Inside Diagnostics Ontario

The diagnostic Newsletter for Healthcare Providers

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DECEMBER 2019

LifeLabs®

CLOSED FOR Christmas

Please note that we will be **CLOSED** on:

CHRISTMAS DAY, Wednesday, December 25th, 2019
BOXING DAY, Thursday, December 26th, 2019
NEW YEAR'S DAY, Wednesday, January 1st, 2020

Closed at 12:00 Noon:
Tuesday, December 24th
Tuesday, December 31st

Regular Working Hours:
December 27, 28 & 30
January 2, 3 & 4

AST, SERUM FOLATE, AND RBC FOLATE - UPDATED CRITERIA FOR INSURED TESTS

J. Timothy (Tim) Feltis
MD FRCPC
Ontario Medical Director, LifeLabs

Effective February 2, 2020, LifeLabs will begin charging patients for the serum AST, serum folate and RBC folate tests, except in certain circumstances, where they will be insured. This is being done on a directive from the Ontario Ministry of Health and Long-Term Care, with details outlined below.

AST

Aspartate aminotransferase (AST) is an enzyme found in liver, along with several other organ systems, such as heart and skeletal muscle; and, as such, is relatively non-specific marker of liver disease. The Alanine Aminotransferase (ALT) test is more specific for assessment of liver damage. Consequently, ALT is the test of choice for assessing the liver disease.

For an AST test to be insured, it can only be ordered by a health care provider (HCP) with experience in treating diseases of the liver, such as hepatologists and gastroenterologists. In addition, the HCP MUST indicate on the requisition that the test is insured for the patient not to be charged.

SERUM FOLATE

Since mandatory fortification of grain products with folic acid, a true folate deficiency has been rare. In addition, the historical notion that Red Blood Cell (RBC) folate is a better indicator of folate stores in the body compared to serum folate test is no longer accepted, as newer evidence indicates equal utility in assessment of folate deficiency (Galloway M and Rushworth J Clin Pathol 2003; 56: 924; Gilfix BM, Clin Biochem 2014; 47:533).

In order for a serum folate test to be insured, it MUST be ordered by a HCP with expertise in gastroenterology or hematology. The HCP MUST indicate on the requisition that the test is insured for the patient not to be charged.

AST, SERUM FOLATE, AND RBC FOLATE - UPDATED CRITERIA FOR INSURED TESTS (CONT'D)

RBC FOLATE

In order for RBC folate test to be insured, the HCP MUST indicate one of the following three indications on the requisition: a) anemia with an elevated MCV b) evidence of malabsorption, or c) evidence of malnutrition.

NOTE: In some instances, the HCP will only order a "folate" on the requisition and not specify serum or RBC folate test. The test will then default to a serum folate.

If the above criteria for AST, serum folate and RBC folate insured tests are not met, the patient will be charged for the testing. The exact costs for performing these tests will be determined closer to the implementation, but will be in the following ranges:
AST: $10.00 to $12.00; Serum Folate: $20.00 to $25.00; RBC Folate: $33.00 to $38.00.

Thank you for your understanding of this utilization initiative. If you have any questions, please contact us at 1-877-849-3637.

J. Timothy (Tim) Feltis
MD FRCPC
Ontario Medical Director, LifeLabs

POINTS TO REMEMBER:

- Effective February 2nd, AST, Serum Folate and RBC Folate tests will become uninsured unless indicated otherwise on the requisition by the health care provider (HCP).
- To be insured:
  - AST test can only be ordered by a HCP with experience in treating diseases of the liver, such as hepatologists and gastroenterologists. In addition, the HCP **MUST** indicate on the requisition that the test is insured.
  - Serum Folate test **MUST** be ordered by an HCP with expertise in gastroenterology or hematology. In addition, the HCP **MUST** indicate on the requisition that the test is insured.
  - RBC Folate test requisition **MUST** contain one of the following three indications: a) anemia with an elevated MCV b) evidence of malabsorption or c) evidence of malnutrition.
- All requests for "folate", without indication of RBC Folate or Serum Folate test, will default to Serum Folate test.

