KRESSER INSTITUTE
FOR FUNCTIONAL AND EVOLUTIONARY MEDICINE

Blood Chem Iron Overload Review

CAUSES OF IRON OVERLOAD

More Common	Less Common
Hereditary hemochromatosis	Sideroblastic anemia
Iron supplementation	Dysmetabolic iron overload syndrome
African siderosis	Glucose-6-phosphate-dehydrogenase (G6PD)
Beta-thalessemia	
Sickle-cell anemia	
Alcohol abuse	
Viral hepatitis	

The most common causes you'll see in clinical practice are genetic mutations that contribute to excess iron storage and excess iron supplementation. Impaired iron metabolism causes excess iron to accumulate in organs and tissues.

HEMOCHROMATOSIS

- Classic hereditary hemochromatosis is an autosomal recessive disorder. A mutation of both copies of the HFE gene on chromosome 6. Two major types are C282Y and H63D.
- At least 20 other mutations of the HFE gene have been identified.
- Mutations in other genes that can cause iron overload, including transferrin receptor 2, ferroportin 1, chromosome number 19, hepcidin, and CDA2.
- Unfortunately, the effects of these mutations are still poorly understood.
- One of the most common misconceptions about iron overload is that heterozygous carriers of these mutations are not affected. However, research over the last two decades has shown this to be clearly false.

It's well established in the scientific literature that iron overload is associated with a long list of pathologies and diseases, including metabolic conditions affecting the liver, metabolic syndrome, gout, cardiovascular disease, neurological issues, endocrine problems, immune imbalances, infections of all types, and musculoskeletal disorders.

EVIDENCE FROM PHLEBOTOMY

- Frequent blood donors have lower rates of diabetes.
- Phlebotomy has also been shown to decrease iron levels, blood pressure, resting heart rate, fasting glucose, hemoglobin A1c, and LDL-to-HDL ratio.

PREVALENCE OF SYMPTOMS OF IRON OVERLOAD

Symptom	Reported
Extreme fatigue	46%
Joint pain	44%
Impotence (or loss of libido)	26%
Skin bronzing	26%
Palpitations	24%
Depression	21%
Abdominal pain	20%

Remember that ferritin is also an acute-phase reactant that is elevated in the inflammatory response, so if you see elevated ferritin with normal iron saturation and UIBC, further investigation is often required. Soluble transferrin receptor decreases with reduced cellular need for iron, and unlike ferritin, it's not affected by inflammation.

Other useful markers for distinguishing between iron overload and inflammation

- C-reactive protein and A1-acid glycoprotein.
- Acute-phase reactants that are elevated in the inflammatory response.
- A1-acid glycoprotein elevated in chronic inflammatory conditions.
- Red blood cell indices such as hemoglobin and mean corpuscular volume (MCV) may be elevated in iron overload. However, this is more true with hemochromatosis than with mild or functional iron overload.
- Increased GGT is correlated with increased disease risk and premature mortality.

Please refer to the handouts provided this week as a quick reference to calculating FeGGT LifePro Scores.

HEREDITARY HEMOCHROMATOSIS DNA ANALYSIS

- Mutations in C282Y, H63D, S65C are present in 90 percent of cases of iron overload.
- The most affordable way to get a patient's HFE gene status is 23andMe. See the patient handout for instructions on how to use 23andMe raw data to obtain this information.
- Heterozygous carriers do have increased iron levels and are at increased risk of disease.

