

BC Newborn Screening Program

Information Sheet

Phenylketonuria (PKU) – Amino Acid Disorder

What are amino acid disorders?

The amino acid disorders are a class of inherited metabolic conditions that occur when certain amino acids either cannot be broken down or cannot be produced by the body, resulting in the toxic accumulation of some substances and the deficiency of other substances.

What is PKU?

PKU is a hereditary disorder in which affected individuals cannot use the amino acid phenylalanine properly so that it builds up in the blood (hyperphenylalaninemia).

What is its incidence?

PKU affects about 1 out of every 12,000 babies born in BC.

What causes the disease?

Mutations in the phenylalanine hydroxylase (PAH) gene produce a defective enzyme that is unable to process phenylalanine properly.

What are the clinical features of the disease?

Babies with PKU are clinically indistinguishable from healthy babies for the first few weeks of life. Without treatment, however, phenylalanine accumulation will cause severe and irreversible mental retardation, eczema, and other problems. Children with untreated PKU may also have a distinctive “mousy” odour.

Phenylalanine levels start rising within 24 hours of birth. Newborns with elevated

levels on blood spot analysis are investigated further.

How is the diagnosis confirmed?

The diagnosis is confirmed by measuring the levels of plasma phenylalanine and tyrosine in the blood. Other tests may also be done to rule out other causes of higher phenylalanine levels. A diagnosis of PKU can also be confirmed by genetic analysis of the PAH gene. Diagnostic testing is arranged by specialists at BC Children’s Hospital.

What is the treatment of the disease?

A low protein diet with low phenylalanine intake should be started as soon as possible to prevent mental retardation and other problems. Some phenylalanine is required by the body for normal growth and development, so it should not be eliminated from the diet. Frequent monitoring of plasma amino acid levels, weight gain, and development are recommended.

Adult women with PKU are at risk to have babies with microcephaly, poor growth, and mental retardation if their phenylalanine levels are persistently elevated during pregnancy. Therefore, pregnant women with PKU should also be monitored closely. Treatment is coordinated by specialists at BC Children’s Hospital.

What is the outcome of treatment?

Infants who are identified early and treated appropriately grow up to be indistinguishable from other children the same age. Women with PKU who carefully

maintain good phenylalanine levels during pregnancy can have babies who have normal growth and development.

Can a family have more than one child with PKU?

PKU is inherited as an autosomal recessive disorder. The parents of a child who has PKU are assumed to be carriers for the disorder and have a 1 in 4 (25%) chance, in each pregnancy, of having another child with PKU. Prenatal testing for PKU can be done as early as 10-12 weeks of pregnancy. Genetic counselling to discuss the benefits of prenatal testing options in more detail is recommended.

Unaffected siblings of a child with PKU have a 2/3 chance of being carriers for PKU. Carriers are healthy and do not have symptoms of PKU.

What other conditions can cause elevated levels of phenylalanine?

Intermediate forms of hyperphenylalaninemia, in which the levels of phenylalanine are lower than what is usually found in classic PKU, can cause variable mental retardation and, in some cases, can be completely asymptomatic (benign). Biopterin is a cofactor for PAH. Defects in biopterin metabolism can cause hyperphenylalaninemia and will also require treatment. Maternal PKU, hyperalimentation (TPN), and liver disease can also lead to the finding of increased phenylalanine levels in newborn screening blood spots.

Resources

<http://www.newbornscreening.info/Parents/minoaciddisorders/PKU.html>

<http://www.geneclinics.org/>

http://www.marchofdimes.com/professionals/14332_1219.asp

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