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Top 4 Reasons to Check Your Iron Level, Not Your Cholesterol

Analysis by Dr. Joseph Mercola Fact Checked | August 10, 2022

STORY AT-A-GLANCE

- While your body requires sufficient iron to stay healthy, elevated levels have been linked to cancer, heart disease, neurodegenerative diseases, gouty arthritis, hepatitis C, liver disease and many other health problems
- Elevated cerebrospinal fluid iron levels are strongly correlated with the presence of the Alzheimer's risk allele, APOE-e4, and elevated iron in your brain may actually be the mechanism that makes APOE-e4 a major genetic risk factor for the disease
- Elevated ferritin has been linked to impaired glucose metabolism, raising the risk of diabetes fivefold in men and fourfold in women, a magnitude of correlation similar to that of obesity
- Iron causes significant harm primarily by catalyzing a reaction within the inner mitochondrial membrane. When iron reacts with hydrogen peroxide, hydroxyl free radicals are formed, causing severe mitochondrial dysfunction
- If your iron level is too high, the easiest way to lower it is to donate blood two or three times a year. If you have severe overload you may need to do more regular phlebotomies. Regular sauna use, which is an effective form of detoxification, is also helpful

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While many health screens are overrated or unnecessary, a few stand out as vitally important. For example, while most people will check their cholesterol on a regular basis, even though high cholesterol has been proven to have no significant impact on heart health, few consider checking their serum ferritin (stored iron) level.

Most doctors also ignore this important health screen. This is tragic, because while your body requires sufficient iron to remain healthy,[1] elevated levels have been linked to cancer,[2] heart disease,[3] neurodegenerative diseases,[4] gouty arthritis[5] and many other health problems.[6]

As noted in a 2007 paper,[7] other iron overload conditions include chronic hepatitis C and end-stage liver disease, and even "mild or moderate increase of iron stores appears to have significant clinical relevance" in these and other conditions.

Iron overload is also of particular concern in Alzheimer's disease.[8,9,10] According to recent research,[11,12] buildup of iron, causing a rusting effect in the brain, plays an important role and is common in most Alzheimer's patients. As noted by the authors:

> *"In the presence of the pathological hallmarks of [Alzheimer's disease], iron is accumulated within and around the amyloid-beta plaques and neurofibrillary tangles, mostly as ferrihydrite inside ferritin, hemosiderin and magnetite.*
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> *The co-localization of iron with amyloid-beta has been proposed to constitute a major source of toxicity. Indeed, in vitro, amyloid-beta has been shown to convert ferric iron to ferrous iron, which can act as a catalyst for the Fenton reaction to generate toxic free radicals, which in turn result in oxidative stress."*

Other research[13] suggests elevated cerebrospinal fluid iron levels are strongly correlated with the presence of the Alzheimer's risk allele, APOE-e4, and that elevated levels of iron in your brain may actually be the mechanism that makes APOE-e4 a major genetic risk factor for the disease.

A primary focus of conventional treatment so far has been to clear amyloid proteins, but while the approach seems logical, such attempts have met with limited success. Now,

researchers suggest clearing out excess iron may be a more effective way to reduce damage and slow or prevent the Alzheimer's disease process.

High Iron Impacts Your Diabetes Risk as Much as Obesity

Iron causes significant harm primarily by catalyzing a reaction within the inner mitochondrial membrane. When iron reacts with hydrogen peroxide, hydroxyl free radicals are formed. These are among the most damaging free radicals known, causing severe mitochondrial dysfunction, which in turn is at the heart of most chronic degenerative diseases.

Importantly, elevated ferritin has been linked to dysfunctional glucose metabolism,[14] raising the risk of diabetes fivefold in men and fourfold in women, a magnitude of correlation similar to that of obesity.[15] High ferritin also doubles your risk of metabolic syndrome,[16] a condition associated with an increased risk of high blood pressure, liver disease and heart disease.

Unfortunately, the first thing people think about when they hear "iron" is anemia (iron deficiency), not realizing that iron overload is actually a more common problem — and far more dangerous.

