



pyruvate carboxylase deficiency

Pyruvate carboxylase deficiency is an inherited disorder that causes lactic acid and other potentially toxic compounds to accumulate in the blood. High levels of these substances can damage the body's organs and tissues, particularly in the nervous system.

Researchers have identified at least three types of pyruvate carboxylase deficiency, which are distinguished by the severity of their signs and symptoms. Type A, which has been identified mostly in people from North America, has moderately severe symptoms that begin in infancy. Characteristic features include developmental delay and a buildup of lactic acid in the blood (lactic acidosis). Increased acidity in the blood can lead to vomiting, abdominal pain, extreme tiredness (fatigue), muscle weakness, and difficulty breathing. In some cases, episodes of lactic acidosis are triggered by an illness or periods without food (fasting). Children with pyruvate carboxylase deficiency type A typically survive only into early childhood.

Pyruvate carboxylase deficiency type B has life-threatening signs and symptoms that become apparent shortly after birth. This form of the condition has been reported mostly in Europe, particularly France. Affected infants have severe lactic acidosis, a buildup of ammonia in the blood (hyperammonemia), and liver failure. They experience neurological problems including weak muscle tone (hypotonia), abnormal movements, seizures, and coma. Infants with this form of the condition usually survive for less than 3 months after birth.

A milder form of pyruvate carboxylase deficiency, sometimes called type C, has also been described. This type is characterized by slightly increased levels of lactic acid in the blood and minimal signs and symptoms affecting the nervous system.

Frequency

Pyruvate carboxylase deficiency is a rare condition, with an estimated incidence of 1 in 250,000 births worldwide. This disorder appears to be much more common in some Algonkian Indian tribes in eastern Canada.

Genetic Changes

Mutations in the *PC* gene cause pyruvate carboxylase deficiency.

The *PC* gene provides instructions for making an enzyme called pyruvate carboxylase. This enzyme is active in mitochondria, which are the energy-producing centers within cells. It is involved in several important cellular functions including the generation of glucose, a simple sugar that is the body's main energy source. Pyruvate carboxylase

also plays a role in the formation of the protective sheath that surrounds certain nerve cells (myelin) and the production of brain chemicals called neurotransmitters.

Mutations in the *PC* gene reduce the amount of pyruvate carboxylase in cells or disrupt the enzyme's activity. The missing or altered enzyme cannot carry out its essential role in generating glucose, which impairs the body's ability to make energy in mitochondria. Additionally, a loss of pyruvate carboxylase allows potentially toxic compounds such as lactic acid and ammonia to build up and damage organs and tissues. Researchers suggest that the loss of pyruvate carboxylase function in the nervous system, particularly the role of the enzyme in myelin formation and neurotransmitter production, also contributes to the neurologic features of pyruvate carboxylase 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

- Ataxia with Lactic Acidosis, Type II
- PC deficiency
- Pyruvate Carboxylase Deficiency Disease

Diagnosis & Management

These resources address the diagnosis or management of pyruvate carboxylase deficiency:

- GeneReview: Pyruvate Carboxylase Deficiency
<https://www.ncbi.nlm.nih.gov/books/NBK6852>
- Genetic Testing Registry: Pyruvate carboxylase deficiency
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0034341/>

These resources from MedlinePlus offer information about the diagnosis and management of various health conditions:

- Diagnostic Tests
<https://medlineplus.gov/diagnostictests.html>
- Drug Therapy
<https://medlineplus.gov/drugtherapy.html>
- Surgery and Rehabilitation
<https://medlineplus.gov/surgeryandrehabilitation.html>

- Genetic Counseling
<https://medlineplus.gov/geneticcounseling.html>
- Palliative Care
<https://medlineplus.gov/palliativecare.html>

Additional Information & Resources

MedlinePlus

- Health Topic: Genetic Brain Disorders
<https://medlineplus.gov/geneticbraindisorders.html>
- Health Topic: Mitochondrial Diseases
<https://medlineplus.gov/mitochondrialdiseases.html>
- Health Topic: Newborn Screening
<https://medlineplus.gov/newbornscreening.html>

Genetic and Rare Diseases Information Center

- Pyruvate carboxylase deficiency
<https://rarediseases.info.nih.gov/diseases/7512/pyruvate-carboxylase-deficiency>

Educational Resources

- Disease InfoSearch: Pyruvate carboxylase deficiency
<http://www.diseaseinfosearch.org/Pyruvate+carboxylase+deficiency/6120>
- MalaCards: pyruvate carboxylase deficiency
http://www.malacards.org/card/pyruvate_carboxylase_deficiency
- Merck Manual Consumer Version: Disorders of Carbohydrate Metabolism
<http://www.merckmanuals.com/home/children-s-health-issues/hereditary-metabolic-disorders/disorders-of-carbohydrate-metabolism>
- Orphanet: Pyruvate carboxylase deficiency
http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=3008

Patient Support and Advocacy Resources

- Children Living with Inherited Metabolic Diseases (CLIMB) (UK)
<http://www.climb.org.uk/>
- National Organization for Rare Disorders
<https://rarediseases.org/rare-diseases/pyruvate-carboxylase-deficiency/>
- Resource list from the University of Kansas Medical Center
<http://www.kumc.edu/gec/support/metaboli.html>
- United Mitochondrial Disease Foundation
<http://www.umdf.org/>

GeneReviews

- Pyruvate Carboxylase Deficiency
<https://www.ncbi.nlm.nih.gov/books/NBK6852>

Genetic Testing Registry

- Pyruvate carboxylase deficiency
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0034341/>

ACT Sheets

- Increased citrulline
<https://www.ncbi.nlm.nih.gov/books/NBK55827/bin/Citrullinemia.pdf>

ClinicalTrials.gov

- ClinicalTrials.gov
<https://clinicaltrials.gov/ct2/results?cond=%22pyruvate+carboxylase+deficiency%22+OR+%22Pyruvate+Metabolism%2C+Inborn+Errors%22>

Scientific articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28pyruvate+carboxylase+deficiency%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D>

OMIM

- PYRUVATE CARBOXYLASE DEFICIENCY
<http://omim.org/entry/266150>

Sources for This Summary

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