Phenylketonuria

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What is phenylketonuria?

Phenylketonuria (commonly known as PKU) is an inherited disorder that increases the levels of a substance called phenylalanine in the blood. Phenylalanine is a building block of proteins (an amino acid) that is obtained through the diet. It is found in all proteins and in some artificial sweeteners. If PKU is not treated, phenylalanine can build up to harmful levels in the body, causing intellectual disability and other serious health problems.

The signs and symptoms of PKU vary from mild to severe. The most severe form of this disorder is known as classic PKU. Infants with classic PKU appear normal until they are a few months old. Without treatment, these children develop permanent intellectual disability. Seizures, delayed development, behavioral problems, and psychiatric disorders are also common. Untreated individuals may have a musty or mouse-like odor as a side effect of excess phenylalanine in the body. Children with classic PKU tend to have lighter skin and hair than unaffected family members and are also likely to have skin disorders such as eczema.

Less severe forms of this condition, sometimes called variant PKU and non-PKU hyperphenylalaninemia, have a smaller risk of brain damage. People with very mild cases may not require treatment with a low-phenylalanine diet.

Babies born to mothers with PKU and uncontrolled phenylalanine levels (women who no longer follow a low-phenylalanine diet) have a significant risk of intellectual disability because they are exposed to very high levels of phenylalanine before birth. These infants may also have a low birth weight and grow more slowly than other children. Other characteristic medical problems include heart defects or other heart problems, an abnormally small head size (microcephaly), and behavioral problems. Women with PKU and uncontrolled phenylalanine levels also have an increased risk of pregnancy loss.

How common is phenylketonuria?

The occurrence of PKU varies among ethnic groups and geographic regions worldwide. In the United States, PKU occurs in 1 in 10,000 to 15,000 newborns. Most cases of PKU are detected shortly after birth by newborn screening, and treatment is started promptly. As a result, the severe signs and symptoms of classic PKU are rarely seen.

What genes are related to phenylketonuria?

Mutations in the PAH gene cause phenylketonuria.

The PAH gene provides instructions for making an enzyme called phenylalanine hydroxylase. This enzyme converts the amino acid phenylalanine to other important compounds in the body. If gene mutations reduce the activity of phenylalanine hydroxylase, phenylalanine from the diet
is not processed effectively. As a result, this amino acid can build up to toxic levels in the blood and other tissues. Because nerve cells in the brain are particularly sensitive to phenylalanine levels, excessive amounts of this substance can cause brain damage.

Classic PKU, the most severe form of the disorder, occurs when phenylalanine hydroxylase activity is severely reduced or absent. People with untreated classic PKU have levels of phenylalanine high enough to cause severe brain damage and other serious medical problems. Mutations in the PAH gene that allow the enzyme to retain some activity result in milder versions of this condition, such as variant PKU or non-PKU hyperphenylalaninemia. Changes in other genes may influence the severity of PKU, but little is known about these additional genetic factors.

**Related Gene(s)**

Changes in this gene are associated with phenylketonuria.

- **PAH**

**How do people inherit phenylketonuria?**

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.

**Where can I find information about diagnosis or management of phenylketonuria?**

These resources address the diagnosis or management of phenylketonuria and may include treatment providers.

- Baby's First Test (http://www.babysfirsttest.org/newborn-screening/conditions/classic-phenylketonuria-pku)

You might also find information on the diagnosis or management of phenylketonuria in Educational resources and Patient support.

testing), particularly the difference between clinical tests and research tests

To locate a healthcare provider, see How can I find a genetics professional in my area?

Where can I find additional information about phenylketonuria?

You may find the following resources about phenylketonuria helpful. These materials are written
for the general public.

