Hereditary hemochromatosis

Hereditary hemochromatosis is a disorder that causes the body to absorb too much iron from the diet. The excess iron is stored in the body's tissues and organs, particularly the skin, heart, liver, pancreas, and joints. Because humans cannot increase the excretion of iron, excess iron can overload and eventually damage tissues and organs. For this reason, hereditary hemochromatosis is also called an iron overload disorder.

Early symptoms of hereditary hemochromatosis are nonspecific and may include fatigue, joint pain, abdominal pain, and loss of sex drive. Later signs and symptoms can include arthritis, liver disease, diabetes, heart abnormalities, and skin discoloration. The appearance and progression of symptoms can be affected by environmental and lifestyle factors such as the amount of iron in the diet, alcohol use, and infections.

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, and type 4 (also called ferroportin disease) begin in adulthood. Men with type 1 or type 4 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. 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.

The onset of type 3 hemochromatosis is usually intermediate between types 1 and 2. Symptoms of type 3 hemochromatosis generally begin before age 30.

Frequency

Type 1 hemochromatosis is one of the most common genetic disorders in the United States, affecting about 1 million people. It most often affects people of Northern European descent. The other types of hemochromatosis are considered rare and have been studied in only a small number of families worldwide.

Genetic Changes

Mutations in several genes, including *HAMP*, *HFE*, *HJV*, *SLC40A1*, and *TFR2*, can cause hereditary hemochromatosis. Type 1 hemochromatosis results from mutations in the *HFE* gene, and type 2 hemochromatosis results from mutations in either the *HJV* or *HAMP* gene. Mutations in the *TFR2* gene cause type 3 hemochromatosis, and mutations in the *SLC40A1* gene cause type 4 hemochromatosis.

The proteins produced from these genes play important roles in regulating the absorption, transport, and storage of iron. Mutations in any of these genes impair the control of iron absorption during digestion and alter the distribution of iron to other parts of the body. As a result, iron accumulates in tissues and organs, which can disrupt their normal functions.

Inheritance Pattern

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.

Other Names for This Condition

- bronze diabetes
- bronzed cirrhosis
- familial hemochromatosis
- genetic hemochromatosis
- haemochromatosis
- HC
- hemochromatosis
- hereditary haemochromatosis
- HH
- HLAH
- iron storage disorder
- pigmentary cirrhosis
- primary hemochromatosis
- Troisier-Hanot-Chauffard syndrome
- Von Recklenhausen-Applebaum disease

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Hemochromatosis type 2A
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1865614/
- Genetic Testing Registry: Hemochromatosis type 3
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1858664/
- Genetic Testing Registry: Hemochromatosis type 4
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1853733/
- Genetic Testing Registry: Hereditary hemochromatosis
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0392514/

Other Diagnosis and Management Resources

- GeneReview: HFE-Associated Hereditary Hemochromatosis
  https://www.ncbi.nlm.nih.gov/books/NBK1440
- GeneReview: Juvenile Hereditary Hemochromatosis
  https://www.ncbi.nlm.nih.gov/books/NBK1170
- GeneReview: TFR2-Related Hereditary Hemochromatosis
  https://www.ncbi.nlm.nih.gov/books/NBK1349
- MedlinePlus Encyclopedia: Hemochromatosis
  https://medlineplus.gov/ency/article/000327.htm

General Information from MedlinePlus

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html

Additional Information & Resources

MedlinePlus

- Encyclopedia: Hemochromatosis
  https://medlineplus.gov/ency/article/000327.htm
- Health Topic: Hemochromatosis
  https://medlineplus.gov/hemochromatosis.html

Genetic and Rare Diseases Information Center

- Hemochromatosis
  https://rarediseases.info.nih.gov/diseases/10746/hemochromatosis
- Hemochromatosis type 1
  https://rarediseases.info.nih.gov/diseases/10417/hemochromatosis-type-1
- Hemochromatosis type 2
  https://rarediseases.info.nih.gov/diseases/10092/hemochromatosis-type-2
- Hemochromatosis type 3
  https://rarediseases.info.nih.gov/diseases/10093/hemochromatosis-type-3
- Hemochromatosis type 4
  https://rarediseases.info.nih.gov/diseases/10094/hemochromatosis-type-4

Additional NIH Resources

- National Human Genome Research Institute
  https://www.genome.gov/10001214/learning-about-hereditary-hemochromatosis/
- National Institute of Diabetes and Digestive and Kidney Diseases
  https://www.niddk.nih.gov/health-information/liver-disease/hemochromatosis
- Office of Dietary Supplements: Iron
  https://ods.od.nih.gov/factsheets/Iron-HealthProfessional/

Educational Resources

- Centre for Genetics Education (Australia)
  http://www.genetics.edu.au/publications-and-resources/facts-sheets/fact-sheet-47-hereditary-haemochromatosis
- MalaCards: juvenile hereditary hemochromatosis
  http://www.malacards.org/card/juvenile_hereditary_hemochromatosis
- My46 Trait Profile
  https://www.my46.org/trait-document?trait=HFE-associated%20Hereditary%20Hemochromatosis&type=profile
- Orphanet: Hemochromatosis type 1
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=139498

- Orphanet: Hemochromatosis type 2
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=79230
- Orphanet: Hemochromatosis type 3
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=225123
- Orphanet: Hemochromatosis type 4
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=139491
- Your Genes Your Health from Cold Spring Harbor Laboratory
  http://www.ygyh.org/hc/whatisit.htm

Patient Support and Advocacy Resources

- American Hemochromatosis Society
  http://www.americanhs.org/
- American Liver Foundation
  http://www.liverfoundation.org/aboutheliver/info/hemochromatosis/
- Haemochromatosis Australia
  https://haemochromatosis.org.au/
- National Organization for Rare Disorders (NORD): Classic Hereditary Hemochromatosis
  https://rarediseases.org/rare-diseases/classic-hereditary-hemochromatosis/
- National Organization for Rare Disorders (NORD): Juvenile Hemochromatosis
  https://rarediseases.org/rare-diseases/juvenile-hemochromatosis/

GeneReviews

- HFE-Associated Hereditary Hemochromatosis
  https://www.ncbi.nlm.nih.gov/books/NBK1440
- Juvenile Hereditary Hemochromatosis
  https://www.ncbi.nlm.nih.gov/books/NBK1170
- TFR2-Related Hereditary Hemochromatosis
  https://www.ncbi.nlm.nih.gov/books/NBK1349

ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22hemochromatosis%22

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28Hemochromatosis%5BMAJR%5D%29+AND+%28%28hemochromatosis%5BTI%5D%29+OR+%28haemochromatosis%5BTI%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+720+days%22%5Bdp%5D

OMIM

- HEMOCHROMATOSIS, TYPE 1
  http://omim.org/entry/235200
- HEMOCHROMATOSIS, TYPE 2A
  http://omim.org/entry/602390
- HEMOCHROMATOSIS, TYPE 3
  http://omim.org/entry/604250
- HEMOCHROMATOSIS, TYPE 4
  http://omim.org/entry/606069

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