LifeLabs® Medical Laboratory Services

Inside Diagnostics

HOLIDAY LABORATORY CLOSURES

Taking the time to provide advice to patients who require regular elective testing in anticipation of the holidays in December will facilitate management and possibly patient safety. It is inevitable that some patients will generate results, such as INR, which indicate the need for therapy change. Communication of critical or alert level patient results has proven to be more difficult over the holiday period.

We recommend that patients who require elective testing to be advised to visit a LifeLabs patient service center (PSC) no later than Monday, December 21st .

Please note, LifeLabs PSCs will be closed on December 25th, 26th and January 1st. Some regional PSCs will be open a half day on December 24th or December 28th to provide patient access over the extended holiday weekend. To verify the PSC hours of operation over the holiday period, please call the Customer Care Center at 416-675-3637 or toll free 1-877-849-3637.

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We hope you have a safe and happy holiday season.

WHEN IS FOLATE ANALYSIS IMPORTANT?

Fortification of food including pasta, flour and grains with folic acid was implemented in Canada in 1998. Since that time, the frequency of folate deficiency has decreased dramatically. Statistics collected internally for the community patient population revealed a decline in the RBC folate deficiency rate from 1.78% in 1997 prior to implementation to 0.4% in 1999 and now < 0.01% in 2009 based on a folate cutoff value of 215 nmol/L. [1, 2]

The low incidence rate suggests that there is little post predictive value in measuring the level of serum or RBC folate for the general population. Studies have also demonstrated that the mean RBC folate concentration increased from 680 (669-692 nmol/L) to 852 (841-862 nmol/L) post implementation of the fortification program. [3]

There are situations in which supplementation is important but the need for quanitation of serum or RBC folate is still questionable. Women who are pregnant or are planning to become pregnant, individuals with hemolytic anemias, long term methotrexate therapy or those with excessive alcohol intake require folate supplements. The recommended adult dose is 0.4 mg daily and for women who are pregnant or planning, daily dose is 0.6 mg. In these cases, however test results are unlikely to influence treatment. [3]

Clinical situations for which folate analysis continues to be important include: [3]

- Malabsorption
- Malnutrition
- Alcoholism
- Unexplained significant macrocytosis (with MCV > 105 fL)

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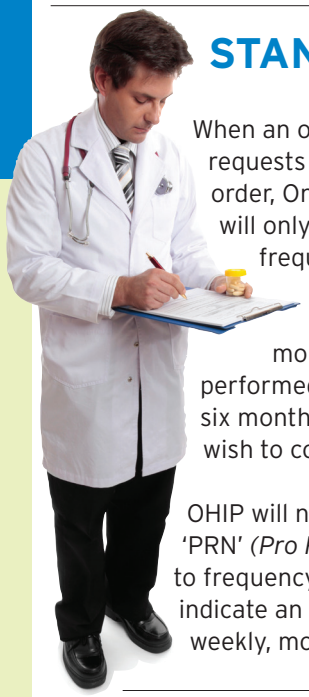


STANDING ORDERS

When an ordering physician/practitioner requests a test to be repeated as a standing order, Ontario Health Insurance Plan (OHIP) will only accept the submission claim if the frequency of the repeat test is indicated on the initial order. OHIP will not accept a repeat test more than six months after the first test has been performed. A new requisition is required every six months should the physician/practitioner wish to continue with the standing order.

OHIP will not recognize the terminology of 'PRN' *(Pro Re Nata)* as an acceptable reference to frequency. All standing order requests must indicate an acceptable frequency such as daily, weekly, monthly, etc.

FAREWELL TO DR. YAMAMURA

Dr. Deborah Yamamura, Medical Microbiologist and Director of Medical Microbiology, has made a decision to leave LifeLabs to focus on her current academic and clinical roles within McMaster University and Hamilton Regional Laboratory Medicine Program. During her eight year tenure with LifeLabs, Dr. Yamamura has provided medical leadership to LifeLabs Microbiology services and has been instrumental in building a strong quality management process within Microbiology and Mycology laboratories. She has also influenced implementation of improved diagnostics within the department including testing for Chlamydia/ GC, antibiotic resistance and urinary pathogens.

