



# inside DIAGNOSTICS

THE DIAGNOSTIC NEWSLETTER FOR PHYSICIANS

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## PLUS ÇA CHANGE, PLUS C'EST LA MÊME CHOSE

This edition of Inside Diagnostics will be the last to bear the name and logo of MDS, under which this laboratory has operated since its inception.

As announced in a recent communication to physicians, MDS Inc. has entered an agreement to sell Diagnostic Services to Borealis Infrastructure, an investment arm of OMERS, one of Canada's largest pension funds.

As a result, our name is about to change but what this really signifies is a return to our roots as an organization dedicated to one thing and one thing alone: Medical Laboratory Service.

As laboratory professionals we are pleased our new owners have chosen to make a long-term investment in our business and recognize that reliable, sustainable service in our area of

endeavor makes sense for you our clients and for those who provide the service. We look forward to continuing to serve you under a new name and logo. ■

**Frank E. Thompson, MD FRCPC**  
*Medical Director*

**Sheila Boss, Ph.D., FCACB**  
*Laboratory Director*

**Peter Catomeris, Ph.D., FCACB**  
*Clinical Biochemist*

**Dr. Deborah Yamamura, B.Sc., M.D., FRCPC**  
*Medical Microbiologist*

## CHANGES TO REPORTING OF THE COMPLETE BLOOD COUNT (CBC)

### Reporting of blood cell morphology

When a CBC is ordered from MDS Diagnostic Services the sample is processed by an automated analyzer. A blood film is made and reviewed by a technologist when the automated results are abnormal or "predetermined flags" suggest a review is necessary.

In other situations, a blood film does not contribute to a diagnosis or assist in the clinical management. Comments in the morphological fields will only be present when a blood film has been examined.

Parameters of the automated differential white and red cell

counts which fall outside the reference interval will continue to be emphasized by Hi or Lo designations but will no longer be accompanied by an automatically appended morphological comment such as 'Macrocytosis.' It follows that when present these comments are the result of the review of a slide by a technologist or pathologist.

Most hematology reports will now end after the automated differential white cell count resulting in less paper to file for a significant number of reports.

### Change to reference ranges

MDS has introduced Sysmex Hematology analyzers. The reference intervals for Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin Concentration (MCHC) and Absolute Monocyte count require adjustment as follows:

<b>MCV</b>	<b>80-100 fL</b>
<b>MCHC</b>	<b>305-360 g/L</b>
<b>Monocytes</b>	<b>0.0- 1.0 xE9/L</b>

You are reminded that when considered in clinical context slight elevations of MCV, in most cases, do not require further action because of the way reference intervals are determined. By definition 2.5% of the normal population will be above and below the upper and lower limits of normal.

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MCV values between 100 and 105 fL may require investigation if the cause is not clear. Unexpected values >105 fL should be investigated. Since the Canadian diet is now fortified with folate, laboratory evidence of folate deficiency is very uncommon except when due to inadequate dietary intake or malabsorption. Liver disease is the most common cause of Macrocytosis in our population.

MCHC. This red cell index is of use mainly within the laboratory. It has very little clinical utility except in rare circumstances.

### Hypochromic Anemia

Hypochromic anemias (iron deficiency, thalassemia minor, anemia of chronic disease, hereditary sideroblastic anemia) are defined by anemias with a low MCV and MCH. It is felt that the mean Corpuscular Hemoglobin (MCH) is the best measure of the amount of hemoglobin in Red Cells and a low MCH is therefore a better indicator of hypochromic anemias than the MCV. The following message will be appended to complete blood count reports with a MCH <26 pg rather than an MCV <80 fL which was our previous practice.

“The possibility of Iron Deficiency or Thalassemia Trait should be considered.”

When the MCH is <25 pg a blood film is also examined. ■

## COLLECTION DEVICES FOR LIQUID BASED GYNECOLOGICAL CYTOLOGY

There is now a choice of devices for the collection of liquid based gynecological cytology.

As well as the Cervex Brush™, which we have provided since 2001, a second type of collection kit, consisting of a plastic spatula and a Cytobrush™ may be ordered if preferred. All of these devices are scored so that the collection tip can be snapped off into the collection fluid.

When the second type of kit is preferred, both spatula and Cytobrush™ should be used in most circumstances and the tips of both devices placed in a single vial of fluid. Please note the Cytobrush™ should not be used on pregnant women or for endometrial sampling. Collection instructions are included with the kits.

You should note the Cervex Brush™ must be rotated five times



Surepath® Cytobrush™

in a clockwise direction while the plastic spatula should be rotated through 360 degrees maintaining tight contact with the cervix. After insertion into the endocervical canal the Cytobrush™ should be slowly rotated through 90 to 180 degrees in one direction. Over-rotation may result in a poor sample.

