

Iron Avidity...Common Phenomenon seen in hemochromatosis patients

"...the paradigm has to shift ...the hemochromatosis patient can also be the iron deficiency anemia patient."

Mark Wurster, MD Ohio State University Health Center

Iron avidity is a common problem, especially among hemochromatosis patients. This patient has a normal to low serum ferritin (e.g. 15-40 ng/mL) with elevated transferrin-iron saturation percentage (Tsat%>50%). The normal condition would be a Tsat% within normal range (25-35%) when the iron stores are in this range of ferritin values.



John Beard, Ph.D

Though there are no data to explain this relationship of iron status markers and HHC, iron avidity may be the body's physiological response to a rapid blood loss (losing too much blood too rapidly by phlebotomy). Compounding the problem, the patient is also consuming a diet low in iron (especially heme) and employing measures to impair the absorption of iron that is consumed, such as drinking tea or coffee with meals, taking supplemental calcium, etc.

According to John Beard, Professor of Nutrition, Penn State University, "With these factors in place and as the iron balance is not fully functional, the various "iron sensors" in the body may be trying to send more iron to bone marrow than is really required."

Beard continues, "It is important to not become iron deficient in the midst of treating HHC as the consequences of overt anemia can be quite unsettling in and of themselves (changes in immune function, cognition, mood, physical endurance, etc.). It is a fine line between too much and too little iron in this kind of individual and diet and bleeding need to be carefully controlled to optimize this balance."

Some patients with hemochromatosis, iron-overload have difficulty grasping the fact that they are at the other end of the iron balance scale and are now deficient in iron. Unfortunately, some physicians also can miss the obvious and continue to try to lower tissue iron levels using Tsat% alone, when what might help is to treat the patient for iron deficiency anemia.

Dr. Susan Leitman, Principal Investigator of the Hemochromatosis Management Protocol at the NIH

Department of Transfusion Medicine, Bethesda, MD says "Treating physicians should not be cavalier about phlebotomy therapy in HHC patients. It is very easy to forget that careful, judicious monitoring must



Susan Leitman, MD

accompany all courses of phlebotomy therapy. Among previously treated patients referred to our protocol, we see about the same number that are "overbled" as those that are "underbled." It is easy to become profoundly iron deficient, with symptomatic fatigue, even exhaustion, if iron stores are totally depleted, and iron deficiency anemia develops.

In the protocol, HHC patients are deironed carefully and are not overbled to the state of becoming iron deficient. Tests such as the complete blood count and iron panel are used to monitor the progress of patients in the program. One marker that is helpful is the mean corpuscular volume (MCV). The MCV drops slightly (about 3%), when the patient's body iron has reached a healthier balance. The MCV is inexpensive and part of the CBC.

Mark Wurster, MD, Ohio State University says that "It is a given that iron is important for many biochemical processes. But there are no data with compelling enough evidence to support there is any benefit to the hemochromatosis patient to suffer iron deficiency anemia."



Mark Wurster, MD

Wurster, Leitman, Beard and Weinberg all agree that iron avid patients should be counseled that they are at increased risk for certain infections. Weinberg writes in his latest book, Exposing the Hidden Dangers of Iron, that in normal persons, the transferrin iron saturation percentage is 25-35%. In untreated hemochromatosis (HHC), it can rise to 100%. In one study, none of eight strains of *V. vulnificus* could grow in the presence of transferrin with 30% saturation; nearly all could grow with transferrin at 100% saturation. In normal mice, an injection of one million bacterial cells of *V. vulnificus* was needed to cause a lethal infection. In mice injected with iron, only one injected bacterial cell resulted in death!

Below is one approach for the iron avid patient to achieve iron balance.

CONSIDERATIONS FOR THE IRON AVID PATIENT:

AVOID exposure to bacteria (see list).
DISCONTINUE phlebotomies for a brief period of time, 3-4 weeks.
DIET: Eat to replenish iron stores
See the diet recommendations for iron deficiency anemia on page 9.

MONITOR: serum ferritin and Tsat% during these intervals
WAIT to perform a phlebotomy until serum ferritin reaches at least 55ng/mL

Serum ferritin drops about 30ng/mL with each full unit of blood removed. Allowing the serum ferritin to rise sufficiently to remain at or above 25ng/mL post phlebotomy, should allow the body to reach iron balance: Tsat% 25-35% with serum ferritin within 25-75ng/mL.

The greatest obstacle to this approach of restoring iron balance is the patient's concern for allowing serum ferritin to rise. Many HHC patients and some physicians still believe that de-ironing is only achieved when ferritin is lowered to less than 10ng/mL. There is no known benefit to lowering serum ferritin below 10ng/mL or even possibly below 20ng/mL when known symptoms of iron deficiency anemia can occur.

Dr. Chris Earley, Johns Hopkins University reports that the symptoms of Restless Legs Syndrome increase in patients whose ferritins are 50ng/mL or lower. Iron Disorders Institute recommends a serum ferritin range of 25-75ng/mL to avoid symptoms of iron deficiency anemia and to protect the patient against becoming iron overloaded.

RESULTS Let us know how this approach works for you. Contact us: comments@irondisorders.org

Resources:

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- Weinberg, ED.** Microbial Pathogens with Impaired Ability to Acquire Host Iron *BioMetals* 13 (2000) 85-9.
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Most Likely Exposure:

Vibrio vulnificus: found in contaminated raw shellfish. Do not consume any raw shellfish or walk barefooted on seacoast beaches.

