Hemochromatosis is the most common genetic disease so far identified, with around 1 in 200 people severely affected. Most people with Hemochromatosis have mutations in the HFE gene, discovered in 1996.

Hereditary Hemochromatosis is classified by type depending on the age of onset and other factors such as genetic cause and mode of inheritance.

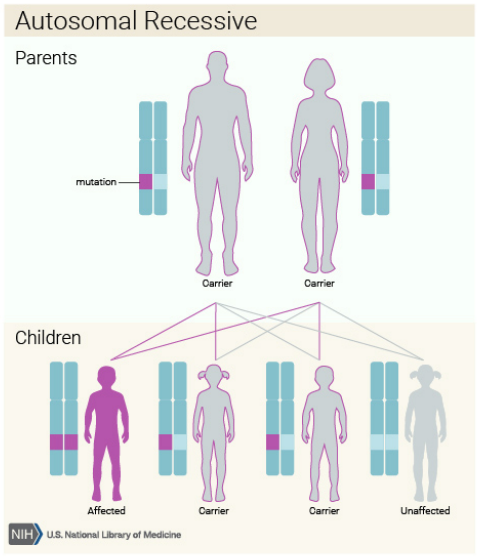
Type 1, the most common form of the disorder, is caused by a mutation in the HFE gene and begins in adulthood. Men with type 1 Hemochromatosis typically develop symptoms between the ages of 40 and 60, and women usually develop symptoms after menopause.

Type 2 Hemochromatosis is a juvenile-onset disorder, caused by mutations in the HAMP or HJV genes. Iron accumulation begins early in life, and symptoms may appear in childhood. By age 20, decreased or absent secretion of sex hormones is evident. Females usually begin menstruation in a normal manner, but menses stop after a few years. Males may experience delayed puberty or symptoms related to a shortage of sex hormones. If the disorder is untreated, heart disease becomes evident by age 30.

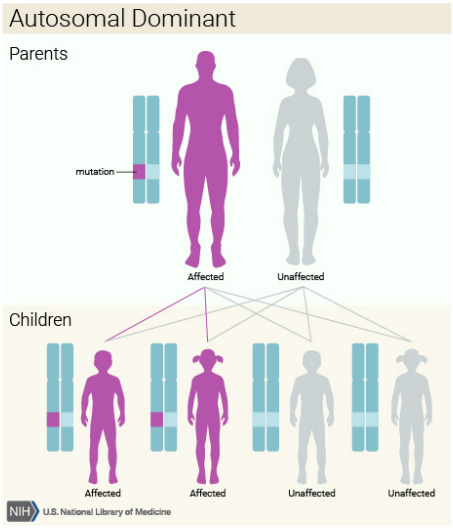
Type 3 Hemochromatosis is characterised by intermediate onset, between types 1 and 2 and is caused by mutation in the TFR2 gene. Symptoms of type 3 Hemochromatosis generally begin before age 30.

Type 4, also called Ferroportin disease, is caused by a mutation in the SLC40A1 gene and also begins in adulthood. Men with type 4 Hemochromatosis typically develop symptoms between the ages of 40 and 60, and women usually develop symptoms after menopause.

Types 1, 2, and 3 Hemochromatosis are inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. Most often, the parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene but do not show signs and symptoms of the condition.



Type 4 hemochromatosis is distinguished by its autosomal dominant inheritance pattern. With this type of inheritance, one copy of the altered gene in each cell is sufficient to cause the disorder. In most cases, an affected person has one parent with the condition.



Most patients with severe hemochromatosis are homozygous for the major C282Y mutation of the HFE gene. This mutation has an allelic frequency of 1-15% in Caucasian populations, being frequent in populations of Celtic ancestry but less common in Mediterranean countries.

The second common mutation is H63D (allelic frequency 10-20%), which usually has less severe effects on iron status than C282Y. Many homozygotes and some heterozygotes, particularly C282Y/H63D compound heterozygotes, will develop clinical Hemochromatosis with aging. Overall estimates suggest 20-40% of people with European ancestry carry at least one mutant HFE allele. Because these mutations are so common, a significant percentage of people can be expected to carry one or more HFE mutations.