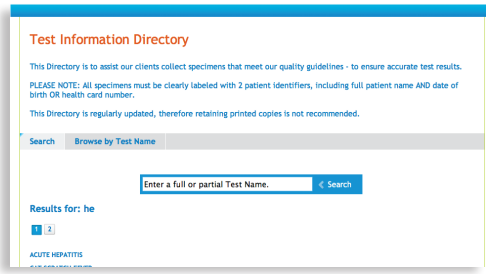
Inside Diagnostics

LIFELABS MOVES TEST DIRECTORY ONLINE

Collection and reporting information at your fingertips

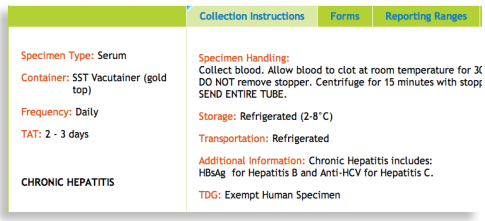
Quick and easy access to information is vital in a fast-paced medical practice. LifeLabs now offers complete information about its test menu via www.lifelabs.com.

The online Test Information Directory features an easy-to-use search functionality, where you can enter in a test name or the first few letters of a test and retrieve a list of available laboratory tests. There is also the ability to browse the complete list alphabetically.

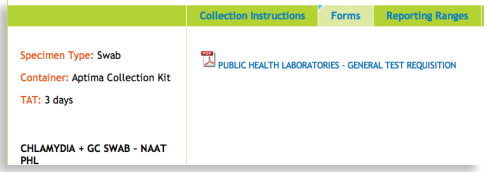


Once you select the test of interest, there are three categories of information available:

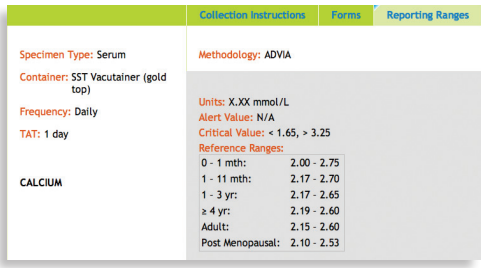
1. **Collection Instructions –** This section details the requirements if you are collecting the specimen. If there is a patient handout available to help the patient prepare appropriately for the test (eg. fasting requirement), this can be printed. You will also find information on proper storage and handling of specimens. If a test has special handling instructions to ensure specimen integrity and a recommendation to send the patient to a patient service centre (PSC) for collection, it will be indicated here.



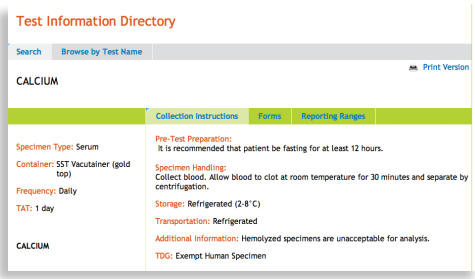
2. **Forms –** In the event there is a unique form or requisition required for a test, you will find the form in this area of the test information. Tests that are to be sent to the public health laboratory will include the appropriate form for downloading and printing.



3. **Reporting Ranges –** With a quick click you can also access the reporting ranges for our tests, as well as information on the methodology we use for testing.



Information available on each test listing includes the type of specimen, the specimen container type, and the turnaround time.



Information in the test directory can be printed, however, this is not recommended. The online directory will be updated as required, so the most current information will be found on the website. This website will provide better access to test information so that all specimens meet quality guidelines. Add it to your browser 'favourites'. Be sure that specimens are clearly labeled with 2 patient identifiers, including full patient name AND date of birth OR health card number. As always, should further consultation be required on test ordering or interpretation, we encourage you to contact us at 1-877-849-3637.

CONTENTS

ONTARIO CERVICAL SCREENING PROGRAM CHANGES

Virginia M. Walley, MD, FRCPC
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The Ontario Cervical Screening Program (OCSP) recently updated its guidelines – and the following restates the OCSP's recent communication to practitioners.

The updated cervical screening cytology guidelines clarifying the age of screening initiation, cessation and the optimum screening interval are as follow:

- Cervical cancer screening should **start at age 21 for women who are or have ever been sexually active.** Women who are not sexually active by 21 years of age should delay cervical cancer screening until they are sexually active. Sexual activity includes intercourse, as well as digital or oral sexual activity involving the genital area with a partner of either gender.
- The prior recommendation was to initiate cervical screening within three years of first vaginal sexual activity.
- Regardless of sexual history, there is no evidence to support screening women under 21 years of age.
- If cytology is normal, **cervical screening should occur every three years.**
- The prior recommendation was for three consecutive, normal, annual Pap test results before extending screening to three-year intervals.

