What is phosphoglycerate dehydrogenase deficiency?

Phosphoglycerate dehydrogenase deficiency is an inherited metabolic disease with variable severity and age at onset characterized by microcephaly, psychomotor delays, and seizures.\(^1\) Individuals with phosphoglycerate dehydrogenase deficiency have defects in the function of the phosphoglycerate dehydrogenase enzyme, which helps the body make the protein building block, serine.\(^1\) Signs and symptoms of phosphoglycerate dehydrogenase deficiency are due to problems with brain development, which requires serine.\(^2\) The most severe form of phosphoglycerate dehydrogenase deficiency is called Neu-Laxova syndrome.\(^3,4\)

What are the symptoms of phosphoglycerate dehydrogenase deficiency, and what treatment is available?

Onset of symptoms is usually in infancy. Symptoms may include:\(^1,4\)

- Microcephaly (small head)
- Psychomotor retardation
- Seizures
- Growth retardation
- Hypertonia (increase in muscle tension)
- Brain malformations
- Brain atrophy, specifically hypomyelination

Onset of symptoms of Neu-Laxova syndrome is prior to birth. Symptoms usually result in neonatal death\(^4\) and may include:\(^3\)

- Ichthyosis (scahy skin)
- Intrauterine growth restriction
- Microcephaly
- Short neck
- Brain malformations
- Incomplete lung development
- Edema (fluid accumulation in tissues)
- Severe proptosis with ectropion (eye abnormality)
- Distinctive facial features
- Flexion contractures (joint deformity)

Treatment is primarily supportive and may include dietary supplementation with oral serine.\(^4\)

How is phosphoglycerate dehydrogenase deficiency, \(PHGDH\)-related, inherited?

Phosphoglycerate dehydrogenase deficiency is an autosomal recessive disease caused by mutations in the \(PHGDH\) gene.\(^1\) An individual who inherits one copy of an \(PHGDH\) gene mutation is a carrier and is not expected to have related health problems. An individual who inherits two \(PHGDH\) mutations, one from each parent, is expected to be affected with phosphoglycerate dehydrogenase deficiency.

If both members of a couple are carriers of mutations in the same gene, the risk for an affected child is 25% in each pregnancy; therefore, it is especially important that the reproductive partner of a carrier be offered testing.
Who is at risk for phosphoglycerate dehydrogenase deficiency, PHGDH-related?

PHGDH-related phosphoglycerate dehydrogenase deficiency can occur in individuals of all races and ethnicities. Having a relative who is a carrier or who is affected can increase an individual’s risk to be a carrier. Consultation with a genetics health professional may be helpful in determining carrier risk and appropriate testing.

What does a positive test result mean?

If a gene mutation is identified, an individual should speak to a physician or genetics health professional about the implications of the result and appropriate testing for the reproductive partner and at-risk family members.

What does a negative test result mean?

A negative result reduces, but does not eliminate, the possibility that an individual carries a gene mutation. The likelihood of being a carrier is also influenced by family history, medical symptoms, and other relevant test results.

Where can I get more information?


References