

Lab Updates

These updates can also be found on our web site: <http://www.ummlabs.org>

June 2006

LYME DISEASE TESTING

Lyme Disease is a systemic illness resulting from an infection with the spirochete *Borrelia burgdorferi*. The disease is most prevalent in children 2 to 15 years of age and in adults 30 to 59 years of age. The onset of the clinical presentation of Lyme Disease typically occurs within 7 to 10 days after a tick bite, with a reported range of 1 to 36 days. Most patients (60-80%) develop the early, localized form of Lyme Disease, which is characterized by *erythema migrans* and influenza like symptoms.

The diagnosis of early Lyme Disease can be made on clinical grounds alone in the presence of classic *erythema migrans*. It is important to be certain of the dermatologic diagnosis since other skin lesions, such as fixed drug eruptions, can look like *erythema migrans*. No laboratory studies are indicated in patients with *erythema migrans*, particularly if there is a history of tick bite, as serological tests are likely to be negative this early in the course of disease.

The antibody response to *Borrelia burgdorferi* infection develops slowly, and only one half of the patients with early stage Lyme Disease will have a positive serology. The Immunoglobulin M (IgM) and G (IgG) antibodies appear 2 to 4 and 4 to 6 weeks, respectively, after the onset of *erythema migrans* and peak at 6 to 8 weeks. Although IgM usually declines to very low levels after 4 to 6 months of illness, IgG remains present at low levels despite successful treatment.

Lyme Disease should never be diagnosed based upon serologic or other laboratory evidence of exposure to *Borellia burgdorferi* in the absence of historical and physical evidence that suggest the diagnosis. In this setting, most "positive" serologic results will be false positives. Serologic confirmation of the diagnosis is indicated when the clinical presentation is not clearly diagnostic, as, for example, when neurologic, cardiac, or arthritic complications occur without a recent or current history of *erythema migrans*.

The Centers for Disease Control and Prevention (CDC) and the Association of State and Territorial Public Health Laboratory Directors (ASTPHLD) recommend a two-test approach for active disease and for previous infection using a sensitive enzyme immunoassay (EIA) or immunofluorescent assay (IFA) followed by a Western immunoblot as the algorithm of choice. All specimens positive or equivocal by a sensitive EIA or IFA should be tested by a standardized Western immunoblot. **Specimens negative by a sensitive EIA or IFA need not be tested further.** When Western immunoblot is used during the first 4 weeks of disease onset (early Lyme Disease), both IgM and IgG procedures should be performed. A positive IgM test result

alone is not recommended for use in determining active disease in persons with illness greater than 1 month's duration because the likelihood of a false-positive test result for a current infection is high for these persons.

If a patient with suspected early Lyme Disease has a negative serology, serologic evidence of infection is best obtained by the testing of paired acute- and convalescent-phase serum samples. Serum samples from persons with disseminated or late-stage Lyme Disease almost always have a strong IgG response to *Borrelia burgdorferi* antigens. It is recommended that an IgM immunoblot be considered positive if two of the following three bands are present: 24 kDa (OspC) *, 39 kDa (BmpA), and 41 kDa (Fla). It is further recommended that IgG immunoblot be considered positive if five of the following 10 bands are present: 18 kDa, 21 kDa (OspC) *, 28 kDa, 30 kDa, 39 kDa (BmpA), 41 kDa (Fla), 45 kDa, 58 kDa (not GroEL), 66 kDa, and 93 kDa.

A negative ELISA, especially in patients with longstanding complaints referred to as "Lyme Disease", should be taken as strong evidence against the diagnosis of Lyme Disease, unless there are extenuating circumstances. In such patients, western blot should not be used as a further "screening tool." Isolated IgM seropositivity is not evidence of longstanding disease in patients with a long history of complaints.

