Iron Overload - Part Seven

All right, let's talk a little bit about prevention and treatment. The first question that is, I'm sure, on many of your minds at this point is should healthy people limit iron in their diet? By healthy people, I mean people without iron overload in this context. The body tightly regulates the storage of iron, and most of us excrete any excess iron that we consume, so in the majority of cases in people who don't have genetic mutations that lean to excess iron storage, it's probably unnecessary to limit dietary iron.

That said, as you know, mutations that cause excess iron storage are common. They're among the most common genetic mutations in North America, so I do recommend avoiding iron supplements as a rule unless the patient is deficient and needs them specifically, and I also recommend regularly screening patients for iron levels given the possibility of iron overload and the potentially serious consequences of it.

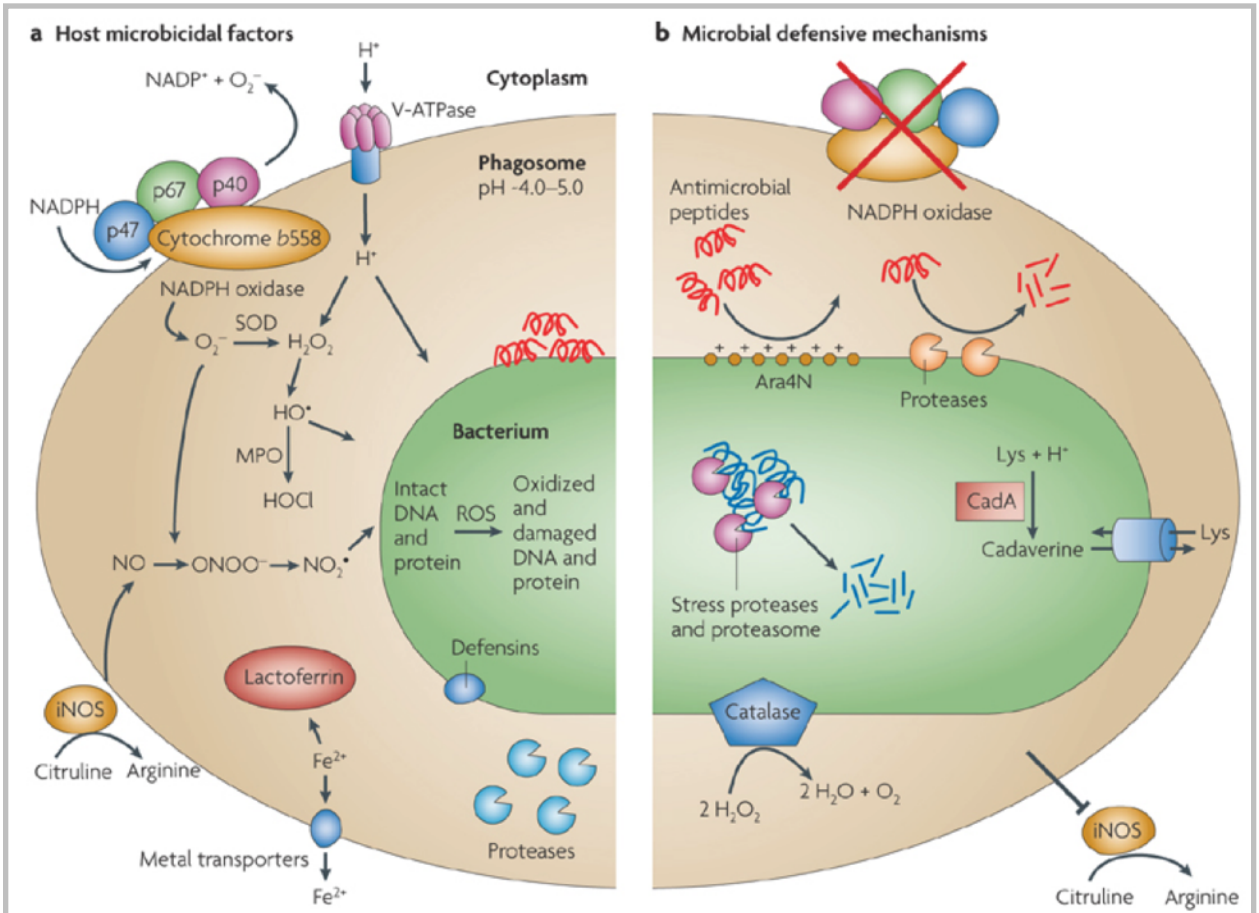
Also, I think it's probably prudent to advise, particularly male patients and menopausal females, to donate blood one to three times a year as a precaution. It's a nice service to provide anyway, and there is little risk to doing it at this point. It can help to prevent iron overload, and there are studies, as you recall from the first unit, that show that reducing iron levels even in people without iron overload led to reduction in cardiovascular risk factors. I think you can make a strong argument for just including that in the patient's health practices.

