

Chapter 1: What is PKU?

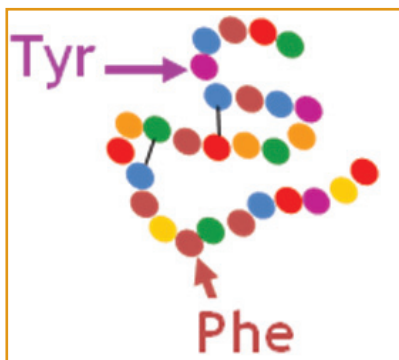


A Parent's Perspective

"If our child with PKU had been our first instead of our third, or if we had wanted more children after we had her, we would have done so, even knowing the child could have PKU. Because after three or four years we saw that our daughter's quality of life was no different from that of our other children. She was quite early walking and talking, she is athletic, and lovely. She was just as normal as her siblings."

What is PKU?

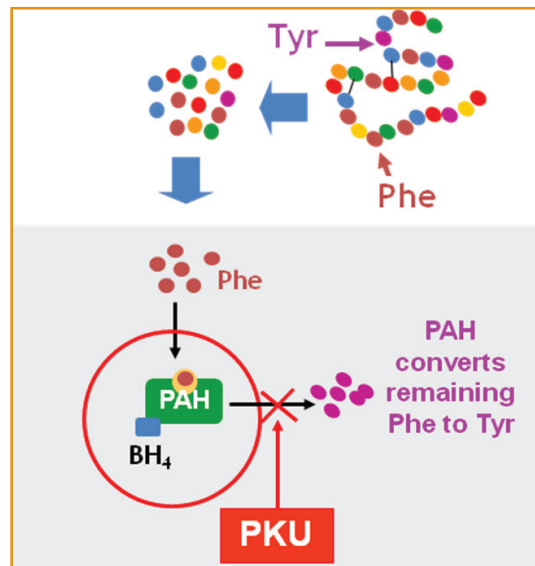
Phenylketonuria (PKU) is an inherited genetic disorder that affects approximately one in 15,000 babies born in the United States¹. A person with PKU does not produce enough of an enzyme in their liver called phenylalanine hydroxylase (PAH). This enzyme is needed to process the amino acid, phenylalanine (Phe), which is found in food items that contain protein². Usually, when people eat protein, it is broken down into different amino acids which are then processed and used for growth and repair of body tissue. Individuals with PKU cannot process Phe in this way, and instead Phe builds up in the blood.



All protein is composed of chemicals called amino acids, joined to each other like beads on a string. When protein is consumed, the string is broken up in the stomach into shorter chains of amino acids and then into individual amino acids in the digestive tract. These individual amino acids are absorbed into the bloodstream and processed for building muscle, making

other chemicals in the body, or providing energy.

In people who do **not** have PKU, some of the Phe is converted directly into another amino acid, tyrosine, with the aid of the enzyme PAH. Tyrosine, generally derived from the protein in food, is essential for several functions, including functions in the brain.



¹National Institutes of Health. Phenylketonuria: Screening and Management National Institutes of Health Consensus Development Statement Available At: <http://consensus.nih.gov/2000/2000phenylketonuria113html.htm> Accessed May 17, 2011

² National Institutes of Health. Phenylketonuria: Screening and Management National Institutes of Health Consensus Development Statement Available At: <http://consensus.nih.gov/2000/2000phenylketonuria113html.htm> Accessed May 17, 2011

What is PKU?

People with PKU cannot convert Phe to tyrosine because their livers do not make an adequate amount of PAH. When a person with PKU consumes protein-rich foods, his or her body cannot break down most of the Phe. As a result, the bloodstream is flooded with excess Phe that is carried to the brain by “transporter cells.” The high Phe causes the brain of an individual with PKU who eats protein-rich food to be overloaded with Phe, causing cognitive as well as behavioral problems and potentially insufficient tyrosine levels, an amino acid that is a precursor to neurotransmitters and hormones³.

There are different categories of PKU that are determined based on diagnostic Phe level, mutation testing (if performed) and the amount of Phe that an individual can tolerate.

