Phenylketonuria (PKU)

Phenylketonuria (PKU) is a genetic metabolic disorder in which a baby is born without an important enzyme known as phenylalanine hydroxylase (PAH). PAH is necessary to break down an amino acid called phenylalanine, commonly found in most foods, into certain hormones, neurotransmitters, and melanin. Patients with PKU have little to no PAH, and so they cannot digest and break down phenylalanine.

Because phenylalanine is involved in the production of the pigment melanin, patients with PKU tend to have lighter skin, hair, and eyes than their siblings. Children born with PKU appear otherwise normal for the first few months. However, if untreated, phenylalanine can build up in the blood and cause severe and irreversible damage to the brain and nervous system. Initial symptoms are a loss of interest in their surroundings, irritability, and behavioral problems. Later complications of untreated PKU include developmental delay, mental retardation, hyperactivity, psychological problems, seizures, and movement disorders. Affected individuals may also smell musty or mouse-like due to excess phenylalanine in the body.

It is very important that women with PKU seek treatment and control their blood phenylalanine levels both before becoming pregnant and throughout the pregnancy, since build-up of this amino acid will damage the developing fetus even if the child has not inherited the disease.

Inheritance

Phenylketonuria is an autosomal recessive genetic disease. This means a person must have two faulty copy of PAH genes, which control the PAH enzyme, in order to develop PKU. Individuals who carry only one faulty copy of the PAH gene are called “carriers”. Carriers do not show any signs or symptoms of the disease. If both parents are carrying the faulty copy of PAH gene, the chances for their offspring to have PKU disease is one in four or 25 %.

Diagnosis and Management

If parents are potentially carriers of PKU, a genetic testing can determine if they each have a mutated copy of the PAH gene. During pregnancy, chorionic villus sampling sampling or amniocentesis can be done to screen the fetus for PKU. More commonly, PKU is tested for with a simple blood test 1-5 days after birth. Many countries mandate PKU testing for all neonates as part of a routine newborn screening program. This ensures that almost all affected newborns are diagnosed and treated early, allowing them to grow up without developmental delays.

Phenylalanine is a component of proteins that are found in milk, cheese, eggs, meat, fish, and other common foods. The main treatment for PKU is a lifelong specialized diet that is very low in phenylalanine, especially during childhood while the patient is growing. A special phenylalanine-free high-protein formula is available for babies with PKU. Unlike infant formula, this supplement is continued throughout childhood and into adulthood as a safe protein source that balances the essential amino acids and nutrients, allowing for normal physical development. Over time, certain vegetables, fruits, low-protein grains, and other low-phenylalanine foods are added to the child’s meal plan. No high-protein animal products are ever allowed. The artificial sweetener aspartame also contains phenylalanine, so “diet” drinks and foods must also be avoided.

This meal plan should be started as soon as possible after birth, ideally within the first seven to

10 days of life. It must be strictly followed and requires cooperation between parents, children, dietitians, and physicians. Regular follow-up blood tests monitor the amount of phenylalanine in the body and may indicate needed adjustments to the child's diet. The outcome of early traetment and then closely following a restricted diet is very good—children tend to develop normally with no phenylalanine buildup or related symptoms. If treatment is delayed or poorly followed, brain damage and developmental delays are likely.

In addition to diet, there are medications that can help reduce blood phenylalanine levels and increase the activity of the PAH enzyme. Although they cannot replace adherence to a proper diet, these drugs are found to be useful for managing PKU in some patients.

PKU in Arab Populations

PKU is found often in Caucasian populations worldwide, with much lower rates in people of African, Hispanic, and Asian ancestry. As a crossroads of these cultures, the Middle East has comparable rates of PKU to much of the Western world. It is one of the more common genetic diseases, with an estimated incidence of 10 cases of PKU per 100,000 live births in Bahrain, 8/100,000 in Qatar, and 5/100,000 in the UAE. In comparison, the rate of PKU in the United States is about 4-6/100,000. Oman seems to be a regional outlier, with only 2.4 cases of PKU per 100,000 live births, although this is still high enough to be of concern. There have also been documented cases in Algeria, Egypt, Kuwait, and Yemen.

PKU is an good candidate for neonatal screening because the blood test is easily performed, the treatment is well known and available, and the consequences of missing the diagnosis and not treating the disease are serious. Rather than caring for patients who are severely physically and mentally disabled, it is very cost effective and highly recommended to screen for and treat the disease at birth. As of 2008 in the Middle East, only Lebanon, Palestine, Qatar, Saudi Arabia, and the UAE had nationwide PKU screening programs. Jordan, Kuwait, and Tunisia had pilot newborn testing that included PKU, and Algeria, Libya, and Yemen were developing plans to begin a pilot program.