Invited Article: **TESTING FOR HERITABLE THROMBOPHILIA IN PATIENTS WITH VENOUS THROMBOEMBOLISM: CHOOSING WISELY**

Heritable thrombophilias are inherited disorders that increase the risk of a first episode of venous thromboembolism (VTE) which include both deep vein thrombosis (DVT) and pulmonary embolism (PE), by about two-fold. These disorders include deficiencies in the natural anticoagulants (**Protein C, Protein S and Antithrombin**), as well as genetic mutations like the **factor V Leiden mutation** which confers resistance to activated Protein C, and the **prothrombin gene mutation**.[1] The population prevalence of the natural anticoagulant deficiencies is very low (about 0.1%). Meanwhile, heterozygosity for the latter two genetic mutations is very common in Caucasian populations (between 2-5%).

In this article, we discuss the current role of heritable thrombophilia testing in the management of patients with VTE. We discourage the routine use of inherited thrombophilia tests outlining the three main reasons why testing for heritable thrombophilias is both inappropriate and unhelpful in the majority of patients with VTE and their asymptomatic relatives.[2]

1. The presence of heritable thrombophilia should not determine the duration of anticoagulation after an episode of VTE.

Clinical and laboratory risk factors that are strongly predictive of a higher risk of recurrence after a first episode of VTE include lack of a major provoking risk factor like surgery or trauma (i.e. unprovoked VTE), male sex, persistently elevated D-dimer, current active cancer and persistent antiphospholipid antibodies.

The knowledge of heritable thrombophilia does not add independent predictive value to this estimate of VTE recurrence and therefore does not change management.[2] Heritable thrombophilia testing should never be undertaken after a VTE episode provoked by a major, transient risk factor such as trauma, major surgery, or hospitalization. The risk of recurrence in these patients is low after receiving a limited duration of anticoagulation therapy and the results of thrombophilia testing do not influence this.[2,3] It is important to highlight that there is no consistent association between heritable thrombophilia and arterial thrombosis, and test results will not provide a causative explanation for such events or influence clinical management.[4] Therefore heritable thrombophilia testing is not indicated and should not be done after myocardial infarction or arterial, ischemic stroke.

2. Routine screening of asymptomatic relatives of patients with VTE for heritable thrombophilia should not be done.

Testing for thrombophilia in asymptomatic relatives of patients with VTE has not been shown to affect clinical outcomes.[2] In limited circumstances, testing for specific thrombophilia may be appropriate – for example, when initiating oral contraception or hormone replacement therapy in a woman with a family history of VTE and / or specific thrombophilia. However, it is important that the benefits and limitations of these tests are reviewed by a hematologist or thrombosis expert to avoid misinterpretation of their results.[1,2] An abnormal test result may also have downstream negative or unintended consequences for patients including anxiety, adverse financial implications for insurance, disease labeling, or overtreatment by other healthcare providers.

3. Testing for heritable thrombophilia is expensive and provides low value to the healthcare system.

Given the questionable utility of these results, testing for heritable thrombophilia provides low value to patients and the healthcare system. A cost analysis of factor V Leiden and prothrombin gene mutation testing in Canada after first

Invited Article: **TESTING FOR HERITABLE THROMBOPHILIA IN PATIENTS WITH VENOUS THROMBOEMBOLISM: CHOOSING WISELY** (CONT'D)

unprovoked VTE concluded that a net economic savings would occur if testing were reduced.[5] These savings would be driven by the cost of testing and inappropriate changes in physician prescribing practices.

Testing for heritable thrombophilia should not be done during acute VTE or while on anticoagulant therapy.