Seroreactivity by ELISA and immunoblot generally indicates the presence of antibodies to the organism that causes Lyme Disease. It does not, however, make the diagnosis of active Lyme Disease, since antibodies may persist long after the Lyme Disease was treated and cured. The diagnosis of Lyme Disease, as note above, should always be based upon the clinical likelihood of the disease, with serologic testing used only for confirmation. Positive and negative tests do have value when used in the right settings. Cross-reacting antibodies can occur in patients with other Borrelial diseases (relapsing fever), spirochetal diseases (syphilis, leptospirosis, pinta, yaws, gingivitis), viral illnesses, and autoimmune diseases (lupus, rheumatoid arthritis). Strong reactivity with the flagellin of intestinal commensals and Gram-negative bacteria causing urinary tract infections can also cause a false-positive test. Epstein-Barr virus and certain parasites, notably malaria, can cause such activation, resulting in ELISA positivity unrelated to Lyme disease. It is estimated that 5 percent or more of the normal population will test positive for Lyme Disease by ELISA due to cross-reacting antibodies elicited by other infections or by the immune response to normal flora.

At UMass Memorial Laboratories, Lyme Screen Serology (Mnemonic: LYME) testing is performed by a highly sensitive qualitative indirect EIA methodology. When requesting testing for Lyme Disease, please order only Lyme Screen Serology. Please do not request Lyme Western Blot – any positive or indeterminate screen results will automatically reflex to a confirmation for both IgG and IgM antibodies by Western Blot.

Changes in High Sensitivity CRP (hsCRP) Reporting Units

The American Heart Association (AHA) and the Centers for Disease Control and Prevention (CDC) have published recommendations for the use of hsCRP (Cardio CRP) testing. The guidelines, published in the January 28, 2003 issue of *Circulation* (2003:107:499-511), help healthcare providers more accurately assess a patient's risk of cardiovascular disease that includes both lipid and inflammatory markers.

The highlights of these recommendations are:

- Screening the entire adult population is not recommended.
- CRP is not a substitute for traditional cardiovascular risk factors.
- Acute coronary syndrome management should not depend on CRP measurements.
- When being used for risk assessment, patients with persistently unexplained CRP levels above 10 mg/L should be evaluated for other non-cardiovascular origins.
- Testing for any risk assessment should not be performed while there is indication of infection, systemic inflammation, or trauma.
- Secondary prevention measures should be based on global risk assessment and not dependent on CRP.
- Serial testing of CRP should not be used to monitor effects of treatment.
- The average of CRP results repeated optimally two weeks apart should be used in performing risk assessment on metabolically stable patients.
- Report CRP, hsCRP, and cCRP measurements in mg/L.

Currently we report the hsCRP (Mnemonic: CRPULTRA) in mg/dL. Based on above recommendations, effective June 26, 2006, the units for reporting will be changed to mg/L. A new canned comment will be included for interpretation:

hsCRP mg/L	Relative Cardiovascular Risk
<1.0	Low
1.0–3.0	Average
3.1–10.0	High
>10.0	Persistent elevations may represent non-cardiovascular inflammation

Changes in Alpha-FetoProtein (AFP) Reporting Units

Alpha-Fetoprotein (AFP) is normally produced by the fetal gut, yolk sac, and liver. It is important in the initial diagnosis of tumors of these areas, as well as monitoring the response of tumors to chemotherapy. Currently we report the AFP (mnemonic: AFPRO) in IU/mL. Based on literature and cited publications, effective June 26, 2006, the units for reporting will be changed to ng/mL. To convert IU/mL to ng/mL, multiply IU/ml by 1.21. The reference range also will be reported in ng/mL, and the new range will be 0.60-6.60 ng/mL.

Changes in Urine Cannabinoids Confirmation Testing

Effective July 6, 2006, the Cannabinoids Confirmation test in urine (mnemonic: CUTHC) will be performed in-house, using a highly specific GCMS technology. This test, which was previously sent to an outside reference laboratory, will be performed every Tuesday and Thursday. The minimum sample requirement is 5 mL of urine. The results will be reported quantitatively with a negative cut off level of 25 ng/mL.