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- Evidence shows that screening every three years is safe and effective and that screening more frequently provides little additional benefit with an increased risk of harm.
- Screening may be discontinued at the **age of 70 if there is an adequate negative cytology screening history in the previous 10 years** (i.e., three or more negative cytology tests).

The "Cervical Screening: Guideline Recommendations," are posted on the CCO website www.cancercare.on.ca/toolbox/qualityguidelines/clinprogram/screening-ebs. They are also featured in the Journal of Obstetrics and Gynaecology Canada (JOGC) (www.sogc.org) in the May 2012 issue.

The guidelines recommend primary Human Papilloma Virus (HPV) testing for women 30 years of age and older, with cytology (Pap test) being the secondary level of testing (triage) for women who are HPV-positive. The implementation of this recommendation within Ontario's organized screening program will be dependent upon public funding of HPV testing, technology assessment and standards development. Planning and implementation for that are underway. Although HPV testing is the preferred screening test for cervical cancer and remains a goal, the OCSP continues to recommend cytology as the primary screening tool.

POINTS TO REMEMBER:

- **Cervical cancer screening should start at age 21 for women who are or have ever been sexually active.**
- **If cytology is normal, cervical cancer screening should occur every three years.**
- **Cervical cancer screening may be discontinued at the age of 70 if there is an adequate negative cytology screening history in the previous 10 years.**

FACTORS CONTRIBUTING TO SHORT-TERM FLUCTUATIONS IN PSA LEVELS

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LifeLabs' biochemists are frequently asked about short-term fluctuations in PSA levels. Most such cases have PSA concentrations in the 4 - 10 µg/L range and physicians have noted that after an initial patient PSA level of close to 10 µg/L, a repeat PSA value a few weeks later is significantly lower with no clinical intervention.

Some of this variability is due to pre-analytical causes – differences in patient preparation, sample handling, or laboratory processing. Within-subject biological variation is another major contributor these fluctuations. The coefficient of biological variation is 15% for total PSA and 17% for free PSA.[1] Alternatively, the difference may relate to assay imprecision. Analytical imprecision, however, is a small contributor to variability as typical coefficients of variation range from 4-6% across the analytical range.

In any case, it is prudent to advise the patient to consistently have their PSA measured at the same laboratory to reduce interlaboratory variation due to method bias. Antibody specificity and traceability between methodologies can lead to significant difference between results.[2] When including the assay imprecision and biological variation, the uncertainty of measurement for total PSA (in the range of 4-10 µg) is as much as 41%.

Both acute and chronic prostatitis may be significant further confounders for PSA-based screening.[3] Acute prostatitis may be easily differentiated. However, other forms of prostatitis, such as category IV NIH prostatitis, may be responsible for an increase in PSA levels without associated symptoms. Category IV prostatitis has a fairly high prevalence, affecting about one third of the adult males.[4] Significant fluctuations in PSA should raise the suspicion of inflammation or infection as an etiology in these patients.

Recent studies have showed that 30% to 60% of patients with PSA levels in the 'grey zone' and without symptoms of prostatitis undergo a decrease in PSA levels of up to 70% after a 2-4-week treatment with antibiotics.[5]

POINTS TO REMEMBER:

- **It is important to repeat PSA analyses using the same method, and ideally in the same laboratory.**
- **Biological variation is a significant contributor to results variability.**
- **Asymptomatic prostatitis can cause significant short-term fluctuations in PSA levels, confounding the interpretation of PSA.**

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1. *Ornstein DK, Smith DS, Rao GS, et al. Biological variation of total, free, and percent free serum prostate specific antigen levels in screening volunteers. J Urol 1997;157(6):2179–82.*
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IRON DEFICIENCY – THE DIAGNOSTIC DILEMMA

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Background

Iron deficiency is defined as a reduction in total body iron to the point that the iron stores are fully depleted leading to tissue iron deficiency and eventual anemia. It is the most common nutritional deficiency worldwide and is frequently encountered in primary practice. It often affects women and young children and can have various causes (Table 1).

TABLE 1: CAUSES OF IRON DEFICIENCY

Increased Requirements	
- Menstruating females	- Pregnancy
- Lactation	- Growing infants and children
- Erythropoietin treatment	
Increased Loss	
- GI bleeding	- Menorrhagia
- Persistent hematuria	- Hemolytic anemias
- Regular blood donors	- Parasitic infections
Decreased Intake	
- Vegetarian diet	- Poor intake, unbalanced diet
- Socioeconomic factors	- Elderly patients
- High risk ethnic groups	- Alcoholism
Decreased Absorption	
- Upper GI pathology	- Gastrectomy
- Medications (eg: Zantac)	

Symptoms of iron deficiency can include fatigue, cold intolerance, irritability, and cognitive or intellectual impairment and typical laboratory findings include a microcytic anemia with a normal or low RBC count. However, early stage iron deficiency can exist before any symptoms or hematological changes occur.

