



What is Hereditary Haemochromatosis?

Hereditary Haemochromatosis (HH) is an inherited condition, whereby too much iron is absorbed from the diet. HH is also known as genetic iron overload, iron storage disease or HFE-associated hereditary haemochromatosis.

What is iron needed for?

Iron is an essential trace element needed for growth and development. It is also required by red blood cells to form a protein called haemoglobin, which carries oxygen in the blood.

What happens when too much iron is absorbed?

We all absorb iron from our diet. The body only absorbs the amount of iron that is required because it has no natural way of removing excess iron. Normally, the liver and other organs can store a small amount of excess iron safely. A person with haemochromatosis absorbs too much iron from their diet. Consequently, their iron stores keep rising. This iron is deposited in various organs, particularly the liver and heart, leading to serious tissue and organ damage. Without treatment, some patients may have premature death.

What are the symptoms?

Haemochromatosis affects everyone differently. Most people with haemochromatosis will never develop any symptoms. The diagnosis may be difficult because most of its symptoms are vague and can mimic the symptoms of many other conditions. In affected patients, symptoms do not appear until age 30 or 40 because iron builds up very slowly.

Early symptoms may include:

Sexual disorders: impotence in men, infertility and early menopause in women, *bronzing of the skin, or a permanent tan, fatigue, weakness, lethargy*

If haemochromatosis is not treated, the following conditions can occur:

Diabetes

Liver disorders: liver cirrhosis and liver cancer

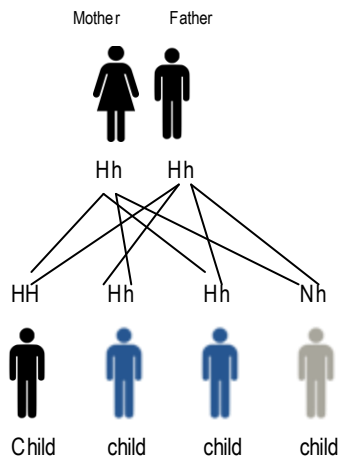
Cardiomyopathy: disease affecting the heart muscle

Arthritis

The need for treatment does not depend on the presence of symptoms. Anybody with this diagnosis should be treated to remove iron.

How is haemochromatosis inherited?

Inherited disorders are caused by defective (mutated) genes in cells. Genes are made of DNA (deoxyribonucleic acid), which contain the instructions for building proteins. In turn, proteins control the structure and function of all the cells that make up your body. Every cell (except sperm and egg cells) contains two copies of each gene, one inherited from the mother and one from the father.



H = Haemochromatosis gene mutation
h = normal gene

Hh = Haemachromatosis carrier
HH = Haemachromatosis patient
Nh = normal

The two important mutations in haemachromatosis are C282Y and H63D. C282Y is the most important and present in most patients. Haemachromatosis is in the HFE gene, a recessive gene disorder. For a person to be at risk of over absorbing iron and developing symptoms of haemachromatosis, he/she must have two copies of the mutated haemochromatosis (HFE) gene. If a person only has one mutated HFE gene, they are known as carriers. In the UK, about one in eight white people are carriers. Carriers do not develop the condition themselves, but may pass the mutated gene onto their children. If two carriers have a child, their child has a 50 per cent chance of inheriting one mutated HFE gene (i.e. becoming a carrier), and 25% chance of inheriting both mutated HFE genes.

What tests are done?

A number of tests are performed depending on the clinical situation.

- 1) Blood tests to measure the iron status at diagnosis and subsequently to monitor the effectiveness of treatment:

Transferrin Saturation (TS)

The transferrin saturation is a measure of the amount of iron carried on the iron transport protein, transferrin.

Serum Ferritin

This indicates the amount of iron stored in the body.

- 2) To confirm the diagnosis of haemochromatosis or to identify family members at risk of loading iron:

HFE Gene Test

A simple blood test for the HFE gene mutation is positive in over 90% of those affected.

To look for evidence of organ damage:



Liver function tests

Blood tests to look at the normal functions performed by the liver.

Fibroscan

This scan measures the stiffness of the liver, which is high if there is any cirrhosis present. It is not completely reliable, so if cirrhosis is suspected, a liver biopsy may be recommended.

Liver Biopsy

This involves removing a small piece of liver tissue with a special biopsy needle. This is then examined under a microscope, which allows assessment of the pattern and extent of iron overload and to look for liver damage, in particular scarring (cirrhosis). It can also exclude other causes of abnormal liver function. The determination of liver cirrhosis helps doctors make a more accurate prognosis, since liver cirrhosis may lead to liver cancer (hepatoma) at a later date. Patients with liver cirrhosis will be followed up more closely with a blood test for alpha-fetoprotein and ultrasound scan every six months to improve the chance of picking up hepatoma at a treatable stage. Because a small number of liver biopsy procedures are associated with morbidity and mortality, the procedure will be discussed with you by a gastroenterology doctor before you decide if you wish to go ahead.

Other tests for organ damage

These may include a random glucose level, thyroid function tests and a scan of the heart, depending on your symptoms.

What is the treatment?

The best method of removing excess iron from the body is by removal of blood. The process is called venesection or phlebotomy therapy, and is identical to giving a blood donation. Treatment is most effective when started early, to prevent or halt tissue and organ damage. Every pint of blood removed contains 250mg of iron. The body then mobilises the excess stored tissue iron to make new red blood cells, which are removed in subsequent phlebotomies.

How many phlebotomies will I need?

The number of phlebotomies varies from patient to patient depending on how much iron overload is present. Treatment may mean weekly phlebotomy for up to one or two years until the iron levels have been reduced to a safe level. Once the iron levels are back to a safe level, you will be put on a maintenance programme. During this time, blood to be removed 2-4 times yearly, depending on how quickly the iron reaccumulates. Because haemochromatosis is not curable, treatment will be needed for life.

How is my treatment monitored?

Treatment is monitored by measuring the remaining iron stores, using serum ferritin and/or transferrin saturation levels.