Although her last day as Director of Microbiology was November 20th, Dr. Yamamura will provide support to LifeLabs through a transition period into February 2010. We extend our best wishes for great success to Deborah in her roles within McMaster and Hamilton Regional Laboratory. Should you have any questions or concerns related to Microbiology, please do not hesitate to call Dr. Huda Almohri or Dr. David Richardson at 416-675-4530.

LABORATORY TESTING FOR THYROID DYSFUNCTION

Screening Tests

It is well established that a sensitive assay for the level of thyroid stimulating hormone (TSH) is the most appropriate initial laboratory test to aid diagnosis of thyroid dysfunction, both hypothyroidism and hyperthyroidism. For initial screening assessment, testing for TSH alone is sufficient.

Who should be screened?

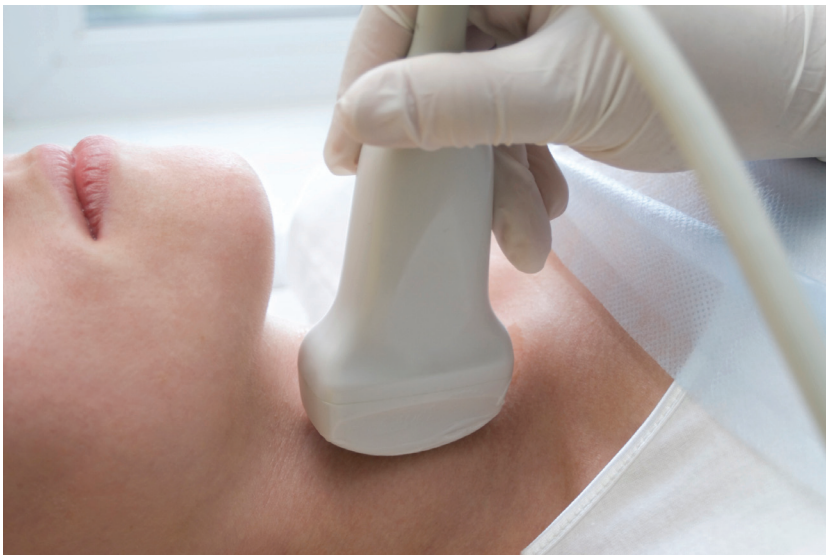
This is still a controversial question. Although the American Thyroid Association recommends screening for thyroid dysfunction after the age of 35 years and every 5 years thereafter, a recent US expert consensus group found after review of current data, that there is insufficient evidence to support population-based screening.[2,4] Aggressive screening of asymptomatic pregnant and post-menopausal women is however, warranted. Other high risk groups that benefit from screening include:

