LifeLabs® Medical Laboratory Services

Inside Diagnostics

ECGS PROVIDED AT LIFELABS PATIENT SERVICE CENTRES

When an ECG or rhythm strip is ordered, the clinician will receive a 12-lead ECG with a rhythm strip at the bottom.

If a longer rhythm strip is required (such as 30 sec. or 1 min.), then an Event Monitor or Holter Monitor should be ordered to assess rhythm correctly.

As a reminder, LifeLabs community laboratories provide ECG services only to patients who are stable and who are not suspected of acute myocardial infarction or other life-threatening cardiac event. No Stat, Urgent or ASAP ECG service is available. Patients suspected of an acute cardiac event must be directed to a hospital or other acute care facility – LifeLabs is not equipped to deal with such patients.

Requests for ECG faxes can be made to our Customer Care Centre at 1-416-675-3637 or 1-877-849-3637.

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GROWTH HORMONE METHOD UPDATE AND REFERENCE RANGE CHANGE

The growth hormone (GH) method used by LifeLabs has been re-standardized by the vendor to align with the preferred calibration process for this analyte using a recombinant 2nd international standard (IS) 98/574. This standard replaces the pituitary derived source from the World Health Organization (WHO), 1st IS 80/505.

Performance of the new reagent has been validated and a decrease in observed GH values of approximately 25% may be expected on patient results. Accordingly, the reference range has been changed as follows:

Male	**< 0.80 µg/L**
Female	**< 8.00 µg/L**

It is advised that baseline GH values be re-established for patients undergoing serial measurements. The reporting range of results remains unchanged.

LABORATORY TESTS FOR INVESTIGATION OF MONOCLONAL GAMMOPATHIES

"Monoclonal gammopathy" is a term that refers to any disorder, both malignant and benign, caused by the disproportionate proliferation of lymphatic B-cells or plasma cells.[1, 2] These diseases include the following:[2-4]

Table 1: Classification of Monoclonal Gammopathies

Group	Class	Types
I	Malignant	• Multiple Myeloma (IgG, IgM, IgA, IgD, IgE, light chain disease, heavy chain disease, biclonal gammopathy, and non-secretory) • Waldenström's acroglobulinemia (IgM, IgA, IgG) • Plasma cell leukemia • Plasmacytoma • POEMS syndrome
II	Primary Amyloidosis	
III	Monoclonal gammopathy associated with other clinical conditions	• Autoimmune disease • Peripheral neuropathy • Epithelial neoplasms
IV	Monoclonal gammopathy of undetermined significance (MGUS)	

Screening for monoclonal gammopathies in the general population is not warranted but investigation should be considered when suspecting:[3, 5, 6]

- Multiple myeloma, macroglobulinemia or amyloidosis
- Patients with unexplained weakness or fatigue, anemia, back pain, osteoporosis, osteolytic lesions or spontaneous fracture, elevation of ESR, hypercalcemia, renal insufficiency, recurrent infections
- Adults with peripheral neuropathy, carpal tunnel syndrome, refractory congestive heart failure, nephritic syndrome, orthostatic hypotension, or malabsorption.

The plasma cell proliferative disorders (PCPD) are generally associated with overproduction and secretion of a monoclonal immunoglobulin (MI). Detection of the MI may be the first clue to the diagnosis of these diseases and a number of laboratory tests are available for this purpose.

Traditionally, most diagnostic laboratory testing protocols have used a combination of serum and urine protein electrophoresis (PEP) and immunofixation (IFE). More recently, the introduction of quantitative serum free light chains (SFLC) analysis has prompted some to include this test as part of the algorithm to improve the clinical sensitivity.[5, 7] Table 2 summarizes how each of these tests can be used, the diagnostic information and limitations inherent to the assay in the diagnosis and monitoring of monoclonal gammopathies.

To request these tests, write "PEP" (specify serum or urine), "IFE" (specify serum or urine) and/or "Serum Free Light Chains" in the "Other Tests" section of the OHIP requisition. The SFLC test is not OHIP-insured and patients will be billed for the test. Some or all of this cost may be reimbursed by supplemental health plans.

Smaller, ill-defined or discrete bands are often identified by PEP or IFE and may fall into the category of "MGUS". However, these bands are not always benign. Some may be an indicator of early multiple myeloma, while others may be associated with common B-cell neoplasms, and still others may be associated with autoimmune disease and other peripheral neuropathies. If an ill-defined or minor discrete band is detected, repeat analysis of the serum protein electrophoresis in 6-12 months is recommended to monitor the progression or regression of these bands1. If the band was expressed as part of an oligoclonal expression due to infection or other process, it is likely to have regressed by this time. However, if the band represents an early malignant process, it will still be present or progressed to the point where it is easily detectable and/or quantifiable.