GGT Test Is Also Advisable to Rule Out Iron Toxicity

A gamma-glutamyl transpeptidase (GGT) test can also be used as a screening marker for excess free iron and is a great indicator of your sudden cardiac death risk. Recent research also suggests elevated GGT is associated with insulin resistance, cardiometabolic disease[17] and chronic kidney disease.[18]

In recent years, scientists have discovered GGT is highly interactive with iron, and when both your serum ferritin and GGT are high, you are at significantly increased risk of chronic health problems and early death,[19] because then you have a combination of free iron (which is highly toxic), and the iron storage to keep that toxicity going.[20] Hence getting a GGT test in addition to a serum ferritin test is advisable to rule out iron toxicity.

Iron Overload Is Extremely Common

As noted in a recent Nautilus article[21] by Clayton Dalton, an emergency medicine resident at Massachusetts General Hospital in Boston, it's quite possible to come dangerously close to the maximum daily intake of iron thought to be safe simply by eating breakfast, as two servings of fortified breakfast cereal may provide as much as 44 milligrams (mg) of iron in some cases.

Meanwhile, the upper tolerance limit is 45 mg for adults, and the recommended daily allowance is 8 mg for men and 18 mg for premenopausal women (i.e., women who still get their monthly period).

Indeed, most adult men and postmenopausal women are at risk for iron overload and need to be mindful of their intake since they do not lose blood on a regular basis. Blood loss is the primary way to lower excess iron,[22] as your body has no active iron excretion mechanism.

There's also an inherited disease, hemochromatosis, which causes your body to accumulate excessive and dangerously damaging levels of iron. The following can also cause or exacerbate high iron. Just remember you cannot base your risk of iron overload on these factors alone. You have to actually measure your iron level if you are:

- Cooking in iron pots or pans. Cooking acidic foods in these types of pots or pans will cause even higher levels of iron absorption
- Regularly eating processed foods such as cereals and white breads fortified with iron. (What's worse, the iron used in these products is inorganic iron, which has more in common with rust than the bioavailable iron found in meat)
- Drinking well water high in iron. The key here is to make sure you have some type of iron precipitator and/or a reverse osmosis water filter
- Taking multiple vitamins and mineral supplements, as both of these frequently have iron in them

- Regularly consuming alcohol, as this will increase the absorption of iron in your diet. For instance, if you drink wine with your steak, you will likely absorb more iron than you need

Iron's Mechanism of Harm Explained

Your body creates energy by passing the electrons from the carbs and fats you eat to oxygen through the electron transport chain in your mitochondria, which produces adenosine triphosphate (ATP). Ninety-five percent of the time, the oxygen is converted to water, but 0.5% to 5% of the time, reactive oxygen species (ROS) are created.

ROS are not all bad as they are important biological signaling molecules, but excessive ROS leads to mitochondrial damage and dysfunction. Iron can react with hydrogen peroxide in the inner mitochondrial membrane. This is a normal part of cellular aerobic respiration.

However, when you have excessive iron, it catalyzes the formation of excessive hydroxyl free radicals from the peroxide, which decimate your mitochondrial DNA, mitochondrial electron transport proteins and cellular membranes. This is how iron overload accelerates chronic disease. Dalton writes:[23]

> *"As the chemists Barry Halliwell and John Gutteridge — who wrote the book on iron biochemistry — put it, 'The reactivity of the hydroxyl radicals is so great that, if they are formed in living systems, they will react immediately with whatever biological molecule is in their vicinity, producing secondary radicals of variable reactivity.'*
>
> *Such is the Faustian bargain that has been struck by life on this planet. Oxygen and iron are essential for the production of energy, but may also conspire to destroy the delicate order of our cells. As the neuroscientist J.R. Connor has said, 'Life was designed to exist at the very interface between iron sufficiency and deficiency.'"*

If You're a Carb-Burner, Your Risk May Be Magnified

If you eat excessive net carbs (total carbs minus fiber) the situation is further exacerbated, as burning carbs as your primary fuel can add another 30 to 40% more ROS on top of the hydroxyl free radicals generated by the presence of high iron.

