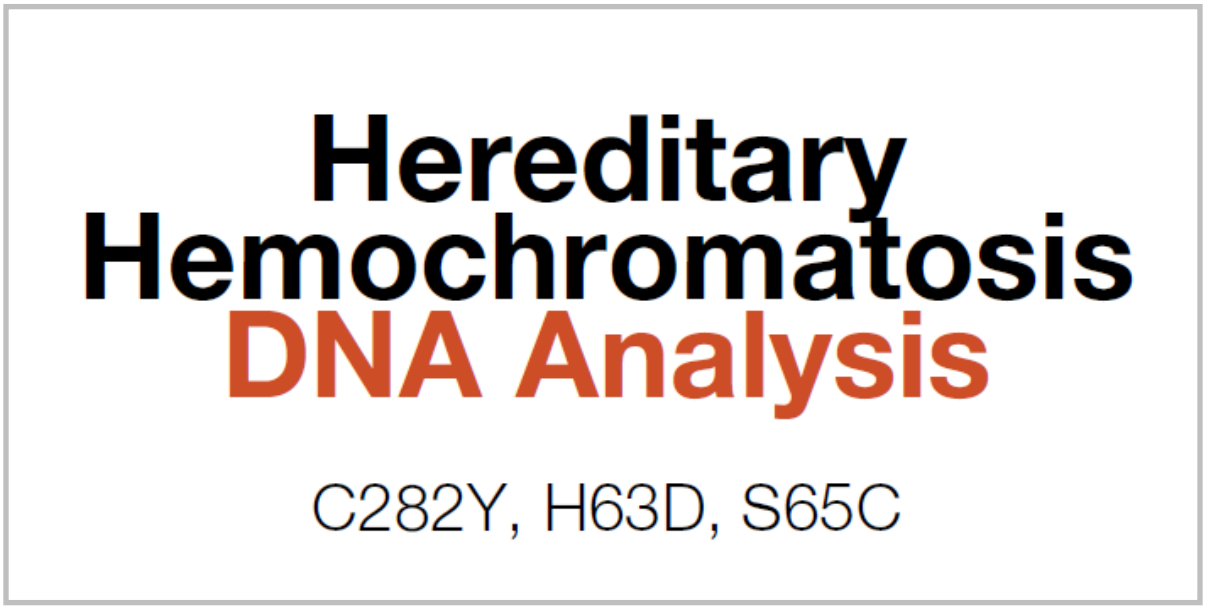
Iron Overload - Part Four

If iron levels are persistently high, do consider a DNA analysis.



It looks at the three most common HFE gene mutations: C282Y, H63D, and S65C, but as I mentioned earlier, in the last decade, we've discovered that there are many more mutations that cause excess iron storage.

That said, these mutations, C282Y, H63D, and S65C, are present in 90 percent of cases of iron overload, so they are by far the most common mutations. It just means that if you get a negative on this test, it doesn't rule out other lesser-known mutations that could be causing excess iron storage, and at the end of the day, the serum markers that reflect actual iron status are more important than the genetic markers because that is what actually does the damage, is the iron levels, the GGT levels, etc.

The most affordable way to get a patient's HFE gene status is 23andMe. 23andMe doesn't provide this information automatically, however. The patient has to do a hack to get this by looking at their raw data. We have a patient handout that describes how to do this, and we will provide this handout as well for you. It's really easy to do. It just involves them accessing the raw data and then sending you that information.

You can also order the genetic testing from a lab such as LabCorp. The last time I looked, it was about $260 or $270. Of course, it depends on the patient's insurance. If the patient has good insurance that will cover it, it would be probably cheaper than doing it through 23andMe. Whatever route you choose, I do recommend doing the genetic testing, although I think the iron status as

defined by the serum iron markers is more important, the genetics still do inform treatment and help you make a plan. For example, if you find that the patient is homozygous for hereditary hemochromatosis, you would be much more aggressive in your approach, and you would monitor him much more closely. You'd likely even refer him out to a hematologist. However, if he doesn't have any mutations that are associated with hereditary hemochromatosis, he may have other mutations that are less serious or less well known, and the causes of his iron overload may be something different. They may not be genetic, and you may need to look elsewhere. So, the genetic testing, I think, is still important and plays a role in the diagnosis and treatment plan.

