What is hemochromatosis?
Hemochromatosis is a disease of iron overload (too much iron in the body). Normally, a small amount of iron is absorbed in the small intestine to provide what your body needs. Most of the iron from your food passes out through the stool. The body automatically controls how much iron is absorbed. This ensures that just the right amount of iron stays in your body. Iron is used by the body to maintain proper health and a small amount is stored for later use. Storage takes place in different parts of the body, such as the liver, heart, pancreas, skin, and joints. Hemochromatosis happens when too much iron is stored in the body.

How is hemochromatosis diagnosed?
The diagnosis of hemochromatosis is most often made by measuring the amount of iron in your blood using several laboratory tests:

- Serum iron
- Total iron-binding capacity (TIBC)
- Transferrin saturation (TS)
- Ferritin

These blood tests are usually all that is needed to diagnose iron overload. Rarely, a liver biopsy may be done to see if the liver is affected. The blood tests and liver biopsy can tell if there is too much iron in your body, but these tests do not explain why you have iron overload.

What causes hemochromatosis?
Hemochromatosis (iron overload) can happen in different ways.

**Acquired (or secondary) hemochromatosis**
Iron overload can happen when you get extra iron from an outside source, such as taking high doses of iron pills or getting frequent blood transfusions. Liver damage from alcohol and high fat levels can also affect iron levels. Acquired hemochromatosis does not run in families.

**Hereditary (or primary) hemochromatosis**
Hemochromatosis can also be inherited. You can have a genetic difference that causes the body to absorb too much iron from the food you eat. Over decades the amount of stored iron in your body can reach dangerous levels. For someone with hereditary hemochromatosis, environmental risks can also be important. For example, heavy alcohol use can cause iron overload to happen more quickly.

Hereditary hemochromatosis is caused by mutations (genetic changes) in a gene called HFE. Every person has two copies of the HFE gene, one copy from each parent. A genetic mutation in both copies of the HFE gene increases the amount of iron absorbed by the body and makes iron overload more likely to happen. There are more than 20 different HFE mutations that can cause hereditary hemochromatosis, but only two of the mutations are common.

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**Medical problems in hemochromatosis**

A build-up of iron in the body slowly causes damage and can lead to a variety of medical problems, such as:

- Fatigue
- Enlarged liver
- Low hormone levels
- Joint pain
- Liver failure
- Diabetes
- Loss of sex drive
- Heart disease
- Diabetes
- Changes in skin color (“bronzing”)
- Thyroid problems

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The information is not intended to diagnose health problems or to take the place of professional medical care. If you have persistent health problems or if you have further questions, please consult your health care provider.
How is hereditary hemochromatosis diagnosed?
Routine genetic testing can help diagnose hereditary hemochromatosis. Testing looks for the two most common mutations: C282Y and H63D. These two mutations are responsible for almost 90% of people with inherited causes of iron overload. Hereditary hemochromatosis is diagnosed when your blood tests show that you have iron overload AND you also carry two mutations in the HFE gene.

Can anyone have hereditary hemochromatosis?
Hereditary hemochromatosis has been reported in people throughout the world, but mutations in the HFE gene are much more common in the Northern European (Caucasian/White) population.

If I have a mutation in the HFE gene will I develop hemochromatosis?
Most people with HFE mutations never develop hemochromatosis. Severe iron overload due to the HFE gene is a very slow process that takes decades to develop. That means iron overload caused by HFE mutations does not affect children and often does not reach a critical point even for adults. Men are more likely to have problems from iron overload and may show symptoms between 40 and 60 years. Women are partly protected by blood loss through menstruation and are unlikely to show symptoms before menopause. The small chance for problems caused by iron overload is the reason for identifying and treating patients who carry two HFE mutations.

What should I do if I have two HFE mutations?
Someone with two HFE mutations should have iron studies done as needed to watch for signs of iron overload. For most people with two HFE mutations nothing more than blood monitoring is ever needed. Your doctor may recommend dietary changes as a way to slow iron build-up. A hepatitis vaccine may be recommended to protect the liver.

How is hereditary hemochromatosis treated?
Not everyone with hereditary hemochromatosis needs treatment. Treatment is done when iron tests reach critical levels. When treatment is needed, removing blood from the body is the best way to remove excess iron. Blood donation (phlebotomy) under the supervision of a health care provider is recommended for people with critical iron levels, or for people who are having health problems from iron overload. Blood donations are done on a regular schedule until iron levels return to normal. Then, additional blood donations are done as needed to maintain normal iron levels.

What do relatives need to know?
HFE mutations are inherited from your parents and can be passed to your children. Siblings (sisters or brothers) of a person diagnosed with hereditary hemochromatosis are the most likely to inherit two HFE mutations. Blood tests may be recommended depending on your age, gender, and relationship to the person with hereditary hemochromatosis. Since HFE-related hemochromatosis does not cause medical problems in childhood, testing is recommended only for family members 18 years of age or older. You may wish to talk with a genetic counselor about testing options.

References:
Up-To-Date - Clinical manifestations and diagnosis of hereditary hemochromatosis (2017)
What if genetic testing shows:

**C282Y/C282Y**

You have two C282Y mutations

About 1 in every 300 Caucasian people has C282Y/C282Y

- Blood tests often show much higher iron levels and you are more likely to develop iron overload.
- Your doctor should check your iron levels regularly as you get older.
- Avoid too much alcohol and foods high in iron, such as red meat (especially liver) and shellfish.
- Do not take vitamin C or iron supplements.
- About 1 in 5 men with C282Y/C282Y will need medical treatment for iron overload.
- About 1 in 50 women with C282Y/C282Y will need medical treatment for iron overload.

**C282Y/H63D**

You have one C282Y mutation and one H63D mutation

About 1 in every 150 Caucasian people has C282Y/H63D

- Blood tests may show high iron levels but you are unlikely to ever develop iron overload.
- Your doctor may want to recheck your iron levels as you get older.
- About 1 in 50 men with C282Y/H63D will need medical treatment for iron overload.
- Fewer than 1 in 100 women with C282Y/H63D will need medical treatment for iron overload.

**H63D/H63D**

You have two H63D mutations

About 1 in every 100 Caucasian people has H63D/H63D

- Blood tests may show high iron levels but you are extremely unlikely to ever develop iron overload.
- Your doctor may want to check your iron levels periodically.
- It is rare to develop iron overload unless there are other risk factors for hemochromatosis.

**C282Y/normal**

You have one C282Y mutation

About 1 in every 10 Caucasian people has C282Y/normal

- Blood tests rarely show high iron levels and you are extremely unlikely to ever develop iron overload.
- Follow-up blood tests are usually not needed.
- It is rare to develop iron overload without other risk factors for hemochromatosis.

**H63D/normal**

You have one H63D mutation

About 1 in every 5 Caucasian people has H63D/normal

- This does not increase your risk for iron overload.
- If iron overload happens, your doctor should look for other reasons for hemochromatosis.