- Classical PKU is the most common form of PKU. It results when there are two severe mutations of the PAH gene and as a result there is little or no PAH enzyme activity to convert phenylalanine to tyrosine. These are the most severely affected patients.
Phe level in blood: Above 20 mg/dl (>1200 µmol/L)
- Moderate/Mild PKU is associated with elevated Phe levels that require treatment but are lower than those observed in Classical PKU.
Phe level in blood: Above 6 mg/dl but less than 20 mg/dl (360- 1200µmol/L)
- Hyperphenylalanemia (HyperPhe) is used to describe those people whose blood Phe level is above normal, but still low enough that they may not require dietary treatment.
Phe level in blood: less than 6 mg/dl (<360 µmol/L)⁴

PKU CLASSIFICATION	PHE LEVEL
Unaffected individual	1 mg/dl (60 µmol/L)
HyperPhe	< 6 mg/dl (<360 µmol/L)
Moderate/Mild PKU	6 mg/dl – 20 mg/dl (360- 1200µmol/L)
Classical PKU	>20 mg/dl (>1200 µmol/L)

³ Acosta B, Yannicelli S, Marriage B, et al. Nutrient intake and growth of infants with phenylketonuria undergoing treatment. J Pediatr Gastroenterol Nutr 1998;27:287-91

⁴ Maltzman, S, : My PKU Toolkit A Transition Guide to Adult PKU Management. New Jersey : Applied Nutrition Corp. 2007:5

What is PKU?

What are the symptoms and treatment for PKU?

With newborn screening being widely used for PKU, infants are diagnosed early and symptoms are prevented with early, life-long treatment. When PKU is untreated, however, blood Phe levels can become elevated. A high level of blood Phe is toxic to the brain, the following symptoms can occur when untreated or treated too late:

- Mental retardation
- Seizures
- Eczema (skin rash)⁵

PKU is treated with a low Phe diet that includes medical formula and foods specially formulated to be low in Phe and provide essential nutrients needed for growth and development⁶. Some patients with PKU are treated with a combination of diet and a medication (Kuvan®, sapropterin, sapropterin dihydrochloride) which lowers the blood Phe level. A small fraction of patients are treated with medication alone.

Regular visits to the PKU clinic are part of the treatment program. Phe levels are checked by performing regular blood tests and treatment is adjusted if necessary to keep Phe levels in the safe range (see chapter 2 for more details on treatment of PKU).

Key Points about PKU

- *PKU is a genetic condition that is not contagious.*
- *Apart from needing a special diet, a person with PKU is healthy.*
- *A person with PKU can not break down an amino acid called phenylalanine (Phe), found in all foods containing protein.*
- *Phe can build up in the blood and damage the developing brain.*
- *Staying on a low protein diet keeps Phe levels in a safe range, allowing for normal development and a healthy life.*
- *Eating the wrong foods will not make a person with PKU sick right away, but will cause problems over the long-term.*
- *Having food that is not part of the diet should not be considered a 'treat' as it will have implications for an individual with PKU.*
- *A person with PKU will not outgrow it and must stay on the diet for life.*

⁵ Mitchell, J.J., Scriver, C.R., Phenylalanine Hydroxylase Deficiency In: GeneReviews [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2000 Jan 10 [updated 2010 May 04].

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What is PKU?

The Genetics of PKU

Genes are present in every cell in our body. They provide the “blueprint” for each characteristic or trait that we possess, such as eye and hair color, height, and gender. Genes also provide the instructions to make enzymes for metabolism. Children inherit two sets of genes, one from each parent. Not every gene always works properly.

The pattern of PKU inheritance is recessive. A recessively inherited condition typically affects males and females equally. For a recessive disorder to happen, a child must inherit one copy of a disease-causing gene from each parent. When this occurs, the child gets a double dose of the disease-causing gene and no normal copy of the gene.

What are the chances of inheriting PKU?

Children born with PKU have inherited a defective PKU-related gene from each parent. Around 1 in 50 or 60 of us has a defective PKU gene, yet only 1 in 15,000 Americans inherit two defective genes and has PKU. Boys and girls have an equal chance of inheriting PKU.

