

How Excess Iron Raises Your Risk for Alzheimer's

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STORY AT-A-GLANCE

- Your body has limited capacity to excrete iron, which means it can build up in your tissues and organs. This is problematic, as iron is a potent oxidizer, capable of damaging tissues, including your brain
- > Buildup of iron in your brain causes a rusting effect, and appears to play an important role in the development and progression of Alzheimer's disease
- > Researchers have also found elevated cerebrospinal fluid iron levels are strongly correlated with the presence of the Alzheimer's risk allele, APOE-e4, and patients with higher iron levels deteriorate earlier and faster than those with low iron
- > Iron overload is easily diagnosed by measuring your serum ferritin. A healthy, ideal level is between 40 and 60 ng/ml
- > Adult men and non-menstruating women with high iron levels would benefit by donating blood two to three times per year to normalize their levels and avoid "rusting" in the brain

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While dietary iron is essential for optimal health¹ — being a key part of proteins and enzymes and playing an important role in energy production and the regulation of cell growth and differentiation, among other things — too much iron in your body can have serious ramifications.² One of the most important roles of iron is to provide hemoglobin (the protein in red blood cells) a mechanism through which it can bind to oxygen and carry it throughout your tissues.

Without proper oxygenation, your cells cannot function properly and eventually die. Common symptoms of insufficient iron include fatigue, decreased immunity or iron deficiency anemia, which can be serious if left untreated.

However, your body has a very limited capacity to excrete iron, which means it can build up in your tissues and organs. This is problematic, as iron is a potent oxidizer, capable of damaging tissues, including your vascular system and brain, thereby raising your risk for both heart disease and dementia.

Excess Iron 'Rusts' Your Brain

You're probably familiar with the fact that Alzheimer's disease is associated with a buildup of amyloid beta plaque in the brain. According to recent research^{3,4} from the Netherlands, buildup of iron, causing a rusting effect in the brain, also 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.

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."

Addressing excess iron may therefore be an effective treatment option. 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 disease process.

Previous Research Supports Rusty Brain Link

This is not the first time scientists have noted a link between excess iron and Alzheimer's disease (AD). In 2012, animal research⁵ suggested a link between abnormal iron metabolism and amyloid beta accumulation. When iron levels in the blood were reduced using an iron chelator, levels of beta-amyloid and phosphorylated tau protein — which disrupt the ability of neurons to conduct electrical signals — both reverted back to normal.

Interestingly, and unfortunately, this still did not reduce the generation of reactive oxygen species. Nor did it actually lower the level of iron in the brain itself. According to the authors:

"These results demonstrate that deferiprone [an iron chelating drug] confers important protection against hypercholesterolemia-induced AD pathology but the mechanism(s) may involve reduction in plasma iron and cholesterol levels rather than chelation of brain iron. We propose that adding an antioxidant therapy to deferiprone may be necessary to fully protect against cholesterol-enriched diet-induced AD-like pathology."

In 2013, UCLA researchers found that Alzheimer's patients tend to have iron accumulation in the hippocampus, and that the iron is responsible for the damage seen in that area. The findings were published in the Journal of Alzheimer's Disease.⁶
According to the researchers, the damage that eventually results in clinical signs of Alzheimer's really begin with iron's destruction of myelin — the fatty coating around your brain's nerve fibers.

This disrupts communication between neurons and promotes the buildup of beta amyloid plaque, which in turn destroys even more myelin. As explained by UCLA:7

"Myelin is produced by cells called oligodendrocytes. These cells, along with myelin, have the highest levels of iron of any cells in the brain ... and circumstantial evidence has long supported the possibility that brain iron levels might be a risk factor for age-related diseases like Alzheimer's. Although iron is essential for cell function, too much of it can promote oxidative damage, to which the brain is especially vulnerable."

