Iron Supplements Increase Infection Risk

It’s been known for some time that iron supplements increase infection risk, because people who take them have more infections. A recent report clarifies some mechanisms.

Evidence for increased infections with iron

Many people in the tropics, especially children, are iron-deficient, given both the relative lack of dietary meat and high rates of intestinal parasites and malaria, so naturally doctors would like to fix that. Unfortunately, the most direct way, giving iron supplements, often backfires.

For example, giving iron to nomads in Somalia greatly increased the number of infections, compared to those who took a placebo.

Seven episodes of infection occurred in the placebo group and 36 in the group treated with iron; these 36 episodes included activation of pre-existing malaria, brucellosis, and tuberculosis. This difference suggested that host defence against these infections was better during iron deficiency than during iron repletion. Iron deficiency among Somali nomads may be part of an ecological compromise, permitting optimum co-survival of host and infecting agent.

Giving iron to children increases their risk of diarrhea and malaria, which in some cases requires hospitalization and can kill the patients. Many other reports (e.g.) and reviews describe similar findings.
Bacteria thrive with iron supplements

This next study is quite neat, since it’s simple and straightforward. A group of adult male volunteers in the Gambia gave a blood sample. They then took one dose of ferrous sulfate, an iron supplement, at 400 mg, which is a typical or even low dose of iron. They then gave another blood sample. Both samples were centrifuged, and the serum was used to grow bacteria. The researchers discovered that oral iron acutely elevates bacterial growth in human serum.

*Escherichia coli*, *Yersinia enterocolitica* and *Salmonella enterica* serovar Typhimurium (all gram-negative bacteria) and *Staphylococcus epidermidis* (gram-positive) showed markedly elevated growth in serum collected after iron supplementation. Growth rates were very strongly correlated with transferrin saturation (p < 0.0001 in all cases). Growth of *Staphylococcus aureus*, which preferentially scavenges heme iron, was unaffected. These data suggest that even modest oral supplements with highly soluble (non-physiological) iron, as typically used in low-income settings, could promote bacteremia by accelerating early phase bacterial growth prior to the induction of immune defenses.

Bacteremia means a blood infection with bacteria, and is a serious, life-threatening condition. Also known as sepsis or septicemia, it’s ranked number 10 in the list of leading killers of people over 65 years old in the U.S.

Below are growth curves for bacteria in serum before iron supplementation (blue lines) and after (red lines).

The y-axis on these charts is a log scale, x-axis is time, so the charts indicate doubling times and final concentration of bacteria. The bacteria grew far faster in serum from individuals after iron supplementation.

Bacteria and other microorganisms require iron

Why should bacteria grow so much faster with excess iron?
The answer is that bacteria, like virtually all living things, require iron for growth. However, in humans and other animals, iron is tightly controlled and sequestered, and one of the main reasons for this is to stop bacteria from acquiring iron.

Control of iron is an important part of the innate immune system.

The frontline of host-pathogen coevolution

Pathogens have to subvert a host’s innate defenses to avoid being killed. Barber and Elde now show that this principle extends to nutrient-transporting proteins, such as transferrin, which binds iron... Without iron, invading pathogens cannot replicate, but iron is sequestered in transferrin, which stops pathogens using it. So pathogens have evolved a succession of transporters that can hijack transferrin's iron. Over time, the primate transferrin binding surface has coevolved to wrestle iron back from the grip of pathogens.

Transferrin is the protein molecule used to transport iron in the bloodstream, and it’s been suggested that infusions of transferrin could be used in the treatment of septicemia.

Meat is a better source of iron

If someone were iron-deficient, a better way to get iron is eating meat. The iron in meat is heme iron, as opposed to the non-heme (unbound) iron in iron tablets. Heme iron is handled more safely by the body, and doesn’t result in spikes of iron in the bloodstream. In addition, heme iron doesn’t cause excess free iron in the gut, so bacteria can’t get it and use it for growth.

Iron supplements increase infection risk

Iron supplements increase the risk of infection.

In the U.S., all flour, corn meal, and rice must be iron-fortified by law. Is this increasing the rate of infections? How many people with gut dysbiosis and other problems such as irritable bowel syndrome owe their problems to iron fortification or supplementation? How many people with septicemia, the 10th leading cause of death among the elderly, got that way due to iron?

No one knows.

PS: For more on the effects of excess iron, see my book, Dumping Iron.
Iron and Fungal Infections

We saw recently that iron is involved, however unlikely it may seem, in producing dandruff, seborrheic dermatitis, and quite possibly, male pattern baldness. These conditions all have in common that a fungus, Malassezia, is involved. In this short post I want to take a look at the evidence of a connection between iron and fungal infections.

Malassezia

Dandruff and seborrheic dermatitis are both associated with several species
of fungus of the genus *Malassezia*. They are specialized to live on human skin. Like all other microbial pathogens, *Malassezia* require iron to grow and reproduce, and they obtain iron from their hosts.

Transferrin is the protein molecule in mammals that binds and carries iron. (Ferritin is for iron storage.) Transferrin is at the center of an evolutionary arms race between microbes and primates. Primates try to withhold iron from microbes, and the microbes try to grab it. Each one of them attempts to fight their respective opponents by evolving molecules that have an ever stronger grip on iron.

Iron sequestration provides an innate defense termed nutritional immunity, leading pathogens to scavenge iron from hosts. Although the molecular basis of this battle for iron is established, its potential as a force for evolution at host-pathogen interfaces is unknown. We show that the iron transport protein transferrin is engaged in ancient and ongoing evolutionary conflicts with TbpA, a transferrin surface receptor from bacteria. Single substitutions in transferrin at rapidly evolving sites reverse TbpA binding, providing a mechanism to counteract bacterial iron piracy among great apes... These findings identify a central role for nutritional immunity in the persistent evolutionary conflicts between primates and bacterial pathogens.

*Transferrin inhibits the growth of Malassezia.* Adding transferrin to a culture of the fungus withholds iron from it so that it can't grow. *Ciclopirox and salicylate*, both iron chelators, also inhibit *Malassezia* in skin.

**Candida**

*Candida* is a genus of fungus with a number of different species and which cause a number of different diseases, including thrush (oral candidiasis), vaginal and skin infections. They can also be invasive and cause blood and other internal infections. Naturally, *Candida* requires iron.

Ciclopirox, the iron chelator, inhibits *Candida*, and the addition of iron reverses the inhibition.

*Candida albicans*, the major species in this genus, is the only microorganism known to directly exploit ferritin for its iron.

Iron is an essential nutrient for all microbes. Many human pathogenic microbes have developed sophisticated strategies to acquire iron from the host as most compartments in the body contain little free iron. For example, in oral epithelial cells intracellular iron is bound to ferritin, a protein that is highly resistant to microbial attack. In fact, no microorganism has so far been shown to directly exploit ferritin as an iron source during
interaction with host cells. This study demonstrates that the pathogenic fungus *Candida albicans* can use ferritin as the sole source of iron. Most intriguingly, *C. albicans* binds ferritin via a receptor that is only exposed on invasive hyphae... Therefore, *C. albicans* uses an additional morphology specific and unique iron uptake strategy based on ferritin while invading into host cells where ferritin is located.

**Cryptococcus neoformans**

*Cryptococcus neoformans* is a fungus that causes an often fatal infection of the meninges and brain, especially in HIV patients. *When it senses that iron is available, it grows*, and elaborates its pathogenic mechanism.

Iron overload is known to exacerbate many infectious diseases, and conversely, iron withholding is an important defense strategy for mammalian hosts. Iron is a critical cue for *Cryptococcus neoformans* because the fungus senses iron to regulate elaboration of the polysaccharide capsule that is the major virulence factor during infection. Excess iron exacerbates experimental cryptococcosis and the prevalence of this disease in Sub-Saharan Africa has been associated with nutritional and genetic aspects of iron loading in the background of the HIV/AIDS epidemic. We demonstrate that the iron-responsive transcription factor Cir1 in *Cr. neoformans* controls the regulon of genes for iron acquisition such that *cir1* mutants are “blind” to changes in external iron levels. Cir1 also controls the known major virulence factors of the pathogen including the capsule, the formation of the anti-oxidant melanin in the cell wall, and the ability to grow at host body temperature. Thus, the fungus is remarkably tuned to perceive iron as part of the disease process, as confirmed by the avirulence of the *cir1* mutant; this characteristic of the pathogen may provide opportunities for antifungal treatment.

There are many other species of fungi that can cause infections, and this is just a quick look at three of them and how they require iron. All other microbes require it as well.

Keeping iron (ferritin) under control may stop these infections from happening. *Iron supplementation is known to increase the infection rate and exacerbate their severity.*

**PS:** For more on iron, see my book, [Dumping Iron](#).

**PPS:** You can support this site by purchasing through my
Iron Increases Infections

Increased body iron correlates with aging, and an increased susceptibility to infections is also related to aging. Coincidence? No, excess body iron increases infections.

Competition for iron and the evolutionary arms race

All bacteria, as well as all fungi and protozoans, require iron in order to live, grow, and reproduce. They share this trait with virtually all other organisms, humans included.

The struggle between parasites and their hosts has been characterized as an evolutionary arms race.

When pathogenic microbes invade a host organism, they need to obtain iron in order for their invasion to succeed, and they have evolved a number of ways to do so.

In the evolutionary arms race, the hosts have evolved numerous mechanisms to withhold iron from invading pathogens. If the host has too much iron available, or if the mechanisms for withholding iron are overridden, infectious agents have an easier time gaining a foothold, and of causing disease.

For example, loss of appetite when ill can be an adaptive, protective response, and at least part of the mechanism behind this is iron withholding from infectious organisms. Critically ill children in an ICU got well faster when they were not fed in the first week, as opposed to being fed
The infection rate among late-fed children was ~8% lower than early-fed (OR .48 vs .35).

Patients who went from a “famine” diet to a hospital diet had higher rates of malaria, brucellosis, and tuberculosis. Force-feeding ill patients can clearly be a bad move.

**Infections in the elderly**

Other than an occasional cold or maybe flu, most people probably don’t worry much about infections, but the elderly have a greatly increased rate of infections, such as pneumonia and urinary tract infections.

Could some of this increased infection rate in the elderly be due to the fat that they have, on average, higher iron stores?

About 10% of elderly men, and 20% of elderly women, have urinary tract infections at any given time. The elderly also have higher rates of pneumonia, diarrhea, and skin infections.

Iron supplementation results in higher rates of diarrhea in children. Blocking bacterial iron receptors via vaccination protects against urinary tract infection.

Serum ferritin (iron) level is an independent predictor of infections in dialysis patients.

**Sepsis**

Sepsis is one of the most serious of infections, and occurs when bacteria (or sometimes, fungi) invade and grow in the bloodstream. It’s often fatal.

Iron chelators have an antibacterial effect in experimental sepsis.

A recent article in Medical Hypotheses suggests the use of iron chelators in sepsis.

In experimental sepsis in guinea pigs, when *E. coli* was injected along with iron, 100% of the animals died, as compared to 0% of animals injected with the bacteria plus saline.