Image of two unaffected carriers and the probability of their child inheriting PKU.

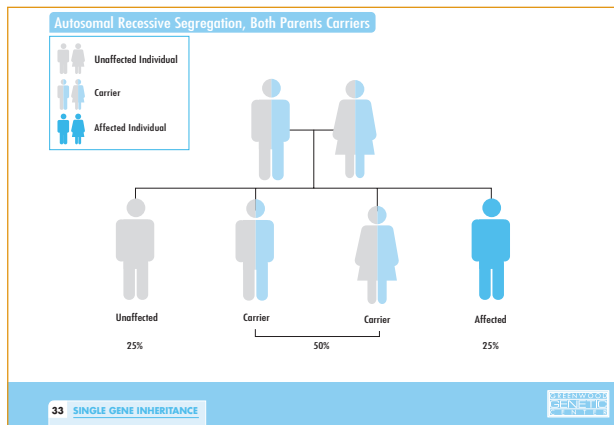


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For a child to inherit PKU, both parents must be a carrier of the PKU gene. Each parent is called a “carrier” because he or she silently carries one copy of the disease-causing gene paired with a normal copy of the same gene. Carriers will not experience any noticeable symptoms. A parent who is a carrier for PKU produces either a normal gene or a PKU gene in each egg or sperm. If both parents are carriers, a child must inherit one copy of the PKU-causing gene from each parent to have PKU.

A baby conceived by two carriers of PKU has a:

- 25% chance of having PKU (inheriting two defective genes)
- 50% chance of being a carrier, who will not have any symptoms of PKU (inheriting one PKU gene and one normal gene)
- 25% chance of inheriting two normal genes

There is a 25 percent chance that another child born to the same parents will also have PKU. Individuals with PKU can have children that do not have PKU if their partner is unaffected. However, their children will be carriers. For more information about PKU patients and pregnancy, see the “Pregnancy” section of this handbook.

What is PKU?

Image of two people with PKU and the probability of their child inheriting PKU.

Image of one person with PKU and one carrier and the probability of their child inheriting PKU.

Image of one person with PKU and one non-PKU/non-carrier and the probability of their child inheriting PKU.

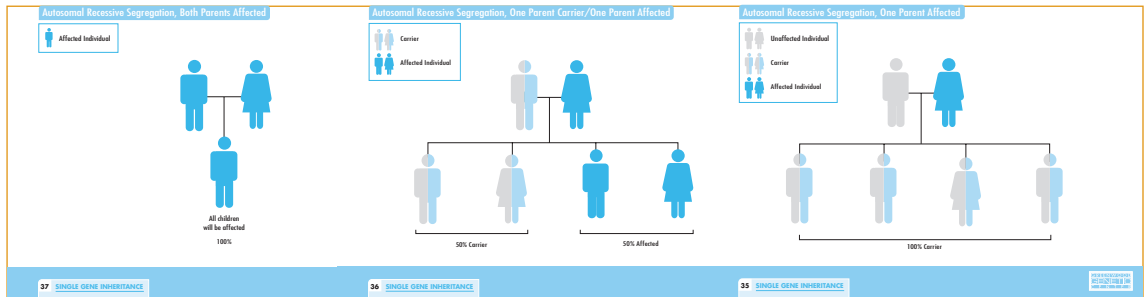


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PARENT 1	PARENT 2	CHILD
PKU	Non-PKU, non-PKU carrier	100% chance of being a carrier of PKU
PKU	Carrier	50% chance of having PKU 50% chance of being a carrier
PKU	PKU	100% chance of being affected with PKU

Parents may be concerned about whether they should have more children. Having more children after having a child with PKU is an individual decision for each family; however, because PKU can be successfully managed, many parents feel there is no reason not to have more children⁷.

⁷ Mitchell, J.J., Scriver, C.R., Phenylalanine Hydroxylase Deficiency In: *GeneReviews [Internet]*. Seattle (WA): University of Washington, Seattle; 1993-2000 Jan 10 [updated 2010 May 04].