In select circumstances where it is deemed that heritable thrombophilia testing is indicated (or will change management), testing should only be done when the patient is clinically stable and after holding all anticoagulants to ensure accurate results and avoid false positives. Protein C, protein S and antithrombin levels are often lower during acute VTE and may not reflect true congenital deficiency.[6] Heparin lowers antithrombin activity and warfarin causes protein C and S deficiency (both Vitamin K dependent proteins). Direct oral anticoagulant therapy may cause overestimation of antithrombin activity, protein C and S activity, and activated protein C resistance ratio depending on the kind of assay used by the testing laboratory.[7,8] Other risk factors such as hormonal therapy or pregnancy also lower protein S activity.[6] Finally, the knowledge of heritable thrombophilia does not influence the choice of initial anticoagulant agent or dose. For all these reasons, testing during an acute episode or on anticoagulants should not be done, as it is likely to be inaccurate and misleading.

REFERENCES

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5. Canadian Agency for Drugs and Technologies in Health. Effectiveness of factor V Leiden and prothrombin mutation testing in patients presenting with a first unprovoked venous thromboembolic episode: a systematic review and economic analysis [Internet]. Ottawa: The Agency; 2015 Mar. (CADTH Optimal Use Report vol.4, no.1a). [cited 2016 Jun 14]. Available from: http://www.cadth.ca/media/pdf/OP0517_Thrombophilia_Science_Report.pdf.
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7. Douxfils J, Ageno W, Samama CM, et al. Laboratory testing in patients treated with direct oral anticoagulants: a practical guide for clinicians. J Thromb Haemost. 2018 Feb;16(2):209-219.
8. Selby R, Elbaz C. No resistance to activated protein C resistance – but choose wisely. J Thromb Haemost 2019; 17: 1443-1445

Guest Contributors:
Eric Tseng, *MD FRCPC*
St. Michael's Hospital, Toronto

Rita Selby, *MD FRCPC*
University Health Network & Sunnybrook Health Sciences Centre, Toronto

POINTS TO REMEMBER:

- After an episode of VTE, testing for heritable thrombophilia does not influence clinical decision-making and has downstream adverse consequences.
- If testing is done, ordering providers should be aware of when to test and how to interpret the test results (including potential for false positives).
- Consider consultation with a thrombosis specialist or hematologist with requisite expertise to decide if testing is indicated.

BIOTIN INTERFERENCE IN LABORATORY TESTS AT LIFELABS AND HOW TO AVOID IT

Why Can Biotin Interfere With Laboratory Tests?

Vitamin supplements are commonly used to obtain essential nutrients that may not be obtained through diet alone. Some of these nutrients may impact laboratory testing, and biotin has received particular attention with regards to its impact on laboratory test results.

Biotin is described in most multivitamin tablets as biotin, vitamin B7, vitamin H, or coenzyme R. Usually, biotin is present in small quantities in multivitamins and does not appreciably impact test results. However, biotin is also marketed as a supplement that can improve nail, hair and skin health and these supplements contain higher doses than what is found in multivitamins.

High doses usually refer to those supplements that contain greater than 5 mg of biotin. Because these supplements are marketed as nutraceuticals, patients may not know they are taking biotin. Additionally, treatment of metabolic disorders such as biotinidase deficiency, or multiple sclerosis, include biotin that can exceed 10 mg per day.

The biotin-streptavidin detection system is used in many laboratory immunoassays, and high levels of biotin can cause false high or false low results, depending on the assay. Some assays are more susceptible to biotin interference than others, and in certain tests, the amount of analyte can impact the degree of biotin interference.

Assays susceptible to biotin interference at LifeLabs:	
Adrenocorticotropic hormone (ACTH)	Gastrin
Alpha-fetoprotein (AFP)	Insulin
Anti-Mullerian Hormone (AMH)	Intact Parathyroid hormone (PTH)
Anti-Thyroglobulin	Sex Hormone Binding Globulin (SHBG)
Anti-Thyroid peroxidase	Total Testosterone
Bioavailable Testosterone	Thyroglobulin
Free Testosterone	Human Chorionic Gonadotropin (hCG)
Cancer Antigen 125 (CA125)	Anti-HAV - IgM
Cancer Antigen 15-3 (CA15-3)	Anti-HAV - Total
Cancer Antigen 19-9 (CA19-9)	Anti-HBc - Total
Carcinoembryonic Antigen (CEA)	Anti-HBe
Connecting Peptide (C-peptide)	HBe
Dehydroepiandrosterone Sulfate (DHEAS)	Anti-HBs
Erythropoietin (EPO)	HBs
Folate – RBC	Anti-HCV
Folate – Serum	Rubella IgG
Human Growth Hormone	

