

SERUM FERRITIN

TERM DEFINITION

Ferritin is the cellular storage protein for iron. It is present in small concentrations in blood, and the serum ferritin concentration normally correlates well with total-body iron stores, making its measurement important in the diagnosis of disorders of iron metabolism.

THE ASSAY

NORMAL VALUES

Adult males

- Mean age 18 years: 60-80 mg/dL
- Upper limit: 300-400 mg/dL

Adult females

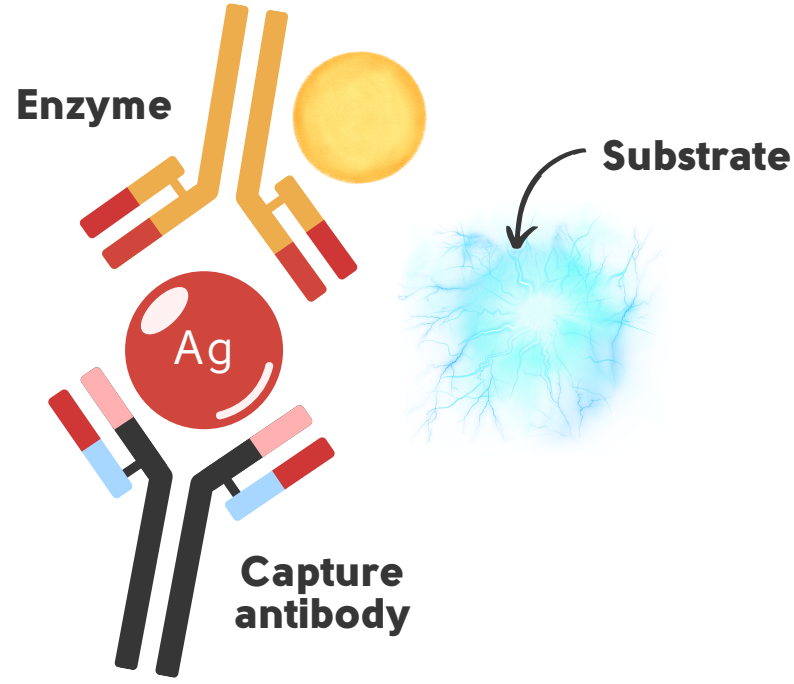
- Mean age 18 years: 25-30 mg/dL
- Upper limit: 15-200 mg/dL

OPTIONS

- Immunoassays—e.g., enzyme-linked immunosorbent assay (ELISA)
- immunochemiluminescence
- Immunoturbidometric assay (rarely used)

SERUM FERRITIN ASSAY

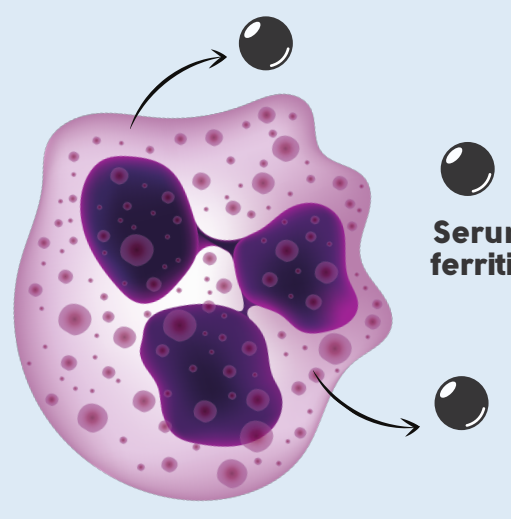
DIRECT SANDWICH ELISA



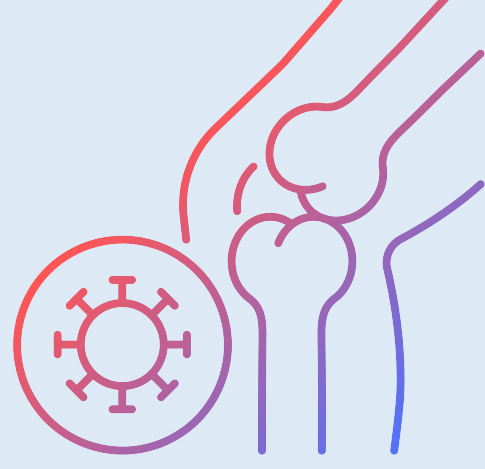
SANDWICH-BASED COLORIMETRIC ELISA



CLINICAL PEARLS



Serum ferritin is a secreted protein; it is primarily made up of L-chains and does not contain iron. Its source and function remain a mystery.



< 10
Serum ferritin

99% specific for iron deficiency (rarely seen in hypothyroidism & ascorbate deficiency).

> 100
Serum ferritin

Iron deficiency unlikely even in setting of inflammation (end-stage kidney disease an exception).

