

Lab Updates

These updates can also be found on our web site: <http://ournet.umhmc.org/C2/Hospital%20Labs/default.aspx>

October/November 2005

Featured Article of the Month

Quantitative BCR/ABL Assay Replaces Ultraquant® Assay

We are pleased to announce that the Diagnostic Molecular Oncology (DMO) Laboratory began performing quantitative BCR/ABL testing on October 1, 2005. The DMO laboratory has adopted a standardized quantitative RT-PCR protocol developed by the Europe Against Cancer Program. This assay replaces the previous assays performed by Specialty Laboratories (BCR/ABL Ultraquant® Major 210 & Minor 190 KD Transcript Whole Blood). The change in methodology does not involve a change in specimen requirements (one to three 8ml EDTA tubes refrigerated after collection and received with 72 hours) but is limited to whole blood and not bone marrow. The assay is performed once per week, and the turn-around time is 3 to 10 days.

The quantitative BCR/ABL assay is intended to identify and monitor Minimal Residual Disease (MRD) levels in patients with the BCR-ABL t(9;22) translocation found in CML, a subset of ALL, and occasionally in AML. When positive at diagnosis this assay is intended to detect minimal residual disease in patients with the common (9;22) translocations, including the b2a2 and b3a2 (p210, Major) or e1a2 (p190, minor) transcripts. This test does not detect the rare (9;22) translocations and should not be used alone for a diagnosis of malignancy.

During the changeover, archived patient specimens will be analyzed using the DMO quantitative BCR/ABL assay and reported as previous test values to provide a reliable baseline and ensure valid trends in MRD levels can be monitored during the transition period. For the time being, DMO quantitative BCR/ABL results will be reported in the anatomical pathology subsection of the patient care inquiry system (PCI). As for all molecular tests, the UMass Memorial Laboratories Molecular Diagnostics Test Requisitions should be utilized. The CPT codes associated with this test are: 83891 (DNA isolation); 83902 x 3 (Reverse transcription) 83898 x 3 (PCR amplification); 83896 x 3 (Nucleic acid probe) and 83912 (Interpretation and Report).

For any questions or comments regarding these tests, please contact: Lloyd Hutchinson, Ph.D. at 508-793-6244 or via email at HutchinL@umhmc.org

Division of Anatomic Pathology Has Moved

On October 17, 2005, the Division of Anatomic Pathology relocated to a new location at Three Biotech, One Innovation Drive in Worcester. Please note that the new telephone number is 508-793-6100. The newly renovated, state of the art space will enhance the performance of pathology services. A limited pathology presence will continue to remain at the University and Memorial campuses to meet the needs of frozen section and cytology services. Supplies normally picked up in the Cytology labs at University and Memorial will still be available (call Cytology's new number, 508-793-6120, for details).

For further information regarding the relocation, contact Dr. Bruce Woda at 508-793-6200 or via email at WodaB@ummhc.org

New Patient Service Center

On October 17, 2005, a new UMMMC Department of Hospital Laboratories Patient Service Center opened in Waltham at 20 Hope Avenue, Suite G03. In addition to blood collection, the site performs Glucose, BUN, Sodium, Potassium, Chloride, Hematocrit and Prothrombin Time testing utilizing the I-STAT®1 Point of Care analyzer.

For further information regarding this site, contact Betsy Harder, Director at 508-334-3845 or via email at HarderB@ummhc.org

Molecular Genetics Test Ordering Changes

On December 1, 2005, the following molecular genetics tests will no longer be orderable through Meditech Order Entry: Factor V Leiden, Factor II (Prothrombin) Mutation Detection and MTHFR Mutation Detection. These tests must be ordered using the UMMMC Molecular Genetics Test Requisition and must be accompanied by either 1) Signed patient consent for molecular genetic testing, 2) Physician attestation that informed patient consent was obtained OR 3) Physician attestation that the patient has symptoms consistent with the disease.

