PHENYLKETONURIA

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Phenylketonuria (PKU) is a hereditary autosomal recessive disease of the group of enzymopathies, associated with impaired metabolism of amino acids, mainly phenylalanine. Accompanied by the accumulation of phenylalanine and its toxic products, which leads to severe damage to the central nervous system, manifested as a violation of mental development.

It is due to mutations in the phenylalanine hydroxylase gene (locus on human chromosome 12q24.1), which results in low levels of the enzyme phenylalanine hydroxylase. Normally, phenylalanine hydroxylase regulates the clearance of about 75% of the excess phenylalanine from our body by converting it to tyrosine. The tyrosine synthesized by the action of phenylalanine hydroxylase is required for the synthesis of various neurotransmitters that act on the nervous system and also control key functions like respiration and heart rate.

Of the mutant alleles that cause PKU 99% map to the PAH gene. The remaining 1% maps to several genes that encode enzymes involved in the biosynthesis or regeneration of the cofactor ((6R)-l-erythro-5,6,7, 8-tetrahydrobiopterin) regenerating the cofactor (tetrahydrobiopterin) necessary for the hydroxylation reaction.

Due to the metabolic block, the side pathways of phenylalanine metabolism are activated and in the body there is an accumulation of phenylpyruvic and phenyllactic acids, phenylethylamine and orthophenylacetate, which normally are practically not formed. An excess of these metabolites causes a disturbance of lipid metabolism in the brain. Presumably, this leads to a progressive decline in the intellect of such patients, even idiocy. Finally, the mechanism of the development of brain dysfunction in PKU remains unclear. Among the causes are also assumed to be a deficiency of neurotransmitters in the brain, caused by a relative decrease in the amount of tyrosine and other amino acids, as well as a direct toxic effect of phenylalanine.

Successful treatment was first developed and conducted in England (Birmingham Children's Hospital) by a group of doctors led by Horst Bickel in the early 50s of the 20th century, but real success came only after the widespread use of early diagnostics of phenylalanine in the blood of newborns (Guthrie, developed and implemented in 1958–1961).

Diagnosis is performed by semi-quantitative test or quantitative determination of phenylalanine in the blood. In untreated cases, it is possible to detect the breakdown products of phenylalanine (phenylketones) in the urine (not earlier than 10–12 days of the child’s life). It is also possible to determine the activity of the enzyme phenylalanine hydroxylase in liver biopsy and to search for mutations in the phenylalanine hydroxylase gene.

At the birth of a child in maternity hospitals for 3–4 days, a blood test is taken and neonatal screening is performed to detect congenital metabolic diseases. At this stage, possible detection of phenylketonuria, and, as a consequence, the earliest possible start of treatment to prevent irreversible effects.

With the timely diagnosis of pathological changes can be completely avoided, if from birth to puberty to limit the intake of phenylalanine with food. The late start of treatment, although it does have a certain effect, does not eliminate the previously developed irreversible changes in the brain tissue. PKU can lead to intellectual disability, seizures, behavioral problems, and mental disorders. It may also result in a musty smell and lighter skin. Babies born to mothers who have poorly treated PKU may have heart problems, a small head, and low birth weight.

Treatment is carried out in the form of a strict diet from the discovery of the disease at least until puberty, many authors are of the opinion that a lifelong diet is necessary. The diet excludes meat, fish, dairy products and other products containing animal and, in part, vegetable protein. Protein deficiency is replenished by amino acid mixtures without phenylalanine. Breastfeeding of children with phenylketonuria is possible and can be successful with certain restrictions. The calculation of the diet for a patient with PKU is performed by a doctor taking into account the need for phenylalanine and its allowable amount.

ANTIOXIDANT AND ANTI-INFLAMMATORY EFFECTS OF RESVERATROL MAKE IT A PROMISING AGENT FOR TREATING OXIDATIVE STRESS-RELATED DISEASES

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Introduction. There is strong evidence that resveratrol (RSV), a polyphenol found in many plants, including grapevines, berries, peanuts, pomegranate, has antioxidant, anti-inflammatory, and anti-proliferative properties. Initially, researches on this compound date back to 1990s when the reports concerning the French paradox appeared. The French paradox is an epidemiological observation of a relatively low incidence of cardiovascular diseases observed in French people despite the high consumption rate of saturated fats and cholesterol in diet. This observation was linked to the relatively high intake of RSV-containing red wine. However, recent researches have aimed at revisiting this concept, challenging the role of RSV. Nevertheless, numerous studies have demonstrated beneficial health-related effects of RSV, making it a promising therapeutic agent. Thus, the **aim** of our paper is to review effects of RSV and evaluate its therapeutic potential.

RSV effects. Given that RSV has a polyphenolic structure, it shows a direct intrinsic antioxidant activity. This substantiates the possibility of using it for the treatment of diseases associated with excessive generation of reactive oxygen