Unfortunately, most people burn carbs as their primary fuel these days. If you struggle with any kind of chronic health problem and have high iron and eat a standard American diet that is high in net carbs, normalizing your iron level (explained below) and implementing a ketogenic diet as described in my book, "**Fat for Fuel**," can go a long way toward improving your health.

Taking extra antioxidants to suppress ROS generated by high iron alone or in combination with a high-sugar diet is inadvisable, as ROS also act as important signaling molecules. They're not all bad. They cause harm only when produced in excess.

Hence your best bet is simply to lower the production of ROS. One of the easiest and most effective ways to do that is to eat a diet high in healthy fats, adequate in protein and low in net carbs. Eating healthy fats can make a bigger difference than you might think, especially if you have high iron.

How Your Body Maintains Iron Homeostasis

Now, your body does have a mechanism for maintaining iron homeostasis, which works well provided you're not getting too much iron from your diet on a regular basis. A key regulator of iron is hepcidin, a protein secreted by your liver. When your iron level is sufficient, your liver secretes hepcidin into your bloodstream.

As your hepcidin level rises, iron absorption in your gastrointestinal tract is inhibited, while cells throughout your body start to sequester iron into ferritin (an iron storage protein). When your iron level is low, your hepcidin level drops, triggering gastrointestinal cells to start absorbing iron from your food again.

Elegant as this system may be, iron overload can still occur if you're consistently consuming too much iron, or if you have a genetic mutation causing impaired iron regulation. A gene called HFE regulates hepcidin; people with hereditary hemochromatosis have two defective copies of this gene, while having just one defective copy is known as heterozygosity. As reported by Dalton:[24]

> *"The prevalence of hereditary hemochromatosis, in which two defective copies of the HFE gene are present and there are clinical signs of iron overload, is actually pretty high — as many as 1 in 200 in the United States.*
>
> *And perhaps 1 in 40 may have two defective HFE genes without overt hemochromatosis. That's more than 8 million Americans who could have a significant short-circuit in their ability to regulate iron absorption and metabolism."*

There's evidence[25,26] to suggest people with a single defective HFE gene may also have impaired iron metabolism, albeit not to the degree seen in those with hemochromatosis.

According to one study,[27] "an estimated 40% to 70% of persons with the C282Y homozygous genotype will develop clinical evidence of iron overload," and estimates suggest more than 30% of Americans are heterozygotes, placing them at this significantly increased risk.[28]

People with a single defective HFE gene have also been shown to be at increased risk of heart disease, heart attack and stroke.[29,30] In one study,[31] heterozygosity raised the risk of cardiomyopathy, a strong risk factor for heart failure, nearly sixfold.

Iron Metabolism and Disease

The discovery of hepcidin in 2000 launched a string of research showing just how dangerous iron overload can be — even if you don't have an HFE gene mutation. I recommend reading through the original article,[32] but here's a quick summary of the highlights:

1. **Iron and cardiovascular disease —** A meta-analysis[33] published in 2013 found that 27 of 55 published studies demonstrated a positive relationship between iron and cardiovascular disease, with higher iron levels being linked to higher risk of disease. Twenty of the studies found no significant relationship, and only eight reported a negative relationship, with higher iron levels being associated with lower risk of disease.

   For example, a Scandinavian study found elevated ferritin levels raised men's risk of heart attack two- to threefold. In another, people with high ferritin were five times more likely to suffer a heart attack than those with normal levels.

   A third found elevated ferritin doubled the risk of heart attack. Importantly, in this study they found that each 1% increase in ferritin raised the risk of heart attack by 4%, and the only risk factor that weighed heavier than ferritin was smoking.

   Canadian scientists have also evaluated the link between serum iron (opposed to serum ferritin) to heart attack risk, as ferritin is not a perfect marker for iron status. They too found that higher iron raised the risk of heart attack in men twofold, and fivefold in women.

2. **Iron and diabetes —** The link between high iron and diabetes has also strengthened over the years. In the late '80s, it was discovered that patients who receive blood transfusions are at significantly increased risk of diabetes, suggesting iron itself, and not just genetic factors, were in fact at play.

