is 2.5.

A screen “**Normal**” result means that the risk of pregnancy with Down syndrome or Trisomy-18 is below the specified risk cut off and/ or AFP levels are less than 2.5 MOM. **A normal test result does not exclude the possibility of an affected pregnancy.**

The ONTD “Pre-test risk” estimate is based on the background of NTD 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%). ONTD “Post-test” risk estimates are based on a single AFP MoM cut-off. For diabetic pregnancies, AFP MoM values are divided by 0.88, and this adjusted AFP MoM value is compared with the cut-off.

A woman’s Pre-test risk of Down syndrome is determined based on chronological age and history of previous Down syndrome pregnancy. The pre test risk of Trisomy-18 is often estimated as 1/10 of the Down syndrome risk.

**Effective March 8, 2010**, UMass Laboratories will begin to perform “Quad Marker” screens (**Mnemonic: MSQ**). After this date we will no longer be sending specimens for quad

marker testing to a reference laboratory. There are no changes in Specimen collection requirements, One full Gold/SST tube (Serum only). Specimen must be accompanied by a completed requisition. The quad marker test will be performed daily, Monday through Friday, with a turn around time of one to three days.

**This test will be performed only between 15 weeks 0 days and 22 weeks 6 days of pregnancy. The best time to screen is between 16–18 weeks of pregnancy.**

Error in the estimates of gestational age is the most common cause 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.

**For any questions regarding methodology and interpretations, please contact:**

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Genetic counselors are available for questions through client services 508-334-2863.

