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Gene test information

HEREDITARY HEMOCHROMATOSIS (HFE GENE TEST)

- **Background**

  Hereditary hemochromatosis is characterized by inappropriately high absorption of iron by the gastrointestinal mucosa, resulting in excessive storage of iron particularly in the liver, skin, pancreas, heart, joints, and testes. Abdominal pain, weakness, lethargy, and weight loss are early symptoms. Without therapy, males may develop symptoms between age 40 and 60 years and females after menopause. Hepatic fibrosis or cirrhosis may occur in untreated individuals after age 40 years. Other findings in untreated individuals may include progressive increase in skin pigmentation, diabetes mellitus, congestive heart failure and/or arrhythmias, arthritis, and hypogonadism.

  The diagnosis of hereditary hemochromatosis is typically based on the results of the screening tests transferrin-iron saturation and serum ferritin concentration, and of confirmatory tests such as molecular genetic testing for the C282Y and HFE H63D mutations in the HFE gene. About 87% of individuals of European origin with hereditary hemochromatosis are either homozygotes for the C282Y mutation or compound heterozygotes for the C282Y and H63D mutations.

- **HFE genotypes**

HFE C282Y and H63D genotypes	Commentary
HFE 282 YY	This genotype is consistent with a diagnosis of hereditary hemochromatosis. In asymptomatic patients, indices of iron overload (serum transferrin saturation and ferritin) should be monitored regularly
HFE 282 CY + HFE 63 HD (compound heterozygous)	This genotype is consistent with the presence of iron overload and may be diagnostic of hereditary hemochromatosis once all other reasons for iron overload have been excluded (e.g. alcohol consumption, hepatitis C, hyperferritinaemia).
All other genotypes:	All other HFE genotypes make a diagnosis of hereditary hemochromatosis very unlikely and such a diagnosis can only be made on a clinical basis.

- **Indications for testing**

  - Confirmation of hereditary hemochromatosis in patients with elevated transferrin saturation or serum ferritin level
  - First-degree relative with hereditary hemochromatosis
  - First-degree relative with susceptibility to hereditary hemochromatosis (homozygosity for 282Y mutation or compound heterozygous for 282Y and 63D)

References:

Bomford A. Genetics of haemochromatosis. Lancet 2002; 360: 1673–81.

Yen AW et al. Revisiting Hereditary Hemochromatosis: Current Concepts and Progress. Am J Med 2006;119:391-9.

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