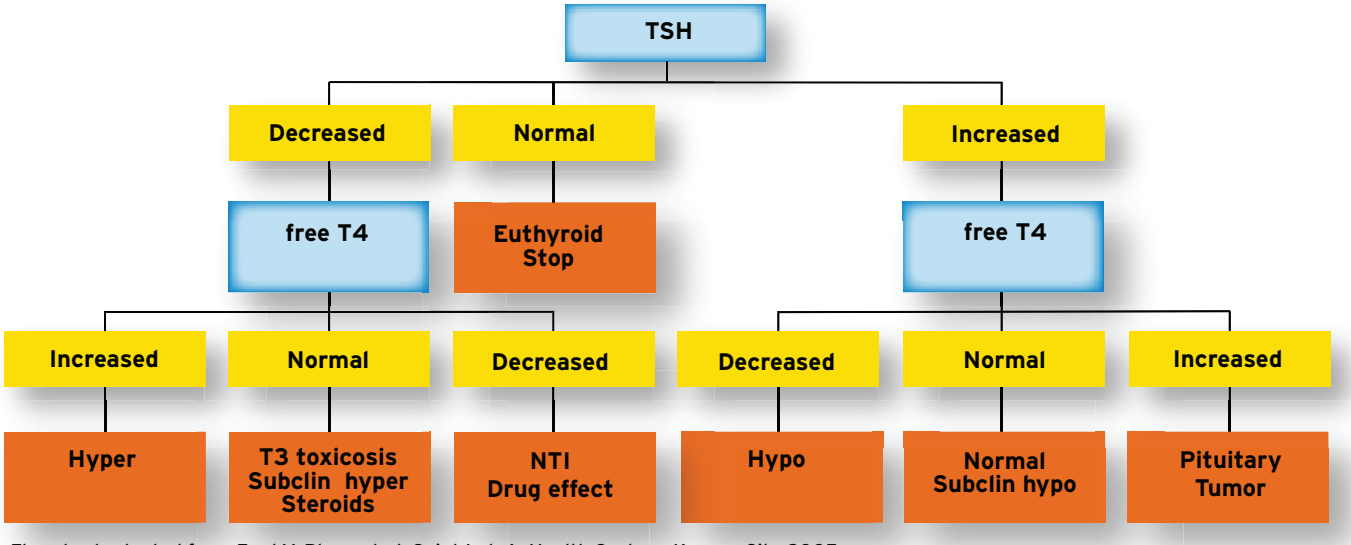
- All newborns (neonatal screening)
- Women trying to conceive
- Women 6 weeks to 6 months postpartum
- Patients with hyperlipidemia, hypertension, and diabetes mellitus
- Patients with a family history of thyroid disease or autoimmune disorders
- Patients on medications known to cause thyroid dysfunction (amiodarone, iodine, dopamine, lithium)

What follow-up investigations for abnormal TSH are needed?

Follow up investigation of TSH results which fall outside the reference interval should include repeat testing of the TSH to confirm the initial result. In suspected hypothyroidism, measurement of FT4 at the time of the repeat TSH is appropriate.

If hyperthyroidism is suspected, measurement of FT4 and T3 (Free or Total) at the time of the repeat TSH is appropriate. FT4 is unlikely to be helpful unless the TSH is < 0.05 mIU/L or > 10.0 mIU/L.





Flowchart adopted from Fred V. Plapp et al. Saint Luke's Health System, Kansas City 2005

Secondary follow-up may include measurement of thyroid antibodies to rule out autoimmune etiology. For suspected hypothyroidism, testing should include anti-thyroid peroxidase or anti-thyroglobulin antibodies. For suspected hyperthyroidism, testing for anti-TSH receptor antibodies or thyroid-stimulating immunoglobulins may be considered.

Condition	Screening Test	Follow-up Testing	Secondary Follow-up Testing
Hypothyroidism	TSH	Repeat TSH Free T4	Thyroid peroxidase or thyroglobulin antibodies
Hyperthyroidism	TSH	Repeat TSH Free T4 T3 (Free or Total)	TSH receptor antibodies or thyroid-stimulating immunoglobulins

Subclinical Hypothyroidism and Hyperthyroidism

Subclinical hypothyroidism is defined as a serum TSH above the upper limit of the reference interval with a normal FT4 concentration. The upper limit of the TSH reference range has drawn much discussion in the literature and some support the use of an upper limit in the range of 2.5 – 3.0 mIU/L. Based on evidence review, the US expert consensus group concluded that, although a TSH concentration in the range of 2.5 – 4.5 mIU/L may identify some individuals with the earliest stage of subclinical hypothyroidism, there was no evidence of associated adverse consequences or benefits of treating patients in this range.[4] The Ontario community laboratories, therefore, continue to report the upper limit of normal in the range of 4.5 – 5.5 mIU/L (LifeLabs defines the upper limit as 5.0).[1]

Patients with a TSH result between the upper limit of normal and 10 mIU/L are at higher risk to progress to overt hypothyroidism but benefits of treatment of these patients are not clearly established.