What do you do if there is excess iron present? There are only two ways of getting rid of it: phlebotomy and chelation. Phlebotomy is the treatment of choice, at least compared with chelation that is done with drugs because the drugs have nasty side effects. They're rarely used in clinical practice for that reason. The only time they are used is when there is a complicated presentation where the patient has iron overload and anemia at the same time, and removing blood would worsen the anemia.

Therapeutic phlebotomy involves the removal of one unit of blood, which is about 200 to 250 mg. It's straightforward and safe. There are few risks. The typical frequency is one to two times a week, and it's done until ferritin reaches near-iron deficiency or 25 ng/mL, and hemoglobin does not drop below 12.5. Then, usually the patient moves into a more maintenance stage of phlebotomy, which would be one unit of blood removed every eight weeks or with a frequency that is required to maintain a serum ferritin in the 50 to 150 range. Different physicians have different targets here. Some recommend keeping it under 75 if the patient has a history of iron overload and iron saturation below 45 percent.

Phlebotomy can also be done by patients without hereditary hemochromatosis, and this doesn't require prescription. They can simply donate blood. They'll also remove one unit of blood in this procedure. It's the same as the therapeutic phlebotomy. The maximum frequency is once every 56 days, and as we've talked about, that may or may not be enough depending on how severe the iron overload and how quickly the patient accumulates iron in between blood draws.

If blood donation is not an option, for example, if the patient has anemia, if hemoglobin is below 12.5, or if the patient lived in the U.K. during the mad cow disease epidemic, and in some states if patients have received tattoos, they won't be allowed to donate blood, so in this case, you have to do chelation or the other iron reduction strategies in order to reduce the iron levels. Luckily for us, we do have an option that's a little bit safer than the drugs that are used for chelation, and that's called apolactoferrin.



Source: Flannagan et al. 2009

Both humans and animals produce apolactoferrin. It's found in various secretions such as breast milk, and it is antimicrobial, so that's one reason that lactoferrin is in breast milk. It suppresses the growth of iron-dependent pathogens, which is important for babies. So if a baby was exposed to a pathogen, the lactoferrin suppresses the growth of those iron-dependent pathogens by binding to the iron, so it protects the baby from infection.

Studies have shown that lactoferrin can remove stored iron. It's one of the few natural substances or the only natural substance that is known to do that. Apolactoferrin is the preferred form. Usually it comes from a bovine source. The brand that we use is Life Extension lactoferrin, and the dose is 300 mg one to two times on an empty stomach between meals, so that's very important to take it between meals, not with food.

Phytic acid or inositol hexakisphosphate, or IP6, does inhibit ferrous iron, so the plant-based forms of iron. It inhibits the absorption of it, but it doesn't inhibit heme iron absorption, and it doesn't remove iron that is already stored in the body, so that's a common misunderstanding. It's really important to get that. It's not an alternative to lactoferrin. It can reduce the absorption of plant-based iron from meals, but as you know, plant-based iron does not contribute as much to the iron stores as heme forms of iron. I think it does have a meaningful effect, but it's not going to treat iron overload once it has already occurred.

Highest sources of heme iron

Food	Amount (mg per 100g)
Clam	28 mg
Chicken liver	13 mg
Oyster	12 mg
Octopus	10 mg
Beef liver	7 mg
Venison	5 mg
Mussel	4 mg
Beef chuck	4 mg
Bison, ground	3 mg
Crab	3 mg
Duck breast	3 mg
Lamb shoulder	3 mg
Pork shoulder	2 mg

In addition to removing accumulated iron, you want to follow three steps to reduce iron levels. Step one is to reduce iron intake, so this, of course, means no iron supplements, and it also means reducing intake of the most iron-rich foods, particularly foods rich in heme iron, and these tend to be mostly shellfish and organ meats, although as you can see at the lower end of the list, we start seeing things like lamb shoulder and bison, but they have almost 10 times less iron than clams, for example, five to six times less than chicken liver. So, organ meats and shellfish are definitely the worst offenders in the case of iron overload, or your best friends in the case of iron deficiency. In most cases, we've found it unnecessary to limit muscle meat. We just have to tell the patients to lay off on organ meats and shellfish, which is a shame because they are so dense in other nutrients as well.

