

What are the Implications for Other Family Members?

The information obtained from DNA testing of genetic diseases is relevant for the person being tested and also for other family members. If a mutation in the *HFE* gene is identified by the Hereditary Haemochromatosis gene test, an investigation of other family members may be appropriate, to determine if they may be at risk of developing iron overload.

Like all genetic tests, Hereditary Haemochromatosis gene testing is something that should be discussed with your Doctor. Your Doctor may provide or recommend counselling before or after this test to assist you with better understanding whether testing is appropriate for you and what the results may mean for you and your family.

What is the Treatment for Hereditary Haemochromatosis?

Treatment involves regular therapeutic venesection where blood is removed from the body to reduce the iron load. Early treatment can prevent tissue damage and lead to a normal life expectancy.

Why Will I Receive an Account?

Yes, you will receive an account and depending upon your clinical history Medicare may make a contribution toward the cost of the test. After the Medicare contribution, if any, there will still be an out-of-pocket charge (For details of the exact cost, see our Billing Guide for Out Patients, **My Pathology Test - What will it cost?**) owing for this test.

In line with our normal billing policy, if you are a Pensioner, current Health Care Cardholder, Veteran with a Gold Card or the resident of a Nursing Home, and you meet the Medicare criteria for a Medicare rebate for this test, you will be exempt from the out-of-pocket charge.

Hereditary Haemochromatosis Gene Test

Information for Patients



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What is Hereditary Haemochromatosis?

Hereditary Haemochromatosis is an inherited disease of iron metabolism and is caused by excessive absorption and storage of dietary iron. It is the most common inherited metabolic disorder in Caucasians, affecting 1 in every 200-300 individuals. The excessive iron build up in the body is termed 'iron overload.' Early diagnosis and management of the disease is important to prevent the increase in iron causing widespread tissue damage to vital organs.

What are the Signs and Symptoms?

Symptoms usually appear between the ages of 40-60 in men and after menopause in women. Severity of disease can vary greatly between individuals. Many patients go to see their Doctor complaining of subtle, nonspecific symptoms before the diagnosis of haemochromatosis is made. These symptoms might include tiredness, a discolouration or 'bronzing' of the skin, loss of libido and joint and abdominal pains.

What Pathology Tests are Usually Performed as the Initial Screen of Hereditary Haemochromatosis?

Most commonly your Doctor will consider a diagnosis of Haemochromatosis after looking at blood tests that assess your iron metabolism. These are usually referred to as "Iron Studies" and include Transferrin Saturation and a Serum Ferritin. Medicare currently require that patients have had at least 2 elevated Ferritin or Transferrin saturation levels or a first degree relative with Haemochromatosis before they will contribute to the cost of testing.

What is the Gene Test for Hereditary Haemochromatosis?

The gene test can be used to confirm the initial suspicion of Hereditary Haemochromatosis and can exclude other causes of iron overload. Alternatively, the test may be used before the disease is clinically evident in individuals with a family history of Hereditary Haemochromatosis.

Hereditary Haemochromatosis is a genetic disorder caused by small abnormal DNA variations in the *HFE* gene. These variations are termed mutations. Everyone has two copies of the *HFE* gene, one inherited from their mother and one from their father. Hereditary Haemochromatosis has a recessive inheritance pattern which means that patients need to have two mutations to be at risk of the condition, one mutation in each of the two copies of the *HFE* gene. If a person has only one mutation they are known as a carrier and are expected to be unaffected (see section on Carriers below).

The Hereditary Haemochromatosis gene test identifies the two most common mutations in the *HFE* gene called C282Y and H63D and the third less significant abnormal variant called S65C. The test requires patient DNA obtained from a blood sample. The DNA is screened for the known DNA mutations using specialised analytical techniques called polymerase chain reaction (PCR) and fluorescence monitoring using hybridization probes.

What do the Results Mean?

The majority of patients with Hereditary Haemochromatosis have two C282Y mutations and are termed homozygotes for this change. Patients who are homozygous for the C282Y mutation have the highest risk for clinically significant iron overload.

Other combinations of 2 abnormal variants can occur also. Some patients have one C282Y mutation and one H63D

mutation, or one C282Y mutation and one S65C mutation. These combinations are termed compound heterozygotes. These patients have a lower risk for clinically significant iron overload and are likely to have milder disease than C282Y homozygous patients.

The identification of two *HFE* gene mutations increases the risk of Hereditary Haemochromatosis but other factors are involved in iron accumulation and not all patients develop disease related to iron overload. Women have some level of protection due to menstrual blood loss and pregnancy. Therefore iron overload may not become evident until after menopause.

What does it Mean if I am a Carrier of Hereditary Haemochromatosis?

Approximately 1 in 10 individuals in the Australian population are carriers of Hereditary Haemochromatosis. Carriers have a single mutation in one *HFE* gene and do not usually develop clinical symptoms. Carriers have a 50% chance of passing the abnormal variant onto their children. However unless the child inherits another abnormal variant from their other parent, or develops a change spontaneously, they will also simply "carry" the abnormal gene.

What are the Limitations of the Test?

The gene test for Hereditary Haemochromatosis identifies the three most common *HFE* gene mutations (C282Y, H63D, and S65C) found in the majority of patients with Hereditary Haemochromatosis. However the diagnosis of Hereditary Haemochromatosis cannot be excluded even in the absence of these changes because there are a small number of patients who have other un-defined genetic abnormalities either in the *HFE* gene or other genes that are responsible for their iron overload. In these rare cases, patients are often reviewed by specialists and other investigations of the cause of iron overload may be considered.