IRON OVERLOAD DISEASE -- HEMOCHROMATOSIS

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Dedicated to John Boudreau, my brother, who was misdiagnosed for decades and then diagnosed too late to recover from multiple organ damage. He lived for decades, assaulted with the ravages of this disease, which finally claiming his life on October 26, 2011. Rest in peace, sweet brother.

This article was first posted in 2009 and revised in 2011 when, with the sudden death of Dr. Malcolm Casadaban, I was reminded of and alarmed at the extent of ignorance regarding an often misdiagnosed, easily preventable but debilitating and even deadly disease — for lack of two blood tests, serum ferritin and transferrin saturation %.

LOOSE IRON — A PLAYGROUND FOR DISEASE

In Sept. 2009 Dr. Casadaban, a genetics and cell biology professor at the University of Chicago, was working in the laboratory with the a strain of the bubonic plague bacterium that had been attenuated (weakened) to make it safe for research. He became ill, checked into hospital and was dead 12 hours later — the first scientist to be killed by the bubonic plague in 50 years. Lab results were positive for the plague bacterium, and the university’s biosafety alarm was triggered.

Dr. Casadaban's liver and blood were awash with iron. His undiagnosed hemochromatosis (iron overload disease) made it possible for genetically weakened and otherwise safe laboratory plague bacterium to thrive in the iron overload milieu and cause his sudden death. Early diagnosis could have been made with two blood tests, something every man over 40 and every woman after menopause should request.

How is it that a scientist with degrees from M.I.T., Harvard, and Stanford in Biology, Genetics, and Cell Biology did not know to be tested for this genetic disease? He ignored the possibility or never took it seriously. Certainly the family care physicians don't bother with it. Why is it not a routine screening test, especially for those of the right age with a northern European heritage? This is not new information. We have known for more than 20 years that iron overload compromises the immune system and nourishes organisms that cause inflammation and infections.

The men among us won’t need to be concerned with this inherited mutated gene until they are 40 and the females until after menopause, although in my daughter, her iron overload became apparent in her early 40's because I insisted that she be tested. This is important enough, common enough, and devastating enough for you to understand it now for yourself and your loved ones. Iron overload is a destructive disease — a sleeper that slowly compromises internal organs and joints, seducing one into thinking "it’s just age catching up" — until years later it has taken over, trashing hopes, dreams and goals; family life, love-life and love of life, and finally – life itself. All for lack of two simple diagnostic blood tests! How incredibly unacceptable!
Exercise can build physical strength, help to keep us focused and healthy, strengthen bones, and for some it has been shown to restore and maintain blood pressure and cholesterol levels within normal range, but no number of life-time workouts can prevent the progress of iron overload disease. So here we go – all you never thought you wanted to know about hemochromatosis.

THE NORMAL

Iron in our diet is essential to health. Most of us absorb about 10 percent of the iron in the foods we eat. When our iron stores are adequate, the body protects us from iron overload by reducing the amount of iron absorbed by the intestines. However, once absorbed, the body cannot rid itself of excess iron except through bleeding or pregnancy.

IRON OVERLOAD

An inherited genetic mutation, called Iron Overload Disease, or Hemochromatosis, causes loss of the body’s rigorous control over intestinal absorption of unneeded iron, allowing it to continue to enter the blood stream from the intestines unabated. Over the years, 5 to 20 times as much iron as normal may be stored, causing damage to major organs such as the liver, heart, pituitary gland, thyroid gland, pancreas, joints, and the retina (macular degeneration). In the retina, excess iron can cause retinal toxicity through the generation of oxygen free radicals. Iron overload in the brain is seen in people with Alzheimer's disease, early onset Parkinson's disease, epilepsy, multiple sclerosis, and Huntington's disease.

PREVALENCE

Hemochromatosis is the most common genetic disorder in the western world. In the United States, Europe, Australia, New Zealand and other western countries there is approximately 1 case in 300 persons, mostly of northern European origin.

AGE AT FIRST MANIFESTATION

The first sign of hemochromatosis may go unnoticed for decades because it requires a blood test showing high iron blood levels, or more precisely, high transferrin saturation percentage and high ferritin levels, that show up in men over 40 and in women after menopause. Later, when physical symptoms of organ or joint damage begin, even then, you will be lucky indeed to have a physician who orders an iron panel to screen for hemochromatosis. File this for later reference and never be afraid to bring up the possibility of iron overload; insist on the test.

My brother, to whom this article is dedicated, was diagnosed by accident. He had an uncontrollable nosebleed that sent him to the ER. The physician stopped the nosebleed and sent blood to the lab asking for an iron panel because of concern for the blood loss. That was his first test ever for iron levels. They sent him home with a supply of iron
tablets to take every day. The next day they called and told him to stop taking the iron. His serum iron levels were off the charts. He had been accumulating iron with no means of off-loading for years. It was too late to repair the damage to his body. After decades of concatenating symptoms and seeing many physicians, any one of whom could have ordered an appropriate iron panel, he was finally diagnosed by accident. A scenario that is very difficult to live with. When caught early and treated effectively, damaged organs can heal, especially the liver, which is amazingly regenerative.