A recent report found that patients who were on long-term, low-dose aspirin had about half the rate of death from sepsis due to *S. aureus* as those who did not take aspirin. If aspirin use results in lower iron stores, which it does, then reduced iron is a potential mechanism of action here.

**Coronary heart disease**

Bacteria have been consistently found in arteries of heart disease patients, and iron appears to be intimately involved, since bacteria need iron.
Is infection involved in all cases of heart disease, i.e. is it the primary cause? I don’t think anyone can say at this point, but bacteria cause inflammation, a characteristic of arteries in heart disease. So bacteria are a potential candidate. They certainly don’t belong in arteries.

**Conclusion**

The topic of infections and iron is a huge one, and I could give many more examples of the role of iron in infectious disease. As with most things iron, this is a very under-appreciated topic. (Don’t bother asking your doctor, in other words.)

It’s clear that iron plays a substantial role in infections, and that withholding iron from pathogenic microorganisms is both a normal function of the human body as well as a promising medical treatment.

Keeping iron levels low could go a long way toward keeping you free of infections. A commenter left this comment just the other day:

> Also, I’ve donated blood twice since last November and eliminated a mild case of folliculitis that I’ve been dealing with for over 12 years. No antibiotics whatever. It’s gone.

He’s had folliculitis for 12 years, never been able to get rid of it, and after donating blood it went away. An anecdote, to be sure, but it could be that he starved the bacteria causing his problem of their iron.

For older people, could keeping iron low reduce the plague of urinary tract infections, pneumonia, and sepsis? Unknown at this point, but I wouldn’t bet against it.

PS: For more on this topic, see my book, *Dumping Iron.*
Young Blood, Aging, and Iron

The by-now famous experiments that have tied the circulations of young and old animals together, showing the rejuvenating effects of “young blood”, have also shown that the harmful effects of old blood may be greater than the rejuvenating effects of young blood. There’s something about old blood—likely many things—that cause a young animal to show signs of aging; I’ve speculated that two of the more important factors might be iron and bacterial lipopolysaccharides—or possibly the bacteria themselves. Here we’ll discuss the links among young blood, aging, and iron.

Of course, other elements in old blood differ in quantity from those in young blood, and scientists are studying a number of candidates that take the form of proteins, as Josh Mitteldorf discusses in his latest article. (See my review of Josh’s book, Cracking the Aging Code.) One of the proteins under investigation is VCAM-1, for vascular cell adhesion molecule, the level of which increases in old blood.

Exposure of young animals to old blood increases the expression of VCAM-1.

Studies from our lab and others have recently shown that brain function—specifically neurogenesis, synaptic plasticity and cognitive function in the hippocampus, a key center for learning and memory—is inhibited in young mice connected to aged mice through heterochronic parabiosis or aged plasma intravenous injections. BECs [brain endothelial cells] upregulate expression of vascular adhesion molecules as a result of increased systemic inflammatory signaling resulting from multiple diseases that afflict the CNS. We discovered that BEC-specific VCAM1 increases in the hippocampus during normal aging. Exposure of young BECs to an aged systemic environment induces BEC activation and upregulation
of VCAM1 both in vitro and in vivo. Specifically, systemic injections of aged human blood into young immunodeficient (NSG) mice—acutely over 4 days or spread over 3 weeks—increased BEC-specific VCAM1 expression, increased brain inflammation as assessed by microglial activation, and inhibited hippocampal neurogenesis. Blocking VCAM1 signaling systemically with a neutralizing monoclonal antibody rescued neurogenesis and prevented aged plasma induced microglial activation. This study suggests preventing BEC-immune cell crosstalk through VCAM1 may be a therapeutic target for ameliorating aged blood induced decline in brain function.

To decipher: old blood injected into young mice → brain inflammation and ↑VCAM-1 production. Blocking VCAM-1 with an antibody abolished this effect, showing that VCAM-1 is the culprit, or one of them, in brain inflammation.

But, what is it about old blood that causes an increase in VCAM-1 expression?

It may very well be iron. The addition of iron chelators to endothelial cell cultures reduces, in a dose- and time-dependent manner, the production of VCAM-1.

These data suggest that iron plays a critical role in TNFα mediated VCAM-1 induction in HDMEC [human dermal microvascular endothelial cells], and the target for iron effects may be IRF-1, NF-kB, and potentially chromatin remodeling.

Iron could be one of the main factors in old blood that causes inflammation and damage.

NF-kappa B is another molecule that’s been suggested as a pro-aging factor in old blood; it’s a master regulator of factors that increase inflammation, which is a key characteristic of aging.

Iron chelators block the increase in NF-kappa B.

These results demonstrate that the iron chelator effectively blocks NF-kappa B activation and coordinate TNF-alpha and IL-6 gene upregulation by HM [hepatic macrophages] in cholestatic liver injury or under in vitro lipopolysaccharide stimulation. These findings support a pivotal role for iron in activation of NF-kappa B and cytokine gene expression by HM in vitro and in vivo.

Iron satisfies a few other requirements for evidence of being involved in aging:

1. Iron increases in aging.
2. Iron promotes oxidative stress, a key characteristic of aging.
3. Iron is implicated in diseases of aging, including heart disease, cancer, and Alzheimer’s.
4. Iron promotes infections, which increase in aging.
5. **Iron promotes mTOR activation**, thought to be critical in aging.

Here we have an element, iron, which looks to me like a prime candidate in aging promotion. Why aging researchers generally don’t see this, I don’t know, but possibly iron just isn’t a sexy topic. Or, I could be wrong, but obviously I doubt it.

I’ll just leave you with one other item of interest.

**Restored Vulnerability of Cultured Endothelial Cells to High Glucose by Iron Replenishment.** When endothelial cells are serially cultured, they lose their sensitivity to damage by high glucose, which is normally toxic. It turns out that serial culturing causes them to lose their iron, to a level only 10% that of normal. When the cells were incubated with iron, they took it up, their iron levels were restored to normal, and high glucose once again became toxic to them.

**PS:** Check out my books, *Dumping Iron*, *Muscle Up*, and *Stop the Clock*.

**PPS:** You can support this site by purchasing through my Supplements Buying Guide for Men.

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**Higher Heart Disease Risk in Post-Menopausal Women Is Due to Iron**

One of the key pieces of evidence leading to the implication that iron causes heart disease is the differential incidence of heart disease between men and
women. Men have far higher rates of heart disease, and they have much higher iron levels, since women lose iron via menstruation. When women cease menstruation at menopause, their risk of heart disease goes way up, and this is not due to hormones, as both of the pieces below note.

That’s the topic of two letters just published in JAMA Cardiology, one by Luca Mascitelli, M.D. and Mark Goldstein, M.D., the other by Virginia Mary Hayes, M.S., Ralph George DePalma, M.D., and Leo Zacharski, M.D., all of them experts on the relation between iron and health. I know a couple of these people, and Dr. Mascitelli kindly sent me these letters, which I’m publishing here because otherwise the public won’t get to see them due to a paywall.
Iron (ferritin) levels above the minimum serve no purpose; it’s merely storage. (Admittedly, if you lost a lot of blood, didn’t die from it, and had no medical care, you might return to health faster if you had more iron stores, but that’s about the only example I can think of where more iron might be better.) Basically, there’s no downside to keeping ferritin within a low normal range, and it could save you from a heart attack.

Premenopausal women have naturally low levels of iron, and this almost completely protects them from heart disease.

By the way, another possible explanation as to how lower iron decreases heart disease risk concerns microbes: iron allows them to grow, and they may cause heart disease.
PS: For more, read my book, Dumping Iron.

PPS: You can support this site by purchasing through my Supplements Buying Guide for Men.

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Does Fungal Infection Cause Male Pattern Baldness and Heart Disease?

Quite the rabbit hole I’ve been down with my research. Does fungal infection cause male pattern baldness and heart disease? There’s an iron link to fungal infection too.

This started when a reader told me that he had started donating blood after reading this site and my book on iron.

He said that he had had seborrheic dermatitis of many years standing. (Click here if you want to see what that looks like.) It’s basically something like really terrible dandruff, but can be on any part of the body. He had tried both anti-fungal medication and topical steroids, and nothing worked. Since it didn’t bother him much, he quit worrying about it.

After his first blood donation, it started clearing up, and after his third donation, it completely disappeared.

What in the world? It turns out that both dandruff and seborrheic dermatitis are linked to a fungal infection by the fungus Malassezia. So is tinea versicolor, a skin infection; when I lived in Sierra Leone, virtually everyone had it to some degree.
In this report, we show that dandruff is mediated by Malassezia metabolites, specifically irritating free fatty acids released from sebaceous triglycerides.

Dandruff is caused by a fungal infection.

All microorganisms that invade man and cause disease require iron. (Every living thing requires iron.) Withholding iron from microbes is at the center of an evolutionary arms race. It stands to reason that donating blood can treat fungal infections of the skin by lowering skin iron levels. (Donating blood will also make you look younger.)

Shampoo that contains salicylate and ciclopirox effectively treats dandruff. Ciclopirox is an iron chelator (attaches and removes iron). So is salicylate. By attaching and removing iron, they deprive fungus of required growth material, it dies, and dandruff is treated.

Ketoconazole, an anti-fungal chemical that works by inhibiting fungal steroid synthesis, also treats dandruff.

Male pattern baldness

Male pattern baldness has been linked to fungal infection as well, and the antifungal drug ketoconazole treats male pattern baldness just as well as minoxidil (Rogaine).

Comparative data suggest that there may be a significant action of KCZ [ketoconazole] upon the course of androgenic alopecia and that Malassezia spp. may play a role in the inflammatory reaction.

If this holds true for many or all cases of male pattern baldness (androgenic alopecia), then our notions of why some men go bald (that it’s due to testosterone metabolites) may be all wrong. Curiously, folklore has it that hats cause baldness — perhaps by giving fungus a warm, moist environment in which to grow?

Male pattern baldness is also associated with heart disease. Severe baldness was associated with a 2.5 fold greater risk of death from heart disease. Huge increase.

If fungal infection in the skin causes both male pattern baldness and dandruff, then iron is implicated, because all invasive microorganisms must take iron from their hosts.

High iron (ferritin) is also associated with heart disease. The mechanism usually postulated is increased oxidative stress of the walls of arteries; iron is a very reactive metal capable of damaging biological structures.

But another mechanism might be the stimulation of fungal growth. “Occult fungal infection is the underlying pathogenic cause of atherogenesis” (from
Atherosclerosis is the underlying cause of coronary heart disease (CHD). Atherogenesis is supposed to result from response to injury and is considered an inflammatory condition. A variety of infectious agents have been investigated as the underlying risk factor for atherogenesis, however, none have been proved to be causally linked. Also several interventions against these agents have not been proved to be of benefit in trials. The role of fungal infection, however, has not been explored in sufficient detail.