Subclinical hyperthyroidism is defined as a serum TSH below the reference interval with normal FT4 and T3 (Free or Total) concentrations. In patients with subclinical hyperthyroidism and a TSH in the range between 0.1 mIU/L and the lower limit of normal, benefits of treating these patients are not clearly established.

Management and Treatment

Algorithms, incorporating clinical findings and laboratory test results, have been developed to help determine appropriate follow up and treatment of both hypothyroidism and hyperthyroidism, although other factors, including family history and medication history should also be taken into consideration.[5]

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1. Ontario Association of Medical Laboratories. Guideline for the Use of Laboratory Tests to Detect Thyroid Dysfunction. CLP 015 (July 2007 Revision). Retrieved from the OAML website: http://www.oaml.com
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FACTORS CONTRIBUTING TO SHORT-TERM FLUCTUATIONS IN PSA LEVELS

We are often asked about interpretation of short-term fluctuations in PSA levels. Most cases are related to PSA concentrations between 4 to 10 ug/L in which the initial PSA level is close to 10 ug/L but decreases to a value less than 4 ug/L within a few weeks with no intervention.

Sources of variation in measured PSA and free PSA

Part of this within subject variability is pre-analytical in nature, related to patient preparation, as well as within-subject biological variation. The coefficient of biological variation is 15% for total PSA and 17% for free PSA.[1] Assay imprecision is a small (5-10%) but measurable contributor to variations in PSA concentration.

Between laboratory differences in method used, assay standardization, sensitivity and antibody specificity may account for a bias of up to 20% between PSA results generated from 2 different methods[2]. It is therefore prudent to direct your patient to consistently have PSA measured at the same laboratory to eliminate fluctuations in PSA concentrations due to between method bias.

Clinical sources of variation

Both acute and chronic prostatitis can be significant confounders for PSA screening[3]. Because the clinical features of acute prostatitis are well defined it can be easily differentiated, however other prostatitis, such as category IV NIH prostatitis, can be responsible for an increase in PSA levels without associated symptoms. Category IV prostatitis has a fairly high prevalence, affecting about one third of adult males[4]. Significant fluctuations in PSA should raise suspicion of inflammation or infection as an etiology in these patients.

Recent studies have shown that 30% to 60% of patients with PSA levels in the grey zone, without symptoms of prostatitis, undergo a decrease in PSA levels up to 70% after a 2-4-week treatment with antibiotics[5]. Use of empiric antibiotics has potential associated risks and repeat PSA measurement after a period of observation should be considered as an alternative.

Points to remember:

- It is important to repeat PSA analysis using the same method and ideally in the same laboratory.
- Repeated PSA measurements provide more valid information for patient management than a single measurement.
- Asymptomatic prostatitis can cause significant short-term flunctuations in PSA levels.

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TESTING DURING PANDEMICS

LifeLabs has a Pandemic Plan, which we have been following during the H1N1 flu pandemic.

Our plan includes protecting our employees and maintaining a healthy workforce through the use of personal protective equipment and encouraging employees to get the H1N1 and regular flu vaccine. These measures help to prevent the spread of the flu in our workplace and ensure we can continue to deliver testing services throughout Ontario and the other provinces where we operate.

LifeLabs will do its best to continue testing and delivering timely results; however, should the flu outbreak escalate in severity and prevalence, LifeLabs, in consultation with the Ministry of Health and Long Term Care, will determine the best use of our testing and collection resources. LifeLabs, in consultation with the client, will prioritize the delivery of services dependent upon both need and the availability of resources.

Information on the status of Ontario testing will be posted on the LifeLabs website at: www.lifelabs.com

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