Determining Iron Deficiency

Iron Corner
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SUMMARY

- Iron deficiency is often the most common cause of anemia.
- Determine if the patient has absolute iron deficiency, functional iron deficiency or both for decisions related to effective management.
- Reticulocyte studies are always indicated when assessing / diagnosing iron deficiency.
- Iron studies should consist of serum iron, total iron binding capacity (TIBC), percent transferrin saturation (Fe/TIBC) and serum ferritin to diagnose iron deficiency.

Is it Absolute or Functional Iron Deficiency?

To forge a useful algorithm for the recognition and management of iron deficiency, it is prudent to have a discussion of the difference between **absolute (overt)** and **functiona**l iron deficiency.

What Is Absolute Iron Deficiency? [1,2]

Body iron stores are depleted.

Absolute, or overt iron deficiency, is due to iron loss from bleeding, or iron absorption that falls short of daily losses.

The most common causes of iron deficiency due to blood loss include:

- Gastrointestinal (including both upper and lower gastrointestinal blood loss)
- Genitourinary blood loss (including menstrual blood loss)

In the western world, iron loss deficiency due to bleeding is, by far, more common. Inadequate iron intake is rare due to fortification of many prepared foods with iron. However, iron deficiency due to decreased uptake or absorption may be seen in malabsorption syndromes such as untreated celiac disease and in unusual diets and with the introduction of cow's milk, rather than formula, in infants younger than 12 months of age.

It is absolutely imperative that the healthcare provider treating iron deficiency meticulously search for sources of blood loss to avoid missing potentially treatable life-threatening illnesses.

What Is Functional Iron Deficiency (aka Iron Restricted Erythropoiesis)? [1,2]

Ample iron is present, but with reduced bioavailability.

Central to this process is hepcidin, an iron regulatory protein synthesized by the liver that blocks iron absorption by binding to and inactivating the membrane-bound, iron transport protein, ferroportin, in intestinal enterocytes and reduces release of iron from macrophages.[3]

Hepcidin is upregulated in a large variety of inflammatory disease states, resulting in anemia due to a reduction in the bioavailability of iron to support normal erythropoiesis. Prior to the discovery of hepcidin, functional iron deficiency was referred to as anemia of chronic disease or anemia of chronic inflammation.

What Laboratory Tests Are Needed?[5]

Absolute Reticulocyte Count

Both overt and functional iron deficiency are associated with decreased red cell production, manifested by reticulocytopenia. The measurement of the reticulocyte count is therefore always indicated.

For practical purposes, an absolute reticulocyte count of <75,000 in the presence of a decreased hemoglobin represents hypoproliferation (or decreased red cell production). Once increased destruction is excluded, confirmatory tests for iron deficiency should be done.

Reticulocyte Index

A convenient way to assess bone marrow response to anemia is through the reticulocyte index. A value <2 suggests a response to anemia is insufficient; a value >3 suggests an adequate response.[6]

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Reticulocyte Hemoglobin Content (CHr, MCHr, RET-He)
Reticulocyte hemoglobin content is a direct measure of iron in the reticulocyte measured in picograms (pg). A mean CHr less than 28 pg is strongly suggestive of iron deficient erythropoiesis.

Iron Status Tests
In an otherwise healthy patient (without concomitant co-morbidities), a serum iron, total iron binding capacity (TIBC), percent transferrin saturation (Fe/TIBC) and serum ferritin should suffice to diagnose iron deficiency and be strongly indicative of functional iron deficiency in the context of the patient's clinical history. If the ferritin is elevated in the face of decreased percent transferrin saturation, a C-reactive protein as an indicator of inflammation may be useful in demonstrating that a normal or elevated ferritin is due to inflammation rather than normal iron stores.

Mean Corpuscular Volume (MCV)
The MCV can be helpful as well; however, the test lacks both sensitivity and specificity. Many patients with iron deficiency, both overt and functional, may have a normal MCV while a decreased MCV may be seen with certain hemoglobinopathies, e.g. thalassemia.

When Should Labs Be Drawn?
These tests are best done fasting. There is a diurnal variation of iron levels and recent food intake can markedly affect the serum iron level, that, in turn, affects the transferrin saturation.

Symptomatic Diagnosis
If long standing iron deficiency is suspected, a simple question about ice craving (pagophagia) can be a useful screening assessment for iron deficiency. Classical physical findings include a glasslike tongue and ridged fingernails (Mees' lines).

References

1. Coyne DW, Kapoian T, Suki W, *et al*. Ferric gluconate is highly efficacious in anemic hemodialysis patients with high serum ferritin and low transferrin saturation: results of the Dialysis Patients' Response to IV iron with Elevated Ferritin (DRIVE) study. *J Am Soc Nephrol.* 2007; 18: 975-984.
2. Wish JB. Assessing iron status: beyond serum ferritin and transferrin saturation. *Clin J Am Soc Nephrol.* 2006; 1(suppl 1): S4-S8.
3. Macrophages and iron trafficking at the birth and death of red cells. Korolnek T, Hamza I. *Blood.* 2015;125(19):2893. Epub 2015 Mar 16.
4. Weiss G, Goodnough LT. Anemia of Chronic Disease *N Engl J Med* 2005; 352:1011-1023
5. Goodnough LT, Nemeth E, Ganz T, Detection, evaluation, and management of iron-restricted erythropoiesis. *Blood* 2010: 116(23): 4754-4761.
6. Hutchinson RE, Davey FR. Hematopoiesis. In: Henry JB, ed. *Clinical Diagnosis and Management by Laboratory Methods 19th edition*. WB Saunders 1996.
7. Cancelo-Hidalgo MJ *et al,* Tolerability of different oral iron supplements: a systematic review. *Curr Med Res Opin* .2013;29:291-303.
8. https://www.thelancet.com/journals/lanhae/article/PIIS2352-3026(17)30182-5/fulltext
9. Arcangelo V, Peterson A. Pharmacotherapeutics for Advanced Practice A Practical Approach. Second Edition, 2006. Philadelphia, Pa. Lippincott Williams and Wilkins. Chapter 55 Anemias (Kelly Barranger) pg 800.

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