Studies involving humans indicate that 80%-90% of the total dose of delta-9-THC (metabolite) is excreted within 5 days--approximately 20% in urine and 65% in feces. The time after marijuana use during which a positive urine test may result depends on the route of administration, potency of THC and frequency of use. Attempts to correlate urine concentration with impairment or time of dose are complicated by variations in individual metabolism, metabolite accumulation in the chronic user, and urine volume changes due to diet, exercise, and age. Therefore, a positive result by the urine cannabinoid test indicates only the likelihood of prior use.

Reference Range Changes

Effective June 26, 2006, the following tests will have new reference ranges. These changes are based on the reevaluation of normal ranges of the population and manufacturer recommended ranges based on large clinical trials.

Test	Mnemonic	Units	Old Range	New Range
Serum Protein Electrophoresis	SPE			
Albumin		g/dL	3.8-5.0	3.5-5.0
Alpha-1- Globulin		g/dL	0.1-0.2	0.1-0.3
Alpha-2- Globulin		g/dL	0.5-0.8	0.5-1.0
Gamma Globulin		g/dL	0.5-1.2	0.6-1.4
Alpha-1-Antitrypsin	A1A	mg/dL	76-190	88-174
Ceruloplasmin	CER	mg/dL	20-52	22-58
Immunoglobulin M	QIM	mg/dL	53-334	46-304

Specimen Requirement Change: LDL Subclasses

Effective immediately, the specimen requirement for LDL subclasses has been updated to include both Red and Lavender top tubes. The prior requirement was strictly Lavender.

New Test: Osmolal Gap

The Osmolal Gap (Mnemonic: OSMGAP) is most effectively used to detect and follow poisonings with low molecular weight toxins such as Ethanol, Methanol, Isopropanol and Ethylene Glycol. The Osmolality Gap is determined by subtracting the Calculated Osmolality from the Measured Serum Osmolality. The Calculated Osmolality is determined by serum concentrations of Sodium, Glucose and Urea (BUN), as per below:

$$\left[-2 \times \text{Na (mmol/L)} + \frac{\text{Glucose (mg/dL)}}{18} + \frac{\text{BUN (mg/dL)}}{2.8} \right]$$

The Measured Serum Osmolality is determined by the Freezing Point Depression method using an osmometer. In normal cases, the Osmolal Gap should be less than <10 mOsm/Kg.

If you have questions, comments or suggestions regarding the preceding articles, please contact:

Dr. L.V. Rao, Director at 508-334-7593 or via email at RaoL@ummhc.org

Ms. Rachel Ambacher, Manager at 508-334-7316 or via email at Ambacher@ummhc.org.

Ms. Judy Rennell, Manager at 508-334-3803 or via email at Rennellj@ummhc.org

Changes to Platelet Aggregation Studies

We recently reviewed our platelet aggregation data and assay literature, and concluded that the concentration of ADP should be changed to 6.4 uM. Effective June 12, 2006, we will report out ADP aggregation at 6.4 uM, instead of the present 3.2 uM.

If there are any questions, please contact:

Dr. Liberto Pechet, Director, at 508-334-0265, or via email at PechetL@ummhc.org

Diane Connor, Manager at 508 334 7153, or via email at ConnorD@ummhc.org

Molecular Testing for Genetic Diseases

Testing for Bloom Syndrome, Canavan, Familial Dysautonomia, Fanconi Anemia, Glycogen Storage Disease Type Ia, Mucopolysaccharidosis type IV, Niemann-Pick Type A and B, Tay-Sachs mutations will be brought in-house starting June, 1st 2006. The analyses will be performed in the UMass Memorial Molecular Diagnostics Laboratory, located in the Reed, Rose and Gordon Building at the UMass Worcester Foundation Campus in Shrewsbury, MA.

Testing will be performed by PCR and mutations will be analyzed by MALDI-TOF mass spectrometry. Each assay will be performed once a week, and the turn-around time will be 10 to 14 days. As for all molecular tests, the UMass Memorial Genetics Requisition should be used with physician attestation of symptomatic disease or that informed consent for carrier testing was obtained.

