

IMPORTANT IMPROVEMENTS IN TESTING TECHNOLOGY AND COLLECTION TUBE REQUIREMENTS

Implementation Date: November 2007

We are pleased to inform you that our laboratory will soon introduce a new generation of Chemistry analyzers with many technological advances including the ability to perform a greater number of assays using a smaller volume of serum.

This technology supports our ongoing initiative to reduce the amount of blood taken from your patients but will require a change in the size of Serum Separator Tubes (SST) as described below. As you can see from the example provided, in many cases, the initiative will have considerable impact on the number of tubes required for chemistry tests. The following example illustrates the advantage to patients when implementation is complete.

Test Name	Current Collection	Future Collection
INR	1 Light Blue	1 Light Blue
CBC	1 Lavender	1 Lavender
Glucose	1 Grey	1 Grey
Lipids, electrolytes	5 SST 13 x 75 mm	2 SST 13 x 100 mm
Ferritin, TSH, FT4		
Net reduction = 3 SST tubes		

In November 2007, we will implement the use of the 13 x 100 mm plastic BD Hemogard SST™ Vacutainer® tube for

collection of Chemistry analytes. The new SST™ tubes have a draw volume of 5.0 mL blood and will replace the 13 x 75 mm (draw volume 3.5 mL) tube in use today. Over the next few weeks and months, you will receive several communications regarding implementation of this change in blood collection practice and technology. Your MDS Client Service Manager or Supervisor will facilitate the transfer of collection tubes to the 13 x 100 mm tube and

will be available to discuss these changes with you if blood specimens are routinely collected in your office. Every attempt will be made to minimize the impact to your office during this period.

The new Chemistry analyzers will be phased in across MDS Ontario laboratories from **December 2007 to April 2008** and will require use of the new tubes. In addition to the reduction in specimen volumes required for analysis, the new Chemistry analyzers support enhanced quality assurance tools and potentially improved turnaround times within the laboratory. It is anticipated that a number of analytes will require a change to reference intervals at implementation. All updates to reference intervals will be highlighted on the patient report together with the effective date of the modification.

We thank you in advance for your help in implementing this change. Please bring this notice to the attention of your staff responsible for specimen collection. ■

IN THIS ISSUE

IMPORTANT IMPROVEMENT IN COLLECTION TUBE REQUIREMENTS	1
THE BIGGEST PROBLEMS CAN BE THE EASIEST TO PREVENT	1
FASTING AND SPECIMEN COLLECTION	2
INCREASED PROLACTIN? CONSIDER MACROPROLACTINEMIA	3
NEW TECHNOLOGY	3
25-HYDROXYVITAMIN D – CHANGE TO REFERENCE RANGES	3
URGENT ACTIVATED PARTIAL THROMBOPLASTIN TIME (APTT) REQUESTS	4
MORE ON HEPATITIS TESTING	4
UPCOMING NAME CHANGE	4

THE BIGGEST PROBLEMS CAN BE THE EASIEST TO PREVENT

Mention by laboratories of proper completion of requisitions with unique identification of patients and specimens appears to induce feelings of anger and frustration, even threats to laboratory directors, or boredom depending on your perspective. Happily, there is a silent compliant majority.

The fact is, we all simply have to manage our working lives to comply with modern standards and train our staff accordingly. The requirement is not about to go away.

Our laboratory does receive important samples without indication of an ordering clinician and without clear and unique identification of the patient and no phone number.

If you are missing a cervical cytology report let us know. We have an HSIL and despite our best efforts cannot identify the patient or submitting clinician.

The significance of this is clear and we go to great lengths to ensure patients are managed in a safe environment. We solve most problems but not all.

Please help by ensuring you and your staff properly complete requisitions and identify specimens and patients. ■

FASTING AND SPECIMEN COLLECTION

A number of tests absolutely require an individual to be in the fasting state for results to be valid under any circumstance.

These include:

- Glucose Tolerance Tests including Gestational Confirmation
- Lactose Tolerance Test
- Insulin Glucose Challenge Test
- by definition Fasting Glucose

For all of these a fast for a minimum of 8 hours is necessary and patients will be asked to return on another day in a fasting state if they do not comply with this requirement.

It is highly recommended that "Lipid Assessment" for cardiovascular risk be performed after a fast for a minimum of 12 hours. Patients who present our Patient Service Centres having fasted for less than this will be told of the recommendation and invited to return on another day.

Because results will be valid under some circumstances, if patients elect to go ahead with testing our staff will draw blood and when results are reported a message will indicate the patient was fasting for less than 12 hours.

When specimens for tests for which fasting is mandatory or recommended are procured in a clinician office we assume the patient was in a fasting state unless otherwise indicated.

Clearly if the results meet lipid targets for an individual they are valid but if they do not, a fasting specimen is required for a valid assessment.

