Phenylketonuria

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Template:Infobox - genetic disease **Phenylketonuria** (PKU) belongs in a category of inherited metabolic disorders and enzymopathies. It is a disorder of the metabolism of the amino acid **phenylalanine** (Phe). Heredity is autosomal recessive with a frequency of occurrence in the Czech Republic of about 1: 6000.

Pathogenesis

The cause of the disease is a mutation in the gene for **phenylalanine hydroxylase** (PAH; 12q24.1; OMIM: 612349 (http://omim.org/entry/612349)) – this enzyme hydroxylates phenylalanine to tyrosine in healthy individuals, but in people with PKU phenylalanine hydroxylase is completely absent or has very low activity. In them, phenylalanine does not hydroxylate to tyrosine, but accumulates in body fluids and damages the myelination of developing nerve fibers, a metabolic pathway is applied, which is normally insignificant, and part of phenylalanine is converted to phenylpyruvate by phenylalanine aminotransferase.

Massive transamination of phenylalanine causes depletion of 2-oxoglutarate in the citrate cycle, so the loss of energy manifests itself first in the CNS.

Symptomatology

náhled|vpravo|Poruchy metabolismu fenylalaninu a tyrosinu. PKU does not appear until after birth, because in pregnancy, excess phenylalanine and other metabolites of the fetus removed from the fetal body by the placenta. As soon as the newborn starts drinking breast milk, the level of phenylalanine in his blood begins to rise and impairs brain development, during infancy and toddlerhood, **mental retardation** gradually develops, which further progresses to moderate to severe.

Phenylpyruvate, phenyllactate and phenylacetate are increasingly excreted in the urine, hence the name phenylketonuria, and give it a **mouse odor**.

The body contains less tyrosine and products of its metabolism, such as melanin, so **weak pigmentation** also typical of the disease.

Other symptoms include microcephaly, a tendency to eczema, seizures and pyramidal and extrapyramidal symptoms.

Diagnosis

náhled|Novorozenecký screening – odběr z patičky novorozence In order to establish the diagnosis before the onset of clinical manifestations, nationwide neonatal laboratory screening is performed from a drop of blood taken between 48 and 72 hours of age. The method of tandem mass spectrometry is used. The Gutrie test was used in the past.

Treatment

The basis of treatment is a **diet low in phenylalanine** and the addition of tyrosine (ie giving foods or supplements that meet the criteria of low phenylalanine and even better increased tyrosine) can affect the level of phenylalanine in the blood and ensure normal development of the child's brain. With early diet, the development is completely normal.

The diet must be followed for life, even in adults, improper metabolism of AMK in patients may reduce cerebral function, due to a disorder of neurotransmitter metabolism.

The critical period is the **pregnancy of phenylketonurics**. In order for a healthy baby to be born, it is necessary to maintain a strict diet before conception and during pregnancy, three months before conception and during pregnancy, the mother's phenylalaninemia (blood phenylalanine level) must be within the normal range. Phenylalanine from the mother's blood would pass into the blood of the fetus and its high level would impair the development of the fetus. The consequence of the so-called **maternal phenylketonuria** is mental retardation, microcephaly, heart defects and the fetus is affected regardless of its genotype (so-called phenocopy). It is also necessary for patients with hyperphenylalaninemia to maintain a diet, as even in these, the level of phenylalanine could harm the fetus.

Summary video

References

External links

- Fenylketonurie (czech wikipedie)
- Phenylketonuria (english wikipedie)

References

- KAPRAS, J., et al. *Kapitoly z lékařské biologie a genetiky I.* 1. edition. Praha : Nakladatelství Karolinum, 1996. ISBN 80-7184-322-9.
- LEDVINA, M., et al. *Biochemie pro studující medicíny II.* 2. edition. Praha : Nakladatelství Karolinum, 2009. ISBN 978-80-246-1415-1.