It's also a mistake, as we've discussed already, to assume that heterozygous carriers of the mutations are not at risk. Carriers do have increased iron levels and are at increased risk of disease, as I've shown, and though it's not nearly as pronounced a risk as it is when they have two mutations, it's still more significant than if they have no mutations at all. Given the significant increase in morbidity and mortality that comes with even high-normal iron levels and an elevated FeGGT LifePro score, I think it makes sense to be cautious. That's our job as functional medicine providers is not just to treat disease after it has occurred but to prevent it from occurring in the first place.

If serum iron markers are elevated with or without HFE gene mutations, other tests may be required to confirm the hemochromatosis diagnosis. Liver biopsy used to be the gold standard, but it's invasive and a little bit risky, and it's accepted now, generally, that it's no longer required to confirm a hemochromatosis diagnosis. This test has been replaced by an MRI of organs where iron is expected to accumulate, such as the liver, the heart, the lungs, the pancreas, and the brain. A test called a FerriScan, which is a special MRI technique for quantifying liver iron content, and then quantitative phlebotomy, where the amount of iron removed is measured to determine if there is

excess iron in the blood. Sixteen to 20 pints of blood should contain about 4 g of iron, and if there are more than 4 g of iron in that amount of blood, then that is a sign of hemochromatosis. If the patient has a serum ferritin over 600 and a very high iron saturation of 70 to 80 percent, I do recommend referring out to a hematologist for further workup.

Unfortunately, many clinicians and even some hematologists are not particularly well educated about the effects of high-normal iron levels. I've referred several patients with an iron saturation of 65 to 75 percent and ferritin levels of 600 to 800 to hematologists only for them to be told that there is nothing to be concerned about unless their ferritin is over 1,000 ng/mL. This is the level at which iron is thought to cause significant organ damage, so don't we want to intervene before that? You may need to treat the patient yourself if the local hematologist won't help, and we're going to talk more about how to do that in Part 2 of this presentation.

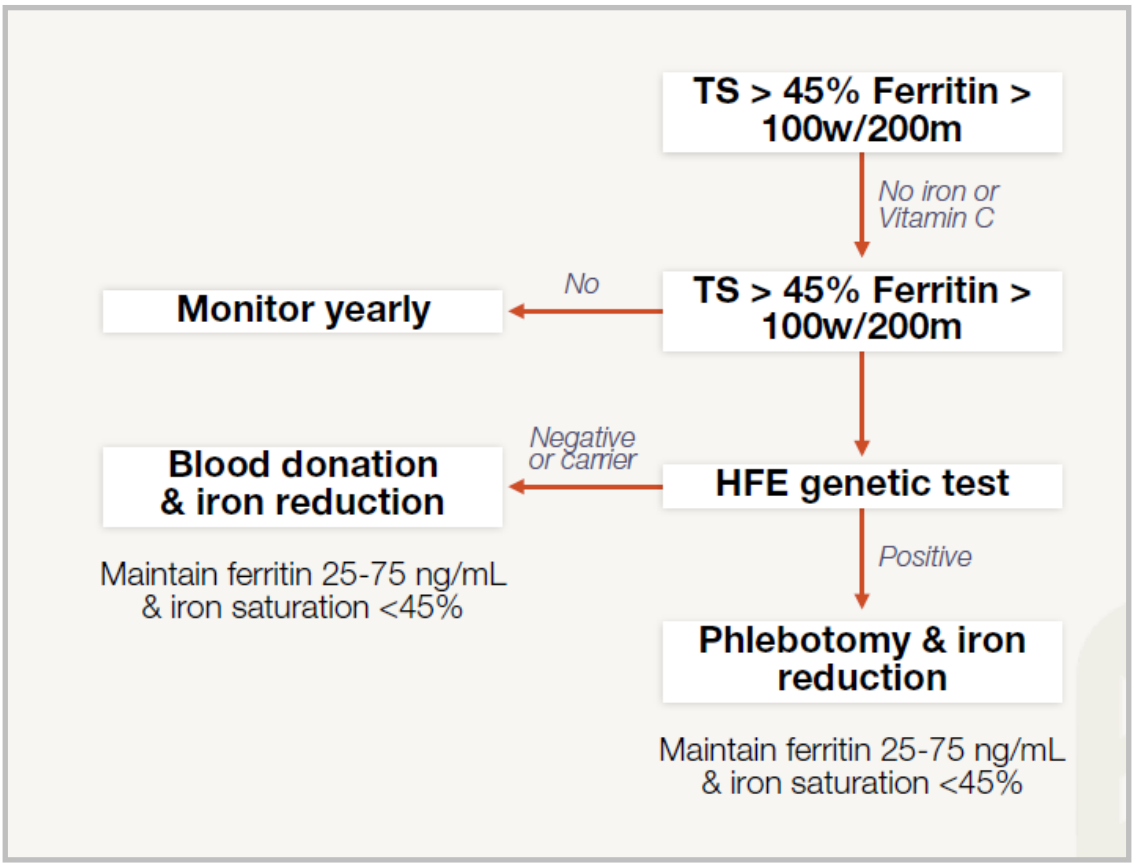
Also note that there are many different presentations of iron overload. Not all patients meet the textbook definition with high ferritin, high serum iron, high iron saturation, and then low UIBC and TIBC, and you'll see this when we go into case studies in the next section. Some patients, for example, might only have high ferritin and perhaps low soluble transferrin receptor with all of their other iron markers normal.