**Baldness particularly male pattern baldness and coronary artery disease have been linked in several epidemiological studies. There is some evidence that this type of baldness could be due to fungal infection and this link is being established even though traditionally male pattern baldness was associated with androgen effect. Seborrheic dermatitis and Pityrosporum [Malassezia] infection have been causally linked and the benefit derived from antifungal shampoo in male pattern baldness, gives further credence to the link with fungal infection. Here it is being hypothesized that fungal infection is the underlying risk factor for both baldness and CHD. Several interventions, which have proved beneficial in CHD like statins and drug coated stents, also have antifungal effects, lending further credence to the present hypothesis.**

*Fungal elements have been detected atherosclerotic plaques* (27% of those examined). *Fungal DNA has also been found in plaques.*

**Male pattern baldness is also strongly linked to insulin resistance and metabolic syndrome.** The Japanese have both a lower prevalence of diabetes and obesity, and **male pattern baldness in Japan develops a decade later and less frequently than in the West.**

**Hemochromatosis, or hereditary iron overload, causes hair loss in the majority of cases,** though apparently mostly body hair.

**Summary**

Admittedly that’s a lot of information. Here’s where we are:

1. Fungal infections of the skin cause dandruff and seborrheic dermatitis. Fungi, like all microorganisms, require iron to grow.
2. Blood donation as well as iron chelators lower iron in the skin, depriving fungi (Malassezia, in this case) of a required nutrient. They then die off. Dandruff and dermatitis cured.
3. Male pattern baldness may very well be caused by fungal infection, together with other factors, such as androgens and genetic susceptibility.
4. The common link between male pattern baldness and coronary heart disease might be fungal infection, in turn caused by too much free iron.
5. Baldness is associated with insulin resistance, and this in turn associates with coronary heart disease.

**Conclusion: What to do**

- If you have male pattern baldness, anti-fungal shampoo may fight it. Blood donation or iron chelators might also.
- If you have male pattern baldness, you’re at higher risk of heart disease. If the fungal/iron connection holds true, getting your ferritin (iron) lower could lower your risk. In fact, even if the fungal connection isn’t solid, lowering your ferritin still lowers your risk.
- Male pattern baldness is strongly linked to metabolic syndrome, which if not taken care of, often ends in diabetes. Taking care of yourself with a low-carbohydrate diet and exercise treats metabolic syndrome. It might make your hair grow back too.

Male pattern baldness is usually discussed in terms of cosmetics only, and is thought to be caused by androgens in the skin. But it could be caused by fungi that feed on iron, and a sign that something deeper and unhealthy is going on.

**PS: Read my book, [Dumping Iron](#).**

**PPS: [You can support this site by purchasing through my Supplements Buying Guide for Men.](#)**

How Iron and Bacteria Combine to
**Promote Aging**

**Microbes in normally sterile body sites**

One of the more remarkable developments in recent years in the field of health and aging is the recognition that bacteria and other microbes such as fungi can be found in many body sites that were formerly considered to be sterile— the bloodstream for instance, or the brain. In this article, I’ll discuss how iron and bacteria combine to promote aging and disease.

I covered this idea in a book review on how bacteria may be largely responsible for many of the ills of aging.

Many body sites are normally covered or filled with bacteria: the gut, the skin, the mouth and throat, for example. But these sites can all be considered to be outside the body. The gut and skin barriers and mucus membranes function to keep bacteria where they belong and to prevent bacterial and fungal illness.

When microbes penetrate to normally sterile body sites, such as the bloodstream, they can cause illness, a fact which has been known at least since the time of Louis Pasteur and Robert Koch.

What current research is uncovering is that apparently healthy people often—maybe always—carry bacteria in normally sterile sites, and that they may be the cause of diseases previously thought non-infectious—heart disease and Alzheimer’s disease, to name two.

Bacteria and other microbes can be placed into one of three categories with regard to their infectiousness: pathogens, opportunistic pathogens, and non-pathogens.

- **Pathogens**: The pathogens are well-known, for example *Yersinia pestis*, which causes the plague, or *Francisella tularensis*, which causes tularemia. Both of these can cause fatal disease in an otherwise healthy human, and generally you don’t want to be anywhere near them.
- **Opportunistic pathogens** are organisms like *E. coli* or *Staphylococcus aureus*, which live in and around healthy people and normally cause no problems. But if they get into body sites where they don’t belong, such as beneath the skin, in the bloodstream, or in the urinary tract, or in people who have compromised immune systems, they can cause disease.
- **Non-pathogens** live on humans, or in soil and water, and do not cause disease.

The story of microbes in normally sterile sites as the cause of aging and disease is largely the story of non-pathogens and/or normally sterile sites like the bloodstream. We already knew about the disease-causing effects of other bacteria, and we knew that blood is not supposed to have microbes in it.
Microbes as the cause of chronic disease

How do we know that bacteria and other microbes cause chronic disease? Are they just bystanders or actual perpetrators?

Take the case of Alzheimer’s disease. Bacteria and fungi have been found in the brains of Alzheimer’s patients, but not in those of controls.

This begins to satisfy the first of Koch’s postulates: the organism must be present in all cases of the disease. Until recently, culturing the microbes, the second of Koch’s postulates, has been difficult, but scientists are working on that.

Culturing the microbes may be difficult. It’s estimated that less than 1% of bacteria can be cultured, which has become known as “the great plate count anomaly”. What this means is that most of the bacteria seen under a microscope cannot be grown in a laboratory, whether because they are dead, non-viable, dormant, or just don’t thrive in laboratory culture media and conditions.[1. Grice, Elizabeth A., et al. “A diversity profile of the human skin microbiota.” Genome Research 18.7 (2008): 1043.]

So, only until the advent of DNA probes has it been discovered that many body sites formerly considered sterile are in fact loaded with microbes.

One of the key factors in Alzheimer’s and other diseases of aging, and of aging itself, is inflammation — an activation of the immune system.

Bacteria and other microbes activate the immune system — that’s what the immune system does, it activates to protect the body from invaders.

Other lines of evidence of a microbial cause of Alzheimer’s include:

- the fact that it only strikes old people, and they have weakened immune systems

Iron and microbes

Virtually all living things require iron to grow, metabolize, and reproduce, and bacteria are no exception.

A key factor in the successful bacterial invasion, colonization, and/or infection of an organism is its ability to get enough iron. If it can’t do so, then it may remain dormant and unsuccessful, as it’s unable to commandeer enough iron to grow.
Because bacteria and other invading microbes require iron, organisms including humans have evolved a number of means of withholding iron from invading microbes. Perhaps the most important is the protein molecule ferritin, which encloses and holds iron atoms tightly in its core and makes it unavailable to microbes that need it.

In turn, microbes have evolved ways to get that iron, and these ways are often very important to a microbe’s pathogenicity – its ability to invade an organism and cause disease.

It’s an evolutionary arms race between host and microbe.

Microbes have developed methods of destroying iron-containing molecules and grabbing the iron within, or have developed their own molecules with a high affinity for iron, and these latch on to any free iron within the organism.

Free iron is the key factor, the bottleneck, that microbes need.

It’s well established that iron supplementation causes infections. In recent years, the seeding of iron in the oceans has been proposed as a method of fighting global warming. In essence, dumping free iron in the form of iron powder eliminates the iron bottleneck for microbial growth, and algae and plankton grow abundantly. This is a good analogy for what happens in the human body when too much iron is available.

Physiological insults can also increase the amount of free iron inside the body and set the stage for microbial infection. Oxidative stress, which increases in aging, causes the release of free iron from ferritin. Solar radiation causes release of free iron in the skin, and this is critical to the mechanism of sun-caused skin damage.[4. Bissett, Donald L., Ranjit Chatterjee, and Daniel P. Hannon. “CHRONIC ULTRAVIOLET RADIATION-INDUCED INCREASE IN SKIN IRON and THE PHOTOPROTECTIVE EFFECT OF TOPICALLY APPLIED IRON CHELATORS 1.” Photochemistry and photobiology 54.2 (1991): 215-223.]

Limiting the amount of free iron is crucial in thwarting infections.

If Alzheimer’s and other chronic diseases are caused by infections, then controlling iron could stop them. Indeed, decreasing the amount of iron in the body either through phlebotomy (bloodletting) or iron chelators has been proposed as a method to treat Alzheimer’s.[5. Dwyer, Barney E., et al. “Getting the iron out: Phlebotomy for Alzheimer’s disease?” Medical hypotheses 72.5 (2009): 504-509.]

Douglas Kell and colleagues, who have done important work in this area, have recently proposed that iron activates dormant bacteria in the brain to cause Alzheimer’s.[6. Pretorius, Etheresia, Janette Bester, and Douglas B. Kell. “A Bacterial Component to Alzheimer’s-Type Dementia Seen via a Systems Biology Approach that Links Iron Dysregulation and Inflammagen Shedding to Disease.” Journal of Alzheimer’s Disease Preprint (2016): 1-20.] They write:

The progression of Alzheimer’s disease (AD) is accompanied by a great many observable changes, both molecular and physiological.
These include oxidative stress, neuroinflammation, and (more proximal to cognitive decline) the death of neuronal and other cells. ... We review the evidence that iron dysregulation is one of the central causative pathway elements here, as this can cause each of the above effects. In addition, we review the evidence that dormant, non-growing bacteria are a crucial feature of AD, that their growth in vivo is normally limited by a lack of free iron, and that it is this iron dysregulation that is an important factor in their resuscitation. Indeed, bacterial cells can be observed by ultrastructural microscopy in the blood of AD patients. A consequence of this is that the growing cells can shed highly inflammatory components such as lipopolysaccharides (LPS). These too are known to be able to induce (apoptotic and pyroptotic) neuronal cell death... This integrative systems approach has strong predictive power, indicating (as has indeed been shown) that both natural and pharmaceutical iron chelators might have useful protective roles in arresting cognitive decline, and that a further assessment of the role of microbes in AD development is more than highly warranted.

Alzheimer’s disease is a signature malady of aging, and if iron is implicated in it, then we may justifiably speculate that iron is involved in other diseases of aging, and in aging itself.

Indeed, iron has been implicated in heart disease, cancer, and diabetes, to name but a few diseases.

While free iron catalyzes harmful chemical reactions that damage cellular components and proteins, its role as a catalyst for bacterial growth, which then causes the diseases of aging, lends a new perspective on how iron causes aging.

Kell et al. also argue that many other chronic, inflammatory diseases are caused by infectious microbes, and that iron may be involved in their successful invasions of human tissue.[7. Potgieter, Marnie, et al. “The dormant blood microbiome in chronic, inflammatory diseases.” FEMS microbiology reviews (2015): fuv013.]

Where do these microbes originate? Humans have protective barrier functions designed to keep microbes where they belong; as noted, the skin, the gut barrier, and mucus membranes do this.

But these barriers are not perfect, and microbes can slip through them on occasion, or in certain pathological states.

In most cases, DNA sequencing has found that most of these disease-causing microbes that are present in normally sterile sites originate in the gut, and secondarily from the oral cavity.

Leaky gut is the condition in which gut microbes, or their constituent parts such as lipopolysaccharides (LPS), slip past the gut barrier and into the
body, there to cause damage or infection. In periodontitis, bacteria from infected gums and bone sheds into the bloodstream.

Kell and colleagues note that tiny amounts of LPS interact with fibrinogen, a blood-clotting protein, and cause hypercoagulability, the tendency of blood to clot faster than normal. This in turn increases the risk of blood clots in veins and arteries, as well as stroke and heart attack.

