Inheritest®
CARRIER SCREEN

Phosphoglycerate dehydrogenase deficiency, *PHGDH*-related

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 (scaly 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 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?

Genetics Home Reference: http://ghr.nlm.nih.gov/condition/phosphoglycerate-dehydrogenase-deficiency

Children Living with Inherited Metabolic Diseases (CLIMB): http://www.climb.org.uk/

References

1. Phosphoglycerate dehydrogenase deficiency. *Genetics Home Reference*. Available at: http://ghr.nlm.nih.gov/condition/phosphoglycerate-dehydrogenase-deficiency. Accessed February 19, 2016.
2. *PHGDH. Genetics Home Reference.* Available at: http://ghr.nlm.nih.gov/gene/PHGDH. Accessed February 19, 2016.
3. Phosphoglycerate dehydrogenase deficiency. OMIM. Available at: http://www.omim.org/entry/601815. Accessed February 19, 2016.
4. Neu-Laxova syndrome. OMIM. Available at: http://www.omim.org/entry/256520. Accessed February 19, 2016.