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REPORT

Excess Iron and Brain Degeneration: The Little-Known Link

By Kathleen Anderson

Iron gradually builds up in certain cells and tissues over the course of the human life span. Too much iron accelerates mitochondrial decay and inflicts system-wide free radical damage to healthy tissues.[1,2] Age-related iron overload is a known contributor to multiple degenerative diseases, including **liver fibrosis**, **heart attack**, and **cancer**.[3-8]

Iron accumulation is often a consequence of aging. In the laboratory, total iron content has been shown to increase exponentially as cells age, resulting in **10-fold higher levels of iron** compared to young cells.[3]

Sadly, owing to physician and patient ignorance, the significant dangers posed by ***excess iron*** in the body remain little known and often overlooked. As a result, most maturing individuals are not taking aggressive measures to ensure ideal ***total-body iron status***—and most doctors do not properly test for it.

In this article, you will discover the results of a **groundbreaking UCLA study** published late last year conclusively linking **excess iron accumulation** in brain tissue to **neurodegenerative brain disorders** like Alzheimer's and Parkinson's.[9,10]

You will also find a multi-pronged approach to prevent and even *reverse* iron-induced tissue damage in the brain, liver, and kidneys using nutrients **Life Extension**® members already take, such as **quercetin**, **curcumin**, **lipoic acid**, and **green tea**.

Brain Iron Levels, Alzheimer's Disease, and Cognitive Decline

Dr. George Bartzokis is a widely published researcher and professor of psychiatry at the Semel Institute for Neuroscience and Human Behavior at UCLA. Much of his work has been devoted to understanding the role that iron plays in human brain development, function, and aging, with a particular emphasis on the link between **iron** and **neurodegenerative disorders**, including **Alzheimer's** and **Parkinson's** disease.

From that work, Bartzokis and his colleagues have generated a detailed picture of iron metabolism across the human life span.

Bartzokis' team showed that they could accurately measure iron levels in living humans' brains by using a highly specialized non-invasive form of magnetic resonance imaging (MRI).[11] Applying this technique to groups of people with and without Alzheimer's disease, the researchers quickly discovered significantly

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larger amounts of stored iron in certain brain regions in those with Alzheimer's than in control subjects.[9,12] Similar findings held true in Parkinson's and Huntington's disease sufferers as well.[10,13]

Those discoveries raised the intriguing question of whether the iron was a potential contributor to the neurodegenerative disease process, or whether it was a byproduct of the disease itself.

Further work revealed the definitive answer. First, the brain scan studies showed that increased iron levels were present at the earliest onset of disease, indicating that they were not a consequence but rather a potential cause of brain degeneration.[13]

Second, even in apparently healthy individuals, iron levels rise steadily with age in some of the very brain regions affected by Alzheimer's, Parkinson's, and Huntington's diseases.[14] Those regions include the basal ganglia, which contain the highest levels of iron in the brain.[13] Third, the researchers found that people with the highest brain iron accumulations had the earliest age at onset of the degenerative diseases.[15]

By now it was clear that the presence of excessive iron in affected brain areas was somehow directly involved in triggering the neurodegenerative disease processes. Iron was fast emerging as a ***potentially modifiable age-related risk factor*** for these conditions.[15]

But it wasn't only neurodegenerative diseases for which excessive iron accumulation was a risk. The UCLA researchers studied a group of healthy older adults, comparing memory and information-processing speed according to their brain iron levels. Those with the highest accumulations of iron in their brain grey matter had the poorest performance, especially among men.[16]

Bartzokis' team was struck by several other gender differences apparent in these diseases: men are more likely to develop these conditions at earlier ages than women, and women have significantly lower iron levels in five vital brain regions than men of similar ages.[17]

A Breakthrough Study

These findings led to a compelling study published in late 2011 demonstrating for the first time that *limiting your body's lifetime exposure to iron can in turn limit your risk of neurodegenerative brain disorders*.

It began with the observation that women not only have lower brain iron levels in their later years, they also have lower iron levels throughout their bodies for most of their lives. It has long been known among physicians that this difference arises because women lose iron during their reproductive years through menstruation. Could that steady, low-level loss of iron be an effective means by which women inadvertently but effectively *limit* their lifetime exposure to iron, thereby protecting themselves from early-onset brain disorders?