Unique identification of specimens is essential in the interest of patient safety. You are reminded that collection vials must bear at least one unique identifier in addition to the patient’s full name as it appears on the Health Card. This may be date of birth or the Ontario Health Card number. ■

## C13 UREA BREATH TEST FOR DETECTION OF HELICOBACTER PYLORI: COLLECTION PROCEDURE UPDATE

H. pylori is associated with the majority of peptic ulcer diseases and is a cocarcinogen for gastric cancer. From 20-40% of the North American population and up to 70% of the South East Asian population has been reported to be infected with H.pylori. The urea breath test is the preferred non-invasive test for the detection of H. pylori in adults and children <sup>(1, 2)</sup>.

The Helikit™ developed by Isodiagnostika is a simple, noninvasive breath test kit that makes use of nonradioactive C<sup>13</sup> labelled substrate to diagnosis active infection with H. pylori. The Helikit™ is recommended for use in children over the age of 6 years.

The following medications can interfere with the Helikit™ breath test results and should be discontinued prior to the test:

Medication	Discontinue
Histamine H2 receptor antagonists	1 day
Proton pump inhibitors	3 days
Bismuth preparations	2 weeks
Antibiotics	4 weeks

### REFERENCES

1. Canadian Helicobacter Study Group Consensus Conference: Update on the approach to Helicobacter pylori infection in children and adolescents – An evidence-based evaluation. Can J Gastroenterol 2005;19:399-408
2. Canadian Helicobacter Study Group Consensus Conference: Update on the approach to Helicobacter pylori – An evidence-based evaluation of six topics relevant to clinical outcomes in patients evaluated for H. pylori infection. Can J Gastroenterol 2004;18:547-554.

# NEW TESTS RECENTLY IMPLEMENTED BY OUR LABORATORY

**Apolipoproteins:** In June 2006, MDS introduced quantitative measurement of Apolipoprotein A and B testing using nephelometric immunoassay technology.

Apolipoprotein A (Apo A) is the primary protein component associated with the HDL particle (90%) and is inversely related to the risk of coronary artery disease.

Apolipoprotein B is an integral protein component of the atherogenic lipoproteins, including LDL (95%), and VLDL (25%). Elevated concentrations are associated with increased risk of cardiovascular disease. Measurement of Apolipoprotein B (Apo B) is recommended by the Canadian Working Group on Hypercholesterolemia and other Dyslipidemias in the evaluation of cardiovascular risk and adequacy of treatment in patients who have metabolic syndrome. It may also be valuable as an alternative measurement to LDL-C particularly for assessment of patients treated with statins. Clinical trials for statins have illustrated that Apo B correlates to clinical outcomes better than levels of LDL-C while on treatment. An optimal concentration of Apo B in a high-risk patient is < 0.90 g/L. A moderate risk patient should be < 1.05 g/L while low risk patients have an optimal level < 1.2 g/L.

## REFERENCES

1. Genest, J, Frohlich J, Fodor G and McPherson R. Recommendations for the Management of Dyslipidemia and Prevention of Cardiovascular Disease. CMAJ 2003; 169 (9); 921-923.

**Anti ENA :** An ELISA based immunoassay for Anti-ENA testing was implemented in July. The presence of these antibodies have been demonstrated to be of significant diagnostic and prognostic value when evaluating patients suspected of a variety of connective tissue diseases such as SLE, scleroderma, Sjorgren's Syndrome and polymyositis. The analysis includes a screening process and reflexive testing of Jo-1, RNP, Scl-70, Sm, SS-A, and SS-B antibodies for all positive samples. The screening assay is performed daily while specific ENA evaluations are assayed twice per week.

**ACTH:** MDS also implemented an assay for quantitation of Adrenocorticotrophic Hormone (ACTH) by chemiluminescent immunoassay in October 2006. ACTH can be used to evaluate the etiology of Cushing syndrome, to differentiate pituitary from other causes of corticosteroid excess and deficiency, and to evaluate ectopic ACTH production by neoplasms.

## New Technologies at MDS

Changes to analytical technology were implemented for the following analytes:

Analyte	Basis of Technology	Implementation Date
Gastrin	Chemiluminescent Immunoassay	May 1 <sup>st</sup>
Anti DNA	ELISA	June 5 <sup>th</sup>
Homocysteine	Chemiluminescent Immunoassay	July 4 <sup>th</sup>
Renin	Radioimmunoassay	Sept 11 <sup>th</sup>

Revised reference intervals were implemented with the new methods for Anti-DNA and renin. A review of pre-implementation validation data and reference intervals for Gastrin and Homocysteine indicated that reference interval changes were not required for either of these tests.

## Investigation of Elevated Creatine Kinase (CK) Levels

Creatine Kinase, CK, is an enzyme that catalyzes the reversible phosphorylation of creatine by ATP. CK is a dimer composed of 2 subunits and can exist as 3 different isoenzymes and two variants.

The three isoenzymes CK-BB (or CK-1), CK-MB (or CK-2), and CK-MM (or CK-3) are primarily, but not exclusively, derived from brain, heart, and striated muscle tissue, respectively. CK variants are less commonly found in serum with a prevalence of less than 3% and are either immunoglobulin-bound CK (Type 1) or mitochondrial-derived CK (Type 2).