Hypercoagulability is characteristic of aging. If iron revive dormant bacteria, which then produces LPS and activates the coagulation system, then here’s another way that iron and bacteria synergize to cause disease.

Conclusion

The study of bacteria and other microbes in sites that were formerly thought sterile is, if not in its infancy, relatively new. Much more remains to be learned about their disease-causing effects, how they got there, what types of microbes they are, and how to prevent their occurrence.

It is well-known, however, that bacteria need iron to thrive, and without it they wither away, become dormant, or die.

Therefore, as documented in my book Dumping Iron, keeping iron levels low and well-controlled can stave off the ravages and illnesses of aging. In my view, iron is a critical factor in aging that so many scientists are overlooking. Whether it is so by virtue of its high reactivity with biological structures, by its role in feeding microbes, or both, remains to be seen.

(NB: As this is a huge topic, not all possible references have been included, but many of them are found in my other articles which are linked above.)

PS: For much more on the role of iron in aging and disease, see my book, Dumping Iron: How to Ditch This Secret Killer and Reclaim Your Health.

PPS: Check out my Supplements Buying Guide for Men. Includes iron chelators!
Why Iron Is the Most Underrated Factor in Health

I wrote an article at Medium.com, Why Iron Is the Most Underrated Factor in Health. I’m reposting it here.

You’ve got your diet and exercise locked down, you sleep well, take a few supplements, in general, you follow good health practices. Is there anything you’ve forgotten?

Yes, excess iron, the most overlooked factor in health. Iron, which accumulates in our bodies over a lifetime, can cause heart disease, cancer, diabetes, Alzheimer’s and Parkinson’s diseases; it can increase the rate and severity of infections and lead to faster aging.

Evolution and Iron

Iron is a required nutrient: we need it to make red blood cells to carry oxygen, for energy production, and for many other critical functions. In the course of our long evolutionary history, iron has not always been abundant in our food; for this reason, as well as its critical necessity, our bodies have evolved mechanisms to grab iron and hold on to it. But we have not evolved any way of getting rid of it.

When humans are growing, they require plenty of iron for their development, but after maturity, the iron accumulates, often to high enough levels to damage cells and lead to disease.

Iron is a reactive element. When exposed to air and water, it rusts, and when inside our bodies, it can react with components of our cells – lipids, proteins, cell walls – and damage them. That’s how it leads to illness and premature aging.
Men, Women, and Iron

Women live longer than men, about four years longer in the present-day United States. Men suffer higher rates of heart disease, cancer, Alzheimer’s, Parkinson’s, and diabetes.

Women also have much lower levels of iron in their bodies than men. Two factors are responsible for this: 1) blood stores most of the iron in the body, accounting for up to 80% of all iron; 2) pre-menopausal women lose blood through the menstrual cycle. As a result, until menopause, women accumulate much less iron than do men.

At age 45, men have about four times the amount of iron in their bodies than women, and at the same age, men have about four times as many heart attacks as women.

For a long time, doctors and scientists ascribed the startling sex difference in heart disease risk to hormonal differences. But in 1981, Dr. Jerome Sullivan first proposed that the difference was due to the far higher iron levels in men.

After menopause, iron levels in women begin to rise, and so do their rates of heart disease, but on average, their levels never catch up to men.

Blood Donors Are Healthier Than Non-Donors

Blood donors lose large amounts of iron with each donation, and they also have lower rates of heart disease, as much as 88% lower.

The immediate objection to this fact is that blood donors are likely to be healthier than non-donors even before they give blood, since they can’t be accepted for donation if they are unhealthy, nor would they be likely to donate if they felt unwell.

To get around this, a number of studies have looked at health differentials between frequent donors and non-frequent donors. Frequent donors have better health and lower heart disease rates than non-frequent donors.

Lowering iron through therapeutic phlebotomy (bloodletting) results in much lower cancer rates: 35% less, and a 60% lower risk of death from cancer.

Coffee, Tea, Chocolate, and the Mediterranean Diet

Many studies have reported on the beneficial effects on health of coffee, tea, and chocolate. Frequent coffee drinkers have lower death rates, and high consumption of chocolate has the same effect, for example.

It turns out that these all inhibit the absorption of iron from food.

The Mediterranean diet, which emphasizes high intake of fruits, vegetables, fish, olive oil, and red wine, and low consumption of red meat, results in lower rates of heart disease and cancer than a typical Western diet.
The Mediterranean diet results in far lower levels of body iron, about half as much as in those eating a typical Western diet. The fruits and vegetables, olive oil, and red wine in the Mediterranean diet all inhibit iron absorption, and red meat, which is high in iron, isn’t consumed as much.

The lower body iron that comes from consuming a Mediterranean diet may be responsible for most or all of its beneficial effects on health.

Why Don’t We Hear More About Iron and Health?

The skeptical reader may wonder, if iron is as important to health and disease as I claim in this article, why we don’t hear more about it.

Physicians and scientists are familiar with the dangers of very high iron, seen in such disorders as hemochromatosis, or hereditary iron overload. But the levels of iron discussed in this article as capable of causing diseases are within a range that doctors consider normal.

In the case of heart disease, the cholesterol theory has held sway for most of the past several decades. Doctors and scientists enamored of this theory may be reluctant to consider the prospect that iron may play a large role. As Max Planck said, science advances one funeral at a time.

In the case of diseases like cancer or Alzheimer’s, the role of iron is a fairly recent discovery and is only now coming to be considered seriously.

Perhaps the most compelling reason why iron has been such a neglected topic in health and disease is because there’s little money to be made from it. Pharmaceutical companies can’t make huge profits from lowering iron and therefore have no incentive to promote the idea. In turn, physicians don’t hear about it.

The interventions that lower iron, which include blood donation, or natural compounds like curcumin and green tea extract, are all cheap or even free.

Conclusion

Iron is an important cause of aging and disease. Keeping iron levels from becoming excessive could prove to be one of the most important things you can do for health and long life.

This article has only touched on some of the most important aspects of iron as it relates to health, and most scientific references have been omitted for the sake of simplicity. But if the reader wants to get the full story on iron, as well as practical ways to control it, see my book, Dumping Iron: How to Ditch This Secret Killer and Reclaim Your Health.

Wheat Grass Chelates Iron and Treats Ulcerative Colitis

Wheat grass is a supplement / cure-all touted by whole-earth, back-to-the-land types, the same people that use Dr. Bronner’s Castille soap. I’ve never used it myself, but according to the Mayo Clinic:

Wheatgrass is a nutrient-rich type of young grass in the wheat family. It’s sold as a dietary supplement in tablet, capsule and liquid forms. Wheatgrass is often used for juicing, or added to smoothies or tea. Proponents say that wheatgrass has numerous health benefits, but there are no significant research studies to support these claims.

Wheatgrass provides a concentrated amount of nutrients, including iron; calcium; magnesium; amino acids; chlorophyll; and vitamins A, C and E. Wheatgrass fans say that its rich nutrient content boosts immunity, kills harmful bacteria in your digestive system, and rids your body of waste. Some proponents tout wheatgrass as a treatment for cancer, anemia, diabetes, constipation, infections, skin conditions, ulcerative colitis and joint pain, among other health concerns. However, there are few research studies about wheatgrass, so it’s difficult to assess such health claims.

As far as its nutrient content goes, it may or may not be superior to greens...
and other vegetables – my inclination is to doubt that.

Wheat grass is definitely superior at something, though: it chelates iron: “Mugineic acid, active ingredient of wheat grass: An oral novel hexadentate iron chelator in iron overloaded diseases.”(1)

Iron chelation therapies are required for the treatment of iron overloaded patients; nonetheless, their side effects are also well known. We have evaluated iron-chelating activity of wheat grass extract (WHE) and its purified compound, mugineic acid in murine model with phenylhydrazine (PHZ) and dextran induced acute and chronic iron overload conditions... The efficacy of mugineic acid and WHE was compared with the potent oral iron chelator ICL670 (Exjade®). PHZ and dextran treatment followed by oral administration of WHE or mugineic acid significantly checked the rise of serum/plasma levels of iron as well as tissue iron and also, haemosiderosis in tissues. The results are highly comparable with known iron chelator ICL670. WHE and purified mugineic acid, both seem to have significant prospect to be the cheap, non-toxic, hexadentate and oral therapeutic agents to prevent or alleviate toxic iron overload in patients.

Wheat grass is as potent an iron chelator as the prescription drug deferasirox (Exjade), which is used in patients with hemochromatosis and transfusion-related iron overload.

That forms a mechanistic basis for the putative benefits of wheat grass.

Has scientific research actually found anything that wheat grass can treat? Indeed it has: ulcerative colitis.(2)

Wheat grass at 100 ml a day for one month significantly improved disease activity ratings in ulcerative colitis when compared to placebo.

It may also reduce toxicity of chemotherapy.(3)

In ulcerative colitis, iron is intimately involved in pathogenic lesions, and iron chelators reduce lesions.(4) Iron supplements can actually cause this disease.(5, 6) One way they can do this is by feeding bacteria what they need, which is iron, resulting in overgrowth of bacteria or in growth of pathogenic species.

A few decades ago, I knew a man about my age (at the time, in other words, young) who had a large length of his intestines removed because of ulcerative colitis. A terrible thing – maybe wheat grass could have spared him that.

So, wheat grass actually works in ulcerative colitis and may work in other gastrointestinal illnesses like Crohn’s disease. I would bet it would treat anything else characterized by iron-induced pathology, which encompasses many, many illnesses.
Addendum: Could wheat grass be the world’s most potent iron chelator? A group in India gave wheat grass to patients with myelodysplastic syndromes, in which the bone marrow fails and blood cells are produced in reduced number. These patients typically require many transfusions, and as a consequence suffer from iron overload.

In the study, the patients consumed 30 ml (about 1 ounce) of wheat grass daily for 6 months. Their average ferritin dropped from 2250 to 950, a greater than 50% decrease. Wheat grass was found to be as effective or more so as a prescription iron chelator.

The time needed between transfusions for these patients increased by 60 to 80% – so the wheat grass either had other beneficial effects besides iron chelation, or less iron in the bodies of the patients caused a lower rate of blood destruction or a higher rate of blood production. Remarkable.

The authors of the study believe that less iron in these patients caused decreased breakdown of red blood cells and hemoglobin. “We may conclude that wheat grass juice is an effective alternative of blood transfusion. It’s use in intermediate thalassaemia patients should be encouraged.”

PS: My book, Dumping Iron, has lots more on this other diseases caused by iron.

PPS: Check out our Supplements Buying Guide for Men.

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**Dumping Iron**

*Dumping Iron: How to Ditch This Secret Killer and Reclaim Your Health* is a game-changer in the world of health and fitness. The accumulation of excess iron in the body, a condition that affects perhaps the majority of adults, leads to much higher risk of heart disease, cancer, diabetes, obesity, brain diseases such as Alzheimer’s and Parkinson’s, and shorter lifespan.

High iron levels affect men much more than they do women, for the simple reason that men’s iron is on average much higher.

