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HEMOCHROMATOSIS

Overview

Of all the minerals you need for good health, iron is one of the most familiar. After all, the producers of everything from breakfast cereals to vitamin tonics tell us that iron builds rich, red blood. Iron does help form oxygen-carrying hemoglobin in your red blood cells, but it's also essential for a number of other body processes, including proper brain function, a strong immune system and healthy muscles. Yet for people with hereditary [genetic] hemochromatosis (HH), even small amounts of iron can cause serious problems.

That's because this disorder causes your body to absorb too much iron from the food you eat. The excess is stored in your organs, especially your liver, heart and pancreas. Sometimes the stored iron damages these organs, leading to life-threatening conditions such as cancer, heart problems and liver disease.

Signs and symptoms of hemochromatosis usually appear in midlife, although they may occur earlier. The most common complaint is joint pain, but the disease can also cause a number of other symptoms, including fatigue, abdominal pain and impotence.

The encouraging news is that a simple and inexpensive test for hemochromatosis exists. What's more, hemochromatosis can be effectively treated by removing blood from your body to lower your level of iron.

Signs and symptoms

Although the genetic defect that causes hemochromatosis is present at birth, most people don't experience signs and symptoms until later in life — usually between the ages of 30 and 50 in men and after age 50 in women. Women are more likely to have symptoms after menopause, when they no longer lose iron with menstruation and pregnancy.

Some people with hemochromatosis never have symptoms. Others experience a wide range of problems. These can vary considerably from person to person and may be different for men and women. In addition, early signs and symptoms of hemochromatosis mimic those of many other common conditions, making hemochromatosis difficult to diagnose. They include:

- Arthritis, especially in your hands

- Chronic fatigue
- Loss of sex drive (libido) or impotence
- Lack of normal menstruation (amenorrhea)
- Abdominal pain
- High blood sugar levels
- Low thyroid function (hypothyroidism)
- Abnormal liver function tests, even if no other symptoms are present

In advanced stages of the disease, you may develop serious conditions such as:

- Cirrhosis — a condition marked by irreversible scarring of the liver
- Liver failure
- Liver cancer
- Diabetes
- Congestive heart failure
- Cardiac arrhythmia

Some people with advanced hemochromatosis develop a bronze color to their skin when iron deposits in the skin cells produce excess melanin — the pigment that gives skin its normal color. Visible iron deposits can also make skin appear gray.

Causes

Iron plays an essential role in the formation of both hemoglobin — a protein in red blood cells that transports oxygen from your lungs to all the tissues of your body — and myoglobin, a form of hemoglobin in your muscles. Iron is also necessary for energy production and a strong immune system and is a component of many important enzymes.

You normally consume about 10 milligrams (mg) of iron every day in the food you eat. Of that, your body absorbs about 1 mg, or 10 percent of the iron you ingest. Most of this is stored in the hemoglobin, but a small amount is stored in your bone marrow, spleen and liver. When these stores are adequate, your body reduces the amount of iron absorbed by your intestine so you don't accumulate excess amounts.

But if you have hemochromatosis, you may absorb as much as 20 percent of the iron you ingest. Because your body can't use or eliminate this extra iron, it's stored in the tissues of major organs, especially your liver. Eventually you may accumulate five to 20 times as much iron as normal. Over a period of years, the stored iron can severely damage many organs, leading to organ failure and chronic diseases such as cirrhosis and diabetes.

Although excess iron (iron overload) is a common problem, it's not always the result of hemochromatosis. Several factors, including frequent blood transfusions, high amounts of dietary iron and certain types of anemia, can cause excess iron in your body. People with chronic liver disease may also have increased iron levels. But in the United States, hemochromatosis is the most frequent cause of high blood iron levels.

The genetics of hemochromatosis

You have approximately 30,000 genes — information centers in your cells that control your body's growth, development and function. A mutation in just one gene can drastically alter the way your body works.

The gene that controls the amount of iron you absorb from food is called *HFE*. The *HFE* gene has two common mutations, C282Y and H63D. In the United States, approximately 85 percent of people with hemochromatosis have inherited two copies of C282Y — one from each parent.

Inheriting just one gene with the C282Y mutation means you're a carrier but aren't likely to develop the disease yourself, although you may absorb more iron than normal. About one in every 10 whites carries one gene for hemochromatosis. If both your parents are carriers, you have a 25 percent chance of inheriting two mutated genes.

A few people inherit one copy of C282Y and one of H63D. Of these, a small percentage develop symptoms of hemochromatosis. An even smaller number of people inherit two copies of H63D. Whether they're at risk of hemochromatosis is a matter of debate.