Mutations Assessed:

Bloom Syndrome: 2281del6ins7;

Canavan: E285A, A305E, Y231X;

Familial Dysautonomia: R696P and IVS20;

Fanconi Anemia: IVS4+4A->T;

Glycogen Storage Disease Type Ia: R83C and Q347X;

Mucopolysaccharidosis type IV: 511del6434 and IVS3-2A->G;

Niemann-Pick Type A and B: R496L, L302P, delR608, fsP330;

Tay-Sachs: IVS12+1G>C, R170Q, 1278 TATC , G269S, deltaF304/305, IVS5-2A>G , R247W.

If you have questions, comments or suggestions regarding the preceding article, 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

Dr. Patricia Miron at 508-334-7815, or via email at MironP@ummhc.org

Hereditary Cancer Risk Assessment and Genetic Testing

UMass Memorial Laboratories is pleased to provide information on behalf of the Department of Genetics regarding the availability of testing services for BRCA and other hereditary cancers.

The Division of Genetics, within the Department of Pediatrics, at UMass Memorial Medical Center offers comprehensive pedigree analysis and discussion regarding hereditary cancer syndromes and genetic testing for patients with personal and/or family history of breast cancer, ovarian cancer, colon cancer, or other malignancies. Genes for which testing is offered through this service include BRCA1/BRCA2 (hereditary breast/ovarian cancer), MLH1/MSH2 (hereditary non-polyposis colon cancer), and APC (familial adenomatous polyposis).

The clinic is serviced by two Geneticists: Beverly Hay, MD and Catherine Nowak, MD and three Board Certified Genetic Counselors: Lisa Blazejewski, MS, CGC, Jessica Douglas, MS, CGC, and Valerie Loik Ramey, MS, CGC. The typical protocol for interested patients who wish to pursue genetic testing involves three visits. The first visit is to elicit family history and do pedigree analysis to determine the risk of a hereditary cancer syndrome in the family, as well as discuss the benefits, risks, and limitations of testing if appropriate. Following that visit, an insurance preauthorization process is initiated for all patients interested in pursuing testing. At the second visit, the patient signs the informed consent and has blood drawn for testing. The third visit is the results disclosure visit. All patients are given their results in person.

Appointments can be made by calling (508) 856-5695. Please note, all patients are seen in the Pediatric Subspecialty Clinic but this is an adult service. Patients will need referrals for three visits. If you have any questions, please contact the UMass Memorial Medical Center Genetics office at 508-856-3949.

Genetic Testing Support Services

With the expansion of our Molecular Diagnostic and Cytogenetics Laboratory testing menus, we are pleased to announce the availability of genetic counselors on staff to assist with testing questions. This service addition to the clinical and technical team of UMass Memorial Laboratories allows us to provide additional opportunities for educational programs and support for our clinicians.

We welcome Board Certified Genetic Counselors Lisa Blazejewski, MS, CGC and Valerie Loik Ramey, MS, CGC who are available Monday through Friday from 12:30-4:30 PM to answer questions regarding available testing, best testing options and also to help with result interpretation. Since Lisa and Valerie have joined our team they have been a tremendous resource for both the laboratory and our clinicians. Please feel free to contact them with questions or for assistance in coordinating contact with additional clinical laboratory staff for technical assistance with genetic testing. They can be reached at (508) 334-7173.

Phone System Upgrade Notification

We are pleased to announce that on Monday, June 26, 2006, the Customer Service Department will be converting to an Automated Call Distribution (ACD) System. This new system will improve the distribution and handling of all incoming calls to Customer Service.

Incoming callers on the (508) 334-2863 number will be greeted with a welcome message, and the call will be routed to the next available Customer Service Representative. If all of the Customer Service Representatives are busy handling other calls, the call will be held in queue for the next available representative. While in queue, the caller will hear music. If the wait extends to 60 seconds, a second message will be heard. Calls will be answered in the order in which they were received.

There will be an exclusive line with the highest priority given for handling critical callbacks. Healthcare providers will be paged to call (508) 334-7100 to receive critical test results. To expedite handling of calls on this priority line, the initial welcome greeting is bypassed to immediately reach a representative.

In order to enhance the professionalism and proficiency of our Customer Service Representatives, calls may be monitored by the Customer Service Manager.