Highest sources of non-heme iron

Food	Amount (mg per 100g)
Spices (thyme, parsley, tarragon, fenugreek)	15–128 mg
Pumpkin seeds	15 mg
Sesame seeds	15 mg
Tomatoes, sun-dried	9 mg
Natto	9 mg
Baked potatoes	7 mg
Sunflower seeds	7 mg
Hazelnuts	5 mg
Soybeans, boiled	5 mg
Spinach, cooked	4 mg
Tomatoes, canned	3 mg
Spinach, raw	3 mg
Beet greens, cooked	2 mg
Swiss chard, raw	2 mg

Nonheme iron is not as well absorbed, as you know now, but it's good to be aware of foods that are higher in nonheme iron. I've posted a list of them on this slide, and we'll put them in a handout as well, as the foods that are high in heme iron on the last slide.

You'd want to tell patients to limit their use of cast iron cookware. This actually can make a meaningful contribution to iron burden, particularly if the pan isn't well seasoned, so it's just something to be aware of. They should use ceramic or stainless steel cookware instead of cast iron.

Substances that increase iron absorption

Substance	Comments
Vitamin C	100 mg increases iron absorption in a meal by over 4-fold
Beta-carotene	Found in apricots, beets, carrots, collards, red grapes, red peppers, spinach, tomatoes, etc.
Hydrochloric acid	HCL supplements
Sugar	Natural forms such as molasses and honey
Alcohol	In moderation only

Step two is to avoid substances that increase iron absorption, so vitamin C. Ascorbic acid at 100 mg increases iron absorption from a specific meal by over fourfold, so that's a very meaningful effect. Beta-carotene significantly increases iron absorption, but it's found in a lot of foods that are really healthy, and I haven't seen a meaningful effect in telling patients with iron overload to avoid beta-carotene. I don't think it's one of the more useful strategies. Hydrochloric acid significantly increases iron absorption, so you'd want to tell patients to avoid taking HCl supplements if they have iron overload. Sugar increases iron absorption, and refined sugar should be avoided anyway, but even natural forms such as molasses and honey can increase iron absorption, so those should be limited. Alcohol, finally, increases iron absorption significantly, so alcohol should be limited, especially during the therapeutic phase where you're getting iron levels down and especially during meals that feature foods with heme iron in them.

Substances that decrease iron absorption

Substance	Comments
Calcium	Inhibits both heme/nonheme
Eggs	Contain phosvitin, which inhibits iron absorption
Oxalates	Found in spinach, kale, beets, nuts, chocolate, tea, berries, some spices/herbs
Polyphenols	Found in cocoa, coffee, teas, apples, berries, walnuts, some spices
Phytate	Found in walnuts, almonds, sesame, dried beans, lentils and peas, and cereals and whole grains

Okay, step three involves consuming substances that decrease iron absorption. Calcium is the only known substance, at this point, that inhibits the absorption of both heme and nonheme iron. Calcium at 50 mg or less has little if any effect on iron absorption, but calcium in amounts of 300 to 600 mg inhibits the absorption of heme iron similarly to nonheme iron. One cup of skim milk contains about 300 mg of calcium for a reference. However, calcium supplements can increase the risk of heart disease in both men and women, and contrary to popular belief, they don't provide much if any benefit for bone health. Some studies have even shown that they decrease bone health. I don't like this as a strategy. I don't like calcium supplementation as a strategy for inhibiting iron absorption, but if the patient tolerates dairy products, consuming a glass of milk or kefir, having some hard cheese, or something like that with a meal can reduce heme iron absorption, and it's one of the few things that can do that.

Eggs contain a compound called phosvitin that impairs absorption of nonheme iron, and that may be responsible for the poor bioavailability of iron in eggs. So, for example, one boiled egg can reduce the absorption of iron in a meal by as much as 28 percent.

Oxalates impair the absorption of nonheme iron, and they're found in foods such as spinach, kale, beets, nuts, chocolate, tea, wheat bran, rhubarb, strawberries, and some herbs. The presence of oxalates in foods such as spinach explains why the iron in those foods is not particularly well absorbed.