   In 1997, the first study[34] to investigate this connection published findings confirming that ferritin is indeed a strong predictor of dysfunctional glucose metabolism. The only factor stronger is body mass index.

   The association between iron and diabetes was confirmed in 1998, when a study[35] found that phlebotomy (blood donation) improved insulin sensitivity and glucose metabolism in both healthy and diabetic subjects. This was later reconfirmed in 2005[36] and 2012.[37]

In 1999, researchers linked elevated ferritin with a fivefold increased risk of diabetes in men and a nearly fourfold increased risk in women.[38] Five years after that, ferritin was linked to a doubled risk of metabolic syndrome, which is also strongly associated with diabetes and cardiovascular disease.[39]

Then, in 2011, a study[40] looking at the connection between transferrin saturation (a measure of the iron load in your transferrin protein) and diabetes risk concluded that having a transferrin saturation above 50% raised the risk of diabetes two to three times and increased mortality rates.

3. **Iron and cancer —** As noted by Dalton, "It had been known since the late 1950s that injecting large doses of iron into lab animals could cause malignant tumors." Unfortunately, it would take three decades before scientists started looking at the link between iron and cancer in humans. Today, there's ample evidence for this connection. Among this evidence are studies showing:

    - Elevated ferritin is associated with a three times higher risk of death from cancer[41]
    - Men who develop cancer have higher transferrin saturation and blood levels of iron than cancer-free men[42]
    - Blood donors are between 20%[43] and 30%[44] less likely to develop cancer than non-donors
    - Elevated ferritin raises your risk of colorectal cancer threefold and lung cancer by 1.5 times.[45] A meta-review of 33 studies that looked at the link between iron and colorectal cancer specifically found more than 75% of these studies supported the link[46]
    - Your risk of dying from cancer increases the higher your serum iron and transferrin saturation levels are. People with the highest levels have double the risk of death as those with the lowest[47]

4. **Iron and neurological disease —** Last but not least, high iron has repeatedly been shown to wreak havoc in the brain. Some of this research has already been mentioned. As noted by Dalton:

   > *"[Your brain] burns 20% of the body's total oxygen requirement. With a metabolism that hot, it's inevitable that the brain will also produce more free radicals as it churns through all that oxygen. Surprisingly, it's been shown that the brain appears to have less antioxidant capacity than other tissues in the body,[48] which could make it more susceptible to oxidative stress … This, in turn, points to a sensitivity to iron."*

   Dalton goes on to cite a number of studies which, when taken together, "suggest that abnormal iron metabolism in the brain could be a causative factor in Alzheimer's and other neurodegenerative diseases."

Ideal Iron and GGT Levels

When checking your serum ferritin, it's important to remember the "normal" ranges for GGT and serum ferritin are far from ideal.[49] If you're in the "normal" range, you're virtually guaranteed to develop some sort of health problem. It's also important to remember that you need both tests to confirm the absence of iron toxicity.

To learn more about this, see my interview with Gerry Koenig, former chairman of the Iron Disorders Institute and the Hemochromatosis Foundation, embedded above for your convenience. The recommended, ideal levels, of ferritin and GGT are as follows:

- **Ferritin —** Adult men and non-menstruating women: 30 to 40 nanograms per milliliter (ng/mL) or 75 to 100 nanomoles per liter (nmol/L[50]).

  The most commonly used threshold for iron deficiency in clinical studies is 12 to 15 ng/mL (30 to 37 nmol/L).[51] You do not want to be below 20 ng/mL (50 nmol/L) or above 80 ng/mL (200 nmol/L). **High iron during pregnancy is also problematic**; having a level of 60 or 70 ng/mL (150 or 175 nmol/L) is associated with greater odds of poor pregnancy outcomes.

- **GGT —** Below 16 units per liter (U/L) for men and below 9 U/L for women. Above 25 U/L for men and 18 U/L for women, your risk of chronic disease increases significantly.

Ferritin and GGT are interactive, and low GGT tends to be protective against higher ferritin. So, if your GGT is low, you're largely protected even if your ferritin is a bit higher than ideal. Still, it would still be wise to take steps to lower your ferritin to a more ideal level. On the other hand, even if your ferritin is low, having elevated GGT levels is cause for concern and needs to be addressed.