A 2015 study⁸ showed that patients with higher iron levels deteriorated earlier and faster than those with low iron. Here, elevated cerebrospinal fluid iron levels were shown to be strongly correlated with the presence of the Alzheimer's risk allele, APOE-e4. According to the authors, "These findings reveal that elevated brain iron adversely impacts on AD progression, and introduce brain iron elevation as a possible mechanism for APOE-e4 being the major genetic risk factor for AD."

Research⁹ published last year in the journal JAMA Neurology also identified brain iron load "as a pathogenic mechanism" in Alzheimer's, and again linked high iron with the presence of the high-risk genetic mutation APOE-e4. As noted by the authors, "The ϵ 4 allele of APOE confers the greatest genetic risk for Alzheimer disease, and recent data implicate brain-iron load as a pathogenic mechanism because ϵ 4 carriage elevates the level of cerebrospinal fluid ferritin."

How Do You End Up With Excessive Iron?

While iron deficiency or anemia is commonly checked for, many doctors are still misinformed about the dangers of iron overload, which is actually a far more common problem. In fact, most men and postmenopausal women are at risk for iron overload since blood loss is the primary way to lower excess iron. The following can also cause or exacerbate high iron:

- Cooking in iron pots or pans. Cooking acidic foods in these types of pots or pans will cause even higher levels of iron absorption.
- Eating processed food products like cereals and white breads fortified with iron.
 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.

There's also an inherited disease, hemochromatosis, which causes your body to accumulate excessive and dangerously damaging levels of iron. About 1 in 3.5 or an estimated 100 million people in the U.S. have the single gene for hemochromatosis. Approximately 1 million people have the double gene variant, considered the genotype most predictive of liver disease complications.

Iron Testing and Maintaining an Ideal Level

The serum ferritin test measures your stored iron. 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. Keep in mind that (as with many other lab tests) the "normal" ranges for serum ferritin are far from ideal. In some labs, a level of 200 to 300 nanograms per milliliter (ng/mL) falls within the normal range for women and men respectively, which is far too high for optimal health.

An ideal level for adult men and non-menstruating women is between 40 and 60 ng/mL. You do not want to be below 20 ng/mL or above 80 ng/mL. Maintaining a healthy iron level is also very important during pregnancy. Having a level of 60 or 70 ng/mL is associated with greater odds of poor pregnancy outcomes. That said, iron deficiency during pregnancy is equally problematic. The most commonly used threshold for iron deficiency in clinical studies is 12 to 15 ng/mL.¹¹

Another valuable test is the serum liver enzyme gamma-glutamyl transpeptidase (GGT) test. While typically used to assess liver damage, it's also a screening marker for excess free iron and is a great indicator of your sudden cardiac death risk.

For women, a healthy GGT level is around 9 units per liter (U/L) whereas the high ends of "normal" are generally 40 to 45 U/L. According to Gerry Koenig, former chairman of the Iron Disorders Institute and the Hemochromatosis Foundation, 12 women with a GGT above 30 U/L have a higher risk of cancer and autoimmune disease. For men, 16 U/L is ideal, while the normal lab range can go as high as 65 to 70 U/L.13

Last but not least, a percentage transferrin saturation test will also reveal elevated ferritin. Ideally, this value should be between 30 and 40%. Above 40%, you have iron overload that is likely damaging your mitochondria and really needs to be addressed.

Dos and Don'ts to Lower Your Iron Level

If your iron level is high, the easiest and most effective solution is to donate your blood. If you're an adult male, you'll want to donate blood two to three times a year once your levels are back to normal. If you are unable to donate blood, ask your doctor to write a prescription for therapeutic phlebotomy.

Also avoid combining foods high in vitamin C with foods high in iron, as the vitamin C increases iron absorption. Alcohol will also increase the absorption of iron in your diet, and is therefore best avoided. On the other hand, calcium will bind to iron, thereby limiting absorption, so eating iron-rich foods with calcium-rich foods can be helpful if your levels tend to be high.