*Dumping Iron* shows how to measure your iron levels, what the test numbers mean, and how to go about lowering iron if necessary.

Humans are adapted to a low-iron environment, so once iron is in our bodies, it virtually never goes away. Our new, high-iron environment leads to iron accumulation, and to ill health and early death.

Iron is the secret killer that no one is telling you about. Finally, in *Dumping Iron*, the scientific and medical data that indicts iron is assembled in one place.

**What the experts say about *Dumping Iron***:

“*Dumping Iron* by P. D. Mangan is a must read by anybody interested in maintaining optimal health, including those in the medical field. Iron overload is an exceedingly common malady in the population and it is easily diagnosed, but it is under-addressed. It leads to heart disease, diabetes, cancer and numerous other chronic and debilitating illnesses. The good news is that iron excess can be prevented and readily treated, which results in a decreased risk of many diseases and improvement in overall health and vitality. *Dumping Iron* clearly tells us how to achieve these goals.”

— Luca Mascitelli, M.D., Lieutenant Colonel, Italian Army, and author of numerous scientific papers on iron and health.

“In *Dumping Iron*, Dennis Mangan has provided the reader access to a massive scientific data pool linking body iron overload to major diseases of mankind... I submit that *Dumping Iron* should be required reading in science and nutrition for high school and above. The ultimate triumph of *Dumping Iron* might be an informed public that will increasingly access ferritin test screening, and health care providers better prepared to interpret tests of iron status, particularly the ferritin level. Acknowledgment of risks of iron overload and proper product labeling might lead to reduced public iron intoxication and improved population health to a degree that would be no less than monumental!”

— Leo Zacharski, M.D., Professor of Medicine, Geisel School of Medicine, Dartmouth College. Dr. Zacharski has written extensively on the connection between iron and disease, and has conducted clinical trials of lowering iron.
“Iron has been compared to fire. A small amount of fire is quite useful in our stoves and furnaces. But when fire is ravaging the contents and walls of our home... BEWARE. In this informative book, Dennis Mangan makes clear the devastation that can be caused by excessive/misplaced iron in the tissues and walls of our bodies. We learn that for essentially all diseases – infections, cancers, Alzheimer’s, Parkinson’s, diabetes, gout, osteoporosis, cardiovascular ills, and more – that the iron burden is a dangerous risk factor. But equally important, the author describes a variety of well tested methods that are readily available to neutralize the iron peril. Adoption of even a few of these methods can remarkably decrease iron-catalyzed disease episodes, enhance well being, and, not least, increase longevity.”

— E. D. Weinberg, PhD, Professor Emeritus of Biology at Indiana University, and the author of over 140 scientific papers, many of them on the role of iron in disease.

Dennis Mangan’s revolutionary new book Dumping Iron: How to Ditch This Secret Killer and Reclaim Your Health is a must read even for the most informed Health and Fitness professional.

For those of us writing in the Medical/Anti-Aging field, it is imperative to cite your work, as much of the research is newly available and stands directly in the face of ‘modern medical advice’. Dennis's work is authoritative and his writing style is clear and thought provoking. In fact, I don’t believe there has been a written book on the risks of elevated iron levels so extensively researched- offering the reader more than 120 citations.

His thesis that excess iron accumulates in the blood as one ages leading to cellular and biological inflammation and ultimately the diseases of aging (heart disease, cancer, and cognitive decline), is impossible to dispute. So much so, I’m going to share it with my inner circle and implore them to get their ferritin levels tested.

Do yourself a favor and read this book immediately. The overall success of your aging process and the extension of your life may depend on it.

— Jay Campbell, author of The Definitive Testosterone Replacement Therapy MANual

Dennis Mangan’s book Dumping Iron is a thorough summary of decades of research on the key role of body iron stores in aging, premature disease, and death.

The depth and span of Dennis’ analysis is rarely seen in modern days, where academics are, not fortuitously, strangled between bureaucracies of Atlantic...
dimensions, the need/desire of easy glory or commercial interests and profit. From the thousands of works done in the field of iron metabolism, Dennis chooses the quality data and discloses in simple and understandable words the double-edged nature of a metal most people and doctors think can only be good for you. Can the size of body iron stores be the key switch signal calling for chronic disease and therefore aging? The decision will be yours, after you read the evidence, never before presented in such simple, engaging and compelling format.

Francesco Facchini, M.D., former Professor of Medicine, University of California, San Francisco.

Amazon Reviews

5 Stars: An excellent, thought-provoking book, April 15, 2016

In “Dumping Iron,” P.D. Mangan has a simple but provocative message: he argues that high iron levels in the human body contribute to a wide range of chronic diseases, including heart disease, dementia, diabetes, and many kinds of cancer.

Here are just a few of the things the book mentions:

• Women live several years longer, on average, than men in the United States and most other countries. This may be because women lose significant amounts of iron through menstruation.

• “At age 45, men have about four times the amount of iron in their bodies as women do, and they also have four times the rate of heart attacks.”

• Nonagenarians and centenarians have significantly lower iron levels than middle-aged people from the same cultures. “This can be attributed to the faster death rate of men with high iron levels and the greater survival of those men with low iron levels.”

• Blood donors, who lower their iron levels when they give blood, are significantly healthier than non-donors. The is true even after accounting for the “healthy donor” effect. “[B]lood donors had an 88% reduced risk of heart attack.”

If iron is so bad, why aren’t its risks better known? The main reason is that it isn’t the root cause of any specific disease. Instead, it’s a general factor that increases one’s susceptibility to a wide range of health problems. For example, bacteria need iron to reproduce, so someone with high bodily iron will be much more susceptible to infections, but iron isn’t the root of those infections so it’s usually overlooked.

Also, iron isn’t always harmful. It’s actually essential, in small doses, to many chemical processes within the body. And dietary iron was scarce in the prehistoric past, and so our bodies have evolved to absorb it readily and let go of it grudgingly. But now that we live in a world of plenty, that tendency
to hold on to iron—and the resulting tendency for one’s iron level to rise steadily with age—causes health problems.

Since mainstream medical advice almost never mentions iron as a health risk, skeptical readers might wonder if this is just some kooky fringe theory. Quite the opposite: “Dumping Iron” has nearly 150 scientific references, along with testimonials by several medical researchers who have studied iron’s effects on the body. I think this book represents the best of alternative medicine: it offers an idea that’s far outside the medical consensus while staying rooted in research.

But “Dumping Iron” isn’t just a scientific treatise. It also offers practical advice about how to measure iron levels, what the ideal level of bodily iron is, and how people can attain that ideal level. The best way to do so is to donate blood, but many people aren’t eligible to donate, so the book offers several alternatives.

This is my favorite health/nutrition book of the past few years, and I’d encourage everyone to check it out and consider its ideas.

5 Stars: The most important health book I’ve read for years, 15 April 2016

Dumping Iron covers a topic I’d never even considered before: the danger of excess iron for your health and the unexpected commonness of it. It turns out that levels considered in the normal range carry a lot of risk across a wide range of conditions.

I found the book to be very well structured. Each section has a takeaway points summary and the whole work builds up a convincing case against iron and then shows clearly what you can do for your own health. In fact I have already signed up and donated blood based on the advice. When talking with friends about the topic I found I could recall a lot of details for a single reading so I think it worked.

Also I should note that I chased up a small sample of the references to make sure they were being accurately reported and they were. Very highly recommended.

5 Stars: It finally makes sense, March 30, 2016

Potentially the most important book on health and healthy life-longevity I’ve read. I’ve spent my entire life reading how green tea, coffee, red wine, a Mediterranean diet, exercise, baby aspirin, etc. are so very healthy without a clear underlining reasoning. Mangan has made a thorough case regarding iron intake. There is too much evidence to ignore that iron is an underlining cause— or at least a contributor— to disease, longevity, and possibly even appearance.
Does Fungal Infection Cause Alzheimer’s?

Some scientists have proposed infection as a cause of Alzheimer’s disease, and now a group of researchers may have retrieved the smoking gun: Different Brain Regions are Infected with Fungi in Alzheimer’s Disease.(1) Does fungal infection cause Alzheimer’s?

The researchers found that in brain matter from ten different patients with Alzheimer’s, all of them were infected with fungi. There was no fungi in the brains of ten control patients.

The amyloid plaques that are characteristic of Alzheimer’s are composed of a protein, amyloid beta, and they show strong antimicrobial activity. In fact the pathogen that is most sensitive to amyloid beta is the fungus, Candida albicans.(2)

As fungi are typically slow-growing organisms, this can explain the disease’s slow progression. There are also at least two reports in the literature of people being cured of Alzheimer’s disease when doctors found fungi (Cryptococcus) and treated the patients with anti-fungal drugs. Their mental status returned completely to normal.(3,4)

If true, this makes sense of many of the facts around Alzheimer’s and provides a basis for prevention and treatment.

Fungi thrive on sugar and iron

Alzheimer’s disease has been called “type 3 diabetes”(5); the brain in Alzheimer’s is characterized by insulin resistance and faulty insulin and IGF-1 signaling.
Fungi thrive on sugar. If glucose levels in the brain and its blood vessels was chronically high or uncontrolled, then it provides a an easy food source for fungi. A list of the different species of fungi found in Alzheimer’s brains (6) shows *Candida albicans* and *Saccharomyces cerevisiae* among them.

In one study, a full 25% of diabetics had an oral Candida infection.(7) Poor blood sugar control was associated with a **13-fold increase in risk** of a *Candida* infection. Candida is the most common cause of fungal infections, and it thrives on sugar.

*Saccharomyces cerevisiae* is the yeast that ferments beer and wine, and also can cause infections. In fermentation, it uses the sugar in mash or grape juice to make alcohol. So it thrives on sugar too.

Therefore there’s a mechanistic link.

1. Alzheimer’s is characterized by loss of control of blood sugar in the brain
2. Fungi thrive on sugar
3. Fungi have been found in Alzheimer’s brains, but not controls

There’s another factor, iron, which has been shown to be elevated in the brains of Alzheimer’s (and Parkinson’s) patients.

Here, I could do no better than quote Eugene D. Weinberg (whom I interviewed) on iron and infection:

> Iron is dangerous because it is an essential growth factor for most bacterial, all fungal and all protozoan infections as well as for all cancer cells. Although viruses do not have independent metabolism, enhanced host iron is needed for viral synthesis.(8) [My emphasis. Link downloads a PDF.]

Iron is crucial growth factor for pathogenic microorganisms, and they have a number of ways of obtaining it, including breaking down tissue (such as in hemolysis) or ingesting ferritin. In the eternal arms race between pathogens and hosts, we have developed a number of ways to withhold iron from pathogenic invaders.

Of course, if iron is abundant and dysregulated and therefore just lying around, pathogens including fungi have an easy time of it. So if iron is abundant and dysregulated in the brain, then pathogenic fungi may invade and cause Alzheimer’s.

One further mechanism links infection with Alzheimer’s, and that is the declining immune system in aging. Older people suffer from more infections because of this.
How to prevent Alzheimer’s

It follows from all of the above that Alzheimer’s can be prevented.

