PHENYLKETONURIA

In Lithuania, newborn screening for phenylketonuria (PKU) has been implemented since 1975. All neonates are tested for phenylalanine (Phe) levels in dry blood samples.

What is phenylketonuria?

Phenylketonuria is a hereditary metabolic disorder characterized by accumulation of amino acid phenylalanine in the body, leading to severe physical and intellectual disability.

What is incidence of phenylketonuria?

Phenylketonuria is one of the most common hereditary metabolic disorders. In Europe, average incidence of PKU is 1 in 10 000 births. In Lithuania, incidence of PKU is 1 in 8,300 births, and 1 in 50 people is a carrier of PKU mutation.

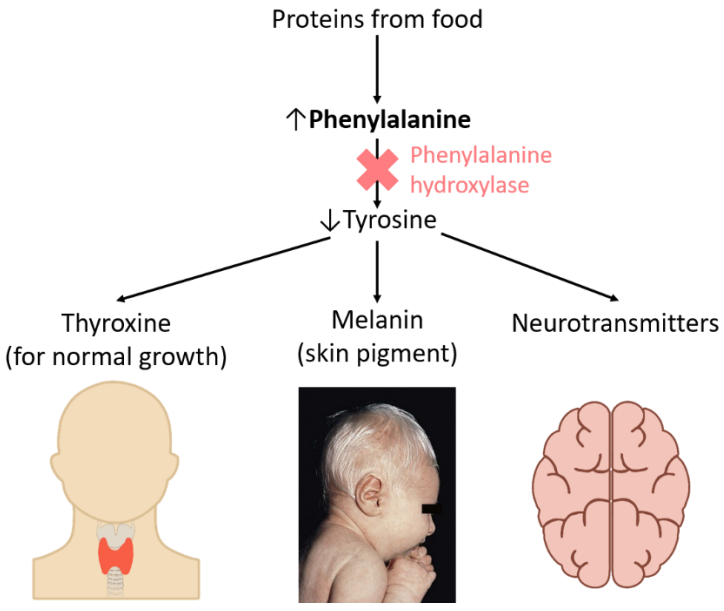
What causes phenylketonuria?

Disease is caused by deficiency of enzyme phenylalanine hydroxylase (PAH), which breaks down amino acid phenylalanine.

Phenylalanine is abundant in many protein-rich foods. Patients with PKU lack or have very little of enzyme PAH, so this amino acid remains unmetabolised.

Normally, enzyme converts phenylalanine to tyrosine – a necessary component for normal brain development after birth and other biochemical processes such as production of thyroid hormone thyroxine, pigment melanin, neurotransmitters.

In patients with PKU, phenylalanine accumulates and tyrosine decreases, excessive levels of phenylalanine are detected in the blood.



However, high blood phenylalanine levels are not specific to PKU. Phe concentration may increase in patients with severe liver impairment, in which case tyrosine levels also increase, and neonates should be tested immediately.

About 1–2 % of hyperphenylalaninemia is due to a deficiency of tetrahydrobiopterin (BH4).

How does phenylketonuria manifest?

Concentration of Phe in blood of a fetus with PKU is normal because activity of enzyme PAH is compensated by maternal enzyme. Therefore, newborns with PKU usually do not have any symptoms of the disorder.

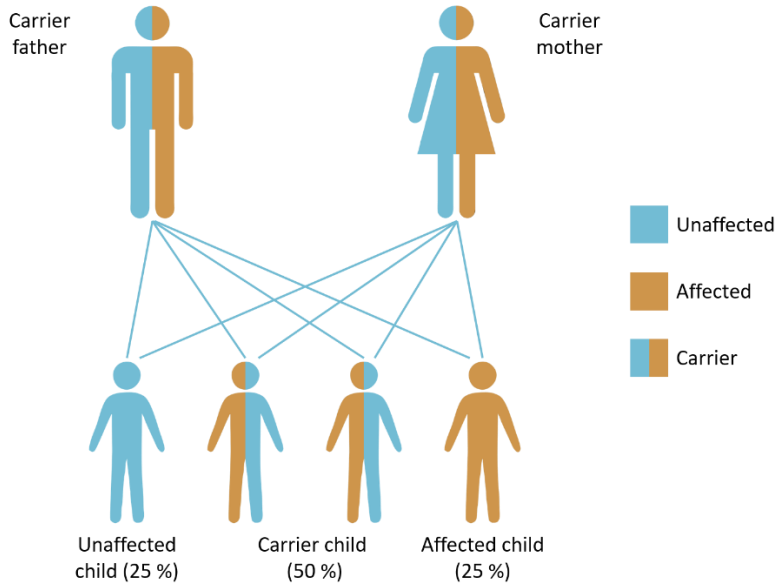
When a newborn starts consuming protein, blood levels of Phe rises gradually. Baby may become anxious, irritable or drowsy, sluggish. Skin becomes easily damaged, rashes can be observed.

Deterioration of the untreated child becomes more noticeable around the 5th-6th month of life: impaired psychomotor development, spasms, convulsions, impaired production of pigment melanin (patients with PKU are more likely to have pale skin and hair), foul urine odor due to accumulating by-product metabolites are observed.

In the first year of life, neurological disorders appear, and, over time, severe intellectual disability, behavioral or social problems such as hyperactivity, destructiveness, agitation develop.

How is phenylketonuria inherited?

Phenylketonuria is inherited in autosomal recessive manner. Usually both parents are healthy carriers of the disease-causing mutation. If a child receives an altered gene from both parents, he or she is born with PKU. Each pregnancy holds 25 percent chance of having a healthy child who will not be a carrier of the disease, 50 percent probability that the child will be a healthy carrier of the disease and 25 percent chance of having a child with FKU.



How is phenylketonuria treated?

PKU treatment is very effective if started early.

Patient should strictly follow a special diet low in phenylalanine. Diet limits intake of natural protein. Specific mixtures of amino acids that do not contain phenylalanine are prescribed as well. Breastfeeding is continued.

Main goal of treatment is to keep levels of Phe in blood within or very close to normal limits, therefore, regular blood tests are performed to check for Phe levels. Based on results, diet plan is adjusted by dietitian and geneticist.

It is recommended for treatment to be started as soon as diagnosis is made and continued throughout patient's life. Even if diagnosis of PKU is made later, dietary treatment is still recommended as it is proved to reduce some of the symptoms of PKU.

Phenylketonuria and pregnancy

Women with PKU must follow a strict diet during pregnancy since their newborns are at risk for developmental disorders. Elevated Phe levels in mother's blood are toxic to fetus and can result in microcephaly (small head), mental and physical developmental delay, congenital heart defects, and low birth weight. This phenomenon is called maternal phenylketonuria syndrome.

Families with children with phenylketonuria in Lithuania are united by “Dalia” association.