

Iron Deficiency - Part Six

Okay, let's talk a little bit about iron supplementation. Until 1999 in the U.S., the majority of iron supplements were made with ferrous iron salts. These are positively charged iron ions and its counterion. The popular counterions are sulfate, gluconate, and fumarate. Once these are ingested, the stomach acid is required to dissolve the iron salt, so if a person is taking H₂ blockers or PPIs, acid-suppressing drugs, or has low stomach acid for another reason, such as they are elderly and they have atrophic gastritis, they have H. pylori, or they're on a low-protein vegetarian diet, they will not dissolve the iron salt, and they won't receive any benefit from the supplement. What's more, they will probably have a number of gastrointestinal side effects that are associated with these kinds of iron.

There are a few speciality manufacturers that make iron tonics or capsules that keep iron soluble so it can be absorbed even by people with low HCl, but this is still not my preferred form of iron for reasons that you'll soon learn.

Heme iron supplements are a much better option than iron salts. Proferrin from Colorado Biolabs contains heme iron. In one study, the change of serum iron from Proferrin was almost 23 times higher than from an identical dose of ferrous fumarate, a common iron salt. In addition, heme iron supplements are much better tolerated and less likely to cause GI distress, which is a common complaint of patients taking ferrous forms. In the study above, patients were able to tolerate 60 mg of Proferrin on an empty stomach with far fewer side effects.

As an additional benefit, patients can take Proferrin with meals, unlike ferrous salts that have to be taken away from meals because so many foods and beverages impair iron absorption when it is in the ferrous form. Again, only calcium inhibits heme iron absorption, so you'd want to make sure if the patient is taking calcium supplements that they don't take them at the same time as the proferrin.

Ferritin itself from a bovine or equine source is also available as a supplement. However, ferritin is not part of a nonheme pool of dietary iron that is readily exchangeable in and is similarly absorbed from the intestinal lumen. Studies show that oral ferritin is poorly absorbed and has a lower absorption than even iron salts, which are much less efficiently absorbed than heme iron.

Liposomal iron is the newest form, which has only recently become available. In fact, there is only one company that is selling it that I know of at the time of this recording. Like heme iron, it has a high bioavailability and low side effect profile. In one randomized open label trial, 99 patients with chronic kidney disease were split into two groups. One received oral liposomal iron at 30 mg per day, the other a total dose of 1,000 mg of IV iron gluconate at 125 mg infused weekly for three months. The short-term therapy with IV iron produced a more rapid hemoglobin increase compared with liposomal iron, but the final increase in hemoglobin over the entire course of the treatment was similar. IV iron can get iron levels up more quickly, but over the longer term of several months, liposomal iron was shown to be equivalent to even IV.



Another study comparing liposomal versus intravenous iron gluconate found a significant increase in iron in the liposomal treatment but not in IV, so in that case, liposomal outperformed IV. One study in rats showed that liposomal iron increased serum iron levels by 119 percent higher than ferric citrate and 54 percent higher than even a heme iron supplement. At this time of this recording, the only liposomal iron that I am aware of is called IronSmart, and it offers 10 mg of liposomal iron per dose. The recommended dose is one dose three times a day for a total of 30 mg, and 30 mg per day of this liposomal iron is thought to be equivalent to about 300 mg of ferrous iron salt.

Parenteral iron is administered by infusion or injection. It is often given to patients who have malabsorption or who have had gastric bypass or portions of their intestine removed. As the last slide suggested, liposomal iron is equivalent or better than IV iron in many studies. If a combination of diet, supplements, foods that increase iron absorption, Proferrin, and liposomal iron doesn't work, you will probably want to refer that patient out for parenteral iron. There are a lot of considerations with IV or injected iron that you should be aware of and experienced with if you're going to offer this kind of treatment. If you're not already experienced with it, it's good to at least work with someone who is or to refer out.

With all forms of supplementation, and even diet, remember that more is not always better. Too little iron is a problem, certainly, but so is too much, as we'll learn in the next section of this presentation. I've seen many patients who were prescribed iron by their doctor and never told to stop, and when I tested their blood, they had toxic levels. Side effects of iron overload can be acute, such as anaphylactic shock, or chronic, such as all of the consequences of iron overload such as fatigue, low libido, neurological problems, etc. Side effects of excess iron supplementation include GI problems such as nausea, vomiting, and cramps.



