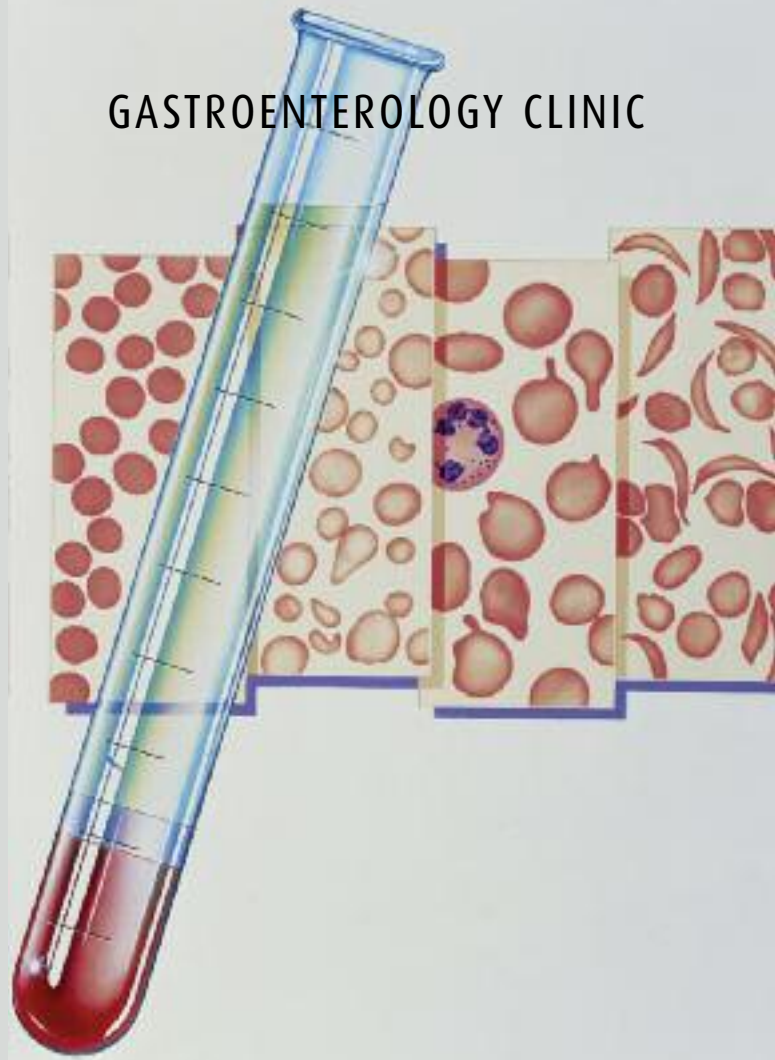


Interpretation of iron studies: a practical approach



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When interpreted with care, iron studies can be very useful biochemical tests. The clinical scenario of the individual patient must always be taken into account.

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REMEMBER

- A low serum ferritin level is the single most reliable indication of true iron deficiency.
- Unexplained iron deficiency is concerning for underlying gastrointestinal pathology such as coeliac disease or malignancy.
- A normal or high serum ferritin level is often the result of inflammation, infection, liver disease or cancer and can therefore mask the presence of iron deficiency. C-reactive protein (CRP) level, erythrocyte sedimentation rate (ESR) and liver function tests may provide useful additional information.
- A low serum iron level as an isolated abnormality has poor diagnostic specificity for iron deficiency.
- A high transferrin saturation (>50%) on a fasting blood sample is the earliest abnormality revealed on iron studies of haemochromatosis.

TEST INTERPRETATION

- Iron studies are commonly ordered to investigate microcytic anaemia and fatigue. Iron overload is often an incidental finding. Common components of iron studies are described in the Table.
- The main challenges in the interpretation of iron studies are usually making an accurate diagnosis of iron deficiency and

TABLE. COMMON COMPONENTS OF IRON STUDIES

	Ferritin	Serum iron	Total iron binding capacity (TIBC)	Transferrin saturation
Function	Total body iron stores	Amount of circulating iron bound to transferrin	Blood capacity to bind iron with transferrin	Ratio of serum iron to TIBC
Interpretation	High: acute phase reactant, iron overload or liver disease Low: iron deficiency	High: iron overload, iron therapy Low: iron deficiency, chronic illness	High: iron deficiency Low: chronic disease	High: iron overload, iron therapy Low: iron deficiency, chronic disease
Important notes	False normal or elevated result due to inflammation, hepatocellular damage or malignancy	Low result due to inflammation, malignancy or hypoproteinaemia	Increased result in pregnant women and in patients taking oestrogen supplements (i.e. oral contraceptive pill)	Falsely elevated result due to recent iron ingestion (fasting blood samples are needed)

distinguishing between iron deficiency anaemia and anaemia of chronic disease. Additional causes of microcytic anaemia include haemoglobinopathies and, rarely, lead poisoning.

- Iron studies should be performed on fasting blood samples because recent ingestion of iron results in a falsely high serum iron concentration and, therefore, transferrin saturation level.
- Classic iron deficiency will lead to low serum ferritin and serum iron levels and a high total iron binding capacity (TIBC).¹ This picture may be masked by inflammation, infection or cancer because the ferritin level can be falsely elevated; inflammatory markers such as ESR and CRP are usually elevated in these settings. Ferritin is stored in hepatocytes, so any condition causing hepatocellular damage will result in a raised ferritin level.^{1,2} Diagnosis of iron deficiency when these clinical conditions coexist can be difficult or even impossible using biochemical tests.³
- The soluble transferrin receptor assay adds little clinically useful information and is largely unavailable. The gold standard test of bone marrow aspiration is rarely performed due to

its invasive nature and associated risks of bleeding and infection.

- If iron deficiency is suspected, a therapeutic trial of iron supplementation with close monitoring for response is more practicable than progressing to bone biopsy. Increasing mean cell volume and haemoglobin level within four weeks are the usual markers of response. If iron deficiency is present, a diagnostic work up is always indicated. This should include a history, focusing on iron intake and symptoms of blood loss, and a targeted physical examination, with or without further diagnostic tests.^{3,4}
- Iron studies in anaemia of chronic disease usually show a normal or elevated ferritin level. The serum iron level is often low and TIBC can be low or normal.⁵
- Iron studies can also be useful in diagnosing conditions of iron overload, including haemochromatosis and transfusion-related iron overloading. A high ferritin level, and in particular a high transferrin saturation, will usually be present.⁶
- Extremely elevated values of ferritin (i.e. >10,000 µg/L) are sometimes found and should lead to consideration

of rare diseases such as adult-onset Still's disease, haemophagocytosis and haemochromatosis.⁶

CONCLUSION

- Iron studies can be very useful biochemical tests if interpreted using the recommendations above. The clinical scenario of the individual patient must always be taken into account. **MT**

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