In normal serum, CK exists almost exclusively as CK-MM and is the result of normal muscle breakdown. Elevation of one or more of the CK isoenzymes can be found in various pathologies, as indicated below:

**CK-MM:** Diseases of skeletal muscle (including muscular dystrophy, myositis, acute rhabdomyolysis), direct trauma to muscle and at pharmacological doses of a number of drugs including clofibrate and statins.

**CK-MB:** Acute myocardial infarction (AMI), other cardiac conditions and diagnostic or therapeutic procedures, and skeletal muscle injury.

**CK-BB:** Normal childbirth, certain gastrointestinal disorders, various lung tumors and to various extents in tumors of the prostate, bladder, testes, breasts, ovaries and uterus.

**Type 1 Variant:** Mainly in elderly women and mostly of no clinical significance but has been associated with gastrointestinal diseases, adenoma or carcinoma, myocardial and vascular diseases.

**Type 2 Variant:** Adults severely ill with malignancies or liver disease and children with myocardial disease.

## Tests Available at MDS

MDS offers the following tests, in addition to Total CK:

- **“CK-MB”** testing, which uses a chemiluminescent immunoassay and quantitatively measures only the CK-MB isoenzyme

- **“CK Fractionation”** testing, which uses electrophoresis technology and is able to detect all three isoenzymes and both variants

**“CK-MB”**-specific testing is used in the investigation of suspected myocardial injury. As CK-MB can also be increased in muscle diseases, CK-MB is reported in mass (ug/L) and as a “relative index” (ratio of CK-MB to Total CK). A relative index greater than 3.0% is suggestive of an AMI and an index less than 2.0% is suggestive of muscle disease. Indices between 2.0-3.0% are borderline high and warrant further clinical correlation.

As a community-based laboratory service, MDS does not perform urgent requests for CK-MB analysis. If AMI is suspected, the appropriate medical response is to direct the patient to a nearby hospital with emergency services, so that immediate care can be provided.

**“CK Fractionation”** may be helpful in the investigation of patients with persistent asymptomatic elevated total CK and patients with rare isoenzyme-secreting tumors. CK Isoenzyme analysis does not provide added value to total CK measurement in monitoring patients suspected of muscle disorders. This test should not be used as a routine test for investigating AMI. Beginning September 5th, 2006, MDS will perform this test only once per week, upon approval of the laboratory medical director. ■

## REFERENCES

1. Moss, D.W. and Henderson, A.R. Clinical Enzymology in Tietz Textbook of Clinical Chemistry, 3rd Edition. Burtis, C.A. & Ashwood, E.R., editors. W.B. Saunders Co. 1999. Pp. 657-666.
2. Laboratory Test Handbook, 5<sup>th</sup> Edition. Jacobs, D.S., DeMott, W.R., and Oxley, D.K., editors. Lexi-Comp, Inc. 1994.

## SAMPLES WHICH MUST BE FROZEN

In order to maintain specimen integrity and yield valid test results some samples must be frozen at -20°C and maintained at this temperature prior to analysis.

Our Directory of Laboratory Services indicates when freezing is required and in most cases it is preferable to send your patient to a Patient Service Center for procurement of these samples. Because of the time required to properly freeze at -20°C, samples collected later in the day may need to remain in the freezer over night which will result in some delay in turnaround time.

In most situations and for most tests which required freezing of samples, this is not of clinical importance; however, samples for Activated Partial Thromboplastin Time (APTT) must be centrifuged then frozen. We therefore recommend you instruct your patients requiring this test to visit a Patient Service Center by 2:00 pm, preferably in the morning, to avoid a potential delay in time to

analysis. APTT samples may potentially generate a critical value. This potential delay is increased later in the day prior to a weekend or long weekend, so it is particularly important that patients understand and should avoid collections of APTT samples at this time period. ■

## CHRISTMAS HOLIDAYS

Our patient service centres will close for the holiday Monday, December 25, 2006 and Tuesday, December 26, 2006.

From our experience, we recommend you advise patients who require regular testing for assays such as INR to visit our locations preferably by Wednesday, December 20 or Thursday, December 21 at the latest. This helps ensure you receive results well before the holidays and when these are unexpected and require action such as adjustment of the dose of medication this can be easily achieved. If you obtain specimens in your office it is best to follow the same guideline.

Less common but elective tests are best delayed until after the holiday when a normal analytical production schedule is resumed.

On behalf of all our staff we would like to thank you for your help and convey, in advance, our best wishes for the Holiday and 2007.

## Contacting Us In the Future:

**Please note:** the number of our Customer Care Centre will remain the same following our separation from MDS Inc.

You can reach us at:

**Customer Care Centre**  
416-675-3637 or 1-877-849-3637

In addition, the location of our main reference laboratory in Ontario remains the same:

**100 International Blvd.,  
Toronto, Ontario, M9W 6J6**

## For more information, CONTACT:

**Dr. Frank Thompson**  
Medical Director, Ontario  
416-675-4530 ext. 4209  
frank.thompson@mdsinc.com