

Blood Chem Iron Deficiency Review

IRON:

- An essential micronutrient, needed for many functions in the body, including hemoglobin, myoglobin, enzyme production, and our immune system.
- Iron cannot be absorbed by the body. It must be oxidized to ferric oxide first, then exposed to an acidic environment, hydrochloric acid in the stomach to be turned into ferrous iron, which can be absorbed, primarily in the duodenum.
- Unabsorbed iron, about 90 percent obtained in a typical diet, is excreted in the feces.

IRON DISTRIBUTION

Location	Amount
Hemoglobin	70%
Myoglobin and enzymes	15%
Ferritin	14%
In transit in serum	1%

Transferrin is the main transport protein of iron. Normally 25 to 35 percent of the transferrin protein is saturated with iron (transferrin saturation 25 to 35 percent).

Ferritin is the long-term storage form of iron. Ferritin is produced in nearly every cell in the body, which stores iron when it is in ample supply or when it has the potential to be harmful.

The average adult requires 8 to 12 mg of iron per day, of which 85 to 90 percent is absorbed, and we excrete about 1 to 1.5 mg of iron per day, and that allows us to maintain iron balance.

TWO PRIMARY CAUSES OF IRON DEFICIENCY

Increased demand	Decreased intake/absorption
Heavy menstruation	Plant-based diets
Pregnancy	Foods that inhibit iron absorption
Fibroids	Medications (e.g. PPIs)
GI bleeding	Low stomach acid
Surgeries and accidents	Low intrinsic factor
Excessive blood donations	Celiac disease
Medications & supplements	Crohn's disease
Alcohol abuse	Autoimmune disease
Lead/metal poisoning	Hormone imbalance

Populations that are most at risk for iron deficiency include women; children; the elderly; people on vegetarian and vegan diets; endurance athletes or those who perform intense exercise; women with heavy menstruation or fibroids; patients with inflammatory bowel disease, celiac, and atrophic gastritis; long-term PPI users; and alcoholics.

SYMPTOMS OF IRON DEFICIENCY

Fatigue	Poor cognitive function
Tachycardia	Reduced exercise tolerance
Palpitations	Inability to maintain proper body temperature
Rapid breathing on exertion	Brittle & spoon-shaped nails
Restless leg	Sores at corner of mouth
Infections	Pica

THREE STAGES OF IRON DEFICIENCY

1. Ferritin 10 to 15 ng/mL; may be asymptomatic
2. Iron stores exhausted; ferritin <10 ng/mL
3. Iron-deficiency anemia

IRON DEFICIENCY MARKERS

Marker	Value
Serum iron	Low
Serum ferritin	Low
Transferrin saturation	Low
Total iron binding capacity	High
Unsaturated iron binding capacity	High
RDW	High
Soluble transferrin receptor	High

Ferritin, transferrin saturation, and UIBC or unsaturated iron-binding capacity, are the most sensitive for detecting iron deficiency, in that order.

These iron markers go out of range much sooner than you'll see changes in the red blood cell indices on the CBC.

SERUM IRON

- Least reliable marker for determining iron status.
- Tests iron contained in plasma that is generally bound to transferrin.
- Alcohol and drugs such as oral contraceptives and methotrexate can increase iron levels in serum.
- Testosterone, large doses of aspirin, metformin, and ACTH can decrease them. Stress and sleep deprivation can also temporarily decrease serum iron levels.

FERRITIN

- Considered the most sensitive marker for detecting iron deficiency, and it's often the first to go out of whack along with RDW.
- However, ferritin is also an acute-phase reactant that increases in the inflammatory response, much like C-reactive protein.

RDW, OR RED CELL DISTRIBUTION WIDTH

- Measures variation of red blood cell size or volume.
- One of the first markers to go out of range in iron deficiency.
- However, it can also be high in B12 and folate deficiency.
- RDW is an inverse marker, which means that when it is high, it indicates low iron.

TRANSFERRIN SATURATION

- Percentage is calculated by dividing serum iron by TIBC and then multiplying by 100.
- The optimal range of transferrin saturation, or iron saturation as it's also known, is generally between 25 and 35 percent on standard lab tests.
- Less than about 17 percent indicates iron deficiency

UNSATURATED IRON-BINDING CAPACITY (UIBC)

- Refers to the portion of transferrin binding sites that are not bound with iron, which is usually about one-third of the binding sites.
- UIBC at or above the high end of the lab range indicates an excess capacity for transferrin molecules to accept iron = iron deficiency (inverse marker).

TOTAL IRON-BINDING CAPACITY TIBC = UIBC PLUS SERUM IRON (INVERSE MARKER).

SOLUBLE TRANSFERRIN RECEPTOR, ALSO KNOWN AS SERUM TRANSFERRIN RECEPTOR, OR STFR

- Cleaved extracellular portion of the transferrin receptor 1 that is released in the serum.
- Used to clarify iron deficiency or overload in patients who may have inflammation, infection, chronic disease, and other conditions in which ferritin does not correlate with iron status, such as cystic fibrosis or insulin-dependent diabetes.
- Iron deficiency = increased sTfR levels.
- Iron overload = decreased sTfR levels, so it's an inverse marker.
- For example, patient has transferrin saturation percentage and UIBC levels that indicate iron deficiency but has a high ferritin level.

- Order a soluble transferrin receptor to determine if it truly is iron deficiency, and perhaps the ferritin is elevated because of an inflammatory condition.

