Fatigue, irregular menstrual cycle, high blood pressure did not fit the profile of a healthy eater and runner—but before the age of 40, these were signs for Melanie that her health was failing. No matter how many doctors she saw over the next fifteen years, none of them would attribute her symptoms to genetic hemochromatosis. Driven by increasing symptoms, Melanie persisted; she knew that her life depended on it. She would eventually solve the mystery of her declining health with the help of a friend.

Melanie recalls being fatigued in high school but decided that it was just typical adolescent changes in hormones. At the age of 37 she would undergo a partial hysterectomy. By the age of 40 she would develop high blood pressure. She was surprised by this development. She didn’t smoke; she exercised regular and was not overweight. Family history would offer a few clues but only half the story. Her mother was in great health with no history of high blood pressure. Her mother is still with us at 82, and her father died of lung cancer at the age of 52. She knew nothing about her father’s family history because he was adopted. Other than arthritis and gout, Melanie remembered her father to be in good health.
Following the onset of high blood pressure, and three years after a complete hysterectomy more serious symptoms began to emerge. While her home state of Louisiana was dealing with the ravages of Hurricane Katrina Melanie was dealing with the ravages of a silent killer: hemochromatosis. By now, Melanie was working in the financial investment industry. She had a very demanding job. It made sense to attribute each emerging symptom to stress caused not only by the demands of work, but from being on the road so much. Because her job required her to travel, this meant staying in hotels. In these unfamiliar surroundings Melanie was not sleeping well and the fatigue grew worse; stress seemed the likely cause. On one occasion, Melanie recalls being exhausted to the point of telling a colleague that if she could, she would crawl under her desk and sleep.

One night at home, the pounding of her heart was so severe that her husband said he could feel the bed move. Melanie thought it was a panic attack and reported this to her doctor. He tested her kidneys and heart function and diagnosed her with a prolapsed mitral valve. Melanie was given beta blockers but things did not improve. Her health would continue to decline. At the age of 54, Melanie had serious digestive issues, and it was decided she needed her gall bladder removed.

Melanie would nearly die as a result of the laparoscopic removal of her gall bladder. “I knew that I was too sick to go home.” remarks Melanie. But never-the-less, she was sent home, with a fever caused by infection due to stones in the common bile duct. Complaining that she felt like she had the flu Melanie was rushed back to the hospital. She was septic. “Now that I know infection is amplified in the presence of high iron, I am astonished that I survived.” Melanie concludes. After the ordeal with this surgery, which would not be Melanie’s last, she had just about reached her breaking point.

“I was still dealing with extreme fatigue and body aches. I continued to seek answers from my physicians; and both my gynecologist and internist diagnosed me with clinical depression. After all, hadn’t I just been through Katrina and then a near death experience? At first I would not fill...
the prescription for an antidepressant. But then, my husband was so concerned for me that he insisted I at least try the drugs. I just hated it; but for him, I took the meds...for three days. I hated these pills. At this time, I was retired from investments, and had been doing contract work for DirectLabs for about 2 years. I called a co-worker and friend at DirectLabs, Leigh Wilkerson. I asked her to help me select any and every test that would help me figure out what was wrong with me. I was convinced that depression was a symptom, not a diagnosis. If it were not for my knowledge of DirectLabs and Leigh’s support, I am convinced I would not be alive today. I knew that a blood test was the best way to determine what was going on with me.”

“I can still recall the desperation in Melanie’s voice,” says Leigh Wilkerson, CEO, DirectLabs, Mandeville, Louisiana. “She asked me to run every test I could imagine. I see this a lot; people are frustrated, needing answers and they just do not know where to turn.” Leigh continues.

“It was more like pleading than asking”. Melanie adds. “I felt like I was on the brink of doing something drastic. I could not tolerate the vicious cycle of symptom, drug, symptom, new drug. I wanted to know The Why!”

“I wanted to know The Why!”

Both Parents Homozygous Different Mutations

Children

100% chance: Compound Heterozygote

Risk of iron loading increased

Approximately four million people in the USA have the H63D/C282Y genotype.


Edward A Doisy Department of Biochemistry and Molecular Biology, Saint Louis University School of Medicine, St Louis, MO 63104, USA.

