Haemochromatosis Information Sheet 1

Haemochromatosis Australia
Inherited Iron overload disorder

Genetic Test Results and Haemochromatosis Mutations

What is your genotype?

We each have two copies of all genes: one from our mother's egg cell, and one from our father's sperm cell. In hereditary haemochromatosis, genes which regulate iron absorption and storage in the body don't work normally and this can lead to iron overload. These genetic mutations are inherited from our parents and can be passed on to our children.

The C282Y and H63D mutations in the HFE gene are the two common gene mutations that have been identified, and there are many more mutations that are very rare and more still that have not yet been identified.

The C282Y mutation is the "strongest" known HFE mutation. It causes a fault in an iron sensor in the body. One copy of this mutation isn't usually enough to cause problems, but when there are two copies of this mutation, the body thinks incorrectly that it is iron deficient, and inappropriately continually absorbs higher amounts of iron from the diet.

The H63D mutation is a "weak" mutation for iron overload, and is much less likely to cause iron overload, even if two copies exist.

The S65C mutation is not always routinely tested for and it is a "weak" mutation that rarely causes iron overload.

Blood Tests for Iron – TS and SF

If a person with hereditary haemochromatosis has iron overload, their blood test results are abnormally high for the transport protein called transferrin saturation (TS) and the iron storage protein

called serum ferritin (SF). This is due to their genetic mutations causing their body to transport more iron from their intestine to their bloodstream and store more iron in their liver.

If a person with hereditary haemochromatosis has a raised TS but normal SF, this is okay. The raised TS shows that the person is absorbing more iron from their food (due to their genetic mutations) but their normal SF shows that the amount of stored iron in their body isn't excessive.

If a person without hereditary haemochromatosis has a raised SF, there are many other common causes for high SF (such as drinking alcohol daily, being overweight/obese, having diabetes, liver disease, an inflammatory or infectious disease).

If someone has testing for hereditary haemochromatosis and their results show normal TS and a low risk HFE genotype, then even if they have a raised SF, they don't have hereditary haemochromatosis.

What is your genotype?

Two copies of C282Y mutation
Highest risk genotype.

Also known as
- C282Y homozygous
- C282Y homozygote
- C282Y/C282Y
- C282Y +/+

1 in 200 Caucasian Australians.
Highest genetic risk of developing iron overload.
Family members need testing for hereditary haemochromatosis.

One copy of C282Y mutation + one copy of H63D mutation
Medium risk genotype.

Also known as
- Compound heterozygous
- Compound heterozygote
- C282Y/H63D

1 in 50 Caucasian Australians.
Medium genetic risk of developing iron overload.
Family members need testing for hereditary haemochromatosis.

One copy of C282Y mutation
Low risk genotype.

Also known as
- C282Y carrier
- C282Y +/-

1 in 8 Caucasian Australians.
Low genetic risk of developing iron overload.
If TS <45% and SF is raised, this is usually due to alcohol use, obesity, diabetes, liver disease, infection or inflammation rather than iron overload.

Two copies of H63D mutation
Low risk genotype.

Also known as
- H63D homozygous
- H63D homozygote
- H63D/H63D
- H63D +/+

1 in 50 Caucasian Australians.
If TS <45% and SF is raised, this is usually due to alcohol use, obesity, diabetes, liver disease, infection or inflammation rather than iron overload.

One copy of H63D mutation
Low risk genotype

Also known as
- H63D carrier
- H63D +/-

1 in 4 Caucasian Australians.
If TS <45% and SF is raised, this is usually due to alcohol use, obesity, diabetes, liver disease, infection or inflammation rather than iron overload.

No mutations
Low risk genotype

Also known as Wildtype.

2 in 3 Caucasian Australians.
If TS <45% and SF is raised, this is usually due to alcohol use, obesity, diabetes, liver disease, infection or inflammation rather than iron overload.

Haemochromatosis Australia
Inherited Iron overload disorder

Web: www.ha.org.au
Email: admin@ha.org.au
INFO LINE 1300 019 028
/haemochromatosis
@HaemAus
/HaemochromatosisAust