Hemochromatosis

National Digestive Diseases Information Clearinghouse

National Institute of Diabetes and Digestive and Kidney Diseases

What is hemochromatosis?

Hemochromatosis is the most common form of iron overload disease. Too much iron in the body causes hemochromatosis. Iron is important because it is part of hemoglobin, a molecule in the blood that transports oxygen from the lungs to all body tissues. However, too much iron in the body leads to iron overload—a buildup of extra iron that, without treatment, can damage organs such as the liver, heart, and pancreas; endocrine glands; and joints.

The three types of hemochromatosis are primary hemochromatosis, also called hereditary hemochromatosis; secondary hemochromatosis; and neonatal hemochromatosis.

What causes hemochromatosis?

Primary Hemochromatosis

Inherited genetic defects cause primary hemochromatosis, and mutations in the *HFE* gene are associated with up to 90 percent of cases.[1] The *HFE* gene helps regulate the amount of iron absorbed from food. The two known mutations of *HFE* are *C282Y* and *H63D*. *C282Y* defects are the most common cause of primary hemochromatosis.

People inherit two copies of the *HFE* gene—one copy from each parent. Most people who inherit two copies of the *HFE* gene with the *C282Y* defect will have higher-than-average iron absorption. However, not all of these people will develop health problems associated with hemochromatosis. One recent study found that 31 percent of people with two copies of the *C282Y* defect developed health problems by their early fifties.[2] Men who develop health problems from *HFE* defects typically develop them after age 40.[1] Women who develop health problems from *HFE* defects typically develop them after menopause.[1]

People who inherit two *H63D* defects or one *C282Y* and one *H63D* defect may have higher-than-average iron absorption.[3] However, they are unlikely to develop iron overload and organ damage.

Rare defects in other genes may also cause primary hemochromatosis. Mutations in the *hemojuvelin* or *hepcidin* genes cause juvenile hemochromatosis, a type of primary hemochromatosis. People with juvenile hemochromatosis typically develop severe iron overload and liver and heart damage between ages 15 and 30.

Secondary Hemochromatosis

Hemochromatosis that is not inherited is called secondary hemochromatosis. The most common cause of secondary hemochromatosis is frequent blood transfusions in people with severe anemia. Anemia is a condition in which red blood cells are fewer or smaller than normal, which

means they carry less oxygen to the body's cells. Types of anemia that may require frequent blood transfusions include

- congenital, or inherited, anemias such as sickle cell disease, thalassemia, and Fanconi's syndrome
- severe acquired anemias, which are not inherited, such as aplastic anemia and autoimmune hemolytic anemia

Liver diseases—such as alcoholic liver disease, nonalcoholic steatohepatitis, and chronic hepatitis C infection—may cause mild iron overload. However, this iron overload causes much less liver damage than the underlying liver disease causes.

Neonatal Hemochromatosis

Neonatal hemochromatosis is a rare disease characterized by liver failure and death in fetuses and newborns. Researchers are studying the causes of neonatal hemochromatosis and believe more than one factor may lead to the disease.

Experts previously considered neonatal hemochromatosis a type of primary hemochromatosis. However, recent studies suggest genetic defects that increase iron absorption do not cause this disease. Instead, the mother's immune system may produce antibodies—proteins made by the immune system to protect the body from foreign substances such as bacteria or viruses—that damage the liver of the fetus. Women who have had one child with neonatal hemochromatosis are at risk for having more children with the disease.[4] Treating these women during pregnancy with intravenous (IV) immunoglobulin—a solution of antibodies from healthy people—can prevent fetal liver damage.[4]

Researchers supported by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) recently found that a combination of exchange transfusion—removing blood and replacing it with donor blood—and IV immunoglobulin is an effective treatment for babies born with neonatal hemochromatosis.[5]

Who is more likely to develop hemochromatosis?

Primary hemochromatosis mainly affects Caucasians of Northern European descent. This disease is one of the most common genetic disorders in the United States. About four to five out of every 1,000 Caucasians carry two copies of the *C282Y* mutation of the *HFE* gene and are susceptible to developing hemochromatosis.[1] About one out of every 10 Caucasians carries one copy of *C282Y*.[1]

Hemochromatosis is extremely rare in African Americans, Asian Americans, Hispanics/Latinos, and American Indians. *HFE* mutations are usually not the cause of hemochromatosis in these populations.

