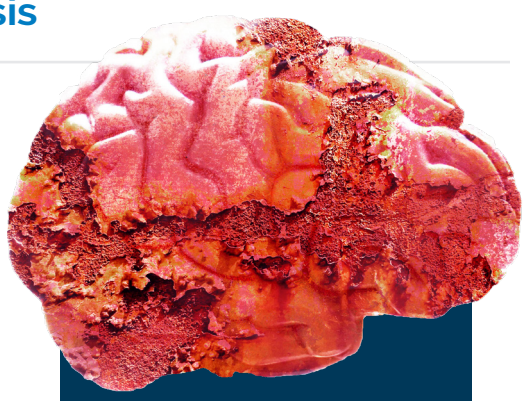
The Great Plains Laboratory, LLC

Rust Brain

The Dangers of Excess Iron and Hemochromatosis

Although low iron can lead to anemia, excess iron is equally important as a factor that can affect virtually every aspect of health. The most common cause of excess iron is a genetic disorder called hemochromatosis, which can affect people at any age. It has been diagnosed in newborns up to the very elderly. Pregnant women with hemochromatosis may lose developing children who may have inherited the disease. The disease is most frequently diagnosed in males over 50 since the iron deposition in the tissues accumulates slowly, but may occur in much younger men who take iron supplements or who eat large amounts of red meat.

Hemochromatosis causes the absorption of iron to be increased. Two common genetic SNPs for this exist and the high prevalence of individuals with two copies makes this the most common genetic disease in many countries. With an incidence of 1 in 200 live births, hemochromatosis affects 1.5 million people in the United States. Approximately, 10-12.5% of the population are carriers for the most common mutations. Carriers have much higher iron levels than people without the mutations. Men are many times more affected than women. Presumably, individuals with limited dietary sources of iron in the past were at a selective evolutionary advantage so that this mutation allowed them to thrive on an iron deficient diet. Even individuals with a single copy of one of the hemochromatosis genes may develop the disease if they have a very high iron intake from the diet.



10-12.5% of the population are carriers for hemochromatosis genetic SNPs

Diseases Associated with Iron Excess

- Diabetes mellitus
- Arrhythmias
- Liver cancer and other cancers
- Amenorrhea
- Bipolar depression
- Friedreich ataxia (FA)
- Kufor-Rakeb disease (KRD)
- Aceruloplasminemia
- Neuroferritinopathy
- Stroke
- Hepatomegaly
- Hypogonadism
- Parkinson's Disease
- Arthritis
- Epilepsy
- Immune suppression with increased infectious diseases
- Pantothenate kinase-2-associated neurodegeneration (PKAN)
- Cardiac insufficiency
- Cirrhosis
- Amyotrophic laterosclerosis
- Alzheimer's Disease
- Autoimmune disease
- FA2H-associated neurodegeneration (FAHN)
- PLA2G6-associated neurodegeneration (PLAN)

Total Iron and Iron-Binding Capacity Test

Total Iron and Iron-Binding Capacity Test (TIBC)

Iron excess is a very common problem in adult men and in post-menopausal women. Iron excess can result from excessive iron supplementation or excessive intake of red meat. Men or post-menopausal women should avoid iron supplementation unless there are conditions causing excessive blood loss. In addition, individuals with deficiency of the protein transferrin have excessive free iron even if the total iron is not excessive. This transferrin deficiency is readily evaluated in the Total Iron and Iron-Binding Capacity Test (TIBC). Low values of TIBC indicate deficient transferrin and excessive free iron. Since ferritin might be normal in such situations, total iron and total iron binding capacity are preferred iron tests. The % transferrin saturation is calculated by dividing the total serum iron by the total iron binding capacity and multiplying by 100. A transferrin saturation higher than 40% is indicative of the disease according to the American Hemochromatosis Society. Thus, the upper limit of normal used at The Great Plains Laboratory is 39%. The optimal range for % saturation is considered to be from 25-35%. Those in the % saturation range of 36-39% may want to cut down on high iron foods and donate blood on a regular basis.