Who to screen?

Universal testing for iron deficiency is not required. At risk patients (Table 1) or those patients with undiagnosed microcytic anemia should be considered for screening. While microcytic anemia is often due to iron deficiency, it can also be caused by anemia of chronic disease and thalassemia or hemoglobinopathy, both of which should be considered in the differential diagnosis. However, it is important to exclude iron deficiency before further testing is initiated.

What test(s) do I order?

Ferritin is the most specific test for screening and diagnosis of iron deficiency - when serum ferritin levels are low iron stores are depleted.

Unfortunately there are limitations to this simple test. Ferritin is an acute phase reactant and will be elevated secondary to acute and chronic inflammatory disorders, malignancy, or liver disease even if iron stores are depleted.

Ancillary testing such as total iron binding capacity (TIBC), percent transferrin saturation (%sat), and serum iron should not be used for screening and have limited diagnostic utility. In response to inflammation, transferrin decreases (negative acute phase reactant) leading to unreliable test results. Therefore, these tests have the same limitations as serum ferritin and would not be reliable if used when serum ferritin is elevated due to inflammation.

To avoid over-utilization of these tests LifeLabs does not process orders for serum ferritin and ancillary tests together unless a valid clinical reason is stated on the requisition. Valid clinical diagnoses include chronic inflammation, chronic kidney failure, iron overload, iron excess, hemochromatosis, and hemosiderosis. If a valid clinical diagnosis is not indicated on the requisition, only a serum ferritin will be performed.

Interpretation of Serum Ferritin Results

Serum ferritin results below the normal range are diagnostic of iron deficiency. This result should prompt investigation and treatment. However, a serum ferritin level above the normal range for age but below 100ug/L does not exclude iron depletion or reduced iron stores (Table 2).

Summary

Iron deficiency is the most common nutritional deficiency worldwide and a common cause of microcytic anemia. Serum ferritin is the recommended test for screening and diagnosis of iron deficiency.

These recommendations are reflected in the revised OAML guideline "Guidelines for the Use of Serum Tests for Iron Deficiency" released in February 2012.

If you have any questions regarding this article please contact Dr. Miranda Wozniak, Discipline Head for Hematology at 416-675-4530 ext. 2040.

POINTS TO REMEMBER:

- **Iron deficiency is the most common nutritional deficiency worldwide.**
- **Screening for iron deficiency should be limited to at risk patients.**
- **Serum ferritin is the recommended test for screening and diagnosis of iron deficiency.**

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Cook JD. Diagnosis and management of iron deficiency anemia. Best Practice and Research Clinical Haematolgy. 2005;18:319-332.

Firkin F, Rush B. Interpretation of biochemical tests for iron deficiency: diagnostic difficulties related to limitations of individual tests. Aust Prescr 1997;20:74-76.

British Colombia Guidelines and Protocols Advisory Committee. Iron Deficiency: Investigation and Management. June 15, 2010.

OAML Guidelines for the use of serum test for iron deficiency (CLP 002) Revised February 2012 www.oaml.com

TABLE 2: INTERPRETATION OF SERUM FERRITIN RESULTS

Serum Ferritin (ug/L)*	Interpretation
<22 (adult males) <17 (male children 2-17yrs) <10 (female adults and female children)	Diagnostic of iron deficiency
Above normal range up to 50ug/L	Depletion of iron stores, probable iron deficiency
50-100	Reduced iron stores, possible iron deficiency
>100	Normal iron stores, iron deficiency unlikely
>1000	Probable iron overload in the absence of inflammation

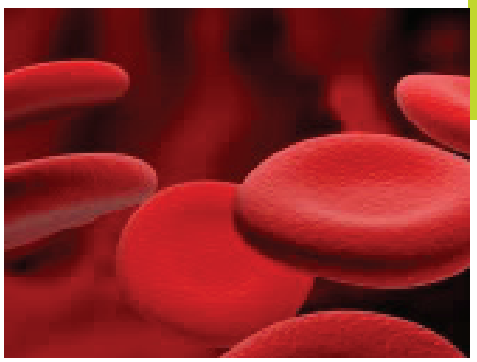
**Based on LifeLabs reportable ranges, always refer to current report*

If ancillary tests results are available, a single result on its own is unreliable for diagnosis of iron deficiency; they should only be interpreted in combination (Table 3).

TABLE 3: INTERPRETATION OF ANCILLARY TEST FOR IRON DEFICIENCY

Test	Result IDA	ACD	IDA and ACD
Serum ferritin	▼	▲	▼ or normal
Serum iron	▼	▼	▼
Total iron binding capacity	High normal to ▲	▼	▼ or low normal
% Transferrin saturation	▼	▼ or may be normal	▼

IDA – Iron deficiency anemia ACD – Anemia of chronic disease



BLASTOCYSTIS: TO TREAT OR NOT TO TREAT

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Members of the genus Blastocystis are ubiquitous parasites with a worldwide distribution. Blastocystis is the most frequently isolated stool parasite according to many epidemiologic surveys, with a higher prevalence in underdeveloped countries; this may be attributed to poor hygiene, exposure to animals, and consumption of contaminated food or water. Blastocystis is transmitted via the fecal-oral route and reside in the gastrointestinal tract. The relationship between Blastocystis infection and human disease remains unclear.

