Iron Levels

This article adds to the discussion of my previous articles on iron and how its accumulation drives aging and disease. Please see them for fuller explanations of the physiology of iron and the implications of iron overload. The articles so far have been:

Iron accelerates aging

Iron the primary driver of aging?

Eugene D. Weinberg on iron toxicity

Excess iron promotes obesity?

Iron and the brain: iron's crucial role in aging

This article shows how blood donation, phytochemicals, and diet affect iron levels. **Please be aware that this article is for informational purposes only, and is not medical advice. If you have concerns about your iron levels, see your doctor. Please read our disclaimer.**

1. Ferritin and hemoglobin tests

Ferritin is a protein that cells make in order to sequester and store iron.

Free iron, that is, iron that is unattached to any other chemical moiety, can catalyze dangerous chemical reactions that damage cell structures. The body therefore strives to keep free iron under control by attaching it to ferritin. While the correlation between excess body stores of iron and ferritin levels is not perfect, in most cases the result is close.

The major storage site of iron in the human body is not ferritin, however, it is hemoglobin, which is the oxygen-transporting molecule of red blood cells.

Around 80% or so of total body iron is found in hemoglobin.

The difference between hemoglobin and ferritin when it comes to iron storage is that hemoglobin levels are, in most cases, kept within a narrow range. Exceptions: in anemia, not enough hemoglobin is made, iron deficiency anemia being the most common form. In polycythemia, too many red cells are made and thus there's too much hemoglobin. Therefore, for anyone without these conditions, the amount of iron stored in hemoglobin is roughly the same for everyone, the main variations depending on male vs female (male hemoglobin levels are higher) and body size.

In contrast, ferritin levels can rise without limit.

Unless a doctor suspects either hemochromatosis (hereditary iron overload) or iron deficiency anemia, he or she is unlikely to order a ferritin test, so one would have to ask for it.

The result of a ferritin test will be accompanied by a laboratory normal range, also called reference range or normal values. This is the range of values for a test that the laboratory has determined that 95% of all apparently healthy people will have. For example, the Mayo Clinic has determined that, for men, the ferritin reference range is 24 to 336 ng/ml, and for women, 11 to 307. Values below that level are deemed iron deficient, above it, iron overload.

There's considerable evidence that there can be adverse effects of high ferritin even within the reference range. If a ferritin is, say, 250, a doctor will most likely do nothing, since it's within the reference range. Evidence shows, however, that 250 may be too high; ferritin above a minimum amount causes damage, and the relation is linear with no threshold. In other words, any level of ferritin above what is necessary to prevent iron deficiency appears to be enough to cause damage and accelerate aging. (1.)

> These results suggest no threshold and are consistent with a study of vascular function where when two groups, both with low ferritin levels (52 vs. 17), were compared, flow mediated vascular dilation was significantly greater in the very low ferritin group. It is also consistent with the study described above where ferritin levels correlated with oxidative stress and insulin resistance with no apparent threshold.

So, the published reference ranges for ferritin appear to be wanting, with the upper range of normal possibly too high. It appears that getting ferritin as low as possible without causing iron deficiency may be beneficial for health.

The reference cited above argues for a reference range of 50 to 70 for men, and 20 to 40 for women.

There are a few reports of iron deficiency without anemia at a ferritin of about 50. (2) What happens is that iron stores are not low enough to cause

anemia, but low enough to interfere with other physiological processes, causing fatigue and exercise intolerance. Most commentators on this topic do not appear to consider a ferritin of 50 to be a sign of iron deficiency, however.

Hemoglobin

In most cases, apparently healthy people have a normal hemoglobin level, but sometimes people have low hemoglobin without knowing it, and this indicates anemia.

Before a blood donation, the blood bank tests for hemoglobin, and will not allow a donation if it's too low.

In the course of an annual physical or checkup, doctors often order a CBC (complete blood count), and hemoglobin is part of this test.

While the blood bank will prevent people from donating if their hemoglobin is low, many supplements (discussed below) are iron chelators, so knowledge of the hemoglobin level can be useful even putting blood donation to the side.

2. Blood donation

Blood donation is the quickest and surest method of lowering ferritin levels, since 80% or so of body iron stores are found in red blood cells.

Total body iron for an adult man is about 3 to 4 grams, and one blood donation of 450 ml (may be 500 ml outside the U.S.) represents 200 to 250 milligrams of iron.

After the blood donation, red blood cell production in the body ramps up from baseline in order to make up for the lost cells. To do this, more hemoglobin needs to be made, and the iron which goes into hemoglobin is taken from body iron stores. Hence, donating blood lowers iron.

After a donation, it may take several weeks to up to two months for the body to manufacture enough red cells to bring their level back to normal. Recovery of blood volume, however, is much faster, perhaps as little as 24 hours.