A 12 hour fast is also recommended when Gastrin Assays are performed. This assay is now rarely required, almost exclusively for diagnosis of Zollinger-Ellison Syndrome in which levels of Gastrin are very high. For this uncommonly requested test patients will be invited to return in a fasting state but not refused service if they request collection.

When Lipemia interferes with an analytical methodology, the patient should be fasting when the test is repeated. The table below provides more detailed information.

MANDATORY

Minimum 4 hour Fast

- Urea Breath Test (H. Pylori)

Minimum 8 hour Fast

- Oral Glucose Tolerance Tests Including Gestational confirmation.
- Lactose Tolerance Test
- Insulin Glucose Challenge Test
- Fasting tests by Definition e.g. Glucose, Insulin.



Minimum 12 hour Fast

- Apolipoproteins A1, B,E
- Lipoprotein a
- Lipoprotein Phenotype
- Free Fatty Acids
- Bile Acid
- Calcitonin
- Growth Hormone (when a single test)

RECOMMENDED

Minimum 12 hour Fast

- Lipid Assessment including Cholesterol, (Total, HDL LDL) and Triglycerides
- Parathyroid Hormone
- Iron/TIBC
- Homocysteine
- Gastrin
- Cryoglobulin, Cryofibrinogen
- Lactic Acid
- Phytanic Acid

For some assays lipemia may interfere with analysis. When this occurs the assay should be repeated after a minimum 12 hr fast. ■

INCREASED PROLACTIN? CONSIDER MACROPROLACTINEMIA

The majority of circulating prolactin exists in "monomeric" form, as a single polypeptide with molecular weight of about 23 kDa. It is the biologically active form and, therefore, clinically-significant.

Macroprolactin is a high molecular weight form of prolactin, which usually contributes only a small amount to circulating levels of prolactin. Its composition is variable but is most frequently a prolactin- IgG immunoglobulin complex, which is cleared from serum at a slower rate than the monomeric form. Evidence suggests that macroprolactin does not have the same bioavailability or bioactivity as the monomeric form.

Prevalence of macroprolactin in the general population is low (Females: 0.3 %; Males: <0.02 %), but is significantly higher in the hyperprolactinemic population. Several studies suggest that it can be as high as 25% in this population, and is a significant cause of increased prolactin results.

All methods used to quantitate prolactin react to both the monomer and macroprolactin forms, although not necessarily with the same equivalency. The prolactin result reported,

therefore, actually reflects the sum of all forms, or the “total” prolactin. The methodology currently in use in our laboratory (Bayer Centaur chemiluminescent immunoassay) has a relatively low cross-reactivity to macroprolactin, however in some patients with macroprolactinemia, the total prolactin can still be elevated.

Macroprolactin has not been shown to be associated with any pathological condition and is not related to symptoms of the hyperprolactinemic syndrome.

An elevated total prolactin result may reflect a “pseudo-hyperprolactinemia” due to the presence of biologically inactive macroprolactin, leading to a misdiagnosis. Accurate diagnosis of hyperprolactinemia must be based on the monomeric prolactin concentration. For this reason, it is recommended that elevated prolactin results be investigated further, to rule out “pseudohyperprolactinemia” due to macroprolactin. This can be easily done by requesting a “**Macroprolactin**” test on the OHIP requisition.

Interpretation of results

To improve the clarity of the interpretation of macroprolactin results, the reporting of prolactin and macroprolactin will be updated. Please note:

- If “**Prolactin**” is ordered, only the Total Prolactin will be reported.
- If “**Macroprolactin**” is requested, the total prolactin, monomeric prolactin, and macroprolactin, each with an appropriate reference range, will be reported.

Guidelines for the interpretation follow:

Parameter	Interpretation
Total Prolactin	An elevated total prolactin result, which has been confirmed by repeat sampling, may be indicative of true hyperprolactinemia and/or pseudohyperprolactinemia, due to macroprolactin. Recommend follow-up analysis of “ macroprolactin ” to rule out pseudohyperprolactinemia. If macroprolactin is requested, an elevated total prolactin result must be interpreted in the context of both the monomeric prolactin and macroprolactin results.
Monomeric Prolactin	A monomeric prolactin result above the reference range is consistent with true hyperprolactinemia, irregardless of whether macroprolactin is present or not.
Macroprolactin	A macroprolactin result above the reference range indicates the presence of increased levels of biologically-inactive macroprolactin ■

REFERENCES

1. Gibney J, Smith TP, and McKenna TJ. Clinical relevance of macroprolactin. *Clinical Endocrinology* (2005) 62: 633-643.
2. Fahie-Wilson MN, John R, and Ellis AR. Macroprolactin: high molecular mass forms of circulating prolactin. *Ann Clin Biochem* (2005) 42: 175-192.
3. Fahie-Wilson. In hyperprolactinemia, testing for macroprolactin is essential. *Clin Chem* (2003) 49: 1434-1436.

