Triosephosphate isomerase deficiency

Triosephosphate isomerase deficiency is a disorder characterized by a shortage of red blood cells (anemia), movement problems, increased susceptibility to infection, and muscle weakness that can affect breathing and heart function.

The anemia in this condition begins in infancy. Since the anemia results from the premature breakdown of red blood cells (hemolysis), it is known as hemolytic anemia. A shortage of red blood cells to carry oxygen throughout the body leads to extreme tiredness (fatigue), pale skin (pallor), and shortness of breath. When the red cells are broken down, iron and a molecule called bilirubin are released; individuals with triosephosphate isomerase deficiency have an excess of these substances circulating in the blood. Excess bilirubin in the blood causes jaundice, which is a yellowing of the skin and the whites of the eyes.

Movement problems typically become apparent by age 2 in people with triosephosphate isomerase deficiency. The movement problems are caused by impairment of motor neurons, which are specialized nerve cells in the brain and spinal cord that control muscle movement. This impairment leads to muscle weakness and wasting (atrophy) and causes the movement problems typical of triosephosphate isomerase deficiency, including involuntary muscle tensing (dystonia), tremors, and weak muscle tone (hypotonia). Affected individuals may also develop seizures.

Weakness of other muscles, such as the heart (a condition known as cardiomyopathy) and the muscle that separates the abdomen from the chest cavity (the diaphragm) can also occur in triosephosphate isomerase deficiency. Diaphragm weakness can cause breathing problems and ultimately leads to respiratory failure.

Individuals with triosephosphate isomerase deficiency are at increased risk of developing infections because they have poorly functioning white blood cells. These immune system cells normally recognize and attack foreign invaders, such as viruses and bacteria, to prevent infection. The most common infections in people with triosephosphate isomerase deficiency are bacterial infections of the respiratory tract.

People with triosephosphate isomerase deficiency often do not survive past childhood due to respiratory failure. In a few rare cases, affected individuals without severe nerve damage or muscle weakness have lived into adulthood.

Frequency

Triosephosphate isomerase deficiency is likely a rare condition; approximately 40 cases have been reported in the scientific literature.
Causes

Mutations in the \( TPI1 \) gene cause triosephosphate isomerase deficiency. This gene provides instructions for making an enzyme called triosephosphate isomerase 1. This enzyme is involved in a critical energy-producing process known as glycolysis. During glycolysis, the simple sugar glucose is broken down to produce energy for cells.

\( TPI1 \) gene mutations lead to the production of unstable enzymes or enzymes with decreased activity. As a result, glycolysis is impaired and cells have a decreased supply of energy. Red blood cells depend solely on the breakdown of glucose for energy, and without functional glycolysis, red blood cells die earlier than normal. Cells with high energy demands, such as nerve cells in the brain, white blood cells, and heart (cardiac) muscle cells are also susceptible to cell death due to reduced energy caused by impaired glycolysis. Nerve cells in the part of the brain involved in coordinating movements (the cerebellum) are particularly affected in people with triosephosphate isomerase deficiency.

Death of red and white blood cells, nerve cells in the brain, and cardiac muscle cells leads to the signs and symptoms of triosephosphate isomerase deficiency.

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

- deficiency of phosphotriose isomerase
- hereditary nonspherocytic hemolytic anemia due to triosephosphate isomerase deficiency
- TPI deficiency
- TPID
- triose phosphate isomerase deficiency

Diagnosis & Management

Genetic Testing Information

- What is genetic testing? /primer/testing/genetictesting
Other Diagnosis and Management Resources

- MedlinePlus Encyclopedia: Hemolytic Anemia
  https://medlineplus.gov/ency/article/000571.htm
- National Heart, Lung, and Blood Institute: Hemolytic Anemia Treatment
  https://www.nhlbi.nih.gov/health-topics/hemolytic-anemia#Treatment

Additional Information & Resources

Health Information from MedlinePlus

- Encyclopedia: Hemolytic Anemia
  https://medlineplus.gov/ency/article/000571.htm
- Health Topic: Anemia
  https://medlineplus.gov/anemia.html
- Health Topic: Movement Disorders
  https://medlineplus.gov/movementdisorders.html

Genetic and Rare Diseases Information Center

- Triosephosphate isomerase deficiency
  https://rarediseases.info.nih.gov/diseases/5287/triosephosphate-isomerase-deficiency

Additional NIH Resources

- National Heart, Lung, and Blood Institute: What is Cardiomyopathy?
  https://www.nhlbi.nih.gov/health-topics/cardiomyopathy
- National Heart, Lung, and Blood Institute: What is Hemolytic Anemia?
  https://www.nhlbi.nih.gov/health-topics/hemolytic-anemia
- National Institute of Neurological Disorders and Stroke: Dystonias Information Page
  https://www.ninds.nih.gov/Disorders/All-Disorders/Dystonias-Information-Page

Educational Resources

- Ann & Robert H. Lurie Children's Hospital of Chicago: Hemolytic Anemia
  https://www.luriechildrens.org/en/specialties-conditions/hemolytic-anemia/
- Cincinnati Children's Hospital: Hemolytic Anemia
  https://www.cincinnatichildrens.org/health/h/hemolytic-anemia
- Johns Hopkins Medicine: Hemolytic Anemia
  https://www.hopkinsmedicine.org/health/conditions-and-diseases/hemolytic-anemia
- Kennedy Krieger Institute: Movement Disorders
  https://www.kennedykrieger.org/patient-care/conditions/movement-disorders
• MalaCards: triosephosphate isomerase deficiency
  https://www.malacards.org/card/triosephosphate_isomerase_deficiency

• Merck Manual for Healthcare Professionals: Overview of Hemolytic Anemia

• Orphanet: Triose phosphate-isomerase deficiency
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=868

• Washington University, St. Louis: Neuromuscular Disease Center
  https://neuromuscular.wustl.edu/msys/glycogen.html#tim

Patient Support and Advocacy Resources

• Dystonia Coalition
  https://www.rarediseasenetwork.org/cms/dystonia

• National Organization for Rare Disorders (NORD)
  https://rarediseases.org/rare-diseases/triosephosphate-isomerase-deficiency/

Scientific Articles on PubMed

• PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28triosephosphate+isomerase+deficiency%5BTIAB%5D%29+OR+%28triose+phosphate+isomerase+deficiency%5BTIAB%5D%29+OR+%28tpi+deficiency%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D

Catalog of Genes and Diseases from OMIM

• TRIOSEPHOSPHATE ISOMERASE DEFICIENCY
  http://omim.org/entry/615512

Medical Genetics Database from MedGen

• Triosephosphate isomerase deficiency
Sources for This Summary


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