The first step is to avoid insulin resistance and diabetes to ensure less of a food supply for pathogenic fungi. You do this by:

1. Staying lean
2. Exercise, preferably a combination of strength training and HIT.
3. Avoid large amounts of refined carbohydrates.

The second step is to keep iron levels in the low normal range. This deprives invading pathogens of their critical growth factor.

Practicing hormesis will also increase the degree to which iron is regulated and sequestered, so that free iron isn’t available to cause damage and provide sustenance for microorganisms.

The authors of the first-cited paper point out that

There are at present a number of highly effective antifungal compounds with little toxicity. A combined effort from the pharmaceutical industry and clinicians is needed to design clinical trials to test the possibility that AD is caused by fungal infection.

I know that if I or a loved one had Alzheimer’s, I wouldn’t be waiting around for a clinical trial that may never happen. (There’s little money in anti-fungal drugs.) I would be harassing a doctor until he agreed to a course of anti-fungal treatment.

PS: More like this in my books Dumping Iron and Stop the Clock.

PPS: Check out our Supplements Buying Guide for Men.
Iron the primary driver of aging?

Not long ago I wrote an article about how iron accumulation, that is, body stores of iron, could be an important cause of the maladies of aging. I set forth quite a bit of evidence in that article, but I’ve been revisiting this topic and am becoming more convinced that excess iron may be one of the most important drivers of aging. This article will set forth further evidence.

What is aging?

First of all, to see how iron could be important to aging, we need to ask what aging is. Aging is a loss of homeostasis such that the organism is unable to bring its biochemical and physiological systems into proper balance. Aging means that rejuvenation and repair of systems, so important to maintaining health, deteriorate. Rates of disease increase with age, as the organism cannot repair its systems nor fight off infections and cancer as well.

In aging, we see a progressive increase in inflammation, oxidative stress, mitochondrial dysfunction, and a loss of autophagy intensity. These processes normally rise and fall together, so that an improvement or deterioration in one means the same for the others. One reason I’ve emphasized autophagy so much on this blog is because simple interventions like fasting and certain supplements can readily increase autophagy to youthful levels, leading to an improvement in all aspects of aging.

Could iron be the cause of these important aspects of aging? I believe that they could.

Consider insulin resistance, which increases with age and is strongly related to many disease states, including heart disease, cancer, and sarcopenia (1), not to mention diabetes. Insulin resistance features elevated levels of inflammation, oxidative stress, mitochondrial dysfunction, and decreased autophagy, making it an archetype of aging.

In insulin resistance, serum ferritin, the most important measure of body iron status, is strongly correlated with glucose tolerance. (2) The correlation coefficient was 0.73, i.e. high. Ferritin also correlated with blood pressure.

In men, a high serum ferritin, >300, was associated with a 5-fold increased risk of being diagnosed with diabetes. (3)

Many of these studies control for body mass index (BMI), but consider that visceral and subcutaneous fat both also correlate with ferritin. (4)

Metformin is a drug commonly used to treat diabetes, and in contrast to other diabetic drugs, actually extends lifespan in lab animals. (5) There have been suggestions that diabetics treated with metformin may actually live longer than non-diabetics without metformin, leading to the idea that metformin is a true anti-aging drug. Some people are now taking metformin for the purpose of
How does metformin work? In a cell culture model in which metformin protects against damage from chemotherapy, it was found that the mechanism is restoration of iron homeostasis. Without going too deep into the biochemistry, the body keeps iron under tight control, and metformin restores that control.

Metformin is also effective on non-alcoholic fatty liver, and the mechanism may be decreased iron absorption.

**The Mediterranean diet**

The Mediterranean diet has been extolled because those living around the Mediterranean have much lower rates of heart disease than elsewhere. There are many confounding factors, however, including red wine, sunshine (vitamin D), social patterns, etc.

Could iron levels have anything to do with better health in the Mediterranean? Yes. A study was done to look at markers of oxidative stress in men in Crete versus men in the Netherlands (Zutphen). Men in Crete had half the level of ferritin in their blood than the men of Zutphen, 69.8 vs 134.2. This data point might be able to account completely for the difference in health between the two populations.

The Cretan men may have lower serum ferritin through less consumption of red meat and through drinking of red wine; iron fortification of food could play a role (not sure whether they do that in Crete), as well as a diet high in fiber, which inhibits iron absorption.

**Iron is involved in the pathology and toxicology of everything**

A scientist by the name of Douglas Kell, who is at the University of Manchester in England, has written a magnum opus of an article on how iron could be involved as a central mechanism in the pathology and toxicology of nearly everything: “Towards a unifying, systems biology understanding of large-scale cellular death and destruction caused by poorly liganded iron: Parkinson’s, Huntington’s, Alzheimer’s, prions, bactericides, chemical toxicology and others as examples.”

**Growth hormone, fasting, and hepcidin**

Growth hormone is the focus of much study in aging, as it appears to promote aging. Calorie restriction, which reliably increases lifespan in animals, is thought to work at least in part by lowering levels of IGF-1, which is produced in the liver by the action of growth hormone; prolonged fasting also lowers IGF-1 levels. (For more, see Fasting-mimicking diet slows aging.)

Of interest here is the hormone hepcidin, which was discovered only 15 years ago.
Hepcidin, a peptide hormone made in the liver, is the principal regulator of systemic iron homeostasis. Hepcidin controls plasma iron concentration and tissue distribution of iron by inhibiting intestinal iron absorption, iron recycling by macrophages, and iron mobilization from hepatic stores. Synthesis of hepcidin is homeostatically increased by iron loading and decreased by anemia and hypoxia. Hepcidin is also elevated during infections and inflammation, causing a decrease in serum iron levels and contributing to the development of anemia of inflammation, probably as a host defense mechanism to limit the availability of iron to invading microorganisms. At the opposite side of the spectrum, hepcidin deficiency appears to be the ultimate cause of most forms of hemochromatosis, either due to mutations in the hepcidin gene itself or due to mutations in the regulators of hepcidin synthesis. The emergence of hepcidin as the pathogenic factor in most systemic iron disorders should provide important opportunities for improving their diagnosis and treatment.

Hepcidin controls iron levels through raising and lowering the amount that is absorbed from the gut. It bears repeating that the body has no way to rid itself of excess iron; it can only detect when iron levels are sufficient and then decrease its rate of uptake from the gut.

It turns out that growth hormone decreases hepcidin, and prolonged fasting increases it.\(^{10}\)

Our results indicate that in humans, hepcidin-25 exhibits diurnal changes that can be altered by prolonged fasting, which increases hepcidin-25 concentrations approximately 3-fold after 3 days of fasting, possibly owing to a suppression of erythropoiesis that may occur during the fasting state to preserve tissue iron concentrations. In contrast, GH administration decreased hepcidin-25 concentrations by approximately 65%, presumably by stimulating erythropoiesis. These results indicate that circulating hepcidin-25 concentrations display much more dynamic and rapid variation than might have been anticipated previously.

From a mechanistic point of view, this makes complete sense. Tissue growth requires iron, so stimulation of growth by HGH causes hepcidin to decrease, which increases intestinal iron absorption. Fasting promotes an anti-aging state in which growth is suppressed, so hepcidin increases, and intestinal iron absorption decreases.
The effect of fasting on the iron-regulatory hormone hepcidin.

The effect of supplemental growth hormone on levels of the iron-regulatory hormone hepcidin.

What I’m saying here is that the effects of fasting on aging (slowing it) and the effects of growth hormone on aging (accelerating it) may be completely explainable by their respective effects on iron levels. Exercise even has an iron component to its healthful effects: it increases hepcidin.\(^{(11)}\)
If that sounds outrageous, consider that we know that excessive levels of iron (ferritin) are a major risk factors for all of the diseases of aging, whether heart disease, cancer, dementia, even sarcopenia. We also know that growth hormone (through its influence on IGF-1) and fasting are reliable interventions in aging, one promoting it, the other decreasing it.

Therefore iron may be a major mechanism of aging, and could be added to Douglas Kell’s list above.

Obviously iron is not the only promoter of aging, since even with a low ferritin level, you won’t live forever. But the fact that is accumulates throughout the lifespan, correlating with chronological age, and that it can induce oxidative stress, insulin resistance, inflammation, and mitochondrial dysfunction, is highly suggestive. It appears that excess iron, by promoting the production of lipofuscin, also reduces autophagy.(12)

Gordon Lithgow of The Buck Institute for Research on Aging agrees.

“We fed iron to four day-old worms, and within a couple of days they looked like 15 day-old worms,” said Lithgow. “Excess iron accelerated the aging process.” Lithgow says excess iron is known to generate oxidative stress and researchers expected to see changes in the worm based on that toxicity. “Instead, what we saw looked much more like normal aging,” said Lithgow. “The iron was causing dysfunction and aggregation in proteins that have already been associated with the aging process. Now we’re wondering if excess iron also drives aging. ”[…]

Lithgow says the work has implications for the aging research field. “Maintaining the proper balance of metals is key to good health throughout the lifespan, and it’s pretty obvious that this delicate balance can go off-kilter with age,” he said. “This is a phenomena that has not been extensively studied by aging researchers and it’s an area that has potential for positive exploitation.”

Is iron the primary driver of aging?

When I recently checked, my ferritin level was 137, which is too high, so I’m interested in lowering it. Blood donation or therapeutic phlebotomy are the best ways to lower iron stores, since 70% of body iron is contained in red blood cells.

It’s not hard to find advice about iron levels, and yet, as part of a standard anti-aging program, I’ve never seen it recommended to keep them in the low normal range. It could be one of the most important anti-aging interventions available.
Mycobacterial tattoo infections

Hipsters are hurting: Tattoo infections in U.S. linked to contaminated ink

Aug 22 (Reuters Health) – Contaminated tattoo ink caused at least 22 skin and soft tissue infections last fall in four U.S. states, according to an analysis released on Wednesday. […]

The bacteria got into the containers when the manufacturer used distilled or reverse-osmosis water, which is not necessarily sterile. In the New York cases, which led to a recall by the Arizona-based manufacturer, the water was used to dilute black ink into various shades of gray.

The New York cases involved infection with a bug called Mycobacterium chelonae, which caused reddish or purple raised bumps in the areas tattooed with gray. The infection can mimic an allergic reaction and be difficult to treat.

“They were not getting better” with standard care, said Dr. Byron Kennedy of the Monroe County Department of Public Health in New York, the chief author of the New England Journal of Medicine study. “You had some folks who were on treatment for 6 months or more.”

I’m sure that all of those hipsters think that infection with a bug related to the one that causes tuberculosis and leprosy, as well as six months of antibiotic treatment, is a small price to pay so they can look hip.

Tattoo ink also contains heavy metals, including mercury, cadmium, lead, antimony, nickel, chromium, and cobalt. The irony is that a lot of these tattooed folks probably shop at Whole Foods.
Could the Health Benefits of Moderate Alcohol Consumption Be Due to Its Bactericidal Effect?

Note to the reader: I published this piece recently elsewhere, but since it probably won’t be seen by many people, I’m publishing it here.

