Glutathione synthetase deficiency

Glutathione synthetase deficiency is a disorder that prevents the production of an important molecule called glutathione. Glutathione helps prevent damage to cells by neutralizing harmful molecules generated during energy production. Glutathione also plays a role in processing medications and cancer-causing compounds (carcinogens), and building DNA, proteins, and other important cellular components.

Glutathione synthetase deficiency can be classified into three types: mild, moderate, and severe. Mild glutathione synthetase deficiency usually results in the destruction of red blood cells (hemolytic anemia). In addition, affected individuals may release large amounts of a compound called 5-oxoproline in their urine (5-oxoprolinuria). This compound builds up when glutathione is not processed correctly in cells.

Individuals with moderate glutathione synthetase deficiency may experience symptoms beginning shortly after birth including hemolytic anemia, 5-oxoprolinuria, and elevated acidity in the blood and tissues (metabolic acidosis).

In addition to the features present in moderate glutathione synthetase deficiency, individuals affected by the severe form of this disorder may experience neurological symptoms. These problems may include seizures; a generalized slowing down of physical reactions, movements, and speech (psychomotor retardation); intellectual disability; and a loss of coordination (ataxia). Some people with severe glutathione synthetase deficiency also develop recurrent bacterial infections.

Frequency

Glutathione synthetase deficiency is very rare. This disorder has been described in more than 70 people worldwide.

Genetic Changes

Mutations in the *GSS* gene cause glutathione synthetase deficiency. The *GSS* gene provides instructions for making an enzyme called glutathione synthetase. This enzyme is involved in a process called the gamma-glutamyl cycle, which takes place in most of the body's cells. This cycle is necessary for producing a molecule called glutathione. Glutathione protects cells from damage caused by unstable oxygen-containing molecules, which are byproducts of energy production. Glutathione is called an antioxidant because of its role in protecting cells from the damaging effects of these unstable molecules. Mutations in the *GSS* gene prevent cells from making adequate levels of glutathione, leading to the signs and symptoms of glutathione synthetase 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

- 5-oxoprolinemia
- 5-oxoprolinuria
- deficiency of glutathione synthase
- deficiency of glutathione synthetase
- pyroglutamic acidemia
- pyroglutamic aciduria

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Glutathione synthetase deficiency of erythrocytes, hemolytic anemia due to
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1856399/
- Genetic Testing Registry: Gluthathione synthetase deficiency
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0398746/

Other Diagnosis and Management Resources

- Baby's First Test
  http://www.babysfirsttest.org/newborn-screening/conditions/pyroglutamic-acidemia

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

- Health Topic: Genetic Brain Disorders
  https://medlineplus.gov/geneticbraindisorders.html
- Health Topic: Metabolic Disorders
  https://medlineplus.gov/metabolicdisorders.html
- Health Topic: Newborn Screening
  https://medlineplus.gov/newbornscreening.html

Genetic and Rare Diseases Information Center

- Glutathione synthetase deficiency
  https://rarediseases.info.nih.gov/diseases/10047/glutathione-synthetase-deficiency

Educational Resources

- Basic Neurochemistry (sixth edition, 1999): Glutathione Metabolism
  https://www.ncbi.nlm.nih.gov/books/NBK28123/
- Disease InfoSearch: 5-Oxoprolinuria
  http://www.diseaseinfosearch.org/5-Oxoprolinuria/52
- Illinois Department of Public Health Newborn Screening Program
  http://www.idph.state.il.us/HealthWellness/fs/5oxy.htm
- MalaCards: glutathione synthetase deficiency
  http://www.malacards.org/card/glutathione_synthetase_deficiency
- Orphanet: Glutathione synthetase deficiency
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=32

Patient Support and Advocacy Resources

- Children Living with Inherited Metabolic Diseases (CLIMB) UK
  http://www.climb.org.uk/
- National Organization for Rare Disorders (NORD)
  https://rarediseases.org/rare-diseases/glutathione-synthetase-deficiency/
- Organic Acidemia Association
  https://www.oaanews.org/5-oxoprolinemia.html

ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22glutathione+synthetase+deficiency%22

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28glutathione+synthetase+deficiency%5BTIAB%5D%29+OR+%285-oxoprolinuria%5BTIAB%5D%29+OR+%28pyroglutamic+acidemia%5BTIAB%5D%29+OR+%28pyroglutamic+aciduria%5BTIAB%5D%29+OR+%285-oxoprolinemia%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+2520+days%22%5Bdp%5D

OMIM

- GLUTATHIONE SYNTHETASE DEFICIENCY
  http://omim.org/entry/266130
- GLUTATHIONE SYNTHETASE DEFICIENCY OF ERYTHROCYTES, HEMOLYTIC ANEMIA DUE TO
  http://omim.org/entry/231900

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