

DIOS: dysmetabolic iron overload syndrome

Iron Overload different from classic hemochromatosis

Key words: hyperferritinemia; iron overload; hemochromatosis; neurodegenerative diseases; HFE; C282Y, H63D, S65C; cholesterol, triglycerides, glucose, uric acid, insulin, blood pressure; body fat; fatty liver; obese; overweight; metabolic syndrome

It is well established that moderately elevated body iron is associated with chronic disease and premature death. Nearly 16 million Americans have some degree of iron overload by inherited or acquired means.

Depending upon the degree and cause of iron overload, the consequences can include bone and joint disease, liver disease including cancer, cirrhosis, fatty liver, metabolic syndrome, cardio-vascular disease or heart failure, diabetes mellitus, hypogonadism, impotence, infertility, hypothyroidism, abnormal adrenal function, increased infection, hearing and vision loss, skin color changes (bronze, gray-green or reddish color), depression, or suicidal tendencies. Elevated iron increases risk for earlier onset of symptoms for neurodegenerative diseases: Alzheimer's disease, Huntington's, or Lou Gehrig's disease; and excess iron is prominent in areas of brain with multiple sclerosis lesions. Having mutations of the *HFE* gene, increases the risk of iron overload and these consequences.

HFE is the gene for classical hemochromatosis (type I) hemochromatosis, a leading cause of iron overload disease. Mutations of *HFE* occur in a variety of patterns, the most at risk are those who are: C282Y/C282Y or H63D/H63D (homozygotes) or C282Y/H63D (compound heterozygotes). Another rare mutation S65C is believed to cause less severe iron overload. Hereditary hemochromatosis type I (HHC) is very common in the white population; about one million Caucasians in the USA have the C282Y/C282Y inheritance pattern—as many as four million have other *HFE* inheritance patterns of hemochromatosis. When people appear “tan” without being in the sun or early deaths due to heart or liver failure, or where there is a history of suicide often undetected hemochromatosis will arise as suspect by people knowledgeable about the disease. Some think that the suicide, alcoholism and depression of Ernest Hemingway and the cirrhosis experienced by Beethoven were due to hemochromatosis.

HHC is characterized by serum transferrin-iron saturation percentage (TS%) above 45% (fasting), accompanied by an elevated serum ferritin above 200ng/mL in adult females or 300ng/mL in adult males. When these patients are diagnosed before serum ferritin is above 1,000ng/mL and they undergo successful iron reduction (phlebotomy or blood donation), the risk of liver damage is less than 1% and they can expect normal lifespan. When serum ferritin is allowed to rise above 1,000ng/mL the risk of serious, irreversible organ damage increases 20-200 fold! For this reason alone, early detection and treatment of iron overload are imperative.

More recently, a condition called dysmetabolic iron overload syndrome (DIOS) is described. DIOS also results in mild iron loading, but unlike classic hemochromatosis, it is characterized by normal TS% with elevated serum ferritin.

Generally, people with DIOS have elevated levels of blood pressure and serum cholesterol, triglycerides, glucose, uric acid, insulin. These individuals are likely to have mildly elevated liver enzymes, especially GGT and have a fatty liver. Two-thirds will have elevated urine levels of hepcidin. People with DIOS will likely be overweight or obese (varying degrees) with central (belly) fat with increased

percentage of body fat to muscle.

**Ideal body fat percentage for adult men
age 41-60: 11-22; obese >27%**
**Ideal body fat percentage adult women
age 41-60: 23-35; obese >39%**

No known studies have focused on the treatment of dysmetabolic iron overload syndrome and as such, treatment guidelines are not well defined. Physicians may choose to address the individual diseases with medications and use phlebotomy to lower the elevated ferritin. In one study investigators found that patients with DIOS whose ferritin levels were greater than 450ng/mL benefited from phlebotomy (blood donation).

Some patients with dysmetabolic syndrome and only mildly elevated levels of cholesterol, triglycerides or blood pressure, but who have not yet developed diabetes may be able to correct or normalize these levels with a strict diet and exercise program directed at reduction of the percentage of body fat and the improvement of antioxidant capability. There may still be a role for iron reduction in such persons.

When the serum ferritin is abnormally high, and TS% is abnormally high, this requires iron reduction with blood donation or phlebotomy.

When the serum ferritin is high but TS% is normal, generally, the cause is due to a fatty liver and inflammation a pattern often seen in people with DIOS.

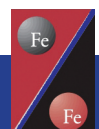
When the TS% is high but the SF is normal or low, this is called iron avidity.

elevated iron	IRON TESTS	
	Serum Ferritin (SF)	Transferrin-iron Saturation Percentage (TS%)
Hemochromatosis (classic—type I)	↑	↑
DIOS (dysmetabolic iron overload syndrome)	↑	NORMAL
Anemia of Chronic Disease (inflammatory response)	↑	↓
Iron Avidity	↓	↑

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Iron Disorders Institute nanograms: DIOS



DIOS Resources: journal articles and abstracts

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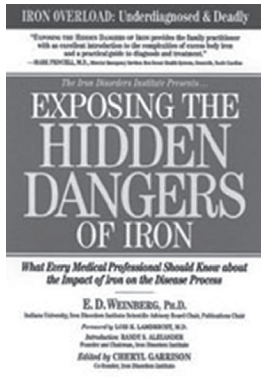


Read Cheryl's story: a case of mild DIOS managed with diet and exercise program.

Excerpts from Cheryl's Story:

Cheryl Garrison, co-founder and Executive Director of Iron Disorders Institute (IDI) was told by her physician in 2008 that she had hemochromatosis. Her doctor was basing the diagnosis on an elevated serum ferritin. Cheryl's blood pressure and lipids were elevated; she had a fatty liver and serious gall bladder issues. After re-reading the books about iron published by IDI she realized that her condition was more in line with dys-metabolic syndrome (DIOS). "I remember Dr. Herbert Bonkovsky telling us in 2000 that fatty liver disease was going to be the next big health issue." recalls Cheryl. Blood pressure and lipid lowering medications were not well tolerated. "I had no choice but to try diet and exercise. After a few weeks on a particular approach, I began to see the first improvements in fat reduction. I am still working on blood pressure." she remarks. Cheryl is willing to share with you what she did, but points out that her approach is not stated as policy for Iron Disorders Institute (IDI).

Contact Cheryl for a copy of her experience:
cgarrison@irondisorders.org



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"Physicians are probably seeing one case of hemochromatosis every two weeks and are likely misdiagnosing these cases as diabetes, arthritis, heart problems, liver disease, impotence, or depression."
—VINCENT J. FELITTI, M.D., Director, Department of Preventive Medicine, Kaiser Permanente, San Diego, California

THE IRON DISORDERS INSTITUTE
Guide to
HEMOCHROMATOSIS

• *A Leading Cause of Iron Overload Disease* •

According to the U.S. Centers for Disease Control and Prevention...
"MORE THAN A MILLION PEOPLE IN AMERICA HAVE HEMOCHROMATOSIS."

KNOW THE SIGNS:

• Chronic Fatigue	• Diabetes	• Emotional Changes
• Joint Pain	• Abdominal Pain	• Depression
• Heart Arrhythmia	• Elevated Liver Enzymes	• Hair Loss
• Chest Pain	• Cirrhosis	• Infertility
• Heart Attack	• Elevated Iron	• Loss of Desire for Sex
• Skin Color Changes	• Cancer	• Impotence

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