Moderate alcohol consumption is associated with better health

Moderate alcohol consumption is associated with better health and lower mortality, particularly with regard to cardiovascular disease. Moderate drinkers, those who consume 1 to 2 drinks (14 to 28 grams of ethanol) daily have about a 25% lower mortality rate than non-drinkers.[1] While this relationship shows association only, a number of mechanisms have been postulated as to why alcohol might benefit cardiovascular health, such as better insulin sensitivity, lower platelet adhesion, lower levels of PAI-1, and higher HDL cholesterol.[2] The protection of alcohol against cardiovascular disease is mediated in part by an inhibition of atherogenesis.[3]

Moderate alcohol consumption also shows an association with lower risk of Alzheimer’s disease and vascular dementia, with light to moderate drinking associated with a 42% lower risk of any dementia, and a 71% lower risk of vascular dementia.[4]

Women who consumed more than 3 drinks weekly had a 52% lower risk of rheumatoid arthritis.[5]

Alcohol consumption may protect against Parkinson’s disease, with ever-drinkers having about a 40% lower risk compared to never-drinkers.[6]

Moderate alcohol consumption is associated with a 30% lower risk of type 2 diabetes.[7]
Current alcohol consumption is associated with a lower risk of incident amyotrophic lateral sclerosis.\cite{8}

All of these diseases for which alcohol is associated with lower risk are diseases of aging.

Alcohol (ethanol) is known to be an effective bactericidal agent, at least at high concentrations, and this may be related to its presumptive health benefits.

**Microorganisms may be a cause of the diseases of aging**

In recent years, it’s been demonstrated that bacteria are present in the blood of a large fraction of otherwise healthy people.\cite{9} These bacteria include species known to cause infections. A diverse microbiome exists in the blood of healthy blood donors, most of it residing in the buffy coat fraction, which consists of white blood cells.\cite{10}

These bacteria, and other microorganisms, may be implicated in chronic diseases, which are outside of what are normally considered infections, whether acute or chronic.\cite{11} They may be wholly or partially causative of cardiovascular disease, Alzheimer’s, Parkinson’s, type 2 diabetes, and rheumatoid arthritis.

Fungal elements have been found in the brains of Alzheimer’s patients; species included *Candida* species, *Malassezia* species, and *Saccharomyces cerevisiae*, among others.\cite{12} Fungal infection may be involved in causing amyotrophic lateral sclerosis as well.\cite{13}

Bacterial components have major involvement in rheumatoid arthritis, and recurrent infections are a risk for that disease.\cite{14}

Higher levels of bacterial lipopolysaccharides (LPS) are found in type 2 diabetes.\cite{15}

Periodontal disease, in which bacteria may be shed into the bloodstream, is associated with atherosclerosis.\cite{16} Infection with *Chlamydia pneumoniae* may contribute to atherosclerosis.\cite{17}

Any agent or intervention that kills or inhibits these bacteria and/or fungi may also prevent these diseases.

**Alcohol, even at very low concentrations, inhibits microorganisms**

Alcohol is known to be a powerful antiseptic, but at concentrations much higher than can be obtained through moderate drinking. However, even very low concentrations of alcohol (ethanol) can inhibit certain bacteria, for example the pathogen *Staphylococcus aureus*.\cite{18} Very low concentrations of ethanol (0.1%) inhibit bacterial utilization of specific amino acids, such as
glutamate, proline, and ornithine, and also affects the cell walls of E. coli. At a concentration of 0.1% (vol/vol), S. aureus growth is significantly inhibited. Concentrations of ethanol as low as 0.2% prevents fungi from growing in food.[19]

A concentration of 0.1% ethanol is similar to the blood alcohol concentration after ingesting two standard drinks, or ~30 g ethanol, depending on the body weight of the person drinking.[20]

Someone who drank moderate amounts of alcohol might be ingesting enough to inhibit or kill bacteria and/or in the blood, and therefore help to prevent the degenerative diseases that have a connection to bacteria.


[18] Very Low Ethanol Concentrations Affect the Viability and Growth Recovery in Post-Stationary-Phase Staphylococcus aureus Populations


Non-Aspirin NSAIDS Can Cause Heart Attacks

Not long ago, the FDA issued a warning that non-aspirin NSAIDs such as ibuprofen could cause heart attacks and strokes. Does this mean that we should never take these drugs, and how serious is the harm that they cause?

Non-aspirin NSAIDs

NSAID stands for non-steroidal anti-inflammatory drug. This group of drugs treats pain, fever, and inflammation, and includes ibuprofen, naproxen, diclofenac, and celecoxib. Aspirin is also an NSAID, but is not included in the FDA warning. Acetaminophen (Tylenol) is not an NSAID, although this drug has problems of its own, and is responsible for huge number of ER visits due to overdose.

The FDA (U.S. Food and Drug Administration) states:

- The risk of heart attack or stroke can occur as early as the first weeks of using an NSAID. The risk may increase with longer use of the NSAID.
- The risk appears greater at higher doses....
- NSAIDs can increase the risk of heart attack or stroke in patients with or without heart disease or risk factors for heart disease. A large number of studies support this finding, with varying estimates of how much the risk is increased, depending on the drugs and the doses studied.
- In general, patients with heart disease or risk factors for it have a greater likelihood of heart attack or stroke following NSAID use than patients without these risk factors because they have a higher risk at baseline.
- Patients treated with NSAIDs following a first heart attack were more likely to die in the first year after the heart attack compared to
patients who were not treated with NSAIDs after their first heart attack.

- There is an increased risk of heart failure with NSAID use.

The main evidence that these drugs cause heart attacks and strokes had come from epidemiological studies, but a meta-analysis of randomized controlled trials found the same link.

Celecoxib and related drugs increased the risk of a heart attack by 76%, and of all cardiovascular events by 37%.

Ibuprofen doubled the risk of heart attack.

All NSAIDs together approximately doubled the risk of heart failure.

Naproxen seemed to be relatively safe.

All NSAIDs greatly increased the risk of gastrointestinal complications such as bleeding and ulcers; for instance ibuprofen quadrupled the rate of GI complications. That’s ironic considering that one of the reasons these drugs are touted so much more than aspirin is because of aspirin’s ability to cause bleeding.

Noteworthy from the above is that these drugs can increase the risk of heart attack and stroke almost immediately, which means that even occasional use could increase risk. Many people, including myself, have been in the habit of taking an ibuprofen or other similar drug for minor aches and pains. I will no longer do this. If needed, I’m going to use aspirin.

**Why non-aspirin NSAIDs increase heart attack risk**

NSAIDs decrease pain and inflammation by inhibiting cyclooxygenase, or COX, of which there are two variants, COX-1 and -2. The form that primarily but not exclusively affects pain is COX-2, while COX-1 is associated with GI side effects.

All NSAIDs affect both COX isoforms, but to different degrees. Ideally, a drug would affect only pain and have no adverse effects, but the search for such a drug has proved fruitless. The chart below (previous link) shows the relative degree to which each of these drugs inhibits COX-1 vs COX-2 at a given concentration.
From this chart, it appears that the more a drug inhibits COX-2 without affecting COX-1, the more dangerous it is in terms of heart attack risk.

Note that aspirin, which prevents heart attacks, has the lowest ratio, meaning that it inhibits COX-1 much more strongly than COX-2.

Resolvins

One reason that aspirin prevents heart attacks may be because of unique metabolic products that it creates, resolvins, which are anti-inflammatory molecules produced from the omega-3 fatty acid DHA. Resolvins are potent regulators of immune function and appear to have many beneficial effects, for example against cancer, and infection.

Resolvins are protective against cardiovascular disease.

Aspirin prevents heart attacks

It’s been known since 1950, or at least suspected, that aspirin prevents heart attacks. In that year, Dr. Lawrence Craven, a general practitioner in Southern California, published the first report on aspirin and heart attacks.

In the midst of a heart disease epidemic that was cutting down millions of middle-aged men, the search for a preventative was urgent. Dr. Craven had noted that some of his patients who took aspirin had excessive bleeding during surgery, and he also thought that platelets were involved in heart attacks. (He was right.) So, putting those together, he urged hundreds of his middle-aged male patients to take aspirin, and a lot of it, a minimum of 2 standard aspirin tablets daily, or 650 mg.

Craven eventually treated over 1,500 male patients with daily aspirin, and reported than not one of them suffered a heart attack.
This of course was not very scientific, since there was no control group, and
his sample of patients wasn’t necessarily representative of the wider
population. Still, at a time when men were dropping like flies of heart
attacks, his results were remarkable.

Craven experimented on himself to get a handle on how aspirin increased
bleeding risk, and reported,

Ingestion of 12 aspirin tablets daily resulted after five days in
spontaneous profuse nosebleed. In order to check on the reliability
of this observation the test was repeated twice over, with
precisely the same results. The proof seemed to be all the more
convincing as the author had not experienced nosebleed for more
than fifty years.

**Confirmation of NSAID risk**

A study published last year in BMJ reaffirms the risk of heart attack with
NSAID use.

All NSAIDs, including naproxen, were found to be associated with an
increased risk of acute myocardial infarction. Risk of myocardial
infarction with celecoxib was comparable to that of traditional
NSAIDS and was lower than for rofecoxib. Risk was greatest during
the first month of NSAID use and with higher doses.

Does this mean that taking a single dose on an NSAID could cause a heart
attack? If you were at high enough risk, yes, probably. If you’re at low
risk, even short-term use could increase risk, however.

With use for one to seven days the probability of increased
myocardial infarction risk (posterior probability of odds ratio
>1.0) was 92% for celecoxib, 97% for ibuprofen, and 99% for
diclofenac, naproxen, and rofecoxib.

So, be careful with NSAIDs.

**PS: I discuss aspirin extensively in my most recent book, Best
Supplements for Men.**
Older People with High Cholesterol Live Longer

High cholesterol among older people is associated with longer life. In Japan, high cholesterol is associated with longer life at all ages. More recent evidence indicates that the relation of high cholesterol to longevity is as robust as ever, and that older people with high cholesterol live longer.

Consider the following an “out of sample” study in which results are verified, associations confirmed, and the risk of data mining undercut.

Cholesterol and mortality

A newly published study looked at 3090 adults aged 60 and up in the Swedish
National study on Aging and Care. Baseline date was 2001-04. The study followed the subjects until the end of 2011.

The results:

Compared to normal total cholesterol (<5.18 mmol/l), borderline-high (5.18–6.21 mmol/l) and high (≥6.22 mmol/l) total cholesterol were associated with a decreased risk of all-cause mortality, with the multiple-adjusted hazard ratio (95% confidence interval, CI) of 0.71 (0.61–0.83) and 0.68 (0.57–0.80), respectively (P for trend <0.001). Reduced all-cause mortality associated with high total cholesterol (≥6.22 mmol/l) was mainly due to the reduced risk of non-cardiovascular mortality (hazard ratio = 0.67, 95% CI = 0.51–0.88). These associations were statistically evident only among individuals without use of cholesterol-lowering medications.

Conclusions

The inverse association between high total cholesterol and reduced all-cause mortality in older adults is primarily due to non-cardiovascular mortality, especially among those who are not treated with cholesterol-lowering medications.

