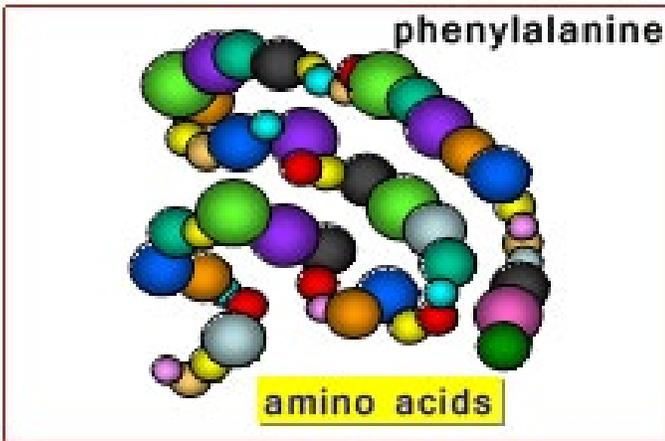


# PHENYLKETONURIA

## WHAT IS PHENYLKETONURIA?

Phenylketonuria (PKU) is a congenital disorder of the metabolism of phenylalanine, caused by a deficiency of the enzyme phenylalanine hydroxylase (PAH).

## WHAT IS PHENYLALANINE?



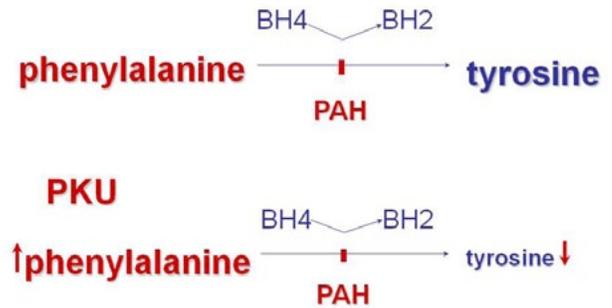
Phenylalanine is an amino acid, a simple molecule that is part of proteins. Proteins are formed by a very long chain of amino acids, which bind as the pearls of a necklace, in a special order for each protein, which determines their spatial shape and thereby, their correct function. When proteins degrade, amino acids are released and can be used to form new proteins or other compounds in our body or to generate energy.

Phenylalanine has its own metabolic pathway by which is capable of forming an amino acid very similar to it, tyrosine, thanks to the action of an enzyme, phenylalanine hydroxylase (PAH) and a coenzyme that facilitates the reaction, tetrahydrobiopterin (BH4).

## WHAT HAPPENS IN PKU?

When there is an alteration in the metabolism of phenylalanine, this amino acid can't be converted easily into tyrosine because the enzyme PAH involved in this reaction fails. This causes a massive accumulation of phenylalanine in blood, urine, tissues and brain. In addition to phenylalanine, some derivatives also accumulate the phenyl ketones. Phenyl ketones are eliminated in the urine and give the name to the disease, Phenylketonuria, also known as PKU (Phenyl-Keton-Uria).

## PKU: PAH deficiency



Another consequence of this defect is the lack of synthesis in tyrosine, an important amino acid as a precursor for neurotransmitters (chemical messengers that release neurons for intercommunication).

## WHY DOES A DEFICIENT ACTIVITY OF PAH TAKE PLACE?

The deficiency of PAH activity occurs due to gene mutations (stable and heritable changes) in the PAH gene which codify for this enzyme. PKU is an autosomal recessive genetic disorders, i.e., parents are carriers of mutations in the PAH gene, although they don't suffer from the effects of the enzymatic deficiency. If both parents transmit a mutation to their child, depending on the severity of the mutations, the child will show a total or partial enzymatic defect that will lead to a PKU or a mild hyperphenylalaninemia, respectively.

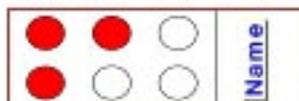
## WHAT HAPPENS WHEN A CHILD IS BORN WITH PKU?