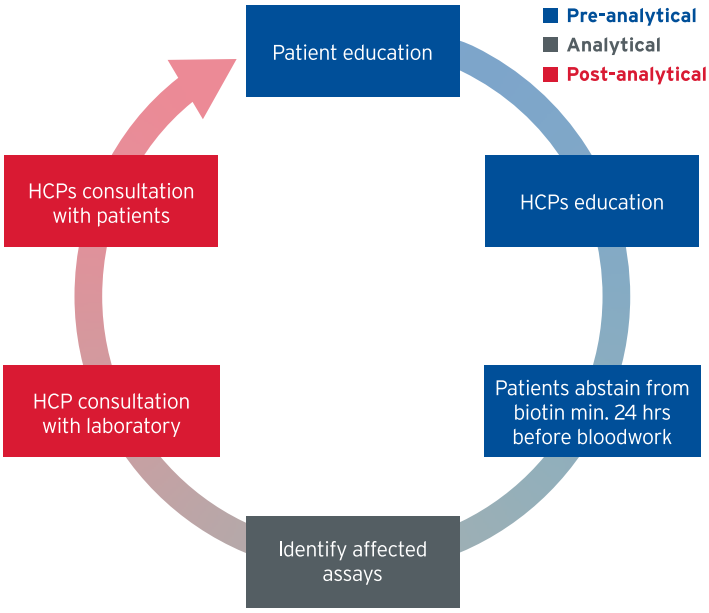
BIOTIN INTERFERENCE IN LABORATORY TESTS AT LIFELABS AND HOW TO AVOID IT (CONT'D)

What is LifeLabs doing to mitigate the risk of biotin interference?

To decrease the impact of biotin on lab test results, the following initiatives are employed by LifeLabs (Figure 1):

1. ***Patient Education*** TV screens at the Patient Service Centres (PSCs) will inform patients of the impact of biotin on laboratory tests; a website dedicated to biotin interference is being developed and will inform patients on strategies to reduce the risk of false test results due to biotin.
2. ***Health Care Providers (HCPs) Education*** In addition to this Inside Diagnostics article that provides the information regarding the affected assays and mitigation strategies, the LifeLabs online lab test information (Test Directory) will identify the tests affected.
3. ***Laboratory Staff Education*** LifeLabs staff will be educated on assays susceptible to biotin interference.
4. ***Encourage Health Care Provider Consultation with the Laboratory*** HCPs should communicate with the lab if a test result does not match the clinical presentation, and if they suspect biotin as a possible source of error. LifeLabs contact number is 1-877-849-3637.
5. ***Encourage Health Care Provider Consultation with Patients*** LifeLabs recommends that patients refrain from taking biotin supplements for ***minimum 24 hrs*** before blood collection, if medically appropriate.

Figure 1. LifeLabs strategy to mitigate risk of biotin interference:



RESOURCES:

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Uvaraj Uddayasankar, *PhD FCACB*
Clinical Biochemist

Nicole White-Al Habeeb, *PhD FCACB*
Clinical Biochemist

POINTS TO REMEMBER:

- High dose biotin can cause false high or false low results depending on the type of test.
- High dose biotin is being marketed as a supplement that can help improve hair, skin and nails and many patients may not realize they are taking biotin.
- Health care providers should contact LifeLabs if they see a result that does not match the clinical presentation and suspect biotin interference.
- Health care providers are encouraged to discuss the risks of high dose biotin with patients and recommend patients refrain from taking biotin for minumum 24 hrs before bloodwork is done.