If you are thin, with a body mass index below 22 or 23, Koenig suggests getting a transferrin test as well, which gives you a percentage saturation level. A level of 25% to 35% is typically considered healthy. In the 1970s, the transferrin saturation test was used as a marker for early death. Having a transferrin saturation percentage of over 55 indicated a 60% increased risk for premature death.

How to Lower Your Iron and GGT Levels

If your iron level is too high, the easiest way to lower it is to donate blood two or three times a year. If you have severe overload you may need to do more regular phlebotomies. Regular sauna use, which is an effective form of detoxification, is also helpful.

While I've long recommended donating blood as the solution to iron overload, I now believe a balanced approach using phlebotomy, detoxification and reducing dietary iron, especially meat, is the best way to go about it.

Keep in mind that trying to control high iron through your diet alone can be risky, as you will also forgo many valuable nutrients. That said, to avoid maximizing iron absorption, avoid eating iron-rich foods in combination with vitamin C-rich foods or beverages, as the vitamin C will increase iron absorption. If needed, you could also take a curcumin supplement. Curcumin acts as a potent chelator of iron and can be a useful supplement if your iron is elevated.

As for lowering GGT, you'll need to implement strategies that boost glutathione, a potent antioxidant produced in your body, as GGT is inversely related to glutathione. As your GGT level rises, your glutathione goes down. This is in fact part of the equation explaining how elevated GGT harms your health. By elevating your glutathione level, you will lower your GGT.

The amino acid cysteine, found in whey protein, poultry and eggs, plays an important role in your body's production of glutathione. Red meat, which does not contain cysteine, will tend to raise GGT, as will alcohol, so both should be avoided.[52]

Research also suggests eating at least 10 servings of fruits and vegetables rich in vitamin C, fiber, beta-carotene, anthocyanins and folate per week can help reduce GGT.[53] Examples include carrots, romaine lettuce, spinach, sweet potatoes, apricots and tomatoes.

Also, be aware that certain medications can raise your GGT. If this is the case, please confer with your doctor to determine whether you might be able to stop the medication or switch to something else, and avoid over-the-counter medicines, including ibuprofen and aspirin, both of which can damage your liver.

General detoxification is another important component if your GGT is high, as your liver's job is to remove toxins from your body. The fact that your GGT is elevated means your liver is under stress.

Take Control of Your Health: Check Your Iron Status Annually

I strongly suggest most adults seriously consider getting a serum ferritin test on an annual basis to confirm you're neither too high nor too low. Again, keep in mind that the "normal" ranges for serum ferritin are far from ideal.[54] In some labs, a level of 200 to 300 ng/mL (499 to 749 nmol/L) falls within the normal range for women and men respectively, which is far too high for optimal health.

When it comes to iron overload, I believe it can be every bit as dangerous to your health as vitamin D deficiency, and checking your iron status is far more important than your

cholesterol. While a full iron panel that checks serum iron, iron-binding capacity and ferritin can be helpful, you really only need the serum ferritin test, plus the GGT test. Your doctor can write you a prescription for these tests.

So, to reiterate some of the most important take-home messages, to prevent ill health due to iron overload, be sure to:

1. Regularly screen for iron overload with a serum ferritin or GGT level to confirm that you don't have excess iron and, if you do, donate blood to lower your levels. Recent U.S. legislation allows all blood banks to perform therapeutic phlebotomy for hemochromatosis or iron overload. All you need is a doctor's order
2. Lower your net carb intake and increase healthy fats to switch over to fat-burning mode and protect your mitochondria. This will help to radically reduce ROS and secondary free radical production
3. Don't avoid iron-rich foods. Just avoid combining them with vitamin C-rich foods, and combine them with calcium-rich foods instead to limit absorption. Also avoid alcohol, which will increase the absorption of iron in your diet. You could also consider a curcumin supplement to reduce your iron load without risking the elimination of other valuable minerals
4. Unless you have a lab-documented iron deficiency, avoid iron-containing multivitamins, iron supplements and mineral supplements that contain iron

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