- **MedlinePlus - Health information**

- **Genetic and Rare Diseases Information Center - Information about genetic conditions and rare diseases**
  (http://rarediseases.info.nih.gov/gard/7383/phenylketonuria/resources/1)

- **Additional NIH Resources - National Institutes of Health**
  - National Human Genome Research Institute (http://www.genome.gov/25020037)
  - National Institute of Child Health and Human Development (http://www.nichd.nih.gov/health/topics/pku/Pages/default.aspx)

- **Educational resources - Information pages**
  - Disease InfoSearch: Phenylketonuria (http://www.diseaseinfosearch.org/Phenylketonuria/5714)
  - Genetic Science Learning Center, University of Utah (http://learn.genetics.utah.edu/content/disorders/singlegene/pku/)
  - Genetics Education Materials for School Success (GEMSS) (http://www.gemssforschools.org/conditions/pku/default)
  - Iowa Department of Public Health (http://www.idph.state.ia.us/genetics/common/pdf/pku.pdf)
  - March of Dimes (http://www.marchofdimes.org/baby/phenylketonuria-in-your-baby.aspx)
- Montreal Children’s Hospital (http://www.pahdb.mcgill.ca/?Topic=Information&Section=Clinical&Page=1)
- My46 Trait Profile (https://www.my46.org/trait-document?trait=Phenylketonuria&type=profile)
- National Genetics and Genomics Education Centre (UK) (http://www.geneticseducation.nhs.uk/genetic-conditions-54/277-phenylketonuriapku)
- New England Consortium of Metabolic Programs (http://newenglandconsortium.org/for-families/phenylketonuria-pku/pku-a-guide-for-parents-of-babies-recently-screened/)
- Orphanet: Phenylketonuria (http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=716)
- Screening, Technology, and Research in Genetics (http://www.newbornscreening.info/Parents/aminoaciddisorders/PKU.html)
- Swedish Information Center for Rare Diseases (http://www.socialstyrelsen.se/rarediseases/phenylketonuria)
- Virginia Department of Health (http://www.vdh.virginia.gov/ofhs/childandfamily/childhealth/gns/vnsp/Parents/documents/FactSheetsEnglish/Parent%20Fact%20Sheet_PKU_English.pdf)
- Your Genes Your Health from Cold Spring Harbor Laboratory (http://www.ygyh.org/pku/whatisit.htm)

**Patient support - For patients and families**
- Children Living with Metabolic Disorders (CLIMB) (UK) (http://www.climb.org.uk/)
- National Organization for Rare Disorders (NORD) (https://rarediseases.org/rare-diseases/phenylketonuria/)
- National PKU Alliance (http://npkua.org/)
- National PKU News (http://pkunews.org/)
- NBS Connect (https://nbs.patientcrossroads.org/)
- Resource list from the University of Kansas Medical Center (http://www.kumc.edu/gec/support/pku.html)
- University of Washington PKU Clinic (http://depts.washington.edu/pku/)

You may also be interested in these resources, which are designed for healthcare professionals and researchers.

- Genetic Testing Registry - Repository of genetic test information
What other names do people use for phenylketonuria?

- Deficiency Disease, Phenylalanine Hydroxylase
- Folling Disease
- Folling's Disease
- PAH deficiency
- Phenylalanine Hydroxylase Deficiency Disease
- PKU


What if I still have specific questions about phenylketonuria?

Ask the Genetic and Rare Diseases Information Center (https://rarediseases.info.nih.gov/gard).

What glossary definitions help with understanding phenylketonuria?

- amino acid
- autosomal
- autosomal recessive
- cell
- deficiency
- disability
- eczema
- enzyme
- gene
- inherited
- maternal
- microcephaly
- newborn screening
- phenylalanine
- recessive
- screening
- toxic

You may find definitions for these and many other terms in the Genetics Home Reference Glossary.

References


The resources on this site should not be used as a substitute for professional medical care or advice. Users seeking information about a personal genetic disease, syndrome, or condition should consult with a qualified healthcare professional. See How can I find a genetics professional in my area? (http://ghr.nlm.nih.gov/handbook/consult/findingprofessional) in the Handbook.

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