The presence of a MI by itself is not diagnostic and must be interpreted with other clinical information. While diagnostic criteria for MGUS, asymptomatic and symptomatic myeloma have been developed, no single technique can reliably differentiate a patient with a benign monoclonal gammopathy from one who will subsequently develop symptomatic multiple myeloma or other malignant disease.[6, 8] Periodic evaluation should include repeat serial measurement of the amount of monoclonal protein, as well as complete blood count bone marrow, and radiologic studies to aid in the diagnosis.

It is important to note that there is a subclass of nonsecretory multiple myeloma which releases little or no monoclonal protein. The techniques listed above may not be helpful in these situations.

References

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4. Katzman JA, Kyle RA et al. Screening Panels for Detection of Monoclonal Gammopathies. Clin Chem (2009) 55: 1517 – 1522.
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6. Smith A, Wisloff F et al. Guidelines on the diagnosis and management of multiple myeloma 2005. Br J Haematol (2005) 132: 410 – 451.
7. Dispenzieri A, Kyle RA et al. International Myeloma Working Group guidelines for serum-free light chain analysis in multiple myeloma and related disorders. Leukemia (2009) 23: 215 – 224.
8. International Myeloma Working Group. Criteria for the classification of monoclonal gammopathies, multiple myeloma and related disorders: a report of the International Myeloma Working Group. Br J Haematol (2003) 121: 749 – 757.

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Table 2: Laboratory Evaluation of Monoclonal Gammopathies

Test Name	Information Provided by Test	Limitations
Serum PEP	• Provides both qualitative and quantitative information. • Used to screen for presence of a MI fraction. • If the MI is present in sufficient amount, PEP provides an estimate of the amount of MI. • Provides an estimate of the total amount of immunoglobulins (IgG, IgA, IgM).	• Some MI's in low concentrations or those migrating in the alpha-2 and beta regions of the electrophoretic gel can be "hidden" within the normal protein bands and, therefore, missed by this technique. • Does not provide a measurement of each of the individual immunoglobulin subclasses, i.e. cannot determine if one or more of the subclasses is suppressed or elevated.
Serum IFE	• Qualitative test, generally used as a follow-up test to characterize the heavy and light chains of the MI fraction, after initial detection bv PEP. The MI may be intact, heavy chain only, light chain only, or a combination. The identity of the MI is reported as IgG, IgA, IgM, IgD or IgE with kappa, lambda light chain molecules. * • Can detect the presence of MI in low concentrations in the alpha-2 and beta regions, missed by PEP.	• **Cannot** quantitate the amount of the MI.
Serum Free Light Chains (kappa and lamba)	• Provides an accurate quantitative measurement of the amounts of free kappa and free lambda light chains in serum • Can be used as a first line screening test for amyloidosis or other light chain related diseases. • Has been proposed as an alternative to Urine PEP and/or IFE for many of the PCPD.	• **Cannot** quantitate the amount of the MI, if it is intact or heavy chain. • SFLC is not an OHIP-insured test.
Urine PEP	• Provides both qualitative and quantitative information. • Since urine is concentrated prior to analysis, this technique can provide a sensitive screen for the presence of MI in urine.	• The presence of a MI requires further investigation by IFE to confirm identity.
Urine IFE	• Can detect and identify the presence of free light chains.	• **Cannot** quantitate the amount of the MI.
Serum Quantitative immunoglobulins (IgG, IgA, IgM)*	• Provides an accurate measurement of each of the immunoglobulin subclasses (IgG, IgA, IgM). • Useful for detection of hypogammaglobulinemia.	• **Cannot** differentiate between monoclonal and polyclonal increases of immunoglobulins. • **Cannot** quantitate the amount of the MI in the presence of other immunoglobulins.

* IgD and IgE monoclonal gammopathies also exist but these are very rare. If a MI has been identified as being IgD or IgE, quantitation of these immunoglobulin subclasses is also available.

MPO TEST FOR CARDIAC HEALTH

Myocardial cell injury is associated with platelet activation but there is now growing evidence that it is preceded by activation and degranulation of neutrophils. One of the principle mediators of neutrophil activation is myeloperoxidase (MPO).

What is MPO and what is its function?

MPO is a hemoprotein enzyme linked to both inflammation and oxidative stress. Literature has demonstrated its role in: [2-8]

- Host defense, by generating anti-microbial reactive oxidants
- Decreasing nitric oxide bioavailability, leading to endothelial dysfunction
- Oxidizing LDL, contributing to cholesterol deposition and transformation of macrophages into foam cells
- Oxidizing HDL, impairing its protective effect and inhibiting cholesterol transport
- Mediation of vascular inflammation that propagates plaque formation
- Destabilizing atherosclerotic plaque
- Sudden cardiac death due to atherosclerosis.

Thus, MPO initiates the development of atherosclerosis and is believed to be a valuable biomarker in cardiovascular risk stratification.[8-12] Elevated concentrations of MPO have been noted to occur independently of CRP or other inflammatory markers.[10]

Why measure MPO?

