

Hyperferritinemia

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1 Ferritin is a cellular iron storage protein and an acute phase reactant

Clinicians obtain ferritin levels when they suspect iron deficiency or overload; they may also obtain ferritin levels during the work-up of some hematologic or autoimmune conditions.¹⁻⁴ Levels may be elevated in many chronic conditions (Box 1) or during acute illness, which can confound interpretation.² Levels that return to normal after resolution of illness do not require further investigation.

2 Transferrin saturation testing can identify iron overload states

If the transferrin saturation is above 45% and ferritin levels are greater than 300 µg/L in men or than 200 µg/L in women, genetic testing should be done to assess for hemochromatosis.⁴ Secondary causes of iron overload (e.g., iron-loading anemias, exogenous iron administration) can also have elevated transferrin saturation. Hyperferritinemia without elevated transferrin saturation suggests an alternate cause.^{2,4}

3 Ferritin elevations above 10 000 µg/L should prompt consideration of specific diagnoses

Although elevations above 10 000 µg/L may be seen in malignant disease, chronic kidney disease or liver dysfunction,³⁻⁵ high levels could also suggest adult-onset Still disease and hemophagocytic lymphohistiocytosis in acutely ill patients with suggestive features (e.g., fever, hepatosplenomegaly, rash, neurologic findings, pancytopenia).^{1,5}

4 Patient history and examination should guide additional investigations

Further testing may include evaluating markers of inflammation and autoimmune disease, serologic evidence of infection and ultrasonography of the liver. Alcohol intake and risk factors for metabolic syndrome should also be reviewed.^{2,3}

5 Patients with stable, mild ferritin elevation do not require further testing

Patients with serum ferritin levels below 1000 µg/L without an elevated transferrin saturation or clear underlying cause should be counselled about alcohol cessation and dietary changes aimed at managing metabolic syndrome. Stable repeat levels at 3–6 months do not require additional testing.² Ferritin levels persistently above 1000 µg/L without a clear cause should be investigated further by a general internist or hepatologist.^{3,4}

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Box 1: Causes of hyperferritinemia.¹⁻⁴

- Alcohol use
- Alcoholic and nonalcoholic fatty liver disease
- Chronic kidney disease
- Hematologic causes
 - Thalassemia
 - Chronic hemolytic anemia
 - Sickle cell anemia
- Parenteral iron overload or red blood cell transfusions
- Myelodysplastic syndromes
- Hemochromatosis
- Infectious causes
 - Viral hepatitis
 - HIV
 - Osteomyelitis
- Inflammatory causes
 - Connective tissue disorders
 - Rheumatoid arthritis
- Metabolic syndrome
- Neoplastic causes
 - Solid organ and hematologic malignant diseases

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