Dr. Todd A. Tishler, a protégé of Dr. Bartzokis at UCLA, discovered a way to test that hypothesis. Tishler, Bartzokis, and colleagues studied brain scan images of 39 postmenopausal women, of whom 15 had undergone a hysterectomy prior to menopause.[18] Those women obviously had stopped menstruating prior to menopause, prematurely ending their bodies' ability to lose iron on a regular basis. The other women had experienced regular periods until menopause. For comparison, the researchers included brain scans of 54 men of similar ages.

Not surprisingly, the men's brains had higher iron levels than those of women who had reached menopause naturally, without hysterectomy. But in a compelling validation of Tishler's hypothesis, the brains of the women with hysterectomies exhibited iron levels not only *higher* than normal menopausal women but *identical* to levels in male subjects.[18]

The UCLA study demonstrated that lifelong menstruation grants most mature women beneficially lower brain iron levels and affords significant protection against early onset of neurodegenerative brain disorders.

It also underscores the critical need for humans to aggressively limit *lifetime* exposure to iron and thereby *substantially* lower their risk of neurodegenerative brain disorders and cognitive decline.

WHAT YOU NEED TO KNOW: HOW EXCESS IRON INFLICTS SYSTEM-WIDE DAMAGE

The interplay between dietary iron intake and total health is more complex than most people grasp.

Here's why: iron-rich red blood cells typically die after about 90 days. Much of the iron contained in their hemoglobin molecules is recycled to generate *new* hemoglobin and new red blood cells. (The same is true of the iron in muscle cells.)

The problem? A significant amount of this iron is not recycled. Instead, it accumulates in cellular repositories called ***lysosomes.***

Our bodies use iron because it is a powerful ***catalyst***, speeding chemical reactions essential to life. But it is precisely that catalytic function that makes iron so dangerous in excess. "Useful" iron in your body is bound to carrier proteins and enzyme systems that isolate it from bodily tissues, and that direct its catalytic activities to where they are needed.72 But iron in its **unbound state** is free to react unselectively with a variety of chemical compounds.15

Unbound iron from age-related overload reacts volatilely with water and oxygen to produce highly *reactive oxygen species* or free radicals.19,41,42 These in turn damage cell membranes, DNA, mitochondria, and multiple tissues and organs.4,73

Natural Ways to Limit Iron-Induced Tissue Damage

There are several ways you can limit the damaging effects of excessive iron in your body. The most obvious is to monitor how much iron you ingest. Experts now typically recommend that older adults limit their intake of red meat, which is our major natural dietary source of iron. You should also choose your vitamin and mineral supplements carefully. Unless you have iron-deficiency anemia, you are unlikely to benefit from extra supplemental iron, and it is absent from properly formulated dietary supplements.

But what can you do about the iron your body has already absorbed and has now accumulated in potentially dangerous ways in your tissues? There are two main approaches you should take. The first is to supplement with nutrients that can bind up, or ***chelate*** the iron in molecular complexes. Chelation isolates iron from tissues and limits its ability to catalyze the oxidant reactions that damage them. Chelation also hastens excretion of excess iron from your body.[19] Ultimately, that means that chelation limits your body's exposure to the destructive effects of iron accumulations.

The second approach to minimizing long-term iron damage is to optimize your antioxidant regimen. That can help you prevent any further damage by iron's catalytic reactions with oxygen.

We'll now examine the compelling data for nutrients that can protect your body from excess iron accumulations by chelating iron, enhancing your antioxidant defenses—or both.

THE LINK BETWEEN EXCESS IRON AND BRAIN DEGENERATION

- Accumulation of iron in bodily tissues is an inevitable consequence of aging.
- Pathologic age-related ***iron overload*** damages cells and tissues and is a causative factor in numerous degenerative diseases, including **liver fibrosis**, **cardiovascular disease**, and **cancer**.
- Few doctors inform their patients of the dangers of high total-body iron distributions, nor do they test for total-body iron status.
- Excessive iron accumulations are found in affected brain areas of people with Alzheimer's, Parkinson's, and other neurodegenerative diseases.
- Even in normal older adults, people with higher brain iron accumulations perform more poorly on cognitive tests than do those with lower brain iron concentrations.
- A breakthrough UCLA study demonstrates that limiting lifetime exposure to iron can reduce brain iron accumulations.
- A number of nutrients can help reduce your body's total exposure to iron through chelation (binding to free iron atoms) and antioxidant activity, including **quercetin**, **curcumin**, **R-lipoic acid**, and **silymarin**.