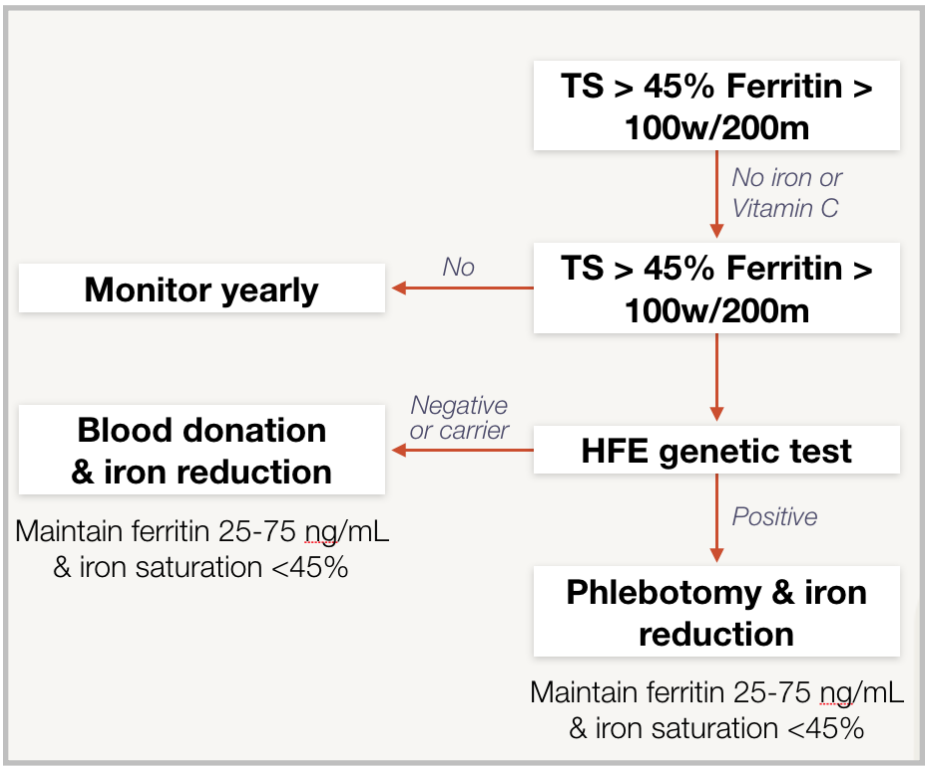
If serum iron markers are elevated with or without HFE gene mutations, other tests may be required to confirm the hemochromatosis diagnosis. Consider FerriScan MRI and quantitative phlebotomy.

High iron saturation with normal ferritin can occur in the earliest stage of iron overload.

I recommend that you have patients complete an iron panel in a fasted state. Iron levels are highest after meals, so postprandial transferrin saturation level may be falsely elevated.

Transient iron overload is possible so always retest to confirm iron overload.

ALGORITHM FOR IRON OVERLOAD WORKUP



PREVENTION AND TREATMENT

- Avoid iron supplements unless a patient is deficient and specifically needs it.
- Regularly screen patients for iron overload.
- Consider advising, particularly male patients and menopausal females, to donate blood one to three times a year as a precaution.

APOLACTOFERRIN

- Produced in breast milk and has antimicrobial properties.
- Suppresses the growth of iron-dependent pathogens.
- Lactoferrin can remove stored iron. The prefered form is apolactoferrin.
- Supplement with Lactoferrin by Life Extensions 300 mg two times a day between meals, not with food

PHYTIC ACID OR INOSITOL HEXAKISPHOSPHATE, OR IP6

- Inhibits absorption of ferrous iron, plant-based forms of iron.
- Does not inhibit heme iron absorption and doesn't remove stored iron
- Can be helpful but will not treat iron overload once it has already occurred.

In addition to removing accumulated iron, follow these three steps to reduce iron levels:

1. Reduce iron intake
    a. No iron supplements
    b. Reduce intake of the most iron-rich foods- particularly foods rich in heme iron, mostly shellfish and organ meats.
    c. Limit use of cast iron cookware- use ceramic or stainless steel cookware instead.
2. Avoid substances that increase iron absorption
    a. Vitamin C. 100 mg of vitamin C increases iron absorption in a meal by over fourfold.
    b. Beta-carotene. Found in apricots, beets, and carrots, collards, red grapes, red peppers, spinach, tomatoes, etc.
    c. Hydrochloric acid (HCL) supplements.
    d. Sugar. Avoid refined sugar and limit natural forms such as molasses and honey.
    e. Alcohol. Consume in moderation only.
3. Consume substances that decrease iron absorption
    a. Calcium. Inhibits both heme/nonheme iron absorption.
    b. Eggs. Contain phosvitin, which inhibits iron absorption.

c. Oxalates. Found in spinach, kale, beets, nuts, chocolate, tea, berries, and some spices/herbs.

d. Polyphenols. Found in cocoa, coffee, teas, apples, berries, walnuts, and some spices.

e. Phytate. Found in walnuts, almonds, sesame, dried beans, lentils and peas, cereals, and whole grains.

See summary handout on iron reduction strategies.