Hereditary fructose intolerance

Hereditary fructose intolerance is a condition that affects a person's ability to digest the sugar fructose. Fructose is a simple sugar found primarily in fruits. Affected individuals develop signs and symptoms of the disorder in infancy when fruits, juices, or other foods containing fructose are introduced into the diet. After ingesting fructose, individuals with hereditary fructose intolerance may experience nausea, bloating, abdominal pain, diarrhea, vomiting, and low blood sugar (hypoglycemia). Affected infants may fail to grow and gain weight at the expected rate (failure to thrive).

Repeated ingestion of fructose-containing foods can lead to liver and kidney damage. The liver damage can result in a yellowing of the skin and whites of the eyes (jaundice), an enlarged liver (hepatomegaly), and chronic liver disease (cirrhosis). Continued exposure to fructose may result in seizures, coma, and ultimately death from liver and kidney failure. Due to the severity of symptoms experienced when fructose is ingested, most people with hereditary fructose intolerance develop a dislike for fruits, juices, and other foods containing fructose.

Hereditary fructose intolerance should not be confused with a condition called fructose malabsorption. In people with fructose malabsorption, the cells of the intestine cannot absorb fructose normally, leading to bloating, diarrhea or constipation, flatulence, and stomach pain. Fructose malabsorption is thought to affect approximately 40 percent of individuals in the Western hemisphere; its cause is unknown.

Frequency

The incidence of hereditary fructose intolerance is estimated to be 1 in 20,000 to 30,000 individuals each year worldwide.

Causes

Mutations in the ALDOB gene cause hereditary fructose intolerance. The ALDOB gene provides instructions for making the aldolase B enzyme. This enzyme is found primarily in the liver and is involved in the breakdown (metabolism) of fructose so this sugar can be used as energy. Aldolase B is responsible for the second step in the metabolism of fructose, which breaks down the molecule fructose-1-phosphate into other molecules called glyceraldehyde and dihydroxyacetone phosphate.

ALDOB gene mutations reduce the function of the enzyme, impairing its ability to metabolize fructose. A lack of functional aldolase B results in an accumulation of fructose-1-phosphate in liver cells. This buildup is toxic, resulting in the death of liver cells over time. Additionally, the breakdown products of fructose-1-phosphate are needed in the body to produce energy and to maintain blood sugar levels. The
combination of decreased cellular energy, low blood sugar, and liver cell death leads to the features of hereditary fructose intolerance.

Inheritance Pattern
This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition
• ALDOB deficiency
• aldolase B deficiency
• fructose-1-phosphate aldolase deficiency
• fructose-1,6-bisphosphate aldolase deficiency
• fructose aldolase B deficiency
• fructose intolerance
• fructosemia

Diagnosis & Management
Genetic Testing Information
• What is genetic testing?
  /primer/testing/genetictesting
• Genetic Testing Registry: Hereditary fructosuria

Research Studies from ClinicalTrials.gov
• ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22hereditary+fructose+intolerance%22+OR+%22Fructose+Metabolism%2C+Inborn+Errors%22+OR+%22Fructose+Intolerance%22

Other Diagnosis and Management Resources
• Boston University: Specifics of Hereditary Fructose Intolerance and Its Diagnosis
  http://www.bu.edu/aldolase/HFI/hfiinfo/detail.html
• GeneReview: Hereditary Fructose Intolerance
  https://www.ncbi.nlm.nih.gov/books/NBK333439
• MedlinePlus Encyclopedia: Hereditary Fructose Intolerance
  https://medlineplus.gov/ency/article/000359.htm
Additional Information & Resources

Health Information from MedlinePlus

• Encyclopedia: Hereditary Fructose Intolerance
  https://medlineplus.gov/ency/article/000359.htm

• Health Topic: Carbohydrate Metabolism Disorders
  https://medlineplus.gov/carbohydratemetabolismdisorders.html

Genetic and Rare Diseases Information Center

• Hereditary fructose intolerance
  https://rarediseases.info.nih.gov/diseases/6622/hereditary-fructose-intolerance

Additional NIH Resources

• National Institute of Diabetes and Digestive and Kidney Diseases: Low Blood Glucose (Hypoglycemia)
  https://www.niddk.nih.gov/health-information/diabetes/overview/preventing-problems/low-blood-glucose-hypoglycemia

Educational Resources

• Boston University: Specifics of Hereditary Fructose Intolerance and Its Diagnosis
  http://www.bu.edu/aldolase/HFI/hfiinfo/detail.html

• MalaCards: fructose intolerance, hereditary
  https://www.malacards.org/card/fructose_intolerance_hereditary

• Merck Manual Consumer Version: Overview of Hereditary Metabolic Disorders

• Orphanet: Hereditary fructose intolerance
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=469

Patient Support and Advocacy Resources

• American Liver Foundation: Cirrhosis
  https://liverfoundation.org/for-patients/about-the-liver/diseases-of-the-liver/cirrhosis/

• Metabolic Support UK
  https://www.metabolicsupportuk.org/

• National Organization for Rare Disorders (NORD)
  https://rarediseases.org/rare-diseases/fructose-intolerance-hereditary/

Clinical Information from GeneReviews

• Hereditary Fructose Intolerance
  https://www.ncbi.nlm.nih.gov/books/NBK333439
Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28Fructose+Intolerance%5BMR%5D%29+AND+%28hereditary+fructose+intolerance%5BTH%5D%29+AND+english%5Bla%5D+AND+human%5Bath%5D+AND+%22last+3600+days%5D

Catalog of Genes and Diseases from OMIM

- FRUCTOSE INTOLERANCE, HEREDITARY
  http://omim.org/entry/229600

Sources for This Summary


Reprinted from Genetics Home Reference:

Reviewed: June 2011
Published: October 9, 2018