Quercetin

Flavonoids are naturally occurring plant molecules that offer both powerful antioxidant protection and the ability to bind to free iron atoms.[19-21] Quercetin, a flavonoid found in berries and other plants, chelates iron atoms as powerfully as the prescription drugs used in managing severe cases of iron overdose.[22,23] Quercetin's antioxidant effects are likely to be closely related to its strong iron-chelating capacity, and account for its ability to prevent the DNA strand damage that precedes cancer development.[24,25]

Studies of quercetin reveal that it can prevent the **kidney damage** associated with acute iron overload from muscle breakdown, one of the leading causes of acute renal failure.[26] Similarly, liver injury from long-term exposure to iron is prevented in laboratory animals supplemented with quercetin.[27,28] Quercetin is included in properly formulated resveratrol supplements since it boosts resveratrol's beneficial effects in the body.

Cranberry and Pomegranate

Dark-colored and red fruits are known to have many health benefits, in large part because of their high content of polyphenols. Cranberry and pomegranate extracts rich in polyphenols have now been shown to have potent iron-chelating capabilities, in some cases completely suppressing iron-catalyzed oxidant reactions.[22,29]

We've long known that cranberry juice and extracts are active in preventing urinary tract infections with some of the most common pathological organisms. The traditional view has been that the extracts' antioxidant and anti-adhesive powers are the primary mechanisms.[30] New evidence shows that another way cranberry extracts work is by *depriving infecting bacteria of the iron they need for survival through chelation*.[30,31]

Green Tea Extract

After water, tea is the most commonly-consumed beverage in the world.[32] Green, unfermented tea leaves have numerous health benefits, chiefly attributable to their content of a polyphenol molecule called epigallocatechin-3-gallate, or **EGCG**.[32] EGCG is a well-known antioxidant.[33] In recent years, it was shown to powerfully chelate unbound iron and protect vulnerable tissues.[34,35]

Green tea extracts rich in EGCG bind to iron, and scientists have proposed their use as an alternative or adjunct to commercial iron chelators, which, while effective, may come with negative side effects.[36,37] Such drugs are used to treat *thalassemia*, a condition which when severe enough, can cause massive iron accumulations as the result of frequent blood transfusions. EGCG from green tea has now been used safely and effectively to bind and remove iron from the blood of individuals with thalassemia.[37,38] And in studies of animals deliberately overloaded with iron to mimic aging, green tea extracts are able to bind free iron and reduce iron-related tissue oxidation in **brain** and **liver** tissue.[36,39,40]

Unlike many drugs and nutrients, EGCG readily crosses the **blood-brain barrier**.[41,42] This allows it to capture and isolate iron from the brain regions affected in Alzheimer's, Parkinson's, and Huntington's diseases.[43] In contrast to many current drug therapies, which can only *modify* symptoms in these tragic conditions, iron chelation by EGCG rich green tea extract offers the potential to prevent and reverse the progression of the disease process itself.[44-46]

SHOULD YOU REALLY BE TAKING IRON?

Curcumin

Despite the dangers posed by *excessive* iron accumulation, aging individuals still require sufficient iron intake for optimal health.

In order to know whether you are getting adequate (or excessive) amounts of iron in your diet, you need to know your ***total-body iron status***. This requires a series of blood tests *beyond* those normally administered to determine whether you suffer from anemia.

For a *comprehensive* snapshot of your current total-body iron status, ask your doctor to include **serum ferritin** and **total iron-binding capacity** in addition to the ***hemoglobin*** and ***hematocrit*** measured in a typical blood count. Your doctor may order additional tests based on these results.

If you don't have iron deficiency or anemia, ***taking supplemental iron is not advisable*** and may contribute to onset of the degenerative disorders associated with iron overload, from Alzheimer's and Parkinson's to cancer and cardiovascular disease. Multivitamin and mineral formulations for maturing individuals should *not* contain extra iron for that very reason. Pregnant women have increased iron requirements and should consult their physician to determine if iron supplementation is appropriate. Be certain that your supplements are appropriate to your own body's iron status.