Graphs showing survival curves shown below. Those with the highest cholesterol, >240 mg/dl, lived the longest, those at 200-240 mg/dl were in the middle, and those with cholesterol <200 had the highest death rate. (To convert cholesterol from mmol/L to mg/dl, multiply by 38.67.)
Noteworthy, those who had high cholesterol but took cholesterol-lowering drugs such as statins had no survival advantage.

The reduced risk of death seen in those with high cholesterol was mainly due to lower risk of non-cardiovascular death. High cholesterol was associated with a ~30% lower mortality rate.

The authors speculate that higher cholesterol may modulate inflammation, or that low cholesterol is a sign of frailty and poor health. Proponents of the harmfulness of cholesterol argue the latter case, but even if true, why would you want your cholesterol in the range of unhealthy, frail people?
In men aged 85 or more, who are described as “very elderly”,

... total mortality in the low-TC [total cholesterol] group was 1.7-fold higher than that in the high-TC group. Mortality, adjusted for the same factors, decreased 0.9% with each 1 mg/dL increase in the serum TC concentration and decreased 0.8% with each 1 mg/dL increase in the serum (low-density lipoprotein) LDL-cholesterol (LDL-C) concentration. Our results indicate an association between lower serum TC concentrations and increased all-cause mortality in a community-dwelling, very elderly population. Mortality decreased with the increases in both TC and LDL-C concentrations, after adjustment for various confounding factors. These findings suggest that low TC and low LDL-C may be independent predictors of high mortality in the very elderly.

Survival curves for all participants (A), men (B), and women (C), shown below.

When I’m 85 years old or more, I don’t plan on being described as “very elderly”. I’ll still be doing deadlifts and won’t be trying to lower my
cholesterol.

**Should the elderly take statins?**

In a review of studies on cholesterol and statins in the elderly – greater than 80 years old – found two basic conclusions:

- total mortality was highest at the lowest cholesterol levels: “Low TC (<5.5 mmol/l) [total cholesterol <212 mg/dL] is associated with the highest mortality rate in 80+-year olds.”
- no benefit of lipid-lowering in this age group: “There is not sufficient data to recommend anything regarding initiation or continuation of lipid-lowering treatment for the population aged 80+, with known CVD, and it is even possible that statins may increase all-cause mortality in this group of elderly individuals without CVD.” [Emphasis added.]

**Hemodialysis patients**

In hemodialysis patients, who are quite ill indeed, higher levels of LDL were associated with reduced risk of infections, and no increase in cardiovascular risk.

**Cholesterol-lowering insanity**

When will the cholesterol-lowering, statin-prescribing insanity end? Probably not any time soon, since Big Pharma has a large influence on medical practices. There’s huge money in prescription drugs including statins.

Cholesterol is a natural molecule synthesized by the human body, and is critical for the function of cell membranes and hormones.

If higher cholesterol is associated with longer life in the elderly, and in all ages in Japan, then that casts considerable doubt on cholesterol as a cause of cardiovascular disease. Since age is a risk factor for CVD, if high cholesterol caused it, we would expect to see higher death rates in the elderly with high cholesterol. But we do not.

**PS: For how iron can cause cardiovascular disease, see my book, Dumping Iron.**
Major Bacterial Involvement in Rheumatoid Arthritis

In a couple of recent articles, we saw that bacteria and iron are accelerants and likely causes of aging, and that the resultant hypercoagulation can be targeted. Etherisia Pretorius (a South African as the name implies) and Douglas Kell (British), two of the authors of the papers which went into those articles, along with colleagues, have recently written about major bacterial involvement in rheumatoid arthritis. This paper is worth bringing to your attention for a couple of reasons at least: 1) it suggests new ways to treat this condition, which is notoriously progressive and refractory to
What rheumatoid arthritis is

Rheumatoid arthritis (RA) is an autoimmune disorder characterized by inflammation, and while it most notably affects the joints, it can damage many other parts of the body. Signs and symptoms include:

- Tender, warm, swollen joints
- Joint stiffness that is usually worse in the mornings and after inactivity
- Fatigue, fever and weight loss

RA affects up to 1% of the population, and is about 3 times as common in women as in men.

The authors of this paper write:

We discuss how the exposure of genetically susceptible individuals to environmental factors (1) that can act as triggers (2), cause an immunological reaction, followed by an autoimmune response (3), can result in RA (4). We review a plethora of evidence, collectively referred to as Ebringer’s theory (5), that points to the environmental trigger as microbial (particularly from e.g. urinary tract infections) (6). We then look at the role of LPS from these microbes (7) in causing an imbalance between pro- and anti-inflammatory cytokines, followed by systemic inflammation, and the effect on the cardiovascular and hematological health of the RA patient (8) (see Figure 1). Finally, recognizing the lack of easy and accessible biomarkers, we suggest that in a truly precision medicine approach, hypercoagulability and also microparticle presence, as well as LPS and β-amyloid analysis could play an important role in tracking the progression of the disease.

Bacteria and iron

A high fraction of those with RA had an infection before diagnosis. One reason that women may have a higher rate of RA is because they have a higher rate of urinary tract infections, especially from the bacteria *Proteus*.

Once infected, antibodies formed against the bacteria can cross-react with human antigens, such as in joints, and cause inflammatory reactions.

How do these bacteria get inside the body? As we’ve previously discussed, body sites that are normally considered sterile, such as the blood, may have quite a lot of bacteria in them.

These bacteria come from the normal flora of the oral cavity and the gut, as well as from infections. Periodontitis is significantly associated with RA, and gut dysbiosis is frequently found in RA patients. Cardiovascular
complications are also common in RA.

One of the keys here is that iron dysregulation allows the bacteria to grow.

We all get some bacteria inside us regularly, but the body’s natural immunity prevents them from growing and reproducing. One of the most important aspects of this natural immunity is iron withholding. Bacteria require iron to grow, as do all living things, and the body tightly holds on to iron to keep bacteria from procuring it for their own uses. Iron is at the center of an evolutionary arms race between animals and microorganisms.

In iron dysregulation, iron escapes from the proteins that hold it, mainly ferritin and transferrin. The free iron is then available for bacteria to use.

An important point is that the more iron in storage, that is, in ferritin, the more there is available to escape and become free iron. Lower body iron stores can mitigate this. This is shown by the fact that in hemochromatosis, or iron hereditary overload, physiological damage occurs, despite the fact that most of the iron is bound by ferritin.

In RA, iron dysregulation and bacterial growth cause hypercoagulation and other damage.

So, would dumping iron via phlebotomy (bloodletting) help treat RA? I couldn’t find a reference to the effect that it’s been tried. But hemochromatosis can masquerade as RA, and iron is found in the joints in RA and other joint diseases.

I’m guessing that someone with RA would not be allowed to donate blood, however. Therapeutic phlebotomy, under a doctor’s care, could be an option.

In addition, attention to gut issues and/or periodontal disease should be of benefit.

Conclusion

Rheumatoid arthritis, a potentially crippling and painful disease, has no known cause. But bacteria are definitely involved, and they are spurred on by excess and free iron.

PS: Check out my book, Dumping Iron, which explains much more about the connection of iron to disease.

PPS: You can support this site by purchasing through my Supplements Buying Guide for Men.
Standard Dietary Advice Makes You Fat and Sick

Standard dietary advice, the advice given by dietitians, doctors, and the Dietary Guidelines for Americans, makes you fat and sick. It’s a combination of unsound science and compromises with the powerful food industry. The people who make and give dietary advice are fighting an intense rearguard action to avoid having to admit that they’ve been wrong all along.

Standard dietary advice is poison, and the medical establishment fully embraces it. It keeps them supplied with customers to whom they can prescribe expensive drugs and procedures.

Standard weight loss diet

Let’s look at a standard weight loss diet. Up to 80% of Americans are overweight/obese, so this is meant for them. (If you’re lean and healthy on what you’re already eating, you presumably don’t need advice.) WebMD has an article on losing weight without fad diets. (I tried for the more authoritative May Clinic diet, but they want you to buy their book to find out what it is. I assume this one is similar.) The WebMD diet advises:

- Practice portion control. In other words, eat less. Brilliant, the same low-calorie strategy that’s been proven to fail for decades.
- Eat a variety of foods, including “whole grains”. An extremely monotonous diet isn’t necessarily harmful at all; it depends on what’s in it. Whole grains are not necessary for health.
- Eat more fruits and vegetables. How are you going to lose weight by eating more of something?
- Eat often. My personal favorite. “Aim for five to six mini-meals per day. Space your meals every 3 to 4 hours.” Eating more often is completely unnatural and will likely actually make you gain weight.
Is there anything good about the standard weight loss diet? Yes, on the plus side they tell you to get rid of junk food like cookies, chips, crackers, and ice cream, and to avoid soda and fruit juice.

The standard weight loss diet is ineffective, and that's partly because it's a compromise between what will cause weight loss and what people are willing to do.

**Standard diabetic diet**

Diabetes is a condition of high blood sugar caused by insulin resistance, and is strongly associated with obesity and/or excess body fat. Diet can make the difference between a return to health and a steady descent downward to kidney failure, amputations, infections, and death.

Here are some highlights of what [the American Diabetes Association recommends for diabetics](https://www.diabetes.org/management/meal-plan.html):

- 3 meals and 2 snacks daily. Basically, eating every 4 hours or so.
- High carbohydrate intake. They call it “moderate”, but it’s 45% of calories as carbohydrate. The average American eats 50% of his calories as carbs.
- Low calories, i.e. the same failed low-calorie diet.

**U.S. Dietary Guidelines**

This is official government advice, vetted extensively by panels of doctors and scientists. Read the summary [here](https://www.dietaryguidelines.gov/what-do-you-think/key-recommendations).

The “Key Recommendations“ state that grains and oils are part of a healthy diet, meaning presumably that if you don’t eat them, you will be unhealthy, which is worse than nonsense.

It allows up to 10% of daily calories as sugar.

It doesn’t allow normal (“full-fat”) dairy, one of the healthiest things you can eat; instead it insists on Frankenfoods, i.e. low-fat or fat-free dairy, and “fortified soy beverages”, a chemical concoction.

**American physicians are fat too**

Suppose you’re overweight/obese or have some kind of other health problem related to your weight. You go to your doctor to get some medical advice.

Chances are good your doctor is overweight or obese himself (or herself, increasingly), and can do little to help you.

A recent survey of U.S. primary care physicians found that 53% of them were overweight or obese. That means that they are either unwilling to keep themselves lean, or unable to do so.

Considering that physicians have very high levels of the personality trait of
conscientiousness — otherwise they wouldn’t be in that occupation — how likely is it that they’re unwilling to stay lean? Very low, I’d say.

That means that they don’t know how to stay lean. If they can’t even provide themselves with good advice, how will they do that for you?

**The medical establishment embraces dietary nonsense**

All of the above is fully within the mainstream of the medical establishment. Is their advice doing any good? With 80% of the population overweight or obese, diabetes becoming an epidemic, and no end in sight, the answer must be “no”.

**PS:** Check out my books, *Dumping Iron*, *Muscle Up*, and *Stop the Clock*.

**PPS:** You can support this site by purchasing through my [Supplements Buying Guide for Men](https://example.com).