Complicating matters further, not everyone with two C282Y gene mutations develops problems with iron overload. Experts aren't sure of the exact number of people who do. Some believe it may be as little as 1 percent. Others place the percentage somewhere between 20 percent and 50 percent. It seems likely, however, that most people with hemochromatosis don't develop serious problems, although it's not possible to determine who will experience symptoms and who won't.

In addition, researchers continue to discover new proteins and genes that are responsible for rare cases of iron overload and that may lead to symptoms in people with *HFE*-related disease.

Other types of hemochromatosis

Other forms of hemochromatosis exist, including:

Juvenile hemochromatosis. This causes the same problems in young people that hereditary hemochromatosis causes in adults. But iron accumulation begins much earlier and symptoms usually appear by age 30. Common complications include diabetes; gonadal failure, which may lead to impotence, amenorrhea and infertility; an irregular heartbeat (heart arrhythmia); and heart failure — a condition in which your heart can't circulate enough blood to meet your body's needs. When not treated, juvenile hemochromatosis can be fatal. Although juvenile hemochromatosis is an inherited disease, the genetic abnormalities that cause it don't involve the *HFE* gene. Instead, it's caused by a mutation in a gene called hemojuvelin.

Neonatal hemochromatosis. In this severe disorder, iron builds up in a baby's liver so rapidly that he or she may be stillborn or die within a few days of birth. Just what causes neonatal hemochromatosis isn't known.

Risk factors

Having two copies of a mutated *HFE* gene is the greatest risk factor for hemochromatosis. Other risk factors include:

Family history. If you have a close relative, such as a parent or sibling, with hemochromatosis, you're more likely to develop the disease.

Ethnicity. People of Northern European descent — British, Dutch, German, Irish and French — are more prone to hemochromatosis than are people of other ethnic backgrounds. Hemochromatosis is less common in blacks, Hispanics and Asian-Americans.

Sex. Men are five times as likely as women are to develop iron overload, and they usually experience symptoms at an earlier age. Because women lose iron with menstruation and pregnancy, they tend to store less of the mineral than men do. After menopause or a hysterectomy, the risk for women increases.

Screening and diagnosis

Hemochromatosis can be difficult to diagnose. Early symptoms such as stiff joints and fatigue can result from a number of conditions that are more common than hemochromatosis. And in the latter stages of the disease, your doctor may focus on treating serious problems such as cirrhosis and heart disease rather than on checking for iron overload. But at any stage — even before symptoms appear — doctors can detect iron overload with two blood tests:

Serum transferrin saturation. This test measures the amount of iron bound to a protein (transferrin) that carries iron in your blood. Transferrin saturation values greater than 45 percent are considered too high.

Serum ferritin. This test measures the amount of iron stored in your body. If the results of your serum transferrin saturation test are higher than normal, your doctor will check your serum ferritin. Because a number of infectious and inflammatory conditions other than hemochromatosis also can cause elevated ferritin, both tests are needed to diagnose the disorder. You may need the tests repeated for the most accurate results.

Serum transferrin saturation and serum ferritin tests aren't a part of routine medical testing. Public health officials recommend that you be tested for hemochromatosis if you have a parent, child or sibling with the disease, or if you have any of the following signs and symptoms:

- Joint disease
- Severe fatigue

- Heart disease
- Elevated liver enzymes
- Impotence
- Diabetes

If you receive a diagnosis of hemochromatosis, your doctor may refer you to a specialist for one of the following:

Liver biopsy. Until recently, this test was the only way to confirm a diagnosis of hemochromatosis. During the procedure, your doctor removes a sample of tissue from your liver, using a thin needle. The sample is sent to a laboratory where it's checked for the presence of iron as well as for evidence of liver damage, especially scarring or cirrhosis. Needle biopsies are relatively simple procedures, requiring only local anesthesia. Risks include bruising, bleeding and infection.

Genetic testing. The discovery of the *HFE* gene made genetic testing for hemochromatosis possible. Some researchers advocate universal screening for *HFE* gene mutations. They point out that hemochromatosis is a common condition that can cause serious complications when it's not treated and that a simple, inexpensive and effective treatment exists.

Other doctors, as well as the Centers for Disease Control and Prevention and the U.S. Human Genome Research Project, recommend this type of testing only for adult family members of someone with hemochromatosis.

Public health officials put forth several reasons for this approach. First, because not all people with two defective *HFE* genes develop symptoms of hemochromatosis, knowing you have the mutated genes could cause unnecessary concern. Second, it's possible to have serious iron overload without *HFE* mutations. That means that a negative genetic test result isn't always a sign of good health. Privacy issues are also a major consideration with any kind of genetic testing. Not all states offer legal protections for people with hemochromatosis.