If you have any questions or comments, please contact:

Cheryl Whitedear, Customer Service Manager at (508) 334-7154, or via email at WhitedeC@umhmc.org

New Patient Service Center Locations

Brockton Patient Service Center

1073 Pleasant Street
Brockton, MA 02301
Mon – Fri 8:00am – 5:00pm
Closed Daily 12:15-1:15pm

Framingham Patient Service Center

61 Lincoln Street, Suite 201
Framingham, MA 01702
Mon – Fri 8:00am – 5:00pm
Closed Daily 12:15-1:15pm

New Laboratory Report Format

During the month of June, UMass Memorial Laboratories will roll out a new report format to clients. This improved version displays laboratory outcomes in a more concise presentation. A scanned version of a report in this new format follows:

UMass Memorial Medical Center, Inc. Clinical Laboratories
 365 Plantation Street, One Biotech Park, Worcester, MA 01605 (508) 334-2863
 L. Michael Snyder, M.D., Medical Director, CLIA # 22D0724619

Ordering Location: LAB FACILITY 123 Anywhere St. Worcester, MA 01605 Ordering MD: LABS ONLY	<table style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 60%;"> PATIENT NAME HEME, NO CHARGE 1313 Mockingbird Lane, Bellvue, WA 00000 Pt Phone: 555-555-5555 </td> <td style="width: 40%; text-align: right;"> Page: 1 FINAL REPORT </td> </tr> <tr> <td> <table style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 33%;">PATIENT ID</td> <td style="width: 33%;">DATE OF BIRTH</td> <td style="width: 17%;">AGE</td> <td style="width: 17%;">SEX</td> </tr> <tr> <td>C0000026863</td> <td>01/01/82</td> <td>35</td> <td>M</td> </tr> </table> </td> <td></td> </tr> </table>	PATIENT NAME HEME, NO CHARGE 1313 Mockingbird Lane, Bellvue, WA 00000 Pt Phone: 555-555-5555	Page: 1 FINAL REPORT	<table style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 33%;">PATIENT ID</td> <td style="width: 33%;">DATE OF BIRTH</td> <td style="width: 17%;">AGE</td> <td style="width: 17%;">SEX</td> </tr> <tr> <td>C0000026863</td> <td>01/01/82</td> <td>35</td> <td>M</td> </tr> </table>	PATIENT ID	DATE OF BIRTH	AGE	SEX	C0000026863	01/01/82	35	M	
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COLLECTED: 06/14/06 0942 RECEIVED: 06/14/06 0942 REPORT DATE/TIME: 06/14/06 0945

TEST	RESULT	OUT OF RANGE	FLAG	REF RANGE/UNITS
Sodium	140			136-145 mmol/L
Potassium		3.4	L	3.5-5.3 mmol/L
Chloride	102			97-110 mmol/L
Carbon Dioxide	25			24-32 mmol/L
Anion Gap	13			5-15
Glucose		201	H	70-99 mg/dL
Blood Urea Nitrogen	10			7-23 mg/dL
Creatinine	1.0			0.5-1.2 mg/dL
GFR	> 60			> 60
Units = mL/min/1.73 m2 African American population multiply result by 1.210.				
Calcium	9.1			8.7-10.7 mg/dL
COMPLETE BLOOD COUNT				
WBC	9.5			4.3-10.3 th/mm3
RBC		4.39	L	4.40-6.00 mil/mm3
HGB	14.1			14.0-18.0 g/dL
HCT	42.1			42.0-52.0 %
MCV		101.1	H	82.0-101.0 fl
MCH	33.0			27.0-34.0 pg
MCHC	35.0			31.5-36.0 g/dL
RDW	13.4			12.1-14.0 fl
Platelet Count	305			140-440 th/mm3
Mean Platelet Vol	10.5			7.8-11.0 fl
PT				
PT	12.1		#	10.0-13.7 seconds
INR	1.0			

H = High L = Low * = Critical # = Delta

** END OF REPORT **

If you have any questions or comments, please contact your Account Representative or Customer Service at (508) 334-2863.