# Hemoglobin A1c as an Option for Diagnosing Diabetes

## *Official endorsement made by the American Diabetes Association*

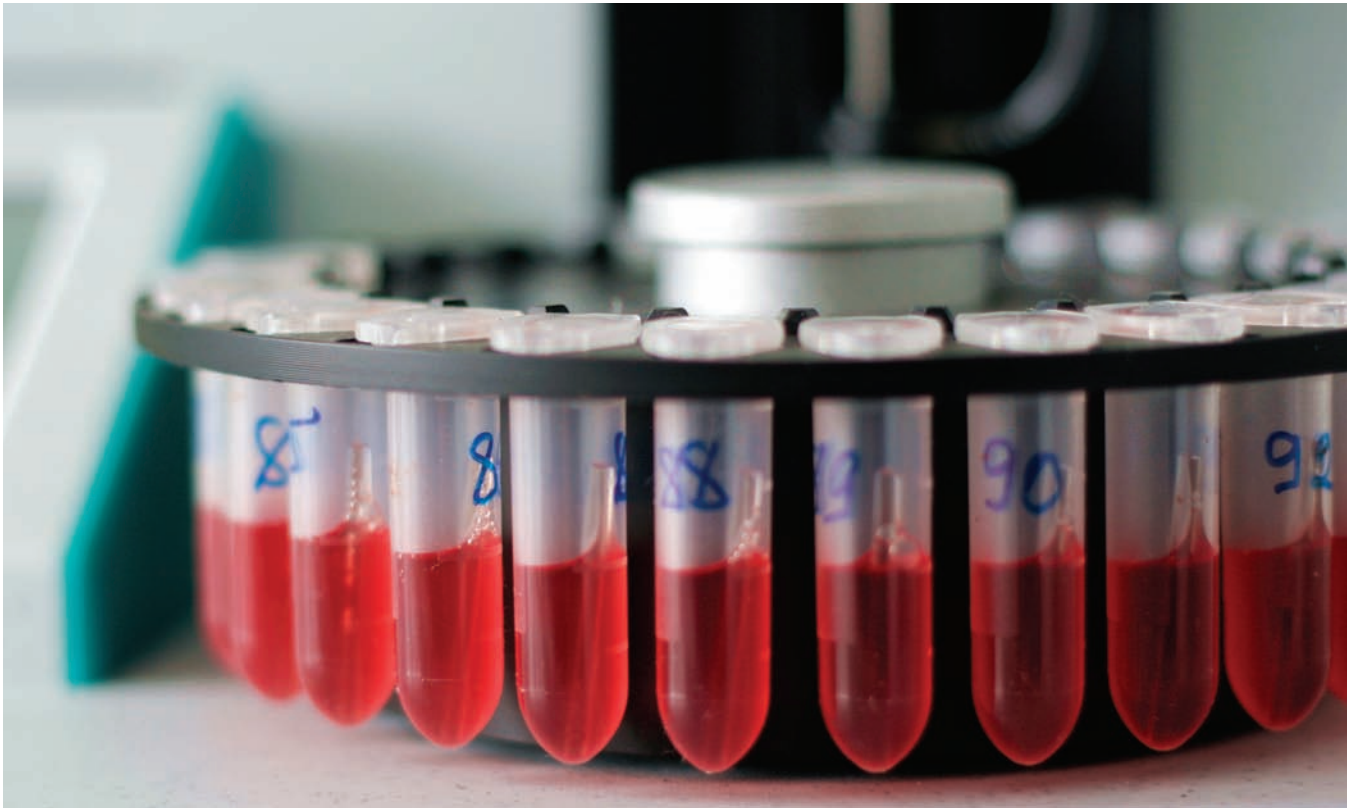


American Diabetes Association (ADA), the International Diabetes Federation (IDF), and the European Association for the Study of Diabetes (EASD) have joined forces to recommend the use of the hemoglobin A1C assay for the diagnosis of diabetes.

In its *Standards of Medical Care in Diabetes*, the ADA for the first time in 2010, officially endorsed the use of HbA1c as one of four options for diagnosing diabetes, with a cut-off of 6.5% or greater. Recommendations for use of the three previous diagnostic criteria remain unchanged, including a fasting plasma glucose (FPG) of 126 mg/dL or above, a 2-hour plasma glucose of 200 mg/dL or greater following a 75-g oral glucose tolerance test, or a random plasma glucose of 200 mg/dL or greater in an individual with classic symptoms of hyperglycemia.

The committee has determined that an A1C value of 6.5% or greater should be used for the diagnosis of diabetes. Along with the 6.5% cutoff for diabetes diagnosis, the ADA now categorizes patients with HbA1c levels of 5.7%–6.4% under the new heading “Categories of Increased Risk for Diabetes,” replacing “Diagnosis of Pre-Diabetes.” This group is defined as having impaired fasting glucose levels of 100 mg/dL to 125 mg/dL or impaired glucose tolerance (2-hr OGTT values of 140 mg/dL to 199 mg/dL) or A1C values between 5.7–6.4%.





Their recommendations include:

- A1C test should be performed at least two times a year in patients who are meeting treatment goals (and who have stable glycemic control).
- A1C test should be performed quarterly in patients whose therapy has changed or who are not meeting glycemic goals.
- Lowering A1C to below or around 7% has been shown to reduce micro vascular and neuropathic complications of type 1 and type 2 diabetes. Therefore, for micro vascular disease prevention, the A1c goal for nonpregnant adults in general is <7%.
- Use of point-of-care testing for A1C allows for timely decisions on therapy changes, when needed.

The A1C has several advantages to the fasting plasma glucose, including greater convenience, since fasting is not required. In addition, it has greater pre-analytical stability, less day to day variations during periods of stress and illness. As with many diagnostic tests a test result diagnostic of diabetes should be repeated to rule out any error, unless the diagnosis is clear on clinical grounds. In scenarios, where two different tests (FPG and A1C) are available for the same patient and both are above diagnostic threshold, the diabetes diagnosis is confirmed. If two different results are discordant, the test whose result is above the diagnostic cut point should be repeated, and the diagnosis is based on the confirmed test.

**Effective March 15, 2010**, the new ADA recommended A1C reference ranges will be reported with every patient test result. The normal range will be less than <5.6%. All values above 5.6% will be flagged. There will be canned comment suggestive of Diabetic range (> 6.5%) and increased risk for Diabetes (5.7%–6.4%). There are no changes in specimen collection requirements.

**Reference:** “American Diabetes Association Clinical Practice Recommendations: Executive Summary”: *Standards of Medical Care in Diabetes – 2010: Diabetes Care* 2010;33, suppl.1: S11-S69.

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

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# Changes in HIV (OHIV) Serology Testing

Current CDC recommendations advocate for routine HIV testing as a part of the normal standard of care provided to patients, regardless of the patient's motivation for seeking services at the health facility or whether the patient presents symptoms of underlying HIV infection. Massachusetts General Law c.111, 70F precludes health care providers from testing patients for HIV infection without written informed consent. Therefore, all HIV screening must be "opt-in-screening". **The testing may be delayed or canceled if informed consent is not submitted or incompletely filled at the Physician's office/ clinic.**

HIV serology testing performed at clinical laboratories is currently being reported as "Retroviral Serology".