A minority will have the opposite presentation. They will have high iron saturation with normal ferritin, and this can occur in the earliest stages of iron overload. An elevated iron saturation correlates with increased gastrointestinal iron absorption, and then ferritin levels will only rise after parenchymal cells are overloaded. Asymptomatic patients or those with arthralgia or other early symptoms such as fatigue may have normal serum ferritin levels.

Although most labs don't strictly require fasting for an iron panel, I recommend that you do have patients take the test in a fasted state. Iron levels are highest after meals, so a postprandial transferrin saturation level may be falsely elevated.

Always re-test to confirm iron overload

In addition, transient iron overload is possible and even somewhat common in my practice where the patient has high iron levels on one test and then normal iron levels on the next one to two retests. The most likely cause of this is that the first test was done in a non-fasted state or unknown iron supplementation; for example, they're taking a multivitamin with iron in it, but they didn't know that. Another possible cause is a high intake of substances that increase iron absorption such as alcohol, vitamin C, or betaine hydrochloric acid, but it's not always clear what causes this transient iron overload. There is a bit of mystery involved, and there is not much written about it in the scientific literature. I've also spoken with researchers and hematologists about it who've had similar experiences, and they're not sure what to make of it either. This is why I think you should always retest at least once after an initial high iron result, as I'll show you on the algorithm on this next slide.



Here's how to do a workup for iron overload. You do an initial test, your case review blood panel, and if you see transferrin saturation above 45 percent, which is the upper end of my functional range, or ferritin above 100 in women or above 200 in men, then you would instruct the patient not to consume any iron-containing supplements or any vitamin C, if they were before that. Then you would wait maybe a week or two weeks, and you would do another test. If transferrin saturation is again above 45 percent and/or ferritin is again above 100 for women or 200 or men, then the next thing I would do would be a genetic test, either through LabCorp or through the 23andMe gene hack. If they are positive, you can refer to a hematologist or start a course of phlebotomy and iron reduction, which we're going to talk more about in the next unit. The goal there is to initially induce near-iron deficiency, which is getting ferritin and transferrin saturation down close to iron-deficient levels and then from there to maintain a serum ferritin of 25 to 75 ng/mL and an iron saturation below 45 percent.

If the patient is negative for hereditary hemochromatosis or they are heterozygous, you would still follow a similar course depending on how high his ferritin and iron levels are. You could either treat him yourself, sending him for a blood donation and following the iron reduction protocol I'm going to teach you in the next section, and the targets would be relatively similar, although they may not need to be as aggressive as the targets for someone who has hereditary hemochromatosis.

Okay, that's it for now. In the next section, we're going to look at a lot of cases, and I'm going to tell you how to treat iron overload. See you then.