Human meningococcal meningitis bacteria: airborne from coughing or sneezing

Escherichia coli: ingested from foods or beverage contaminated with fecal matter

Capnocytophaga canimorsis bacteria: found in saliva of some dogs and cats



Eugene Weinberg, Ph.D

Diet Recommendations for the IRON DEFICIENT Adult

“... intakes of highly bioavailable forms of iron (supplemental iron and red meat) and of fruit, a dietary source of an enhancer of nonheme-iron absorption (vitamin C), promote high iron stores, whereas foods containing phytate (whole grains) decrease these stores. Individual dietary patterns may be important modulators of high iron stores.”

Fleming, D. J., K. L. Tucker, P. F. Jacques, G. E. Dallal, P. W., Wilson, and R. J. Wood. "Dietary Factors Associated with the Risk of High Iron Stores in the Elderly Framingham Heart Study Cohort." American Journal of Clinical Nutrition 76 (2002): 1375-84.

Before recommending oral iron supplements to a patient whose hemoglobin is lower than normal, it is important to distinguish between iron deficiency anemia (IDA) and anemia of chronic disease (ACD). In ACD the lower than normal hemoglobin is in response to inflammation and the underlying cause should be identified and treated. If the patient is found to be iron deficient, often diet can improve hemoglobin values for patients, especially when the cause is due to inadequate dietary iron. The same diet can restore iron balance in the iron avid patient.

Diet Recommendations for an Iron Deficient Patient

Consume at least three 4 oz.... portions of lean red meat per week. For vegetarians an increased consumption of foods with high non-heme iron content along with avoidance of substances that impair the absorption of iron. For a list of iron content in foods visit www.irondisorders.org

Substances that impair iron absorption include: coffee, tea, high fiber, calcium and eggs. Have these items at different times of the day or 2 hours prior to or after meat is consumed. Substances that improve the absorption of iron include naturally occurring beta carotene (not supplemental) and acidic foods such as tomatoes or oranges.

Once iron balance is achieved, continue on a balanced diet such as the following:

Get adequate daily protein from meat, soy or plant food combinations such as beans or lentils with rice. Reduce or eliminate refined sugar from the diet. Small amounts of honey, or molasses are okay. Limit the amount of sugar substitutes as well, especially aspartame. Stevia is a possible sweetener to consider. Do not cut complex carbs (whole grains) from the diet. Eat at least 3 portions of complex carbs per day. Eat at least 5 servings per day of fresh or fresh frozen fruits (berries are best choices especially for diabetics) and vegetables.

Though the iron in fruits and vegetables is not easily absorbed, these food items are essential for nutrients such as vitamin C, beta carotene and chlorophyll. Fruits and vegetables are a good source of antioxidants, which counter harmful free radical activity.

Consume at least two cups of dairy per day such as 8 oz.... glasses of skim-milk, yogurt (one with active cultures and no sugar). Sour cream and cheese are fine in moderation, just try to limit the fatty choices, but remember that fat is necessary for normal metabolism: olive oil, avocados, and most fish are good sources of fat.

SUPPLEMENTS

All patients should be evaluated before considering a diet additive or supplement. Otherwise, they can mask a potentially harmful, even fatal complication.

Following evaluation, a one-dose-daily multiple vitamin with selenium is recommended for all groups with disorders of iron. Hemochromatosis patients should select a daily multi-vitamin without iron, even if they are trying to replenish iron stores caused by overbleeding. Consumption of a high iron diet should be sufficient for these patients because the tendency to load iron must be considered.

For the iron deficient patient, the daily multi-with iron might be beneficial until iron stores are replenished or improved. Taking supplemental iron without benefit of a physician's examination and tests could be harmful. Any use of supplemental iron should be determined appropriate and monitored by the physician. When hemoglobin has improved with diet and supplemental iron, but falls once the supplemental iron is discontinued, the patient should be examined for blood loss or other causes of anemia.

Iron balance can be confirmed by retesting serum ferritin, transferrin-iron saturation percentage (Tsat%) and hemoglobin. Iron Disorders Institute ranges for serum ferritin 25-75ng/mL; Tsat% 25-35%. A complete blood count also provides very helpful information as indicated below.

“Anemia is not a complete diagnosis. If a patient is anemic, the underlying cause must be determined before supplemental iron is given. Iron is not just another vitamin, nor is it a cure for chronic fatigue.” James Cook, M.D.

Comparing blood tests for anemia of chronic disease (ACD) and iron deficiency anemia (IDA)

	ACD	IDA
Hemoglobin	Decreased*	Decreased
Serum ferritin	Increased	Decreased
TIBC	Decreased	Increased
Serum iron	Decreased	Decreased
Tsat% (transferrin/iron saturation percentage)	Decreased	Decreased
Erythropoietin	Inadequate	Adequate
MCV	Normal to slightly Decreased	Decreased
White blood cell	Variable	Normal
Red blood cell	Decreased	Normal to slightly Decreased
Serum transferrin receptor	Normal	Increased

*Hemoglobin can go as low as 7.0g/dL in some ACD patients

RESOURCES:

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