DIFFERENTIAL DIAGNOSIS

ELEVATED SERUM FERRITIN

Iron overload

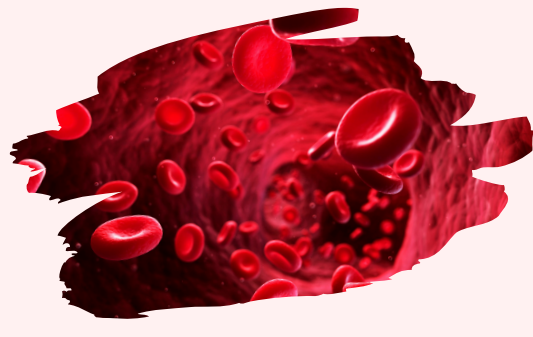
Inflammation

Leak

LOW SERUM FERRITIN

Diagnostic of iron deficiency

* Causes of elevated ferritin are very context-dependent (e.g., inpatient vs. outpatient setting).



HIGH SERUM FERRITIN

Iron overload:

- Hereditary hemochromatosis
- Transfusion
- Ineffective erythropoiesis

Inflammatory disorders:

- Infection
- Rheumatological disorders (e.g., Still's disease)
- Malignancy
- Metabolic syndrome

Leak:

- Acute liver failure

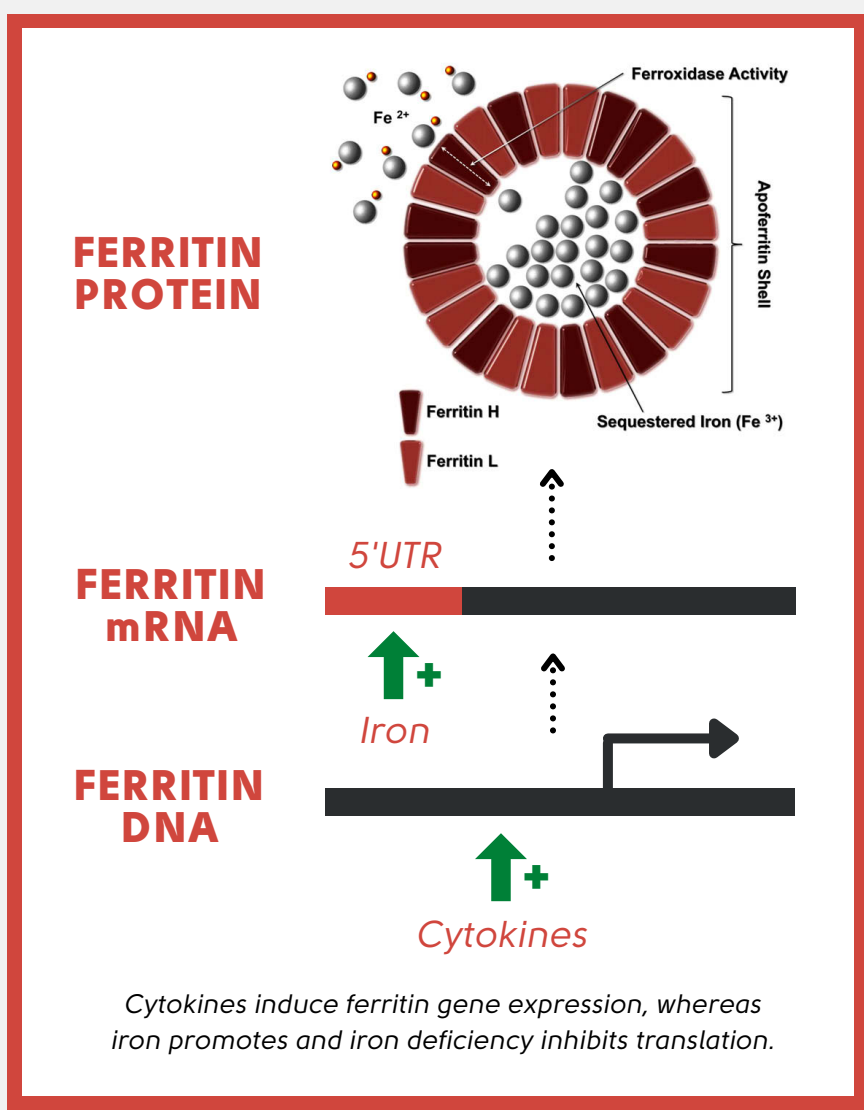
Multiple mechanisms:

- Liver disorders
- Renal disorders
- Hemophagocytic lymphohistiocytosis (HLH; leak & inflammation)

