

**Guidelines for the Use of Serum Tests for Iron Deficiency (CLP 002)**

Revised February, 2012

**1. Purpose**

To provide clinicians with a concise reference document describing the appropriate laboratory tests for assessing patients of all ages suspected of having iron deficiency.

Investigation of the underlying cause of iron deficiency is beyond the scope of this guideline. Iron overload will be covered in a separate OAML guideline.

Readers are reminded that OAML Guidelines will not apply to every clinical situation, nor can they serve as a substitute for sound clinical judgment.

**2. Causes of Iron Deficiency:**

**Table 1: Causes of Iron Deficiency**

<b>Increased Requirements</b>	<ul style="list-style-type: none"> <li>• Menstruating females</li> <li>• Pregnancy</li> <li>• Lactation</li> <li>• Growing infants and children</li> <li>• Erythropoietin treatment</li> </ul>
<b>Increased Loss</b>	<ul style="list-style-type: none"> <li>• GI bleeding</li> <li>• Menorrhagia</li> <li>• Persistent hematuria</li> <li>• Intravascular hemolytic anemias</li> <li>• Regular blood donors</li> <li>• Parasitic infections</li> </ul>
<b>Decreased Intake</b>	<ul style="list-style-type: none"> <li>• Vegetarian diet</li> <li>• Socioeconomic factors</li> </ul>
<b>Decreased Absorption</b>	<ul style="list-style-type: none"> <li>• Upper GI pathology (eg: Celiac and Crohn’s disease)</li> <li>• Gastrectomy</li> <li>• Medications (antacids, Zantac)</li> </ul>

### 3. Indications for Testing

Screening of the general population for iron deficiency is not indicated.

At-risk populations as defined in Table 1 with clinical signs and symptoms and patients with microcytic anemia should be considered for screening.

It should be noted that although microcytic anemia is often due to iron deficiency, it can also be caused by hemoglobinopathies and anemia of chronic disease. The latter disorders are beyond the scope of this guideline, but should be considered in the differential diagnosis and management. Failure to identify these other causes may result in unnecessary iron replacement.

### 4. Testing for Iron Deficiency

A low serum ferritin result indicates that iron stores are depleted, making serum ferritin the most specific test for iron deficiency and the only test that should be used for screening. Ancillary tests such as serum iron, total iron binding capacity, and percent saturation are not indicated and should not be ordered.

Iron deficiency should be suspected when the Complete Blood Count (CBC) demonstrates a microcytic, hypochromic anemia with a normal or reduced Red Blood Cell (RBC) count. These laboratory findings may be present before the onset of clinical symptoms of anemia. Additionally, early stage iron deficiency can exist before any hematological changes occur; a low serum ferritin result would be the only indication of this clinical situation.

**Caution:** In the presence of inflammatory disease, malignancy, or liver disease, serum ferritin may be elevated and will therefore not accurately reflect iron stores. C-reactive protein (CRP) and liver function tests may be ordered when necessary to help determine if a ferritin result is elevated due to inflammation.

### 5. Serum Ferritin Results Interpretation

A serum ferritin result below the normal range for the patient's age is diagnostic of iron deficiency and should prompt investigation and treatment.

Serum ferritin typically has a wide reference range and will vary with age and gender, consult your laboratory's report for the established reference ranges.

Inflammation is common and in its presence ferritin may be elevated and give seemingly normal results, even in the presence of iron deficiency. Therefore, a serum ferritin result within the normal range for the patient's age, but less than 100 ug/L, does not exclude depleted or reduced iron stores (See Table 2 - Interpretation of Serum Ferritin Results on the following page). In this situation it is recommended that the patient's response to iron replacement be assessed or other causes of microcytic anemia be excluded.

**Table 2: Interpretation of Serum Ferritin Results**

Serum Ferritin (ug/L)	Interpretation
<15 <12 (in children)	Diagnostic of iron deficiency
15-50	Depletion of stored iron, probable iron deficiency
51-100	Reduced iron stores, possible iron deficiency
101- 300	Iron deficiency unlikely (in the absence of inflammation)
*>300	May reflect inflammation or iron overload
*>800	Probable iron overload (in the absence of inflammation)

\* Refer to OAML Iron Overload Guideline (CLP 001)

## 6. Ancillary tests for Iron Deficiency

**Serum Iron, Total Iron Binding Capacity (TIBC) and % Saturation (Transferrin Saturation) testing for iron deficiency is not encouraged.** These tests lack specificity and their results can be distorted in several clinical situations limiting their diagnostic use. Transferrin levels often decrease in response to inflammation. Therefore, much like ferritin, these tests for iron deficiency are unreliable in the setting of acute and chronic inflammatory disorders (chronic infection, autoimmune disease), liver disease, and malignancies.

There is an expanding list of biomarkers that in the future may be used to diagnose iron deficiency. Included in this list are soluble serum transferrin receptor (sTfR) and the reticulocyte hemoglobin content (CHr or Ret-He). These tests are not currently available for routine use, but in the future may prove to be useful tools to differentiate iron deficiency from other causes of anemia.

It is recognized that many patients have non-diagnostic ferritin levels yet iron deficiency may still be suspected clinically. In these cases, it is recommended that other causes of microcytic anemia be excluded or the patient's response to iron replacement be assessed. Lastly, in some clinical situations, further testing such as assessment of bone marrow iron stores may be indicated.

## 7. Summary

Iron deficiency is a common disorder with several etiologies. Where confirmation of iron deficiency is indicated, serum ferritin is the best and only test that should be ordered.

The following references were used in the preparation of this guideline:

1. British Columbia Guidelines and Protocols Advisory Committee. Iron Deficiency: Investigation and Management. June 15, 2010.
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9. Wish, J. "Assessing Iron Status: Beyond Serum Ferritin and Transferrin Saturation." Clinical Journal of the American Society of Nephrology 1 (2006):S4-S8.

## Acknowledgements

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