RETICULOCYTE HEMOGLOBIN CONTENT, OR CHR

- Measures the amount of hemoglobin in reticulocytes.
- CHr provides an indirect measure of the functional iron available for new red blood cell production over the previous three to four days.
- Can be ordered at some Quest Diagnostics locations and through Spectra Labs.

TREATMENT OF IRON DEFICIENCY

1. Diet
 - a. Vegetarians and vegans are at higher risk of deficiency.
 - b. Heme iron, found in animal products, is much better absorbed than nonheme iron, which is found in plant sources of iron. Bioavailability of plant sources of iron is lower.
 - c. Absorption of plant-based forms of iron is inhibited by other commonly consumed substances such as coffee, tea, dairy products, supplemental fiber, and supplemental calcium.

HIGHEST SOURCES OF HEME IRON

Food	Amount (mg per 100g)
Clam	28
Chicken liver	13
Oyster	12
Octopus	10
Beef liver	7
Venison	5
Mussel	4
Beef chuck	4
Bison, ground	3
Crab	3
Duck breast	3
Lamp shoulder	3
Pork shoulder	2

If possible, shellfish and organ meats should be a part of the diet, especially when iron is deficient.

HIGHEST SOURCES OF NONHEME IRON

Food	Amount (mg per 100g)
Spices (thyme, parsley)	15-128
Pumpkin seeds	15
Sesame seeds	15
Tomatoes, sun-dried	9
Natto	9
Baked potatoes	7
Sunflower seeds	7
Hazelnuts	5
Soybeans, boiled	5
Spinach, cooked	4
Tomatoes, canned	3
Spinach, raw	3
Beet greens, cooked	2
Swiss chard, raw	2

SUBSTANCES THAT DECREASE IRON ABSORPTION

Substance	Comments
Calcium	Inhibits both heme/nonheme
Eggs	Contain phosvitin, which inhibits iron absorption
Oxalates	Spinach, kale, beets, nuts, chocolate, tea, berries, some spices/herbs
Polyphenols	Cocoa, coffee, teas, apples, berries, walnuts, some spices
Phytate	Walnuts, almonds, sesame, dried beans, lentils and peas, and cereals and whole grains
High doses of zinc	Limit to 20 mg per dose, taken between meals
Medications	Proton pump inhibitors (PPIs) and other antacids

SUBSTANCES THAT INCREASE IRON ABSORPTION

Substance	Comments
Vitamin C	100 mg increases iron absorption in a meal by over 4-fold
Beta-carotene	Apricots, beets, carrots, collards, red grapes, red peppers, spinach, tomatoes, etc.
Hydrochloric acid	HCL supplements
Meat (especially red meat)	100g of red meat increases non-heme absorption by fourfold
Sugar	Fruit, honey, black-strap molasses
Alcohol	In moderation with meals; excess alcohol in conjunction with excess iron damages liver

IRON SUPPLEMENTATION

- Until 1999 in the U.S., the majority of iron supplements were made with ferrous iron salts.
- Stomach acid is required to dissolve the iron salt, which is an issue for individuals with low stomach acid.
- There are a few specialty manufacturers that make iron tonics or capsules that keep iron soluble so it can be absorbed even by people with low HCl, but this is still not my preferred form of iron.
- Heme iron supplements are a much better option than iron salts.
- Proferrin from Colorado Biolabs contains heme iron.
- Heme iron is much better tolerated and less likely to cause GI distress.
- As an additional benefit, patients can take Proferrin with meals, unlike ferrous salts that have to be taken away from meals.
- Don't take Proferrin at the same time as calcium supplements.

LIPOSOMAL IRON IS THE NEWEST FORM

- Like heme iron, it has a high bioavailability and a low side effect profile.

PARENTERAL IRON IS ADMINISTERED BY INFUSION OR INJECTION.

- Often given to patients who have malabsorption or who have had gastric bypass or portions of their intestine removed.
- Studies have found liposomal iron is equivalent or better than IV iron in many studies.

If a combination of diet, supplements, foods that increase iron absorption, Proferrin, and liposomal iron doesn't work, consider referring that patient out for parenteral iron.

With all forms of supplementation, and even diet, remember that more is not always better.

FUNCTIONAL MEDICINE TREATMENT OF IRON DEFICIENCY

Intervention	Comments
Address underlying causes	e.g. GI bleeding, malabsorption, infection, intense exercise, PPI use, etc.
Diet	Increase intake of foods high in iron
Improve absorption	Consume substances that increase iron absorption; avoid substances that decrease absorption

For both omnivores and vegetarians, I recommend supplementing with HCl, hydrochloric acid, and 100 to 300 mg of vitamin C with meals in order to increase iron absorption. It is also not a bad idea to have a glass of wine with meals if your patient tolerates alcohol.

SUPPLEMENTATION FOR MODERATE TO SEVERE IRON DEFICIENCY

Supplementation for moderate to severe iron deficiency

Severity of iron deficiency	Comments
Mild	1 capsule of Proferrin ES/Clear or 6 capsules of Ancestral Supplements desiccated liver or spleen per day
Moderate	2 capsules of Proferrin ES/Clear and/or 3-6 capsules of Ancestral Supplements desiccated liver or spleen per day
Severe	3 capsules of Proferrin ES/Clear and 6 capsules of Ancestral Supplements desiccated liver or spleen per day