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CARRIER SCREEN

Phenylalanine hydroxylase deficiency, includes phenylketonuria (PKU)

What is phenylalanine hydroxylase deficiency?

Phenylalanine hydroxylase deficiency is an inherited disease of variable severity. Individuals with phenylalanine hydroxylase deficiency have a defect in the enzyme phenylalanine hydroxylase, which is responsible for the breakdown of the essential amino acid, phenylalanine, found in a variety of foods including protein and some artificial sweeteners. The most severe form of PAH, phenylketonuria (PKU), is characterized by microcephaly, epilepsy, severe intellectual disability, and behavioral problems.[1]

What are the symptoms of phenylalanine hydroxylase deficiency and what treatment is available?

Phenylalanine hydroxylase deficiency is a disease with variable severity, even within families. There are two main categories of phenylalanine hydroxylase deficiency, PKU and non-PKU, based on levels of phenylalanine found in the blood.[2]

Symptoms of phenylalanine hydroxylase deficiency may include:[1,2]

- Microcephaly (small head size)
- Light skin and hair color
- Intellectual disability
- Eczema
- Musty body odor
- Seizures
- Developmental delays
- Behavioral problems and/or psychiatric disorders
- Osteopenia (low bone mineral density)

Individuals with the non-PKU form of phenylalanine hydroxylase deficiency may have less severe symptoms and a lower risk for intellectual disability than those with PKU.[2] In some cases, individuals with non-PKU phenylalanine hydroxylase deficiency have only mildly elevated levels of phenylalanine in blood, even when untreated.[2]

There is no cure for phenylalanine hydroxylase deficiency; however, early detection and treatment can prevent intellectual disability and other neurological damage. Treatment of PKU requires a lifelong, phenylalanine-restricted diet that may include special formulas and dietary supplements. The artificial sweetener aspartame should be avoided, as it contains phenylalanine.[2]

High levels of phenylalanine in a pregnant woman can cause birth defects in a developing fetus, including poor growth, heart defects, and intellectual disability. Consequently, women affected with phenylalanine hydroxylase deficiency should work with their physician several months prior to conception and during pregnancy to control their phenylalanine levels.[2]

PKU is included on the newborn screening panel in all 50 states.[3]

How is phenylalanine hydroxylase deficiency inherited?

Phenylalanine hydroxylase deficiency is an autosomal recessive disease caused by mutations in the *PAH* gene.[1] An individual who inherits one copy of a *PAH* gene mutation is a carrier and is not expected to have related health problems. An individual who inherits two *PAH* mutations, one from each parent, is expected to be affected with phenylalanine hydroxylase deficiency.

If both members of a couple are carriers of a mutation in the same gene, the risk of having 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 phenylalanine hydroxylase deficiency?

Phenylalanine hydroxylase deficiency can occur in individuals of all races and ethnicities. It is most common in Turkish, Irish, Northern European and East Asian individuals.[2]

Carrier frequency and incidence in select populations[2]

Population	Carrier frequency	Incidence
Turkish	1/26	1/2,600
Irish	1/33	1/4,500
Northern European, East Asian	1/50	1/10,000

Having a relative who is a carrier or is affected can increase an individual's risk of being 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?

March of Dimes: http://www.marchofdimes.com/baby/birthdefects_pku.html

Screening, Technology and Research in Genetics: http://www.newbornscreening.info/Parents/aminoaciddisorders/PKU.html

National PKU News: http://www.pkunews.org/

References

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3. National Newborn Screening Status Report. November 2, 2014. Available at: http://genes-r-us.uthscsa.edu/sites/genes-r-us/files/nbsdisorders.pdf . Accessed January 6, 2016.