Curcumin

Curcumin is the major chemical component of the spice turmeric, which has multiple health benefits as an antioxidant and anti-inflammatory molecule.[47-49] The unexpected discovery that curcumin is also a powerful iron chelator has given us new insight into its multimodal mechanisms of action in gaining control of age-related iron accumulations in the brain, heart, and liver.[50-53]

Iron chelation by curcumin is now recognized as one of the mechanisms by which it prevents cognitive deficits and pathological tissue changes in animal models of Alzheimer's disease.[48] In addition to its direct chelation of iron, curcumin induces increased genetic expression of the body's natural iron-binding and transport protein, ***ferritin***, further sequestering iron away from vulnerable tissues.[50] These multiple capabilities lead directly to reduction in iron levels in iron-overloaded organs.[50,53-55]

Recently, it was discovered that curcumin's iron-chelating ability helps restore **natural DNA repair mechanisms**, an additional means of protecting damaged neurons in Alzheimer's and Parkinson's diseases.[56] And, in a fashion similar to cranberry polyphenols, curcumin can inhibit growth of microorganisms (in this case, yeast) by depriving them of the iron they need to reproduce.[57]

Milk Thistle (Silymarin and Silibinin)

Milk thistle extracts have been used for centuries in managing diseases of the liver and gallbladder.[58] Iron accumulations and the resulting oxidant stress in liver tissue are responsible for progressive ***fibrosis***

(scarring) and ultimately liver failure.[2,59] Early work on milk thistle extracts focused on their antioxidant functions, but more recently evidence for potent iron chelation has been revealed as an additional liver-protective mechanism.[58,60] Iron-overloaded animals can be protected from the liver fibrosis-inducing effects of iron by regular doses of silibinin, a milk thistle component.[2,59]

Impressive human data for the impact of silibinin on iron-overloaded patients is now available. In patients with **chronic hepatitis C**, in whom iron accumulations contribute to liver failure, treatment with a mixture of **silibinin** and **soy complex** resulted in a significant decrease in serum levels of ferritin, the iron-bound protein that reflects total body iron levels.[61] In patients with *thalassemia major*, who have massive iron accumulations as a result of multiple transfusions, **140 mg three times per day** of the milk thistle component ***silymarin*** enhanced the iron-chelating effects of the drug *desferrioxamine*.[62] Similar results have been shown using **140 mg per day** of ***silibinin*** in patients with another form of iron overload, hereditary *hemochromatosis*.[63]

Lipoic Acid and Carnitine

Lipoic acid and ***carnitine*** are small-molecule nutrients vital to your body's management of its energy flow.[64,65] Potent antioxidants, they are both credited with **protecting mitochondria** and thereby slowing the aging process. Exciting work is now emerging that shows that each of these nutrients, in each of several forms, exerts its favorable anti-aging effects by chelating iron as well.[64-66]

A form of carnitine called ***L-propionyl carnitine*** is known to improve **heart muscle recovery** after a heart attack. It acts as an energy source for heart muscles, and also as an anti-free radical agent in damaged heart tissue; the latter effect has now been shown to be the result of iron chelation.[65] Another form, ***acetyl-L-carnitine***, exhibits powerful antioxidant effects that reverse the impact of iron-induced oxidative stress in human cells.[67]

Lipoic acid chelates iron in ***lysosomes***, cellular components that are a site of iron storage, effectively preventing iron-induced oxidative damage.[68,69] This nutrient also reduces iron uptake by cells in the lens of the eye, suggesting a potential role in preventing **cataract formation**.[70]

An important animal study has now demonstrated that supplementation with R-lipoic acid reverses age-related accumulation of iron in rat brain tissue and restores normal antioxidant activity.[71] This study has direct bearing on the prevention and treatment of neurodegenerative diseases in humans, the very conditions that Dr. Bartzokis and colleagues have been studying at UCLA.

Summary

Milik Thistle

Accumulation of iron in cells is a widely overlooked and inevitable consequence of aging. Pathologic age-related iron overload damages cells and tissues and is a causative factor in numerous degenerative diseases, including liver fibrosis, cardiovascular disease, and cancer. Few doctors inform their patients of the dangers of excess iron, nor do they test for total-body iron status. Excessive iron accumulations are found in affected brain areas of people with Alzheimer's, Parkinson's, and other neurodegenerative diseases. Even in normal older adults, people with higher brain iron accumulations perform more poorly on cognitive tests than do those with lower brain iron concentrations. A breakthrough UCLA study demonstrates that limiting lifetime exposure to iron can reduce brain iron accumulation. A number of nutrients can help reduce your body's total exposure to iron through chelation (binding to free iron atoms) and antioxidant activity. These include **quercetin**, **curcumin**, **R-lipoic acid,** and **milk thistle**.

The majority of people should avoid multi-vitamin supplements fortified with iron, as most aging individuals already have too much iron in their bodies. •

If you have any questions on the scientific content of this article, please call a **Life Extension**® Health Advisor at 1-866-864-3027.

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