The Health Effects of Excess Iron and Hemochromatosis

High iron causes toxicity by the Fenton reaction in which hydroxyl free radicals are formed from iron (II) and hydrogen peroxide. Excessive intestinal iron absorption in hemochromatosis leads to net iron accumulation of 0.5 to 1.0g per year. Symptoms typically develop after 20g of storage iron have accumulated. Males predominate (5–7:1 male to female ratio) with slightly earlier clinical presentation, partly because physiologic iron loss (menstruation, pregnancy) delays iron accumulation in women. The proposed mechanism for iron toxicity is through lipid peroxidation by hydroxyl free radicals produced from the Fenton reaction. Direct interaction of such hydroxyl radicals with DNA leads to strand breaks resulting in cytotoxicity and mutagenesis, altering hepatic morphology, and predisposing to hepatocellular carcinoma.

Patients with hemochromatosis manifest hepatomegaly, abdominal pain, bronze skin pigmentation (particularly in sun-exposed areas), deranged glucose homeostasis or frank diabetes mellitus, cardiac dysfunction (arrhythmias, cardiomyopathy, and atypical arthritis). In some patients, the presenting complaint is hypogonadism, with amenorrhea in the female and loss of libido and impotence in the male. The classic triad of pigment cirrhosis with hepatomegaly, skin pigmentation, and diabetes mellitus does not always develop. Death may result from cirrhosis or cardiac disease. Hemochromatosis patients carry a risk for hepatocellular carcinoma that is 200-fold greater than that of the general population. Workers in iron mines develop bronchial cancer five to ten times the rate of the general population. Lung cancer can be nearly eight times higher than expected in patients with hemochromatosis. Other cancers recorded in hemochromatosis are pancreas, stomach, rectum, gallbladder, bladder, prostate, colon and brain, among others. A transferrin saturation higher than 40% is indicative of the disease according to the American Hemochromatosis Society.

In addition, there is a significant association of both neurological and psychiatric symptoms associated with excessive iron including Parkinson's disease, Alzheimer's disease, depression, and bipolar depression. Remarkably, the average % saturation of 130 patients with epilepsy was 39.9%, a value very close to the cutoff value of 40% that is indicative of hemochromatosis.

Missing Link in a Variety of Chronic Diseases

The need for iron in the diet or in supplements is one of the most common nutritional challenges. Iron is one of the most abundant metals on earth and it is thought that iron was involved in the production of oxygen on earth. Iron in our body exists in two valence states, the +2 ion called ferrous ion and the +3 ion called ferric ion. When iron is ingested, ascorbic acid greatly increases its absorption from the intestinal tract. Iron from red meats including beef, bison, mutton, and emu is absorbed more readily than iron from other sources. Absorbed iron is carried through the blood stream by the iron-binding protein transferrin. Excess iron is stored by the iron storage protein called ferritin. Iron is released from ferritin when iron deficiency develops. A very large part of nutritional iron is incorporated into the protein in the red blood cells called hemoglobin. In addition, iron is also present in the respiratory complexes of the mitochondria and in detoxification enzymes like cytochrome p450 enzymes. Deficiency of iron leads to a type of anemia called microcytic anemia. In this anemia, there is a decrease in the amount of hemoglobin in b and the red blood cells are smaller than usual, resulting in low values for the parameter called mean corpuscular volume (MCV). In addition, blood loss can lead to iron deficiency and toxic elements like lead may also cause reduced iron utilization.

Total Iron and Iron-Binding Capacity Test

Case Studies of Iron Excess

A 23 year old man sought medical treatment for symptoms that had persisted for 10 years including testicular pain, anxiety, fatigue, and dizziness. The physicians who examined him found no physical cause for his symptoms and he was referred to a psychiatrist. Psychiatric drugs offered no relief. The % saturation of transferrin was 58%, well over the 40% cutoff for iron overload. All of his symptoms markedly improved after treatments to lower iron and his followup % saturation of transferrin was a normal value of 36%.

A 17 year old female with depression, extreme fatigue, arthritis, reddening of the hair, menstrual irregularities, and heart palpitations failed to respond to antidepressant drugs. On the verge of suicide, the patient had a battery of tests done at a direct-to-consumer laboratory. The tests indicated hemochromatosis. All of her symptoms cleared after finding a physician to treat her iron overload.