The American Red Cross recommends avoiding heavy lifting or vigorous exercise on the day of the donation, and avoiding alcohol for 24 hours. One shouldn't expect to be setting any personal records in the gym in the days following a blood donation.

A rule of thumb for ferritin lowering via blood donation is that each donation lowers ferritin by 30 points. If someone has a high ferritin level, say over 200, it will take several donations to get down to a level below 100.

Table 1. Danish study of the influence of blood donation of serum ferritin levels (ng/mL) in men, 30-66 years of age.[51]

Donation History Per Year	Ferritin Median 5-95 pct*	Ferritin Range
0	137	46-396
2	44	17-122
3	38	14-110
4	31	12-91

* 5th to 95th percentile

The table above was taken from reference 1, and shows average ferritin levels in men in blood donors vs non-donors. It can be seen that even two donations a year causes a large decline in ferritin, and that there are diminishing returns to more donations. The reason for the diminishing returns is that, once ferritin levels decline, the body decreases the level of the hormone hepcidin, which causes an increase in iron absorption from food. In effect, one must pedal faster to stay in the same place.

Fertile (pre-menopausal) women have average ferritin levels of around 35 ng/ml, and they have far lower rates of disease than men the same age. Their blood loss from the menstrual cycle is on average 35 ml a month, or 420 ml a year.

Therefore, one blood donation is about the equivalent of a fertile woman's annual menstrual blood loss. Once ferritin levels are in the lower end of the range, one donation a year may be enough to keep them there.

3. Iron chelation

The American Red Cross estimates that only 38% of the population is eligible to donate blood. (3) While that figure is probably concentrated among the very young and the elderly, plenty of young or middle-aged men are probably unable to donate blood.

Iron chelators, which are natural or synthetic chemicals that are ingested orally or given intravenously, attach to free iron in the body and remove it.

Prescription chelators are out, since they have side effects, and unless someone has demonstrated iron overload, meaning a ferritin well above the upper limit of the normal range, a doctor is unlikely to prescribe them.

A number of non-prescription chelators exist however. As noted in some of the previous articles in this series, many of the polyphenols and other phytochemicals that have been shown to have health benefits also chelate iron. This is not a coincidence.

The following supplements chelate iron:

- curcumin
- quercetin
- green tea polyphenols
- IP6 (inositol hexaphosphate)

It’s difficult to get quality data as to how effective these chelators are, since in most cases no controlled human studies have been done. Nor are they ever likely to be done, since no one stands to make money off of these, as they’re all relatively cheap OTC supplements.

One study (cited in reference 1) found that in diabetics, “a polyphenol–enriched, low-iron carbohydrate-restricted diet over 4 years” dropped average ferritin levels from 325 to 53. So it certainly appears that polyphenols, along with a low-iron diet, can lower ferritin. I’ve seen anecdotal reports on the web of people claiming that they dropped their ferritin 100 points using chelators such as IP6, but as I said, I haven’t seen any controlled studies, so take that with a grain of salt.

As for dosages, there are none other than the label recommendations. My bottle of curcumin, for instance, states that one can take up to 1500 mg, or three capsules, daily, in divided doses.

It’s possible to attain a state of iron deficiency with the use of chelators, and iron deficiency is very much to be avoided. Children and adolescents should avoid chelators unless under a doctor’s advice, since growing bodies need iron and iron deficiency can literally stunt their growth, and cause a host of other problems.

Some iron chelators have the ability to chelate other metals besides iron. Generally one would not want to chelate zinc or magnesium and probably others, and iron chelators may have the ability to cause deficiencies in these other metals.

4. Hindering iron absorption from food

Iron absorption from food can be hindered by the use of various chelators or by the choice of low-iron foods.

Here we should note the difference between free iron and heme iron in food. Free iron is found in plant foods as well as foods that are fortified with iron. Unfortunately, in the U.S., all flour, corn meal, and rice is required by law to have added iron.

Heme iron is that which is found in meat. Red meat (beef and pork) has more iron than chicken or fish.

Heme iron is very readily absorbed from the intestinal tract. The absorption of free iron can be lowered through the use of coffee, tea, red wine, or any of the iron-chelating supplements listed above.

Coffee and tea (black or green) greatly hinder free iron absorption, and red wine does as well, although perhaps less so. The key here is that they must be drunk with the meal.

Avoiding iron-fortified flour, corn meal, and rice would mean less (free) iron in the diet, hence less absorbed.

As for hindering the absorption of heme iron, the only choice that exists is avoiding foods that contain it, mainly red meat.

Conclusion

Published reference ranges for ferritin may have upper limits that are too high for optimal health. Even within the reference range, lower ferritin values generally associate with better markers of health than higher.

Unfortunately, mainstream medicine isn’t going to tell you this. There’s no money to be made by pharmaceutical companies in it, and most doctors are too constrained by the reality of acute care medicine to either know or care much about it.