Polyphenols are a major inhibitor of iron absorption. These include chlorogenic acid found in cocoa, coffee, and some herbs. Phenolic acid is found in apples, peppermint, and some herbal teas, and tannins are found in black teas, coffee, cocoa, spices, walnuts, and some fruits, and these all

have the ability—all these polyphenols have the ability to inhibit iron absorption, and the effect can be quite strong for nonheme iron. Some teas inhibit nonheme iron absorption by up to 90 percent, and coffee can inhibit it by up to 60 percent.

Finally, phytate is a compound contained in soy protein, fiber, nuts, and veggies, and even low levels of phytate, about 5 percent of the amounts found in whole cereal flours, can reduce iron absorption by 50 to 65 percent. Again, that's only nonheme iron, not heme iron.

From a practical perspective, the iron absorption-inhibiting effects of oxalates, polyphenols, and phytate can explain why iron overload is uncommon in contemporary hunter–gatherers who consume iron-rich foods. They also consume foods that are rich in these iron inhibitors, oxalates, polyphenols, and phytate. It's important to advise patients with iron overload or who are at risk for iron overload to eat plenty of fresh fruits and vegetables, because in addition to the other health benefits that these foods have, they will help prevent iron overload.

KRESSER INSTITUTE
FOR FUNCTIONAL AND EVOLUTIONARY MEDICINE

Iron Reduction Strategies

The following strategies will help to reduce both your intake of iron and the iron that is already stored in your body. Not all of these steps will be necessary for all patients. Please consult with your clinician to determine the recommended frequency of blood donation and which of the additional steps listed below are required. (For example, many patients are able to achieve iron balance without limiting beef and lamb if the preceding strategies, i.e., #1-10 below, are followed.)

1. Donate blood at a frequency that maintains serum ferritin <150 ng/mL (men) or <100 ng/mL (women) and iron saturation <45%, ensuring that hemoglobin stays >13% and ferritin does not drop below 30 ng/mL.
2. Do not consume organ meats, venison, clams, oysters, or mussels. These foods are very high in heme iron, the most absorbable form.
3. Consume coffee and/or tea with meals. Coffee and tea are rich in tannins, which inhibit non-heme (plant-based) iron absorption.
4. Consume a variety of fruits, vegetables, and other foods that are high in oxalic acid, phytic acid, and polyphenols, which inhibit non-heme iron absorption. These include dark leafy greens (e.g., spinach, kale), brightly colored fruits and veggies (beets, berries, etc.) nuts, chocolate, lentils (if tolerated), and spices/herbs.
5. Consume dairy products with meals (if tolerated). Dairy products are rich in calcium, which is the only substance known to decrease both heme iron (found in animal products) and non-heme iron.
6. Limit supplemental vitamin C to 200 mg/day (always between meals), which enhances iron absorption. Vitamin C in foods is fine.
7. Avoid sugar. It increases iron absorption by as much as four times in some cases.
8. Avoid alcohol until iron balance has been achieved. Alcohol elevates intestinal iron absorption, possibly by increasing stomach acid secretion. Once iron balance is achieved, moderate alcohol consumption (one drink per day) is permitted.
9. Avoid betaine HCl (hydrochloric acid) supplements or digestive enzymes that contain HCl. HCl increases iron absorption.
10. Avoid fortified foods or supplements/multivitamins that contain iron.
11. Limit consumption of beef and lamb to two to three times per week. They are also high in heme iron.
12. Take 300 mg of apolactoferrin twice a day on an empty stomach. Lactoferrin is the only natural substance known to remove iron that is already stored in the body. It is a safe alternative to pharmaceutical iron chelation for patients with mild iron overload that cannot donate blood (due to anemia or other restrictions), or a means of further reducing iron levels for patients that are able to donate blood.

Okay, we have a handout called Iron Reduction Strategies in the PDF generator. Make sure your patients take this seriously. That is one of the most important things I want to leave you with.

Remember that most patients and even most clinicians don't take it seriously enough, and I've seen so many patients, even those who know they have iron overload, come to me with really significantly elevated iron levels, and that's just putting them at unnecessary risk for a variety of diseases and early death. It's just completely unnecessary, given how relatively easy it is to deal with. Make sure to retest those patients' iron levels regularly. Include a full iron panel and ferritin in your routine blood work so you can catch the patients who have been undiagnosed. Then you can calculate the FeGGT iron score using the **web app** that we built for you to make it as easy as possible, and then you want to keep that FeGGT score in the low-risk category.

Okay, that's it for the iron deficiency and iron overload unit. I hope you enjoyed it and got a lot out of it. We'll see you next time.