Both men and women can inherit the gene defects for hemochromatosis; however, not all will develop the symptoms of hemochromatosis. Men usually develop symptoms at a younger age than women. Women lose blood—which contains iron—regularly during menstruation; therefore, women with the gene defects that cause hemochromatosis may not develop iron overload and related symptoms and complications until after menopause.

What are the symptoms of hemochromatosis?

A person with hemochromatosis may notice one or more of the following symptoms:

- joint pain
- fatigue, or feeling tired
- unexplained weight loss
- abnormal bronze or gray skin color
- abdominal pain
- loss of sex drive

Not everyone with hemochromatosis will develop these symptoms.

What are the complications of hemochromatosis?

Without treatment, iron may build up in the organs and cause complications, including

- cirrhosis, or scarring of liver tissue
- diabetes
- irregular heart rhythms or weakening of the heart muscle
- arthritis
- erectile dysfunction

The complication most often associated with hemochromatosis is liver damage. Iron buildup in the liver causes cirrhosis, which increases the chance of developing liver cancer.

For some people, complications may be the first sign of hemochromatosis. However, not everyone with hemochromatosis will develop complications.

How is hemochromatosis diagnosed?

Health care providers use medical and family history, a physical exam, and routine blood tests to diagnose hemochromatosis or other conditions that could cause the same symptoms or complications.

- **Medical and family history.** Taking a medical and family history is one of the first things a health care provider may do to help diagnose hemochromatosis. The health care provider will look for clues that may indicate hemochromatosis, such as a family history of arthritis or unexplained liver disease.
- **Physical exam.** After taking a medical history, a health care provider will perform a physical exam, which may help diagnose hemochromatosis. During a physical exam, a health care provider usually
  - examines a patient's body
  - uses a stethoscope to listen to bodily sounds
  - taps on specific areas of the patient's body
- **Blood tests.** A blood test involves drawing blood at a health care provider's office or a commercial facility and sending the sample to a lab for analysis. Blood tests can determine whether the amount of iron stored in the body is higher than normal:[1]
  - The **transferrin saturation test** shows how much iron is bound to the protein that carries iron in the blood. Transferrin saturation values above or equal to 45 percent are considered abnormal.

– The **serum ferritin test** detects the amount of ferritin—a protein that stores iron—in the blood. Levels above 300 μg/L in men and 200 μg/L in women are considered abnormal. Levels above 1,000 μg/L in men or women indicate a high chance of iron overload and organ damage.

If either test shows higher-than-average levels of iron in the body, health care providers can order a special blood test that can detect two copies of the *C282Y* mutation to confirm the diagnosis. If the mutation is not present, health care providers will look for other causes.

- **Liver biopsy.** Health care providers may perform a liver biopsy, a procedure that involves taking a piece of liver tissue for examination with a microscope for signs of damage or disease. The health care provider may ask the patient to temporarily stop taking certain medications before the liver biopsy. The health care provider may ask the patient to fast for 8 hours before the procedure.

  During the procedure, the patient lies on a table, right hand resting above the head. The health care provider applies a local anesthetic to the area where he or she will insert the biopsy needle. If needed, a health care provider will also give sedatives and pain medication. The health care provider uses a needle to take a small piece of liver tissue. He or she may use ultrasound, computerized tomography scans, or other imaging techniques to guide the needle. After the biopsy, the patient must lie on the right side for up to 2 hours and is monitored an additional 2 to 4 hours before being sent home.

  A health care provider performs a liver biopsy at a hospital or an outpatient center. The health care provider sends the liver sample to a pathology lab where the pathologist—a doctor who specializes in diagnosing disease—looks at the tissue with a microscope and sends a report to the patient's health care provider. The biopsy shows how much iron has accumulated in the liver and whether the patient has liver damage.

Hemochromatosis is rare, and health care providers may not think to test for this disease. Thus, the disease is often not diagnosed or treated. The initial symptoms can be diverse, vague, and similar to the symptoms of many other diseases. Health care providers may focus on the symptoms and complications caused by hemochromatosis rather than on the underlying iron overload. However, if a health care provider diagnoses and treats the iron overload caused by hemochromatosis before organ damage has occurred, a person can live a normal, healthy life.

Who should be tested for hemochromatosis?

Experts recommend testing for hemochromatosis in people who have symptoms, complications, or a family history of the disease.