**Effective March 22, 2010**, HIV serology test results are reported as "HIV-1, 2 Antibodies". All Positive test results are automatically sent for Western Blot confirmation.

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

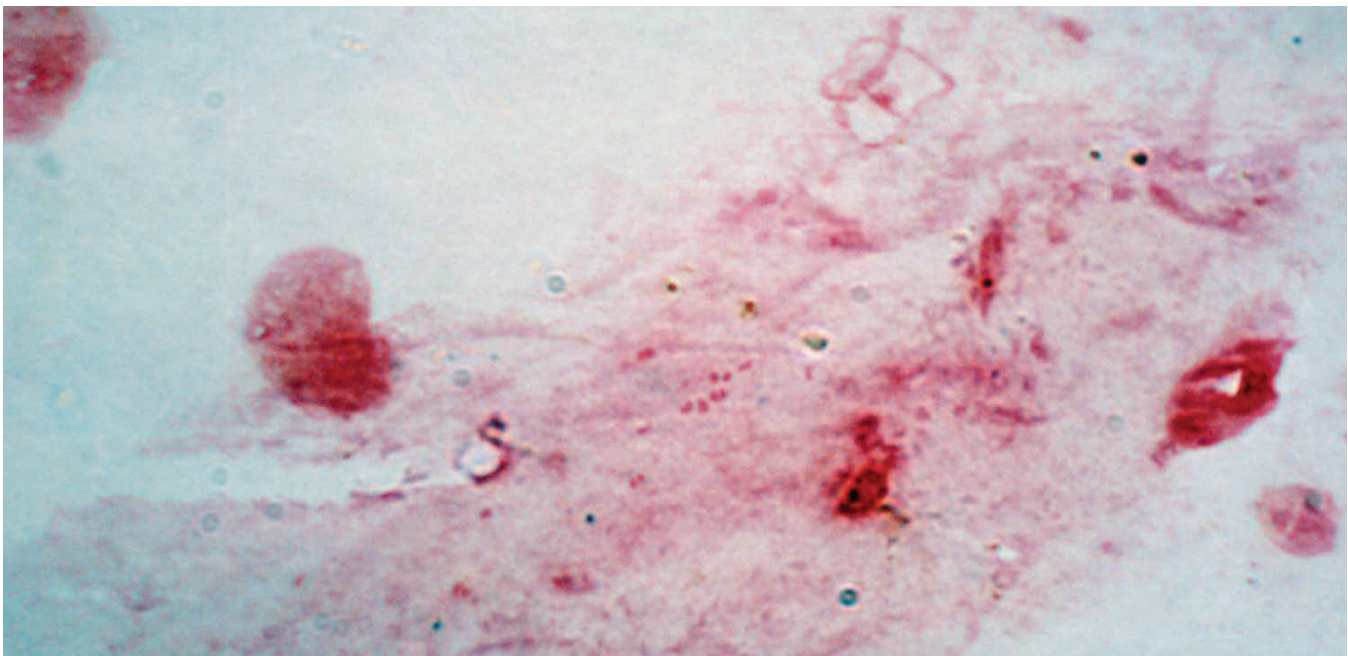
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*Providing a higher level of service. If you don't believe it, put us to the test!™*

## We are one of the largest laboratory providers in New England

UMass Memorial Laboratories has opened a Patient Service Center (phlebotomy draw station) at Stony Creek Medical Center, 6 Business Park Drive, Suite 203, Branford, Connecticut.

## The vision of UMass Memorial Laboratories is:

- To be a leading provider of laboratory services throughout New England, meeting the needs of patients and providers in the region, and
- To be one of the top ten academic medical center-based laboratories in the United States



## **Branford Connecticut PSC**

### **Stony Creek Medical Center**

**6 Business Park Drive, Suite 203, Branford, CT**

Branford/Stony Creek PSC is located at 6 Business Park Dr., Branford, CT.

The hours are Monday through Friday 7:30am-4:00pm.

The phone number at Branford PSC is 203-315-4907.