The requisition and/or consent forms can be printed directly from Meditech at patient care locations and nursing units. To do so, select the patient in PCI and choose the "Forms and Templated Notes" option, followed by "Print Order Sets/Guidelines/Forms", then the "Lab Requisition Forms Menu". Molecular Genetics Test Requisitions (Form# Molecular Dx 2005) and Consent Forms (Form # Genetics Consent) are also available in bulk through the Copy Center at 508-856-2713. Outreach clients can obtain copies by contacting Customer Service at 508-334-2863.

Stool Culture Billing Modification

In the past when a Stool Culture was ordered the test automatically screened for Salmonella spp, Shigella spp, and Campylobacter spp. with only one charge. Effective immediately, there will be two charges associated with the test: one charge for the Salmonella spp. and Shigella spp. screen (CPT code 87045) and a second charge for the Campylobacter spp. screen (CPT code 87046). All three pathogens will still be screened for automatically, and the order mnemonic STOOL will remain unchanged.

For any questions or comments regarding these changes, contact: Brenda Torres, Microbiology Manager at 508-334-3429 or via email at TorresB@ummhc.org

Changes in Drugs of Abuse (DOA) Tests in Urine

Effective December 5, 2005, the following methodological changes will be made to the DOA testing reported from the Clinical Toxicology Laboratory. These tests will be performed using Protein Biochip Array Technology (PBAT) combined with Chemiluminiscent immunoassay (CIA). This biochip array approach of measuring DOA tests offers a significant diagnostic advantage through the simultaneous measurement of numerous analytes on one sample. The DOA panel is in a competitive immunoassay based format, consisting of discrete test regions for the simultaneous identification of 9 drugs of abuse classes detecting Amphetamine, Methamphetamine, Barbiturates, Benzodiazepines, Cannabinoids, Cocaine, Opiates, Methadone and Phencyclidine in urine using cut off values to distinguish Positive from Negative samples.

DOA Test Cut Offs and Class Compounds Detected

<u>Drug Class</u>	<u>Cut Off Levels (ng/mL)</u>	<u>Compounds Detected</u>
Amphetamine	1000	d-Amphetamine , MDA
Barbiturates	200	Phenobarbital , Secobarbital, Pentobarbital, Butalbital, Amobarbital, Barbital
Opiates	300	Morphine , Codeine, 6-MAM, Morphine-3-glucuronide, Hydromorphone, Hydrocodone.
Benzodiazepine	200	Oxazepam , Temazepam, Flunitrazepam, Nitrazepam, Diazepam, Alprazolam, α -Hydroxyalprazolam, Nordiazepam, Nitrazepam, Clonazepam, Clobazam, Midazolam, Chlordiazepoxide, Estazolam, Flurazepam.
Cannabinoids	50	11-Nor-delta-9-THC-9-carboxylic acid , 11-Nor-delta-8-THC-9-carboxylic acid.
Cocaine	300	<u>Benzoyllecgonine</u>
Methadone	300	<u>Methadone</u>
PCP	25	<u>PCP</u>

Three urine DOA panel tests are offered:

- **DOA4 (Drugs of Abuse Screen 4):** Barbiturates, Cannabinoids, Cocaine metabolite, and Opiates
- **DOA7 (Drugs of Abuse Screen 7):** Barbiturates, Cannabinoids, Cocaine metabolite, Opiates, Amphetamines, Benzodiazepines and PCP
- **DOA9 (Drugs of Abuse Screen 9):** Barbiturates, Cannabinoids, Cocaine metabolite, Opiates, Amphetamines, Benzodiazepines, PCP, Methadone and Propoxyphene

These DOA tests are considered screening tests and provide preliminary analytical test results. Presumptive positive tests are **NOT** automatically confirmed by GC/MS. Confirmations are only performed upon written request. Clinical consideration and professional judgment should be applied to any DOA test result, particularly when presumptive positive results are used. If the detection of a specific drug is desired, and it is not listed above, please submit a requisition with the drug name and the Clinical Toxicology Lab will perform the appropriate testing necessary.