Blastocystis is the most common stool parasite seen at LifeLabs; historically this finding was not reported due to its uncertain pathogenicity. However, due to recent physician requests, LifeLabs has started reporting the presence of Blastocystis in stool samples when present in moderate or higher amounts. The report also includes a comment informing physicians that the pathogenicity of this parasite is undefined.

Clinical Symptoms and Epidemiology

There has been debate in the literature concerning the pathogenicity of Blastocystis and its relation to human disease remains unclear. Some studies suggest an association between the parasite and disease, but others do not.

A variety of signs and symptoms, ranging from intestinal symptoms to cutaneous disorders, have been attributed to Blastocystis infection:

- Acute or chronic diarrhea
- Abdominal pain
- Nausea
- Anorexia
- Bloating
- Flatulence

Blastocystis has been investigated as an etiologic agent of Irritable Bowel Syndrome (IBS), although current studies do not suggest a clear role. Controlled trials are needed demonstrating a resolution of symptoms in Blastocystis-infected IBS patients by eradication of the organisms.

Diagnosis

Laboratory diagnosis can be made by several different methods:

- Direct smear
- Concentrated smear
- Culture
- Nucleic acid amplification technique

LifeLabs' method includes a concentrated smear followed by iron hematoxylin stain.

As with other enteric pathogens, the examination of multiple stool specimens increases the diagnostic yield. It is recommended that 3 consecutive stool samples be sent for diagnosis of Blastocystis.

Treatment

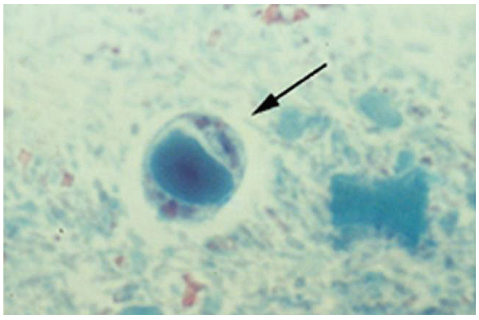
A number of antimicrobial agents have been used for treatment of Blastocystis infection. For example, Metronidazole, Trimethoprim-Sulfamethoxazole, and Iodoquinol all have been reported as options for therapy.

There is still a great deal of debate about the true pathogenicity of Blastocystis and therefore much debate about the need for treatment. Presently there is no consensus as to which patients should be treated for Blastocystis infection. A recent publication in the Clinical Infectious Diseases journal gives more information and guidance on treatment[6].

Conclusion

The pathogenicity and relationship of Blastocystis infection to human disease remains unclear. The risk and benefit of treatment should be carefully considered as many of the drugs used in the treatment of Blastocystis infection have significant side effects.

Figure 1: Trichrome stain showing a cyst of Blastocystis in stool sample.



It is quite possible that patients who respond to treatment for Blastocystis with metronidazole or trimethoprimsulfamethoxazole (TMP-SMX) may actually have clinical improvement owing to treatment of a secondary pathogen. Therefore, isolation of Blastocystis in stool from a symptomatic individual should lead to a thorough investigation for other causes of the gastrointestinal complaints. It is reasonable to initiate a trial of antimicrobial therapy in patients who have persistent diarrhea or those who have undergone an extensive work-up without any other pathogen or gastrointestinal source identified.

In the asymptomatic individual, treatment is not necessarily indicated.

POINTS TO REMEMBER:

- **Blastocystis is a frequently encountered parasite worldwide.**
- **Blastocystis pathogenicity and relationship to human disease remains unclear.**
- **Currently, LifeLabs reports the presence of Blastocystis in stool samples when present in moderate or higher amounts with a comment indicating that pathogenicity of this parasite is controversial.**
- **It is suggested in the literature that symptomatic patients be treated with a trial of antibiotics if thorough investigations for other causes of the gastrointestinal complaints are negative.**
- **Treatment is not indicated in asymptomatic patients.**

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3. *UdkowMP, Markell EK. Blastocystis hominis: prevalence in asymptomatic versus symptomatic hosts. J Infect Dis 1993; 168:242–4.*
4. *Clark CG. Extensive genetic diversity in Blastocystis hominis. Mol Biochem Parasitol 1997; 87:79–83.*
5. *Coyle CM, Verughese J, Weiss, LM , Tanowitz HB Blastocystis to treat or not to treat CID 2012:54 105-110*

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