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 may include extreme tiredness (fatigue), joint pain, abdominal pain, weight loss, and loss of sex drive. As the condition worsens, affected individuals may develop arthritis, liver disease (cirrhosis) or liver cancer, diabetes, heart abnormalities, or skin discoloration. The appearance and severity of symptoms can be affected by environmental and lifestyle factors such as the amount of iron in the diet, alcohol use, and infections.

There are four types of hereditary hemochromatosis, which are classified 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 known as a juvenile-onset disorder because symptoms often begin in childhood. By age 20, iron accumulation causes decreased or absent secretion of sex hormones. Affected females usually begin menstruation normally but menses stop after a few years. Males may experience delayed puberty or symptoms related to a shortage of sex hormones. If type 2 hemochromatosis is untreated, potentially fatal heart disease becomes evident by age 30.

The onset of type 3 hemochromatosis is usually intermediate between types 1 and 2 with symptoms generally beginning 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.

Causes

Mutations in several genes 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 in the body. Mutations in any of these genes impair the control of the intestine’s absorption of iron from foods 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

Formal Diagnostic Criteria

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/21452290
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3149125/

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/26153218
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4929861/

Formal Treatment/Management Guidelines

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/21452290
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3149125/

Genetic Testing Information

- What is genetic testing? /primer/testing/genetictesting

- Genetic Testing Registry: Hereditary hemochromatosis

Research Studies from ClinicalTrials.gov

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

Other Diagnosis and Management Resources

- GeneReview: HFE Hemochromatosis
  https://www.ncbi.nlm.nih.gov/books/NBK1440

- GeneReview: Juvenile Hemochromatosis
• GeneReview: TFR2-Related Hereditary Hemochromatosis
  https://www.ncbi.nlm.nih.gov/books/NBK1349

• MedlinePlus Encyclopedia: Hemochromatosis
  https://medlineplus.gov/ency/article/000327.htm

Additional Information & Resources

Health Information from MedlinePlus

• Encyclopedia: Hemochromatosis
  https://medlineplus.gov/ency/article/000327.htm

• Health Topic: Hemochromatosis
  https://medlineplus.gov/hemochromatosis.html

• Medical Tests: Iron Tests
  https://medlineplus.gov/lab-tests/iron-tests/

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

• 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/Genetic-Disorders/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
Educational Resources

- Centers for Disease Control and Prevention
  https://www.cdc.gov/features/hereditary-hemochromatosis/

- Centre for Genetics Education (Australia)

- MalaCards: juvenile hereditary hemochromatosis
  https://www.malacards.org/card/juvenile_hereditary_hemochromatosis

- Orphanet: Hemochromatosis type 1
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=139498

- Orphanet: Hemochromatosis type 2
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=79230

- Orphanet: Hemochromatosis type 3
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=225123

- Orphanet: Hemochromatosis type 4
  https://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

- Your Genome from Wellcome Genome Campus
  https://www.yourgenome.org/facts/what-is-hereditary-haemochromatosis

Patient Support and Advocacy Resources

- American Liver Foundation
  https://liverfoundation.org/for-patients/about-the-liver/diseases-of-the-liver/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/
Clinical Information from GeneReviews

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

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+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+720+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- HEMOCHROMATOSIS, TYPE 1
  http://omim.org/entry/235200
- HEMOCHROMATOSIS, TYPE 2A
  http://omim.org/entry/602390
- HEMOCHROMATOSIS, TYPE 2B
  http://omim.org/entry/613313
- HEMOCHROMATOSIS, TYPE 3
  http://omim.org/entry/604250
- HEMOCHROMATOSIS, TYPE 4
  http://omim.org/entry/606069

Medical Genetics Database from MedGen

- Hereditary hemochromatosis

Sources for This Summary

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/29158016

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/10802645

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/23418762

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/29423808

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/11518736 
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC209405/

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/11431687

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20542038

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/29722188

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