Because her mother metabolizes all the compounds until delivery and she does it correctly, in spite of being a carrier of wrong information (capable of transmitting the HPA). When the baby starts feeding, milk proteins degrade and release all the amino acids, which are metabolized by their own metabolic pathways. Nevertheless, the transformation of phenylalanine into tyrosine will be interfered due to the fact that PAH hasn't been formed correctly and there will be an accumulation of phenylalanine. Tyrosine, in contrast, will not synthesize in sufficient quantity to be used in the synthesis of proteins that the baby needs to grow and in the synthesis

of neurotransmitters. A metabolic defect will occur. The balance needed between all the organism's compounds in order for metabolism to work correctly will be broken. This could have negative consequences for the baby (a certain level of developmental delay), which would not be detected until some months have passed by.

## HOW IS PKU DIAGNOSED?

PKU is diagnosed by analyzing the amino acids in the blood. Most countries have a neonatal screening program



that allows detecting the disease in newborn babies within the first few days of life. The purpose of these detection programs is to treat the babies before they start exhibiting symptoms of the disease. Once detected, the babies will be referred to a reference hospital to make a differential diagnosis with other less frequent types of disorders, which can cause an increase of blood phenylalanine levels (defects from pterins metabolism) and also to begin the treatment. The study of the PAH gene mutations confirms the diagnosis.

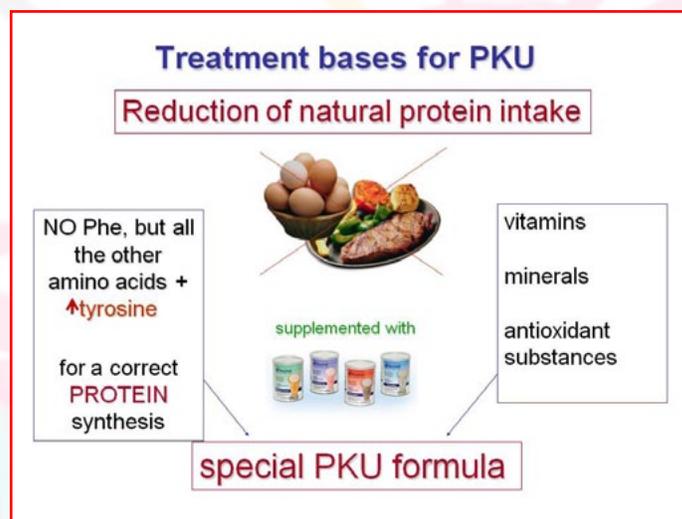
## WHAT SHOULD BE DONE TO AVOID THE CONSEQUENCES OF PKU?

Treatment is needed as soon as possible. The treatment is based on avoiding an accumulation of phenylalanine by limiting it from the child's diet. The diet for kids with PKU is based on restricting natural proteins such as milk, meat, fish, eggs and other types of food that contain phenylalanine) and substituting these proteins with a special formula that contains all the other amino acids, except for phenylalanine.

Additionally, in order to prevent deficiency of tyrosine, the formula has to be supplemented with this amino acid. This way the unbalance, created by interrupting a metabolic path, is mended and the metabolism regains its correct function. Both phenylalanine and tyrosine are important amino acids to form proteins that constitute the newborn's body. Therefore, the restriction of phenylalanine has to be adapted to obtain a correct concentration in the baby's blood and tissues.

Some patients having a moderated PKU respond to the supplementation of BH4 with a decreased concentration of blood phenylalanine. This makes it possible to

substitute the diet restricted in phenylalanine with the supplementation of this coenzyme.



PKU is a hereditary disease, which without treatment could have serious consequences. Nevertheless, if it is diagnosed and treated early and if a proper dietary control is performed, kids with PKU can live a normal life in every sense with minimal restrictions, which would be limited only to the diet.

## Translation

American School of Barcelona



Passeig Sant Joan de Déu, 2  
08950 Esplugues de Llobregat  
Barcelona, España  
Tel: 34 93 203 39 59

[www.hsjdbcn.org](http://www.hsjdbcn.org) / [www.guiametabolica.org](http://www.guiametabolica.org)  
© Hospital Sant Joan de Déu. All right reserved