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September 2025 Updates to Iron Study Testing

The laboratory has been working with clinicians to improve the utilization of tests used to diagnose iron disorders and facilitate interpretation of those results. The changes, effective 9/2/2025 are as follows:

- 1) Low iron results: When the iron result is below the normal range, the following comment will be appended: "If testing for iron deficiency, serum iron is unreliable as the primary test. It is recommended to include ferritin and TIBC with iron (transferrin) saturation for a more reliable assessment."
- 2) Low normal ferritin results: When the ferritin level is in the lower end of the normal range (30-100) the following comment will be appended: "If testing for iron deficiency, iron deficiency can occur with low normal ferritin levels, especially in patients with inflammation because ferritin is a positive acute phase reactant. It is recommended to include TIBC with iron (transferrin) saturation for a more reliable assessment."
- 3) **High ferritin results:** When the ferritin level is above the normal range the following comment will be appended: "If testing for iron overload/hereditary hemochromatosis, the patient should be assessed initially by a fasting morning TIBC with iron (transferrin) saturation test. Because it is an acute phase reactant, ferritin may be elevated in a number of conditions."
- 4) Female reference range for ferritin: The current population based low end of the reference range (15 ng/ml) is below recommended cutoffs (ranging from 30 to 50) for physiologically decreased ferritin levels ^{1,2,3}. The use of a target/desired range is analogous to the way lipid tests are flagged. We are changing the low end to 30 ng/ml. Similarly, the upper end is going from 150 to 250 ng/ml to improve specificity for iron overload diagnosis.
- **5)** Changing the test name for Iron Saturation. Many institutions call this test Transferrin Saturation. Iron Saturation is often used interchangeably. The two names for the same test can lead to confusion. We are renaming the test Iron (Transferrin) Saturation.
- 6) Changing the upper end of the reference range Iron (Transferrin) Saturation.

 Percent saturation often exceeds 45% in hereditary hemochromatosis⁴. The current Bronson reference range is up to 50% in Females and 55% in males. The new ranges will be Male: 20-45% and Female: 15-45%.

The following table, modified from UpToDate³ is a summary of tests related to testing for iron disorders.

Test	Description	Finding in Iron Deficiency	Finding in Iron Overload
Primary Tests			
Serum Iron (Epic LAB94)	 Iron in the circulation Can be transiently elevated after taking iron supplement (including multivitamin) or iron rich meal. Only useful in calculating iron (transferrin) saturation. Not useful in isolation. 	Not used for diagnosis	Not used for diagnosis

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Test	Description	Finding in Iron Deficiency	Finding in Iron Overload		
Transferrin & TIBC (Epic LAB829)	 Iron binding proteins. TIBC is calculated from Transferrin. Increased when iron stores are low. 	• High (TIBC >457 ug/dl)	• Low (TIBC <254 ug/dl)		
Iron Saturation (aka Transferrin Saturation) included in Bronson TIBC panel. (Epic LAB829)	 Percent of iron binding proteins saturated with iron. Calculated from serum iron and TIBC. Helpful in individuals with inflammation that may elevate ferritin. 	• Low (Male <20%) (Female <15%)	• High (Male >45% (Female >45%)		
Ferritin (Epic LAB68)	 Iron storage protein Acute phase reactant: increased in inflammatory states, which can mask iron deficiency Unaffected by recent iron intake. 	• Low < 30 ng/ml	• High (Male >400 ng/ml) (Female >250 ng/ml)		
Second Level Tests – Specialized testing for selected cases					
Reticulocyte hemoglobin content- included in RETIC panel (Epic LAB296)	 Hemoglobin in reticulocytes Not increased in inflammatory states Often used in CKD Unreliable in thalassemia 	• Low < 28.6 pg	Not used for diagnosis		
Soluble transferrin receptor-sent to Mayo Ref Lab (Epic LAB3129)	 Receptor for transfer of iron into cells Not increased in inflammatory states Elevated in patients with hemolysis, thalassemia & sickle cell disease 	Concentrations are inversely related to iron status; sTfR elevates in response to iron deficiency and decreases in response to iron repletion.	Not used for diagnosis		
Bone Marrow Iron Stain	Storage iron (the gold standard test)	• Absent	• Increased		

References

- 1) <u>Diagnosis and management of iron deficiency in chronic inflammatory conditions (CIC): is too little iron</u> making your patient sick? | Hematology, ASH Education Program | American Society of Hematology
- 2) Sex, lies, and iron deficiency: a call to change ferritin reference ranges | Hematology, ASH Education Program | American Society of Hematology
- 3) Diagnosis of iron deficiency and iron deficiency anemia in adults UpToDate
- 4) ACG Clinical Guideline: Hereditary Hemochromatosis PubMed

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