Hereditary Haemochromatosis (HH)

Understanding the Genetics

This leaflet is written for people with hereditary haemochromatosis or people with a family history of hereditary haemochromatosis.

What is hereditary haemochromatosis?

Hereditary haemochromatosis (HH) is a treatable, inherited condition where the body absorbs too much iron from the diet. When too much iron builds up in the body, this is known as **iron overload**. The excess iron is stored in the liver and other organs of the body such as the pancreas, heart, endocrine (hormone producing) glands and joints.

Why is the amount of iron in the body important?

A small amount of iron is stored in the liver and is essential for health. It is needed when new red blood cells are formed. However when too much iron is stored in the liver, the liver may become enlarged and damaged. Excess iron may also be stored in other organs and joints, causing damage.

What causes hereditary haemochromatosis?

HH is most commonly caused by changes in a gene known as **HFE**.

We all have about 25,000 pairs of genes inside every cell of our body. Our genes act as instructions that tell our body how to grow and develop. We inherit one copy of each gene from our mother and one copy from our father. When we have children, we pass on one copy of each of our genes.

HH is a recessive condition. This means that people with HH have changes in both copies of their HFE gene. There are two common gene changes, known as C282Y and H63D.

What is the difference between C282Y and H63D?

C282Y/C282Y
People with two copies of C282Y are at risk of developing HH. However, many people with two copies of C282Y do not accumulate enough iron to become ill. Yearly blood tests are recommended to monitor iron levels, and early treatment offered if indicated.

C282Y/H63D
People with one copy of C282Y and one copy of H63D have a smaller risk of developing HH. It is recommended that iron levels are monitored every three years.

H63D/H63D
People with two copies of H63D are not likely to be at risk of developing iron overload. Therefore, no monitoring of iron levels is recommended.

HH Carrier
People with one copy of either C282Y or H63D, in combination with one unaltered copy of the HFE gene, are known as **carriers** of HH. Carriers are not likely to be at risk of developing iron overload. Therefore, no monitoring of iron levels is recommended.

As HH is genetic, there is more information about at-risk family members below.

How common are changes in the haemochromatosis gene?

The gene changes that cause HH are very common. Approximately 1 in 10 people of Northern European ancestry carry one copy of C282Y. This means about 1 in 300 people have two copies of C282Y and are at risk of developing HH.

Approximately 1 in 5 people of Northern European ancestry are thought to carry one copy of the milder H63D gene change.

How do you test if someone has hereditary haemochromatosis?

A simple gene test can determine if a person has HH and is at risk of developing iron overload. It identifies which versions of the HFE gene a person has.

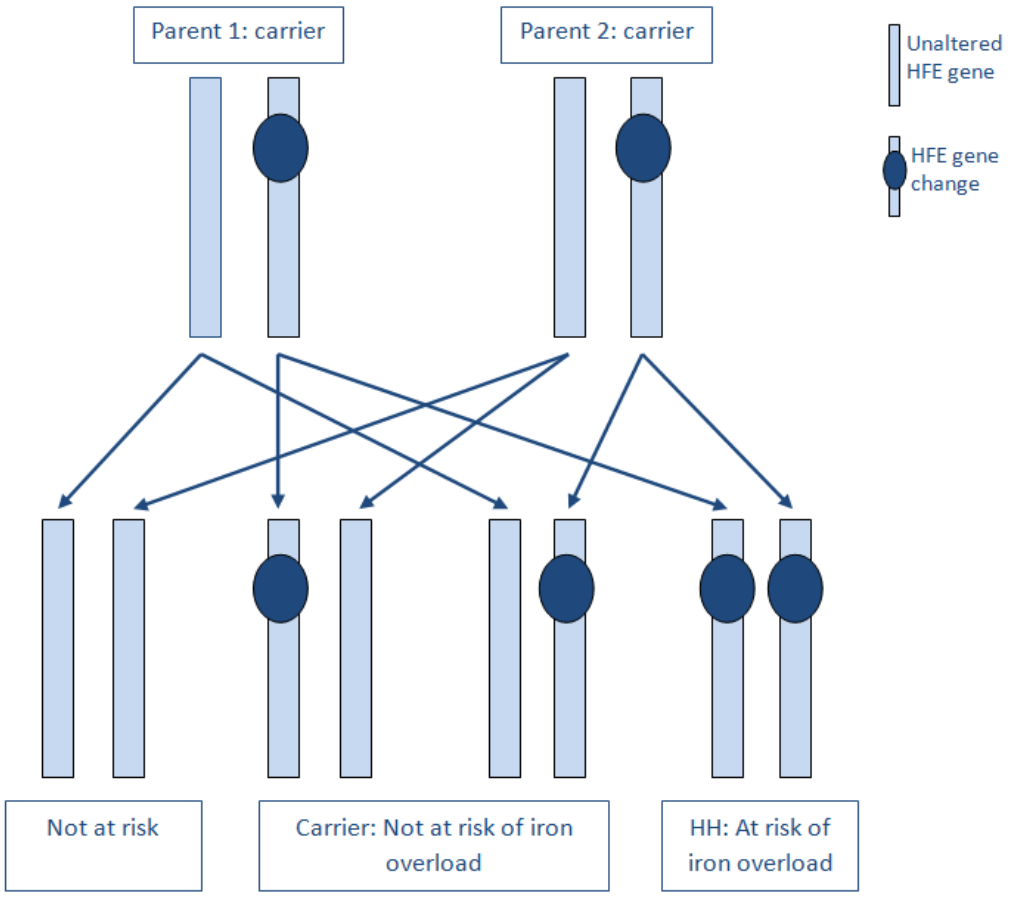
There are also blood tests (fasting serum ferritin and transferrin saturation) that check the amount of iron in the blood.

All of these tests can be carried out by your GP.

Who in the family is at risk of hereditary haemochromatosis?

People with HH have a change in both copies of their HFE gene. They have inherited an HFE gene change from both of their parents. This means that both **parents** of someone with HH will be carriers of HH. Occasionally a parent of someone with HH can have two HFE gene changes, meaning that they are also at risk of developing iron overload themselves.

When both parents are carriers (have one HFE gene change), each of their children has a 1 in 4 chance of having two HFE gene changes. This means that **siblings** of an individual with HH have a 1 in 4 (25%) chance of having HH and being at increased risk of developing iron overload in adulthood.



Each time two carriers have a child there will be a:

- 1 in 4 (25%) chance that both parents will pass on the gene change - the person will be at risk of developing iron overload in adulthood
- 1 in 2 (50%) chance that one parent will pass on the gene change and the other will pass on the unaltered gene - the person will be a carrier of HH and not at risk of iron overload in adulthood
- 1 in 4 (25%) chance that neither parent will pass on the gene change - the person will not be a carrier of HH and not at risk of iron overload in adulthood.

The chances are the same for each sibling.

Should my family members be offered the genetic test?

If your gene combination is as follows:

- **C282Y/C282Y** - your first degree relatives (parents, siblings and children) are recommended to seek advice from their local GP (family doctor). As HH is a condition that affects **adults**, testing is offered in adulthood. This is because there is no medical reason to be tested in childhood. If your children are adults and would like to find out for themselves, they should ask their GP about being tested.
- **C282Y/H63D, H63D/H63D and HH Carriers** - testing is not indicated for first degree relatives (parents, siblings and children).

Where can I find more information?

Haemochromatosis UK (www.haemochromatosis.org.uk)

If you have any questions, you can contact your Clinical Genetics Team on 0131 537 1116.

Remember:

- Carriers are **not** at risk of iron overload
- Not everyone with two altered gene copies develop iron overload or symptoms.