### EARLY SUBJECTIVE SIGNS AND SYMPTOMS

This disease is difficult to recognize by its physical signs and symptoms because of the number of organs and functions involved. Early signs and symptoms include:

- Joint pain (44%), including hand, wrist, knees, feet, back and neck
- Chronic Fatigue (74%)
- Impotence (45%)
- Lack of normal menstruation
- Abdominal pain
- High blood sugar levels
- Low thyroid function (hypothyroidism)

### BLOOD TESTS

Hemochromatosis is diagnosed at any stage with two fasting blood tests. Testing is crucial, as iron can build up to damaging levels in your body before symptoms appear. Ask the physician to write "copy to patient" on the lab order. Keep your own medical file on this.

- **Transferrin Saturation %**. (To achieve the percentage of saturation divide the serum iron (SI) into the total iron binding capacity (TIBC). This test is a more useful indicator of iron status than just SI or TIBC alone. It measures the amount of iron bound to a protein (transferrin) that carries iron in your blood. Iron Overload Diseases (IOD) Association safe range is 12-44%. The Iron Disorders Institute lists the normal range 25-35%.

- **Serum ferritin**. This test measures the amount of iron stored in your body, (whereas serum iron measures the level of iron in your blood.) Safe range listed by the IOD is 5-150 ng/mL. Whereas the Iron Disorders Institute lists the normal range of Ferritin for adult males as up to 300 ng/mL and for women up to 200 ng/mL. That 300 level for males differs greatly from that of the IOD, who list safe range as 5-150 ng/mL. One would hope for some agreement soon with the new research in progress in Europe and the U.S.

- **Note**. You may not be told to fast for the blood draw. Remember to do so. Additionally, for one week prior to the blood test, you should not be taking iron supplements or vitamin C, which enhances intestinal absorption of iron.
TREATMENT

This is a manageable condition. Treatment involves off-loading the iron by giving blood. At first, the blood letting is aggressive (weekly), but once the ferritin levels (reflecting iron storage) are at 10-15, you will be considered "de-ironed" and the schedule for blood-letting is much more tolerable, two or three times/year.

If your iron panel shows elevated Ferritin and Transferrin Saturation %, your physician will hopefully start a regimen of treatment. However, many physicians are uninformed about this genetic condition. So, for your own information and personal guidance, there are treatment and maintenance protocols on www.irondisorders.org or www.ironoverload.org.

Dr. Sharon Moalem, in his book, "Survival of the Sickest", relates the story of Aran Gordon, whose first nebulous symptoms began when he was training for the Marathon des Sables, a grueling 150-mile race across the Sahara Desert. For the next three years, Aran suffered through the uncertainty and frustration with a concatenation of health problems, laboratory tests, and one misdiagnosis after another until finally one physician ordered lab tests for transferrin saturation % and serum ferritin. Voilà! a correct diagnosis – hemochromatosis, so simple to diagnose, yet so unnecessarily illusive without those two simple laboratory tests.

Aran was told that without treatment he had five years to live. Many undiagnosed individuals or those who have been diagnosed too late (like my brother) to repair their ravaged bodies, live in pain and poor health for many more years than that. Once Aran's iron levels were under control, he went after the Marathon des Sables one more time a few months after he was supposed to have died. Aran was cured and healthy again through a carefully controlled regimen of bloodletting, one of the oldest of medical treatments.

ALREADY BEING TREATED BUT STILL CONFUSED?

For those of you who have already been diagnosed, but are uncertain about your treatment here is an article that I found very helpful.

http://bloodjournal.hematologylibrary.org/content/116/3/317.full

DNA TEST

DNA (deoxyribonucleic acid) codes genetic information for identification and for the transmission of diseases. If there is a family history of hemochromatosis, get a DNA test even if you are too young to have symptoms. If you have inherited this gene mutation, you can then be on the alert for an increase in iron levels above normal and start treatment before it becomes a burden. A significant number of people with the genetic
mutation for hemochromatosis do not have elevated blood iron levels. They are not symptomatic, but they are carriers, therefore their children and grandchildren should be alerted. For the details of the genetics of inheritance, [www.irondisorders.org](http://www.irondisorders.org) has excellent charts.

**INTERPRETIVE DATA FOR DNA HEMOCHROMATOSIS MUTATION DETECTION** (Genetics/Molecular Studies; Dominican Hospital, Santa Cruz, CA)

Hereditary hemochromatosis is an autosomal recessive disorder of iron metabolism that varies in clinical severity. Three mutations (H63D; C282Y; and S65C) have been described in the majority of patients with hemochromatosis.

**C282Y Homozygote.** Homozygosity for the C282Y mutation is responsible for up to 90% of the hemochromatosis patients. Penetrance of C282Y is under debate. Current studies estimate penetrance as 80% for men and 38% for women over 40. Additional studies estimate much lower penetrance for liver disease (about 1%).

**C282Y/H63D compound heterozygote.** A second mutation (H63D) has been described in some patients when inherited with the C282Y mutation as a compound heterozygote (C282Y/H63D). This genotype however has a reduced penetrance of less than 2%.

**C282Y/S65C compound heterozygote.** C282Y/S65C compound heterozygotes have also been reported, but the penetrance of this genotype is not known. It may contribute to a mild form of hemochromatosis.

**Heterozygotes for C282Y (C282Y/WT), H63D (H63D/WT), or S65C (S65C/WT) are not significantly associated with hemochromatosis, although other undetected mutations in combination with these mutations may contribute to symptoms of hemochromatosis.**

**Homozygous H63D** genotypes (H63D/H63D) rarely show symptoms of hemochromatosis, but several cases have been reported.

Mutations in unidentified genes or other mutations in the HFE gene, which may cause hemochromatosis, are not ruled out by this analysis.

**REFERENCES**


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