On the other hand, genetic testing can help confirm a diagnosis of hemochromatosis and in many cases may eliminate the need for a liver biopsy. And although genetic testing is substantially more expensive than blood iron screening, it's needed only once, whereas blood tests may be repeated every few years if you're at high risk of hemochromatosis.

If you're considering genetic testing for hemochromatosis, discuss the pros and cons carefully with your doctor or a genetic counselor.

Complications

Untreated, hemochromatosis can lead to a number of complications, especially in your joints and in organs where excess iron tends to be stored — your liver, pancreas and heart. Many of these complications are serious and some may be life-threatening:

Cirrhosis. Because your liver is a primary storage area for excess iron, it's especially likely to be damaged by long-term iron overload. Cirrhosis — permanent scarring of the liver — is just one of the problems that may occur. Cirrhosis itself may lead to serious complications including bleeding from dilated veins in your esophagus and stomach (varices) and severe fluid retention in your abdomen (ascites). Toxins that accumulate in your blood can affect your mental functioning, leading to confusion and even coma (hepatic encephalopathy). A number of factors other than hemochromatosis can also cause cirrhosis — the most common are long-term alcohol abuse and chronic hepatitis.

Liver cancer. If you have both cirrhosis and hemochromatosis, your risk of liver cancer increases greatly. Nearly one-third of people with hemochromatosis and cirrhosis eventually develop liver cancer. Because liver cancer must be diagnosed and treated early for the best outcome, your doctor will likely monitor you for any liver problems.

Diabetes. This disease affects the way your body uses blood sugar (glucose). Diabetes is the leading cause of new blindness in adults and can contribute to serious health problems such as kidney failure and cardiovascular disease.

Congestive heart failure. This potentially life-threatening condition may occur when excess iron in your heart interferes with its ability to circulate enough blood to meet your body's needs. Untreated congestive heart failure can be fatal, but the condition is often reversible when hemochromatosis is treated and excess iron stores reduced.

Heart arrhythmias. Abnormal heart rhythms can cause heart palpitations, chest pain and lightheadedness. In some cases, they may be life-threatening. Like congestive heart failure, arrhythmias can often be reversed with treatment for hemochromatosis.

Pigment changes. Deposits of iron in skin cells can turn your skin a bronze or gray color.

Treatment

Doctors can treat hemochromatosis safely and effectively by removing blood from your body (phlebotomy) on a regular basis, just as if you were donating blood. But in this case, the goal is to reduce your iron levels to normal. The amount of blood drawn depends on your age, your overall health and the severity of iron overload. Some people need many phlebotomies to achieve normal iron levels.

Initially, you may have a pint of blood taken once or twice a week — usually in a hospital or your doctor's office. This process shouldn't be uncomfortable. While you recline in a chair, a needle is inserted into a vein in your arm. The blood flows from the needle into a tube that's attached to a blood bag. Depending on your veins and the consistency of your blood, the time needed to remove a pint of blood can range from 10 minutes to 30 minutes.

Once your iron levels have returned to normal, you may only need to give blood about four times a year.

Donating your blood
Until recently, blood drawn from people with hemochromatosis was discarded. But in 1999, the Food and Drug Administration (FDA) ruled that hemochromatosis blood could be donated to blood banks that applied to the FDA for a variance. You can contact a blood bank in your area to see whether it participates in this program. Or check the American Hemochromatosis Society Web site for more information.

What you can expect from treatment
Treating hemochromatosis before damage to your organs has occurred prevents serious complications such as liver disease, heart disease and diabetes.

If you already have one of these conditions, phlebotomy may slow the progression of the disease, and in some cases even reverse it. People with cirrhosis are often monitored for liver cancer with an abdominal ultrasound and a test called an alpha-feto-protein blood test every six months.

Self-care

You can't prevent hemochromatosis, but if you have the disease, the following measures may help:

Avoid iron supplements and multiple vitamins containing iron. These can increase your iron levels even more. It's also best to avoid a diet high in iron-rich foods, such as red meat, dried peas and beans and iron-enriched breads, cereals and pastas.

Avoid taking vitamin C supplements, especially with food. Vitamin C increases absorption of iron. Try to drink vitamin C-rich juices, such as orange juice, between meals. Whole fruits and vegetables, though, are fine.

Avoid alcohol. Alcohol and iron combine to cause more liver damage.

Avoid eating raw shellfish. People with hemochromatosis are susceptible to infections, especially those caused by certain bacteria in raw shellfish.