Changes in Urine Amylase Testing

Amylase is an enzyme that helps digest glycogen and starch. It is produced mainly in the pancreas and salivary glands. Amylase is normally secreted from the pancreas through the pancreatic duct into the small intestine. Urine Amylase is used in the differential diagnosis of pancreatitis. It is very useful in the diagnosis of pseudocyst of the pancreas, where the urine amylase may remain elevated for weeks after the serum amylase has returned to normal, and after a bout of acute pancreatitis.

Effective December 12, 2005, the specimen requirement will change from random urine to **timed** urine. **The requisition must state the date and time of collection (start and finish) and urine volume.** The new reference range will be 1-17 U/hour.

Changes in Vitamin B12 Reference Range

Vitamin B₁₂ is the name given to any one of a group of substances termed cobalamins. Cobalamins are obtained from animal products such as meat, eggs, milk, and other dairy products. Once in circulation, cobalamins are taken up and stored in the liver. They are released into the plasma as needed where they are carried by B₁₂ binding proteins (transcobalamins).

Vitamin B₁₂ is a coenzyme that is involved in two very important metabolic functions vital to normal cell growth and DNA synthesis: 1) the synthesis of methionine, and 2) the conversion of methylmalonyl CoA to succinyl CoA. Deficiency of this vitamin can lead to megaloblastic anemia and ultimately to severe neurological problems.

Vitamin B₁₂ deficiency can occur for one of several reasons. The most common cause is a defect in the secretion of intrinsic factor, resulting in inadequate vitamin B₁₂ absorption from foods. This condition is called pernicious anemia and is most common in people over age 50. Other causes of vitamin B₁₂ deficiency are gastrectomy, malabsorption due to surgical resections, and a variety of bacterial or inflammatory diseases affecting the small intestine.

The lower reference limit, which is critical to the diagnosis of B12 deficiency, is not clearly established. Because of overlap in serum levels between B12 deficient and normal individuals, the use of an "Indeterminate" range is necessary.

Based on above, effective December 5, 2005, the Vitamin B12 assay will be reported with a new reference range interpretation:

Normal Range:	180-914 pg/mL
Indeterminate Range:	145-180 pg/mL
Deficient Range:	≤ 145 pg/mL

New Test: Corticotropin Releasing Hormone (CRH) Stimulation Test

CRH stimulation test is used to distinguish Cushing's disease from Ectopic ACTH secretion. Patients with pituitary Cushing's disease respond, while those with Ectopic ACTH secretion do not. This test has also been used in the diagnosis of central adrenal insufficiency.

The patient usually fasts for 4 hours or more, after which an i.v. access line is established and synthetic ovine CRH (1 mcg) per kg body weight, or a 100 mcg total dose, is injected as an i.v. bolus. Blood samples for ACTH and Cortisol are drawn at 0, 15, 30, 45, 60 and 90 minutes after CRH injection. Most patients with Cushing's disease respond with ACTH and Cortisol increases within 45 minutes after CRH.

This test will be available December 12, 2005. The ordering mnemonic will be CORTREL.

New Test: Growth Hormone Stimulation Test

Growth hormone affects many of the metabolic processes carried out by somatic cells. The best known is the effect of increasing body mass. Growth hormone deficiency is basically a clinical diagnosis, based on auxological features (i.e., a comparison of a child's growth pattern to established norms), and confirmed by biochemical testing. There is general consensus that a diagnosis of impaired GH secretion can be confirmed only if subnormal GH secretion is observed during an Arginine Stimulation Test.

For an Arginine Stimulation Test, an intravenous infusion of 0.5 g/kg body weight (to a maximum of 30 g) is given over 30 minutes, and serum growth hormone is measured at -15, 0, 15, 30, 60, 90, and 120 minutes. The combination of arginine plus growth hormone-releasing hormone (GHRH) is a more potent stimulus than arginine alone. Despite limitations, this provocative testing remains the "gold standard" in the diagnosis of GHD, and appears to be a useful predictor of response during the first year of treatment with GH. Most pediatric endocrinologists use a cutoff serum GH concentration of 10 ng/mL to define a "normal" response.

This test will be available December 12, 2005. The ordering mnemonic will be ARGSTIM.

If you have questions, comments or suggestions, 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