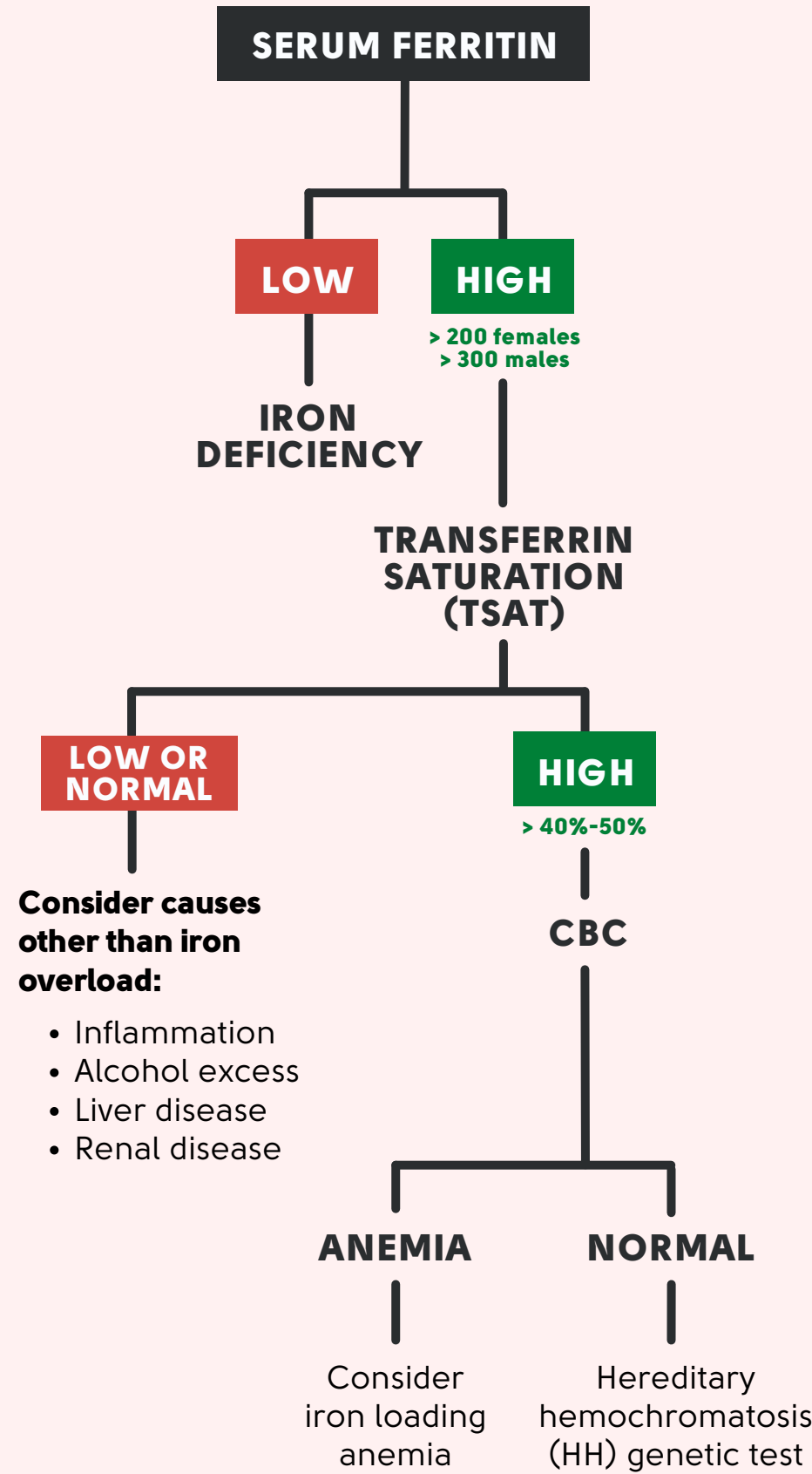
Congenital hyperferritinemia

PROXIMATE MECHANISMS

Ferritin provides intracellular storage of bioavailable iron in a safe and readily accessible form. Ferritin comprises 24 monomer subunits that consist of either Heavy (H) type (21 kDa) or Light (L) type (19 kDa) polypeptide chains encoded by 2 different ferritin genes. The 24 monomer subunits associate to form a hollow spherical particle that can store up to 4000 iron atoms as Fe³⁺ ions.



SERUM FERRITIN WORK-UP



EXTREME HYPERFERRITINEMIA

Markedly elevated serum ferritin is typically thought to occur only in a few conditions, including adult onset Still's disease, and hemophagocytic lymphohistiocytosis (HLH).

However, recent studies show marked elevation in adults occurs in many conditions and is not predictive of HLH.

Blood. 2015;125:1548-52

113 patients with serum ferritin levels higher than 50,000 mg/L

- Renal failure 65%
- Hepatocellular injury 54%
- Infection 46%
- Hematological malignancy 32%
- Inflammatory conditions 18%
- HLH 17%
- Iron overload 12%
- Hemolytic anemia 4%
- Solid tumor 4%

DID YOU KNOW?

HISTORY OF MEDICINE

In 1894, Schmiedeberg reported that iron was attached to a protein in the liver, spleen and bone marrow. He called this protein "Ferratin". Schmiedeberg O. Arch Exptl Path Pharmacol. 1894;33:101.

In 1937, Laufberger isolated from horse spleen a protein to which he gave the name ferritin, in deference to the work of Schmiedeberg. Bull Sot Chim Biol. 1937;19:1575.

In 1972, an immunoradiometric assay was used to show for the first time that normal plasma contains detectable levels of ferritin and that these are lower in patients with iron deficiency anemia.

NOTES

ATTRIBUTIONS

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