# HFE (rs1799945) Report

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The rs1799945 polymorphism corresponds to the H63D mutation in the *HFE* gene, which is one of the primary genetic variants associated with hereditary hemochromatosis (HH). Unlike the more common and penetrant C282Y mutation, homozygosity or heterozygosity for H63D generally exerts a milder effect on intestinal iron absorption, meaning that only a small percentage of individuals with this variant will progress to severe clinical iron overload (Rametta et al., 2020). However, the risk escalates notably in individuals who are compound heterozygotes (carrying one H63D and one C282Y allele) or in those facing external liver stressors such as alcohol use or viral hepatitis (Li et al., 2024). Ultimately, if excessive iron absorption outpaces the body's negligible capacity for excretion, it leads to the gradual, toxic accumulation of iron in major organs, triggering oxidative stress, cellular necrosis, and progressive tissue fibrosis.

**Clinically, the disorder is characterized by a prolonged, asymptomatic preclinical stage, often making early detection reliant on genetic screening and abnormal serum iron indices. When early symptoms do manifest, they are notoriously vague, consisting of chronic fatigue, lethargy, and arthralgia, classically presenting as pain in the second and third metacarpophalangeal joints, sometimes referred to as the "iron fist"** (Palmer et al., 2018). **As iron deposition advances, it causes profound end-organ damage, particularly impacting the liver, heart, and pancreas**. **Patients may develop liver cirrhosis (with a dramatically increased risk for hepatocellular carcinoma), restrictive cardiomyopathy, and diabetes mellitus resulting from pancreatic fibrosis, a condition historically described as "bronze diabetes" due to the simultaneous hyperpigmentation of the skin** (Milman et al., 2019; Palmer et al., 2018). Endocrine disruption from iron infiltrating the pituitary gland frequently causes hypogonadism, loss of libido, and erectile dysfunction.

**Standard conventional treatment for symptomatic hemochromatosis revolves around regular therapeutic phlebotomy (venesection). Phlebotomy effectively and safely depletes the body's iron stores by removing iron-rich red blood cells, which forces the body to mobilize accumulated iron from tissues to produce new erythrocytes** (Szczerbinska et al., 2024). This protocol typically involves weekly or bi-weekly blood draws until serum ferritin and transferrin saturation normalize, followed by lifelong maintenance phlebotomies. For patients who have developed severe cardiac complications or anemia that preclude them from tolerating phlebotomy, iron chelation therapies using pharmacological agents (e.g., deferoxamine) can be prescribed. However, traditional chelation therapy can be burdensome and carries significant side effects, reserving its use primarily as a secondary option for those ineligible for bloodletting (Hollerer et al., 2017). (Note: Repeated phlebotomy at this level will cause

severe vitamin deficiencies and you should get a CMA regularly if being phlebotomized (you'll know you need it because of the severe fatigue you start to feel.)

For patients seeking "natural options" as either an adjuvant therapy alongside phlebotomy or as a stand-alone approach (though patients should be heavily cautioned about the risks of foregoing clinical monitoring), aggressive dietary modifications and the use of natural plant-based chelators provide highly effective avenues to inhibit iron absorption. The foundational step involves adopting a plant-rich diet while strictly avoiding heme-iron sources (mammalian red meat) and highly fortified cereals (Milman, 2021). Crucially, these patients must avoid consuming Vitamin C alongside meals, as it acts as a powerful enhancer of iron absorption. Instead, they should incorporate dietary inhibitors like black or green tea with meals; the catechins and tannins in these beverages strongly inhibit non-heme iron uptake (Perzia et al., 2022).

Furthermore, specific natural polyphenols and flavonoids have demonstrated well-documented abilities to chelate iron safely. Quercetin, an abundant flavonoid found in onions, apples, and green tea, has been extensively shown in both in vitro and in vivo studies to bind directly to iron, significantly downregulating apical iron uptake in the intestines and blocking its release into the bloodstream via the ferroportin transporter (Lesjak et al., 2014). Beyond directly interfering with iron absorption, quercetin and related flavonoids possess robust antioxidant properties that neutralize the lipid peroxidation and free-radical damage induced by excess intracellular iron, essentially shielding vital organs from the downstream damage characteristic of hemochromatosis (Wang et al., 2021). Combining a low-iron, plant-based diet with polyphenol-rich botanical extracts offers a highly synergistic natural strategy to keep iron absorption stunted.

**Also, to help with the oxidative damage your most powerful options will be the VARs TRIAD regularly like 6/4/2 (6 VARs Glutathione a day, 4 VARS SOD a day, and 2 VARS Catalase a day) – these would off the far superior natural options to prevent the damage caused by the iron deposits.**

## References

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