Glucose phosphate isomerase deficiency

Glucose phosphate isomerase (GPI) deficiency is an inherited disorder that affects red blood cells, which carry oxygen to the body’s tissues. People with this disorder have a condition known as chronic hemolytic anemia, in which red blood cells are broken down (undergo hemolysis) prematurely, resulting in a shortage of red blood cells (anemia). Chronic hemolytic anemia can lead to unusually pale skin (pallor), yellowing of the eyes and skin (jaundice), extreme tiredness (fatigue), shortness of breath (dyspnea), and a rapid heart rate (tachycardia). An enlarged spleen (splenomegaly), an excess of iron in the blood, and small pebble-like deposits in the gallbladder or bile ducts (gallstones) may also occur in this disorder.

Hemolytic anemia in GPI deficiency can range from mild to severe. In the most severe cases, affected individuals do not survive to birth. Individuals with milder disease can survive into adulthood. People with any level of severity of the disorder can have episodes of more severe hemolysis, called hemolytic crises, which can be triggered by bacterial or viral infections.

A small percentage of individuals with GPI deficiency also have neurological problems, including intellectual disability and difficulty with coordinating movements (ataxia).

Frequency

GPI deficiency is a rare cause of hemolytic anemia; its prevalence is unknown. About 50 cases have been described in the medical literature.

Genetic Changes

GPI deficiency is caused by mutations in the GPI gene, which provides instructions for making an enzyme called glucose phosphate isomerase (GPI). This enzyme has two distinct functions based on its structure. When two GPI molecules form a complex (a homodimer), the enzyme plays a role in a critical energy-producing process known as glycolysis, also called the glycolytic pathway. During glycolysis, the simple sugar glucose is broken down to produce energy. Specifically, GPI is involved in the second step of the glycolytic pathway; in this step, a molecule called glucose-6-phosphate is converted to another molecule called fructose-6-phosphate.

When GPI remains a single molecule (a monomer) it is involved in the development and maintenance of nerve cells (neurons). In this context, it is often known as neuroleukin (NLK).

Some GPI gene mutations may result in a less stable homodimer, impairing the activity of the enzyme in the glycolytic pathway. The resulting imbalance of molecules involved
in the glycolytic pathway eventually impairs the ability of red blood cells to maintain their structure, leading to hemolysis.

Other *GPI* gene mutations may cause the monomer to break down more easily, thereby interfering with its function in nerve cells. In addition, the shortage of monomers hinders homodimer formation, which impairs the glycolytic pathway. These mutations have been identified in individuals with GPI deficiency who have both hemolytic anemia and neurological problems.

**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**

- glucose-6-phosphate isomerase deficiency
- glucosephosphate isomerase deficiency
- GPI deficiency
- nonspherocytic hemolytic anemia due to glucose phosphate isomerase deficiency

**Diagnosis & Management**

**Genetic Testing**

- Genetic Testing Registry: Glucosephosphate isomerase deficiency
- Genetic Testing Registry: Hemolytic anemia, nonspherocytic, due to glucose phosphate isomerase deficiency

**Other Diagnosis and Management Resources**

- National Heart, Lung, and Blood Institute: Hemolytic Anemia
  https://www.nhlbi.nih.gov/health-topics/hemolytic-anemia

**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: Hemolytic Anemia  
  https://medlineplus.gov/ency/article/000571.htm
• Health Topic: Anemia  
  https://medlineplus.gov/anemia.html

Genetic and Rare Diseases Information Center  
• Glucosephosphate isomerase deficiency  
  https://rarediseases.info.nih.gov/diseases/2502/glucosephosphate-isomerase-deficiency

Additional NIH Resources  
• National Heart, Lung, and Blood Institute: Hemolytic Anemia  
  https://www.nhlbi.nih.gov/health-topics/hemolytic-anemia

Educational Resources  
• Disease InfoSearch: Glucosephosphate Isomerase Deficiency  
  http://www.diseaseinfosearch.org/Glucosephosphate+Isomerase+Deficiency/3100
• Disease InfoSearch: Hemolytic anemia, nonspherocytic, due to glucose phosphate isomerase deficiency  
  http://www.diseaseinfosearch.org/Hemolytic+anemia%2C+nonspherocytic%2C+due+to+glucose+phosphate+isomerase+deficiency/8502
• European Network for Rare and Congenital Anemias  
  https://www.enerca.org/anaemias/34/glucose-phosphate-isomerase-deficiency
• MalaCards: glucose phosphate isomerase deficiency  
  http://www.malacards.org/card/glucose_phosphate_isomerase_deficiency
• Orphanet: Hemolytic anemia due to glucophosphate isomerase deficiency  
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=712

Patient Support and Advocacy Resources  
• National Organization for Rare Disorders (NORD): Hereditary Nonspherocytic Hemolytic Anemia  
  https://rarediseases.org/rare-diseases/anemia-hereditary-nonspherocytic-hemolytic/
Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28glucose+phosphate+isomerase+deficiency%5BTIAB%5D%29+OR+%28glucosephosphate+isomerase+deficiency%5BTIAB%5D%29+OR+%28glucose-6-phosphate+isomerase+deficiency%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D

OMIM

- HEMOLYTIC ANEMIA, NONSPHEROCYTIC, DUE TO GLUCOSE PHOSPHATE ISOMERASE DEFICIENCY
  http://omim.org/entry/613470

Sources for This Summary


  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/22782259
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/7989588
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC330061/

Reprinted from Genetics Home Reference:

Reviewed: December 2013
Published: May 15, 2018

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services