NEW TECHNOLOGY

MDS performs C-peptide testing using a chemiluminescent immunoassay. The manufacturer has changed the configuration of the assay from a rabbit polyclonal, competitive assay to a murine monoclonal sandwich assay. In addition, the manufacturer has recalibrated the assay. Due to these changes, the reference range and the sensitivity of the assay have been changed, effective September 10, 2007. ■

25-HYDROXYVITAMIN D – CHANGE TO REFERENCE RANGES

It has been well established that Vitamin D plays an important role in skeletal development and maintenance. More recent literature has shown that Vitamin D has other important biological roles and that Vitamin D sufficiency is associated with decreased risk of many cancers, diabetes mellitus, multiple sclerosis, rheumatoid arthritis, cardiovascular disease, and lowered mortality in patients with chronic kidney disease.

25-hydroxyvitamin D is considered to be the best indicator of vitamin D nutritional status. Vitamin D deficiency is defined as 25-hydroxyvitamin D below 25 nmol/L, but recent guidelines suggest that 25-hydroxyvitamin D levels greater than 75 nmol/L are considered sufficient and that the following ranges are more appropriate to define 25-hydroxyvitamin D status:

Deficiency:	<25 nmol/L
Insufficiency:	25-75 nmol/L
Sufficiency:	75-250 nmol/L
Toxicity:	>250 nmol/L

MDS will be adopting these reference ranges in the near future.

Based on these guidelines, the literature suggests that there is a high percentage of patients, in the general population, with insufficient vitamin D concentrations. Various guidelines have been proposed, using strategies of supplementation and/or exposure to sunlight or simulated sunlight, in order to ensure that patients maintain sufficient blood levels of vitamin D and optimal health. ■

REFERENCES

1. Holick, MF. High Prevalence of Vitamin D inadequacy and implications for health. *Mayo Clin Proc.* (2006) 81(3): 353-373.
2. Hollis, BW. Circulating 25-hydroxyvitamin D levels indicative of vitamin D sufficiency: implications for establishing a new effective dietary intake recommendation for vitamin D. *J Nutr.* (2005) 135: 317-322.
3. Dawson-Hughes B, Heaney RP, Hollick MFR, Lips P, Meunier PJ, Vieth R. Estimates of optimal vitamin D status. *Osteoporos Int.* (2005) 16: 713-716.

URGENT ACTIVATED PARTIAL THROMBOPLASTIN TIME (APTT) REQUESTS

Unlike the PT/INR test, the APTT assay requires special handling. When blood is collected for a PT/INR test alone, the specimens are stable for 24 hours, as long as the tube is kept at room temperature, and the stopper is not removed. If an urgent PT/INR is requested, the only limiting factor for providing urgent results is the time it takes to deliver the specimen to a testing site.

For the APTT test, however, blood has to be centrifuged and the plasma separated within one hour of collection. This plasma must then be analyzed within four hours which is possible only when collection occurs close to a testing laboratory. If this is not possible the plasma has to be frozen for a minimum of one hour and then transported on dry ice. The requirement for centrifugation and freezing dictates that the blood must be drawn at least 1½ hours prior to transportation to the lab. When ordering urgent APTT assays later during the day, please bear in mind that the same applies and so specimens may need to be frozen overnight before transportation on dry ice to the laboratory. Inevitably results will not be available the same day. Whenever possible, patients should be instructed to visit our Patient Service Centres early in the day for APTT assays particularly when results are required urgently. ■

UPCOMING NAME CHANGE

You may recall that MDS Diagnostic Services was sold by MDS Inc. earlier this year to Borealis Infrastructure. Since then, we have been in the process of obtaining a trademark on a new brand name. Stay tuned for further communications on our new name!

MORE ON HEPATITIS TESTING

Based on expert advice, the testing algorithm for Acute Hepatitis will shortly be modified to include testing for Hepatitis C.

When ALT as the sentinel test is greater than 1.5x the upper reference limit, an anti HCV assay will, in future, be performed along with anti HAV and HBsAg.

If all of these are negative an anti HBc IgM assay will be performed.

The algorithm is essentially that illustrated in the Summer 2007 edition of "Inside Diagnostics" to which you are referred.

It should be remembered that seroconversion may be delayed for several weeks in cases of Hepatitis C. To exclude Hepatitis C as the cause of the acute illness, anti HCV should be ordered as a single test 6 weeks later.

We will modify our testing algorithm when the required changes have been made to our laboratory information system. ■



For more information, CONTACT:

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

Dr. Sheila Boss
Scientific Director, Ontario
416-675-4530 ext. 2296
sheila.boss@mdsdx.com

Dr. Peter Catomeris
Clinical Biochemist
416-675-4530 ext. 2029
peter.catomeris@mdsdx.com

Dr. Wahbi Hammouda
Director of Laboratory Hematology
416-675-4530 ext. 2728
wahbi.hammouda@mdsdx.com

Dr. Deborah Yamamura
Medical Microbiologist
416-675-4530 ext. 2344
deborah.yamamura@mdsdx.com