Inheritest®
CARRIER SCREEN

Pyruvate dehydrogenase deficiency, *PDHA1*-related

What is pyruvate dehydrogenase deficiency, *PDHA1*-related?

Pyruvate dehydrogenase deficiency is an inherited neurodegenerative disease characterized by lactic acidosis, delayed development, and neurological problems.[1] Individuals with pyruvate dehydrogenase deficiency, *PDHA1*-related, have defects in a component of the pyruvate dehydrogenase complex, which is needed to convert energy from food into a form that cells can use.[2] When pyruvate builds up in cells, it is converted to lactic acid.[1] Signs and symptoms of pyruvate dehydrogenase deficiency are due to decreased energy and the buildup of lactic acid in cells, which has the most severe consequences in the brain.[1]

What are the symptoms of pyruvate dehydrogenase deficiency, *PDHA1*-related, and what treatment is available?

Pyruvate dehydrogenase deficiency, *PDHA1*-related, is a disease that varies in age of onset and severity. Signs and symptoms usually appear shortly after birth and may include:[1]

- Lactic acidosis (buildup of lactic acid)
- Nausea and vomiting
- Severe breathing problems
- Abnormal heartbeat
- Developmental delay
- Intellectual disability
- Seizures
- Hypotonia (poor muscle tone)
- Ataxia (loss of muscle coordination)
- Abnormal brain structures

Many individuals with pyruvate dehydrogenase deficiency, *PDHA1*-related, do not survive past childhood, although some may live into adolescence or adulthood.[1] There is no cure and treatment is supportive.

How is pyruvate dehydrogenase deficiency, *PDHA1*-related, inherited?

Pyruvate dehydrogenase deficiency can be caused by mutations in at least five genes, including *PDHA1*, which is responsible for approximately 80% of cases.[1] Pyruvate dehydrogenase deficiency, *PDHA1*-related, is an X-linked disease.[1, 3] A male who inherits one copy of a *PDHA1* gene mutation is affected with pyruvate dehydrogenase deficiency. A female who inherits one copy of a *PDHA1* mutation is a carrier and may have some symptoms.[1, 3]

If a female is a carrier, the risk for each son to be affected is 50% and the risk for each daughter to be a carrier is 50%. If a male is affected, each son is unaffected and each daughter is an obligate carrier.

Who is at risk for pyruvate dehydrogenase deficiency, *PDHA1*-related?

Pyruvate dehydrogenase deficiency, *PDHA1*-related, is a rare condition that can occur in individuals of all races and ethnicities. Its prevalence is unknown.

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/pyruvate-dehydrogenase-deficiency

National Organization for Rare Disorders (NORD): http://rarediseases.org/rare-diseases/pyruvate-dehydrogenase-complex-deficiency/

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

References

1. Pyruvate dehydrogenase deficiency. Genetics Home Reference. Available at http://ghr.nlm.nih.gov/condition/pyruvate-dehydrogenase-deficiency. Accessed on February 23, 2016.
2. PDHA1. *Genetics Home Reference.* Available at http://ghr.nlm.nih.gov/gene/PDHA1. Accessed on February 23, 2016.
3. Lissens, W. et al., Mutations in the X-linked Pyruvate Dehydrogenase (E1) α Subunit Gene (PDHA1) in Patients with a Pyruvate Dehydrogenase Complex Deficiency. *Human Mutations.* 2000. 15: 209-2119.