While researchers are looking at iron-chelating strategies, I don't recommend this. For example, using phytate or phytic acid (also known as IP6) to prevent iron absorption and chelate iron out of your body can easily result in other mineral deficiencies, such as zinc deficiency. A far safer alternative is curcumin. It actually acts as a potent chelator of iron and can be a useful supplement if your iron is elevated.

As I have beta thalassemia that elevates serum ferritin, I have had to be assiduous about using therapeutic phlebotomies to keep my ferritin in a healthy range. For nearly two years now, though, I have not had any phlebotomies; I've merely relied on an optimized detoxification program and my ferritin is typically between 35 and 40 ng/mL.

I hope to write a book on this program but it will not be out until 2020 or possibly 2021, as I am working with some of the finest experts on the planet and the goal is to create the best program ever designed.

Alzheimer's Prevention Strategies

According to Dr. David Perlmutter, a neurologist and author of "Grain Brain" and "Brain Maker," anything that promotes insulin resistance will ultimately also raise your risk of Alzheimer's. To this I would add that any strategy that enhances your mitochondrial function will lower your risk. In 2014, Bredesen published a paper that demonstrates the power of lifestyle choices for the prevention and treatment of Alzheimer's.

By leveraging 36 healthy lifestyle parameters, he was able to reverse Alzheimer's in 9 out of 10 patients. This included the use of exercise, ketogenic diet, optimizing vitamin D and other hormones, increasing sleep, meditation, detoxification, and eliminating gluten and processed food. You can download Bredesen's full-text case paper online, which details the full program.¹⁴ Following are some of the lifestyle strategies I believe to be the most helpful and important:

Eat real food, ideally organic — Avoid processed foods of all kinds, as they contain a number of ingredients harmful to your brain, including refined sugar, processed fructose, grains (particularly gluten), vegetable oils, genetically engineered ingredients and pesticides. Ideally, keep your added sugar to a minimum and your total fructose below 25 grams per day, or as low as 15 grams per day if you already have insulin/leptin resistance or any related disorders.

Opting for organic produce will help you avoid synthetic pesticides and herbicides. Most will also benefit from a gluten-free diet, as gluten makes your gut more permeable, which allows proteins to get into your bloodstream where they sensitize your immune system and promote inflammation and autoimmunity, both of which play a role in the development of Alzheimer's.

Replace refined carbs with healthy fats — Diet is paramount, and the beauty of following my optimized nutrition plan is that it helps prevent and treat virtually all chronic degenerative diseases, including Alzheimer's. It's important to realize that your brain actually does not need carbs and sugars; healthy fats such as saturated animal fats and animal-based omega-3 are far more critical for optimal brain function.

A cyclical ketogenic diet has the double advantage of both improving your insulin sensitivity and lowering your Alzheimer's risk. As noted by Perlmutter, lifestyle strategies such as a ketogenic diet can even offset the risk associated with genetic predisposition.

When your body burns fat as its primary fuel, ketones are created, which not only burn very efficiently and are a superior fuel for your brain, but also generate fewer reactive oxygen species and less free radical damage.

A ketone called beta hydroxybutyrate is also a major epigenetic player, stimulating beneficial changes in DNA expression, thereby reducing inflammation and increasing detoxification and antioxidant production. I explain the ins and outs of implementing this kind of diet, and its many health benefits, in my book, "Fat for Fuel."

In it, I also explain why cycling through stages of feast and famine, opposed to continuously remaining in nutritional ketosis, is so important.

Pay close attention to the kinds of fats you eat — avoid all trans fats or hydrogenated fats that have been modified in such a way to extend their longevity on the grocery store shelf. This includes margarine, vegetable oils and various butter-like spreads.

Healthy fats to add to your diet include avocados, butter, organic pastured egg yolks, coconuts and coconut oil, grass fed meats and raw nuts such as pecans and macadamia. MCT oil is also a great source of ketone bodies.