Functional	medicine	treatment
of ir	on deficie	ncy

Intervention	Comments
Address underlying causes	e.g. GI bleeding, malabsorption, infection, intense exercise, PPI use, etc.
Diet	Increase intake of foods high in iron
Improve absorption	Consume substances that increase iron absorption; avoid substances that decrease absorption

Let's pull all of this together into a discussion of a functional medicine approach to iron deficiency. As always, we start with addressing the underlying cause. Examples could be poor diet, inadequate intake of iron in the diet, dysmenorrhea, inflammatory bowel disease, H. pylori or other sources of GI bleeding and malabsorption, excessive intense exercise, low stomach acid either due to a disease state or to taking acid-stopping drugs, or calcium or zinc supplementation at high dose.

With diet, we want to focus on foods that are highest in heme iron such as shellfish, particularly clams and oysters, beef, chicken liver, and red meat. Limit high-calcium foods such as milk and cheese at mealtimes and coffee and tea as well, although coffee and tea only inhibit plant-based forms of iron. They can inhibit by up to 90 percent, as you saw. I've not found it necessary to limit phytate, eggs, and oxalates in omnivores when they're eating foods that are very high in heme iron such as shellfish and clams because, again, these substances don't decrease the absorption of heme iron, and those foods are so high in iron that they can get enough even when they're consuming phytate and oxalates. Phytate and oxalates are in many very healthy foods: fruits and vegetables, dark leafy greens, etc.

If your patient is a vegetarian or vegan, you can focus on the highest plant-based sources of iron, but again, many of these also contain substances that inhibit iron absorption, so supplementation may be necessary.

For both omnivores and vegetarians, I recommend supplementing with HCI, hydrochloric acid, and 100 to 300 mg of vitamin C with meals in order to increase iron absorption. It is also not a bad idea to have a glass of wine with meals if your patient tolerates alcohol. As I mentioned, I don't really



recommend focusing on beta-carotene as a means of increasing iron absorption because many of the foods that contain it are also high in phytic acid.

If iron deficiency is mild or in the functional range, and it's caused primarily by insufficient intake rather than blood loss or significant malabsorption, dietary changes and doing things that increase absorption may be enough to address the problem. If iron deficiency is more severe and/or it's caused by other conditions, iron supplementation will likely be necessary. I recommend Proferrin extra strength with 10.5 mg per tablet or IronSmart with 10 mg per teaspoon or 15 mg per capsule.

Supplementation for moderate to severe iron deficiency		
Severity of iron deficiency	Comments	
Mild	1 capsule of Proferrin ES or 1 capsule/teaspoon of IronSmart per day	
Moderate	2 capsules of Proferrin ES or 2 capsules/teaspoons of IronSmart per day	
Severe	3 capsules of Proferrin ES or 3 capsules/teaspoons of IronSmart per day	

The dose that your patient would take depends on the severity of iron deficiency. So, I've offered some guidelines here on this slide. With mild functional deficiency, one capsule of Proferrin or one capsule or teaspoon of IronSmart per day in addition to diet and absorption changes. For moderate deficiency, two capsules of Proferrin or two capsules or teaspoons of IronSmart in addition to diet and absorption changes. Then in severe deficiency, three capsules of Proferrin or three capsules of IronSmart in addition to the diet and absorption changes. If that doesn't do the trick, you may need to refer out for parenteral iron.



	EVOLUTIONARY MEDICINE		
1.	Eat clams, oysters, beef and chicken liver, beef, and lamb regularly throughout the week. These are the highest food sources of highly absorbable heme iron. (Note that nonheme iron found in plant foods is poorly absorbed compared to heme iron, which is found exclusively in animal foods.) Plan your meals in advance each week to ensure that you are eating one of these foods daily.		
2.	Take 250 mg of vitamin C (as ascorbic acid) and 200 to 1,200 mg of betaine hydrochloric acid (HCI) with meals. These substances increase iron absorption significantly. If you are taking proton pump inhibitors (PPIs) or other acid-suppressing drugs, please speak with your clinician before taking HCI.		
3.	Consume substances that impair iron absorption—including tea, coffee, dairy products, supplemental fiber, and supplemental calcium and zinc—between meals.		
4.	If you tolerate it, consider a glass of wine or other alcohol with dinner, as alcohol also improves iron absorption.		
5.	Cook in cast iron whenever possible.		
6.	Don't smoke. Tobacco smoking robs the body of oxygen and depletes the immune system, which is already challenged with iron deficiency.		
7.	If the steps recommended above do not improve your iron levels, and/or your clinician suggests it, take a heme iron (e.g., Proferrin ES) or liposomal iron (e.g., IronSmart) supplement at the dose your clinician recommends.		

I've put together an iron repletion protocol handout that you can print out and use as a quick reference.

Okay, that's it for now. In the next section, we're going to talk about the other side of the iron coin, which is iron overload. Thanks for watching and listening.