Hereditary Hemochromatosis (HH)

What is hemochromatosis?

Hemochromatosis is a disease of iron overload (too much iron in the body). Normally, the small intestine absorbs all the iron you need. Any extra iron leaves your body through the stool (feces). The body controls exactly how much iron is kept. This keeps a steady amount of iron in your body. Iron is needed to stay healthy and a small amount is stored for later use. Iron can be stored in different parts of the body, such as the liver, heart, pancreas, skin, and joints. Hemochromatosis happens when too much iron gets stored in the body.

How is hemochromatosis diagnosed?

Hemochromatosis is usually diagnosed by measuring the amount of iron in your blood. Several laboratory tests may be done, including:

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

These blood tests are usually all that is needed to diagnose iron overload. Magnetic resonance imaging (MRI) may be done when blood tests show very high iron levels. MRI can estimate how much iron is stored in the body. Rarely, a liver biopsy may be done to measure iron levels in the liver and check for liver damage. These tests can diagnose iron overload, but they do not explain why you have too much iron.

What causes hemochromatosis?

Hemochromatosis (iron overload) can happen in different ways.

Acquired (or secondary) hemochromatosis

Iron overload can be caused by getting too much iron from an outside source. This could happen by taking too many iron pills or getting frequent blood transfusions. Liver damage from heavy alcohol use, a high fat diet, or a liver infection can also affect iron levels. This type of hemochromatosis does not run in families.

***Hereditary (or primary) hemochromatosis* (HH)**

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 can reach dangerous levels. Iron overload can happen faster in a person with HH if there are other risk factors, like taking iron pills, getting too much vitamin C, or having a liver infection.

HH 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 mutation in both copies of the *HFE* gene increases the amount of iron kept in the body and makes iron overload more likely to happen. There are more than 20 different *HFE* mutations that can cause HH, but only two of the mutations are common.

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	Thyroid problems
Changes in skin color (“bronzing”)		

How is hereditary hemochromatosis diagnosed?

Iron studies are usually done first. If there is too much iron, genetic testing is done to learn if a person has HH. HH is diagnosed when testing shows that a person has iron overload AND also has 2 mutations in the *HFE* gene. Genetic testing may be done first when there is a family history of HH. Genetic testing usually looks for the two most common mutations: C282Y and H63D. These mutations are found in 9 out of 10 people with HH.

Can anyone have hereditary hemochromatosis?

HH has been reported in people throughout the world, but mutations in the *HFE* gene are much more common in people with European (Caucasian/White) ancestry.

If I have a mutation in the *HFE* gene will I develop hemochromatosis?

Probably not. 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 does not reach a critical point for most adults. Men are more likely than women to develop iron-related problems. Symptoms may start between 40 and 60 years of age. Women who menstruate are partly protected by blood loss and are unlikely to show symptoms before menopause. The small chance for iron-related problems is the reason to learn who carries two HFE mutations.

What should I do if I have two *HFE* mutations?

Someone with two *HFE* mutations should have iron studies done to watch for signs of iron overload. For most people with two *HFE* mutations nothing more than blood testing is ever needed. Your doctor may recommend dietary changes to slow down iron build-up. A hepatitis vaccine may be recommended to protect the liver.

How is hereditary hemochromatosis treated?

Not everyone with HH needs treatment. Treatment is done when iron tests reach critical levels or when a person has iron-related health problems. When treatment is needed, removing blood from the body is the best way to remove excess iron. A doctor will recommend blood removal on a regular schedule until iron levels return to normal. Once the levels are normal, blood is removed as needed to keep iron levels steady.

What do relatives need to know?

HFE mutations are inherited from your parents and can be passed to your children. Brothers and sisters of a person with HH are the most likely relatives to inherit two *HFE* mutations. Blood tests may be recommended depending on age, biological sex, and the relationship to the person with HH. Testing is not needed before 18 years of age since HH does not cause problems in children.

References:

GeneReviews – *HFE*-associated hereditary hemochromatosis (2018)

Up-To-Date - Clinical manifestations and diagnosis of hereditary hemochromatosis (2021)

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 high 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.