Keep your fasting insulin levels below 3 — Lowering your insulin will also help lower leptin levels, which is another factor for Alzheimer's. If your insulin is high, you're likely consuming too much sugar and need to cut back.

Optimize your omega-3 level — High intake of the omega-3 fats EPA and DHA help prevent cell damage caused by Alzheimer's disease, thereby slowing its progression and lowering your risk of developing the disorder. Ideally, get an omega-3 index test done once a year to make sure you're in a healthy range. Your omega-3 index should be above 8% and your omega 6-to-3 ratio between 0.5 and 3.0.

Eat plenty of nitrate-rich foods — Beets and other nitrate-rich foods such as arugula provide powerful benefits for your brain and may be a powerful ally in the fight against Alzheimer's disease. Your body transforms plant-based nitrates into nitric oxide, which enhances oxygenation, has beneficial impacts on your circulatory and immune systems, and serves as a signaling or messenger molecule in every cell of your body.

The betanin in beets also helps prevent oxidation, particularly oxidation caused when the beta-amyloid is bound to copper. As noted by coauthor Darrell Cole Cerrato, 18 "We can't say that betanin stops the misfolding [of amyloid beta] completely, but we can say that it reduces oxidation. Less oxidation could prevent misfolding to a certain degree, perhaps even to the point that it slows the aggregation of beta-amyloid peptides ..."

Previous research¹⁹ has also shown raw beet juice helps improve neuroplasticity, primarily by increasing blood flow and tissue oxygenation. Nitric oxide, in its capacity as a signaling molecule, allows your brain cells to communicate with each other better. Importantly, the beets boosted oxygenation of the somatomotor cortex, a brain area that is often affected in the early stages of dementia.

Optimize your gut flora — To do this, avoid processed foods, antibiotics and antibacterial products, fluoridated and chlorinated water, and be sure to eat traditionally fermented and cultured foods, along with a high-quality probiotic if needed. Dr. Steven Gundry does an excellent job of expanding on this in his book "The Plant Paradox."

Intermittently fast — Intermittent fasting is a powerful tool to jump-start your body into remembering how to burn fat and repair the insulin/leptin resistance that is a primary contributing factor for Alzheimer's. Once you have worked your way up to where you've been doing 20-hour daily intermittent fasting for a month, are metabolically flexible and can burn fat as your primary fuel, you can progress to the far more powerful five-day water fasts.

Move regularly and consistently throughout the day — It's been suggested that exercise can trigger a change in the way the amyloid precursor protein is metabolized,²⁰ thus, slowing down the onset and progression of Alzheimer's.

Exercise also increases levels of the protein PGC-1 alpha. Research has shown that people with Alzheimer's have less PGC-1 alpha in their brains and cells that contain more of the protein produce less of the toxic amyloid protein associated with Alzheimer's.

Optimize your magnesium levels — Preliminary research strongly suggests a decrease in Alzheimer symptoms with increased levels of magnesium in the brain. Keep in mind that the only magnesium supplement that appears to be able to cross the blood-brain barrier is magnesium threonate.

Optimize your vitamin D, ideally through sensible sun exposure — Sufficient vitamin D is imperative for proper functioning of your immune system to combat inflammation associated with Alzheimer's and, indeed, research shows people living in northern latitudes have higher rates of death from dementia and Alzheimer's than those living in sunnier areas, suggesting vitamin D and/or sun exposure are important factors.

If you are unable to get sufficient amounts of sun exposure, take daily supplemental vitamin D3 to reach and maintain a blood level of 60 to 80 ng/ml. That said, it's important to recognize that sun exposure is important for reasons unrelated to vitamin D.

Your brain responds to the near-infrared light in sunlight in a process called photobiomodulation. Research shows near-infrared stimulation of the brain boosts cognition and reduces symptoms of Alzheimer's, including more advanced stages of the disease.