BUILDING THE GENETIC TESTING LANDSCAPE IN CANADA

LifeLabs Genetics is proud to announce the expansion of our molecular diagnostic testing capabilities. We are now offering genetic testing for inherited conditions, using next-generation sequencing, from our lab in Surrey, British Columbia.

Our services include:

- Variant interpretation, medical reporting, and clinical services by Canadian board-certified geneticists and genetic counsellors
- A complete portfolio, spanning most clinical areas
- Fixed and custom panels, with reflex options
- Parental testing for segregation, included when medically relevant
- Options for re-evaluating previously negative results
- A commitment to sharing data to increase diagnostic yield

We are committed to working closely with government, researchers, clinicians, and all Canadians to provide the highest quality molecular diagnostic testing.

As part of our continuous improvement plan, and to align with the new facility, we have also updated the following two forms:

- LifeLabs Genetics Requisition Form - Now fillable, making data entry much faster
  https://www.lifelabsgenetics.com/wp-content/uploads/2019/11/Hereditary-National-Requisition-2019_v8_SF-Fillv3.pdf
- MOHLTC Pre-Approval Form - Pre-populated with the LifeLabs Genetics address to ensure your patients' samples and genetic data remain in Canada
  https://www.lifelabsgenetics.com/wp-content/uploads/2019/11/20190916-MOHLTC-Request-Form_fillv1-1.pdf

We are looking forward to supporting you in increasing diagnostic yields!

For any questions please contact: **1-84-GENEHELP** or **Ask.Genetics@lifelabs.com.**

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For more information, please visit our site at **www.LifeLabs.com**

Dr. Huda Almohri
Deputy Ontario Medical Director, Discipline Head, Microbiology
416-675-4530 ext.42105
huda.almohri@lifelabs.com

Dr. Abdel Belhaj
Medical Microbiologist
416-675-4530 ext.42344
abdel.belhaj@lifelabs.com

Dr. Uvaraj Uddayasankar
Clinical Biochemist
416-675-4530 ext.4221 1
Uvaraj.Uddayasankar@lifelabs.com

Dr. Mohamed Abouelhassan
Clinical Biochemist
416-675-4530 ext.42216
Mohamed.Abouelhassan@lifelabs.com

Dr. Afaf Erfaei
Hematopathologist
416-675-4530 ext.42944
afaf.erfaei@lifelabs.com

Dr. Timothy Feltis
Ontario Medical Director
416-675-4530 ext.42801
tim.feltis@lifelabs.com

Dr. Theano Karakosta
Mass Spectrometry Specialist
416-675-4530 ext.42029
theano.karakosta@lifelabs.com

Dr. Danijela Konforte
Discipline Head, Special Chemistry
416-675-4530 ext.42207
danijela.konforte@lifelabs.com

Dr. Daniela Leto
Medical Microbiologist
416-675-4510 ext.32310
daniela.leto@lifelabs.com

Dr. Patrick St.Louis
Clinical Biochemist
416-675-4530 ext.42253
patrick.st.louis@lifelabs.com

Dr. Tracy Morrison
Clinical Biochemist
416-675-4530 ext.42975
tracy.morrison@lifelabs.com

Dr. Dorothy Truong
Clinical Biochemist
416-675-4530 ext.42208
dorothy.truong@lifelabs.com

Dr. Nicole White-Al Habeeb
Clinical Biochemist
416-675-4530 ext.42099
Nicole.White-AlHabeeb@lifelabs.com

Dr. Krystyna Ostrowska
Medical Microbiologist
416-675-4530 ext.42892
krystyna.ostrowska@lifelabs.com

Dr. Difei Sun
Mass Spectrometry Specialist
416-675-4530 ext.42296
difei.sun@lifelabs.com

Dr. Kika Veljkovic
Discipline Head, High Volume Chemistry
416-675-4530 ext.42832
kika.veljkovic@lifelabs.com

Dr. Miranda Wozniak
Deputy Ontario Medical Director, Discipline Head, Hematology
416-675-4530 ext.42040
miranda.wozniak@lifelabs.com