A 26 year old man with schizophrenia had compulsive teeth brushing for 7-8 hours each day. His schizophrenia symptoms were resistant to neuroleptics. He was noticed to have bronzed legs and hepatomegaly, symptoms of hemochromatosis. The % saturation of transferrin was 96%, an extremely high value. Interestingly, his total iron capacity was well below normal, indicating a likely deficiency of the iron-binding protein transferrin. Thus, this patient likely had iron overload due to transferrin deficiency, instead of hemochromatosis. The symptoms of the two illnesses are virtually identical since both illnesses cause excessive free iron. The patient was treated with iron removal which dropped the % saturation to 44%, a value that is still somewhat high. The compulsive teeth brushing stopped completely and the sociability of the patient improved. One might speculate that additional improvements might have occurred with additional iron removal.

A 73 year old male developed sudden memory loss, confusion, headaches, visual hallucinations, and paranoia. It was noted that he had developed bronzed colored skin. His % saturation of transferrin was 72%. Removal of iron resulted in a markedly reduced % saturation of transferrin to 28%, with all symptoms completely cleared except for memory loss that was substantially better.

Severe iron deficiency requiring iron injections may be associated with milk allergy which can be detected by the IgG Food Allergy Test.

Treatment for Excess Iron

The safest treatments for iron are phlebotomy (blood draw) and diet. Phlebotomy can be done perhaps every two months once the illness is under control, but perhaps weekly for two to three years when iron is extremely elevated. Dietary restriction of high iron foods and the use of turmeric supplements are the absolute safest methods. Chelation with oral iron-binding chelators has been reported as extremely dangerous with a mortality rate of 11%.

Iron supplementation may be needed for growing children and women with regular menstrual bleeding, but may not usually be needed by men since they do not experience this bleeding and usually have enough iron from diet alone. It is generally recommended that no men take iron supplements unless they have done testing to document iron deficiency. Parents should not give sweetened vitamins that contain iron to children. Eating entire bottles of these vitamins by children is one of the most common reasons for calls to poison control centers and emergency room visits due to iron toxicity. Severe iron deficiency requiring iron injections may be associated with milk allergy which can be detected by the IgG Food MAP. A woman with this condition had been getting frequent, painful intravenous injections of iron for many years until an IgG Food MAP revealed high IgG milk allergy that was preventing her absorption of iron from the gastrointestinal tract.

Patients with excess iron should avoid the following foods:

- Alcohol
- Lamb
- Ostrich
- Beef
- Vitamin C (more than 100mg per day)
- Iron-fortified breakfast cereals and similar processed foods
- Emu
- Bison
- Any vitamin or mineral supplement containing iron

Foods that Inhibit Iron Absorption

Eggs contain a compound called phosvitin that binds iron. One boiled egg can reduce absorption of iron in a meal by as much as 28%. Phenolic acid found in apples, peppermint, and some herbal teas, and tannins found in black teas, coffee, cocoa, spices, walnuts, fruits such as apples, blackberries, raspberries and blueberries all have the ability to inhibit iron absorption. Although spinach is high in iron, the high oxalate content of spinach prevents iron absorption.

Supplements to Reduce Iron

Turmeric is among the spices known to inhibit iron absorption by 20%-90% in humans, reducing iron absorption in a dose-dependent manner. The stoichiometric qualities of turmeric indicate it could bind nearly all absorbable iron and cause iron deficiency, and it does so in mice. Curcumin, the active ingredient in turmeric, binds ferric iron (Fe^{3+}) to form a ferric-curcumin complex that is dose-dependent and Fe^{3+} specific. Doses up to 12 grams of turmeric per day have been reported to be safe and well-tolerated. Obviously, iron values need to be monitored when supplementing to prevent iron deficiency anemia; people with iron deficiency should avoid turmeric and curcumin. Turmeric extract contains much higher amounts of curcumin than raw turmeric spice which may only contain 3% curcumin. Curcumin may also be taken by itself and is most bio-available as a liposomal supplement. Black pepper assists in absorption of curcumin.

For a list of references, visit the Total Iron and Iron-Binding Test page of our website, **www.greatplainslaboratory.com/iron-binding**

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