Numerous studies have illustrated that elevated MPO levels predict increasing cardiovascular disease (CVD) risk, independent of other classical risk factors.[8-12] An increased risk of heart attack and/or death has been reported when MPO values were in the 400-500 pmol/L range.

- Elevated MPO levels predict the risk of coronary artery disease in subgroups otherwise associated with low risk.[9]
- Elevated MPO levels independently predict the early risk of future cardiovascular events in patients with acute coronary syndromes up to 24 months preceding an event.[10, 11]
- MPO enhances cardiovascular risk prediction when used independently or alongside standard biomarker testing.[12]

How does the patient prepare for the MPO Test?

No preparation is required. A venous blood sample is collected. A fasting sample is not necessary and the patient can continue medications as per routine. MPO test results are specific for inflammation associated with atherosclerosis and are not likely to be falsely elevated due to infections, rheumatologic disorders, or obesity.

When is the MPO Test ordered?

MPO quantitation is recommended in borderline or high risk patients in conjunction with a lipid panel, but may also be ordered separately. It is not recommended for screening low risk patients. This test is not OHIP insured and patients will be charged at the

time of collection. Some or all of this cost may be reimbursed by supplemental health plans.

For more information on this test and our other cardiovascular markers, please call 1-877-849-3637 or visit www.lifelabs.com.

References:

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UPDATE: TECHNOLOGY CHANGE FOR *CHLAMYDIA TRACHOMATIS* AND *NEISSERIA GONORRHOEAE* ANALYSES

In May 2011, LifeLabs will implement new technology for the detection of Chlamydia trachomatis (CT) and Neisseria gonorrhoeae (GC) using the BD ProbeTecTM CT/GC Q^X Amplified DNA Assays performed on the BD Viper™ XTR System. These nucleic acid amplification assays offer enhanced sensitivity and specificity compared to the current method.

The BD reported clinical trial performance of the ProbeTec™ CT/GC Q^X Amplified DNA Assays compared to Patient Infected Status (PIS)[1,2] is summarized in the following table:

Sex	Sample Type	BD Chlamydia Q^X Assay		BD Gonorrhoeae Q^X Assay	
		Sensitivity	Specificity	Sensitivity	Specificity
Male	Urine	98.0%	99.2%	100%	98.9%
	Urethral	92.1%	98.4%	100%	99.1%
Female	Urine	93.0%	99.4%	96.9%	99.5%
	Endocervical	91.3%	98.3%	98.5%	99.7%
	Vaginal	96.5%	99.2%	100%	99.1%

Clinicians may order both CT and GC on a single specimen for urine, male urethral and female endocervical or vaginal swabs. The CT and GC methods are indicated for use with asymptomatic and symptomatic individuals to aid in the diagnosis of chlamydial and gonococcal urogenital disease.

Specimen Collection Changes

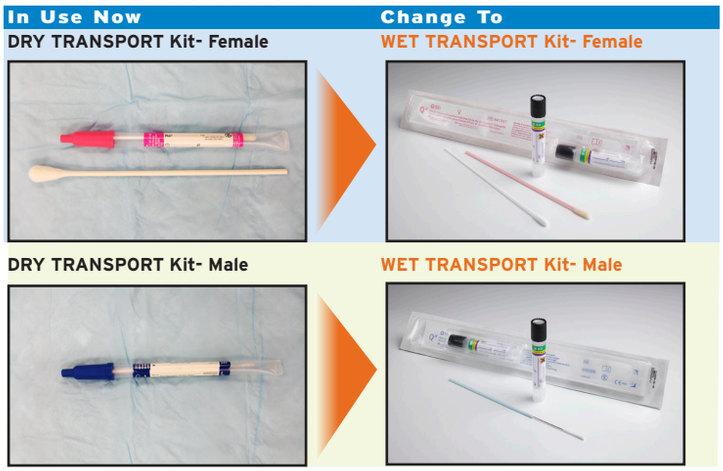
Urine: For male and female urine specimens, there is no change in collection procedures for urine specimens. The optimal specimen is a clean catch urine submitted in a sterile container.

Swabs: For urogenital swab specimens, the new BD Viper technology requires a new collection device and a change from a "DRY" transport kit to a "WET" transport kit. An illustration of the current and new kit formats follow for your consideration.

The collection procedures for male urethral, female endocervical and vaginal swab specimens will remain the same as the current method.

Client communication providing information for ordering new "WET" kits, the process for disposal of old kits and implementation dates for testing will follow in April, 2011.

Collection Device for Swabs



References

1. BD Diagnostics, Package Insert BD ProbeTec™ Chlamydia trachomatis (CT) Q^X Amplified DNA Assay.
2. BD Diagnostics, Package Insert BD ProbeTec™ Neisseria gonorrhoeae (GC) Q^X Amplified DNA Assay.

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