Some researchers have suggested widespread screening for the *C282Y* mutation in the general population. However, screening is not cost-effective. Although the *C282Y* mutation occurs quite frequently, the disease caused by the mutation is rare, and many people with two copies of the mutation never develop iron overload or organ damage.

Researchers and public health officials suggest the following:

- Siblings of people who have hemochromatosis should have their blood tested to see if they have the *C282Y* mutation.
- Parents, children, and other close relatives of people who have hemochromatosis should consider being tested.
- Health care providers should consider testing people who have severe and continuing fatigue, unexplained cirrhosis, joint pain or arthritis, heart problems, erectile dysfunction, or diabetes because these health issues may result from hemochromatosis.

How is hemochromatosis treated?

Health care providers treat hemochromatosis by drawing blood. This process is called phlebotomy. Phlebotomy rids the body of extra iron. This treatment is simple, inexpensive, and safe.

Based on the severity of the iron overload, a patient will have phlebotomy to remove a pint of blood once or twice a week for several months to a year, and occasionally longer. Health care providers will test serum ferritin levels periodically to monitor iron levels. The goal is to bring serum ferritin levels to the low end of the average range and keep them there. Depending on the lab, the level is 25 to 50 μg/L.

After phlebotomy reduces serum ferritin levels to the desired level, patients may need maintenance phlebotomy treatment every few months. Some patients may need phlebotomies more often. Serum ferritin tests every 6 months or once a year will help determine how often a patient should have blood drawn. Many blood donation centers provide free phlebotomy treatment for people with hemochromatosis.

Treating hemochromatosis before organs are damaged can prevent complications such as cirrhosis, heart problems, arthritis, and diabetes. Treatment cannot cure these conditions in patients who already have them at diagnosis. However, treatment will help most of these conditions improve. The treatment's effectiveness depends on

the degree of organ damage. For example, treating hemochromatosis can stop the progression of liver damage in its early stages and lead to a normal life expectancy. However, if a patient develops cirrhosis, his or her chance of developing liver cancer increases, even with phlebotomy treatment. Arthritis usually does not improve even after phlebotomy removes extra iron.

Eating, Diet, and Nutrition

Iron is an essential nutrient found in many foods. Healthy people usually absorb less than 10 percent of iron in the food they eat.[6] People with hemochromatosis absorb up to 30 percent of that iron.[6] People with hemochromatosis can help prevent iron overload by

- eating only moderate amounts of iron-rich foods, such as red meat and organ meat
- avoiding supplements that contain iron
- avoiding supplements that contain vitamin C, which increases iron absorption

People with hemochromatosis can take steps to help prevent liver damage, including

- limiting the amount of alcoholic beverages they drink because alcohol increases their chance of cirrhosis and liver cancer
- avoiding alcoholic beverages entirely if they already have cirrhosis

Points to Remember

- Hemochromatosis is the most common form of iron overload disease. Too much iron in the body causes hemochromatosis.
- Inherited genetic defects cause primary hemochromatosis.
- Primary hemochromatosis mainly affects Caucasians of Northern European descent.
- A person with hemochromatosis may notice one or more of the following symptoms: joint pain; fatigue, or feeling tired; unexplained weight loss; abnormal bronze or gray skin color; abdominal pain; and loss of sex drive. Not everyone with hemochromatosis will develop these symptoms.
- Without treatment, iron may build up in the organs and cause complications, including cirrhosis, diabetes, irregular heart rhythms or weakening of the heart muscle, arthritis, and erectile dysfunction.
- If a health care provider diagnoses and treats the iron overload caused by hemochromatosis before organ damage has occurred, a person can live a normal, healthy life.
- Experts recommend testing for hemochromatosis in people who have symptoms, complications, or a family history of the disease.
- Health care providers treat hemochromatosis by drawing blood. This process is called phlebotomy.

Hope through Research

The NIDDK's Division of Digestive Diseases and Nutrition supports research into diseases that affect the liver, including hemochromatosis.

Clinical trials are research studies involving people. Clinical trials look at safe and effective new ways to prevent, detect, or treat disease. Researchers also use clinical trials to look at other aspects of care, such as improving the quality of life for people with chronic illnesses. To learn more about clinical trials, why they matter, and how to participate, visit the NIH Clinical Research Trials and You website at *www.nih.gov/health/clinicaltrials.* For information about current studies, visit *www.ClinicalTrials.gov.*

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