Hereditary hemochromatosis (HH) is an autosomal recessive disease characterized by iron accumulation in several organs, followed by organ damage and failure. The C282Y mutation in the HFE gene explains 80-90% of all diagnosed cases of HH in populations of northwestern European ancestry. Targeted disruption of the mouse Hfe gene (or introduction of the murine mutation analogous to the C282Y human mutation) produces a murine model of HH. Another mutation in the HFE gene, H63D, is more prevalent than C282Y. However, the physiological consequences of the H63D mutation (as well as C282Y/H63D compound heterozygosity) on iron homeostasis are less well established. To evaluate the phenotypic consequences of the C282Y/H63D and H63D/H63D genotypes, we produced H67D (corresponding to H63D in humans) and C294Y (corresponding to C282Y in humans) knock-in mice. H67D homozygous mice, C294Y homozygous mice, and H67D/C294Y compound heterozygous mice each demonstrated hepatic iron loading. Even on a standard diet, by 10 weeks of age, hepatic iron levels in mice of these three genotypes were significantly higher than those of wild-type littermates. The relative severity of hepatic iron loading was C294Y/C294Y > C294Y/H67D > H67D/H67D. We conclude that the H67D allele, when homozygous or combined with a more consequential mutation like C294Y, leads to hepatic iron loading. These observations indicate that the H67D mutation leads to partial loss of Hfe function and can contribute to murine HH.
Serum iron and serum ferritin were among the tests that were performed through Direct Labs. When the results came back it was like a huge red flag, waving at them. Melanie’s iron was very high; her ferritin was over 1,000ng/mL—the critical zone where organs are damaged permanently.

Armed with clues from the Internet and her lab work, Melanie made an appointment with her doctor—hopefully, to pinpoint the underlying cause of so many health problems.

“What does this high iron and high ferritin alert mean?” Melanie asks her doctor. The response was disappointing. Rather than investigate the possibility of hemochromatosis, an iron disorder known to be associated with high iron, Melanie’s doctor informs her that she just needs to adjust her antidepressant meds.

Baffled by her doctor’s behavior Melanie points to the high iron lab results and tells the doctor to “Look again! What does this mean?”

Frustrated Melanie found another doctor who paid attention to Melanie’s clues. This doctor ordered the genetic test and confirmed the diagnosis of hemochromatosis.

“I am H63D/C282Y positive or otherwise known as a compound heterozygote.” Adds Melanie. “Cheryl Garrison, executive director, Iron Disorders Institute tells me that this combination is more problematic than the C282Y/C282Y homozygote.”

Garrison explains. “Melanie is fortunate to have found a doctor who was informed. One of the problems with the diagnosis is that often the compound heterozygote H63D/C282Y or other heterozygotes are discounted as low risk for the consequences, when in fact they are also at risk if their iron levels are high. For this reason we encourage people to obtain a complete iron panel as part of their investigation.”

“We understand the demands of the medical profession. There’s so much to know and so little time to learn it. Before Melanie’s situation, I too was unfamiliar with high iron. I had seen plenty of low iron results—I believe we are prone to think of low iron first—certainly the medical professionals I know are that way.” Leigh interjects.

Shaun Carpenter, MD agrees. “High iron is not generally on our radar screen when we encounter a patient with so many complaints. We all have to expand our understanding of Iron-Out-of-Balance™ and we need to appreciate the patient more.”

Dr. Carpenter continues. “Physicians are trained to diagnose and manage diseases but what if the one test that reveals high iron is not included in any of the common tests we do?” Patients have the time to read and investigate possibilities. And when they have access to unraveling mysteries as Melanie did, the doctor benefits as well.”

“DirectLabs saved my life!” Melanie says with conviction. “If I had continued on the same path of unknowns, I would not be alive today. I am convinced of that!”

Melanie would undergo yet another surgery, which was to remove three quarters of her liver. She had a premalignant Cyst Adenoma. Today, she is on a strict diet and has regular phlebotomies. As a result of her experience she has informed multiple doctors about hemochromatosis, iron tests and genetics. To date, three families have been diagnosed because of Melanie’s efforts to raise awareness.

Gerald Koenig, Chairman, Board of Directors, Iron Disorders Institute adds. “Because hemochromatosis is not a household word and iron tests are not included in routine blood chemistry panels and because the treatment does not require a drug, hemochromatosis lacks the benefit of a large pharmaceutical sales team bringing it to the attention of doctors. Hemochromatosis depends on patient persistence and information access, exemplified by Melanie’s story.”
“There is a wealth of information about hemochromatosis once you are aware. Besides informing doctors as Melanie did splendidly, individuals can download the Iron Disorders Institute Hemochromatosis Diagnosis and Clinical Management Guidelines, which are compatible with the American Association for the Study of Liver Diseases (AASLD) and the American Academy of Family Physicians (AAFP). People can also purchase the DVD: Iron Men Living with Hemochromatosis. This can be given to family members and to hospital systems that run education programs for doctors.” Garrison concludes.

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**Hemochromatosis DVD**

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