Delivering near-infrared light to the compromised mitochondria synthesizes gene transcription factors that trigger cellular repair, and your brain is one of the most

Vitamin B12 — According to a 2010 study published in the journal Neurology,^{21,22} people who consume foods rich in B12 may reduce their risk of Alzheimer's in their later years. For each unit increase in holotranscobalamin — the marker of vitamin B12 — the risk of developing Alzheimer's was reduced by 2%. Very high doses of B vitamins have also been found to reduce memory loss by preventing brain shrinkage.²³

Curcumin — Recent research shows curcumin supplementation helped improve memory and focus in seniors already suffering mild memory lapses, and reduced amyloid and tau deposits associated with Alzheimer's.²⁴ Overall, the curcumin group improved their memory by 28% over the year-and-a-half-long treatment period.

PET scans also confirmed the treatment group had significantly less amyloid and tau buildup in areas of the brain that control memory, compared to controls.

Curcumin has also been shown to increase levels of brain-derived neurotrophic factor (BDNF),²⁵ and reduced levels of BDNF have been linked to Alzheimer's disease. Yet another way curcumin may benefit your brain and lower your risk of dementia is by affecting pathways that help reverse insulin resistance, hyperlipidemia and other symptoms associated with metabolic syndrome and obesity.²⁶

Avoid and eliminate mercury from your body — Dental amalgam fillings are one of the major sources of heavy metal toxicity, however you should be healthy prior to having them removed. Once you have adjusted to following the diet described in my optimized nutrition plan, you can follow the mercury detox protocol and then find a biological dentist to have your amalgams removed.

Avoid and eliminate aluminum from your body — Common sources of aluminum include antiperspirants, nonstick cookware and vaccine adjuvants. There is some suggestion that certain mineral waters high in silicic acid may help your body eliminate aluminum.

Avoid flu vaccinations — Most flu vaccines contain both mercury and aluminum.

Avoid statins and anticholinergic drugs — Drugs that block acetylcholine, a nervous system neurotransmitter, have been shown to increase your risk of dementia. These drugs include certain nighttime pain relievers, antihistamines, sleep aids, certain antidepressants, medications to control incontinence and certain narcotic pain relievers.

Statin drugs are particularly problematic because they suppress the synthesis of cholesterol, deplete your brain of coenzyme Q10, vitamin K2 and neurotransmitter precursors, and prevent adequate delivery of essential fatty acids and fat-soluble antioxidants to your brain by inhibiting the production of the indispensable carrier biomolecule known as low-density lipoprotein.

Limit your exposure to dangerous EMFs (cellphones, Wi-Fi routers and modems) — Radiation from cellphones and other wireless technologies trigger excessive production of peroxynitrites,²⁷ a highly damaging reactive nitrogen species. Increased peroxynitrites from cellphone exposure will damage your mitochondria,^{28,29} and your brain is the most mitochondrial-dense organ in your body.

Increased peroxynitrite generation has also been associated with increased levels of systemic inflammation by triggering cytokine storms and autonomic hormonal dysfunction.

Optimize your sleep — Sleep is necessary for maintaining metabolic homeostasis in your brain. Without sufficient sleep, neuron degeneration sets in, and catching up on sleep during weekends will not prevent this damage.^{30,31,32} Sleep deprivation causes disruption of certain synaptic connections that can impair your brain's ability for learning, memory formation and other cognitive functions. Poor sleep also accelerates the onset of Alzheimer's disease.³³

Most adults need seven to nine hours of uninterrupted sleep each night. Deep sleep is the most important, as this is when your brain's glymphatic system performs its cleanout functions, eliminating toxic waste from your brain, including amyloid beta.

Challenge your mind daily — Mental stimulation, especially learning something new, such as learning to play an instrument or a new language, is associated with a decreased risk of dementia and Alzheimer's. Researchers suspect that mental challenge helps to build up your brain, making it less susceptible to the lesions associated with Alzheimer's disease.

Watch this video to learn more about how copper affects the iron levels in your body.

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