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My46 Trait Profile

Phenylketonuria

Phenylketonuria is a metabolic disorder caused by an inability to correctly metabolize (i.e. break down) an amino acid called phenylalanine. It is caused by mutations in the PAH gene that makes the phenylalanine hydroxylase enzyme.

Characteristics of Phenylketonuria

Phenylketonuria (PKU) is a metabolic disorder that occurs when the body cannot process the amino acid phenylalanine. This results in the body making and excreting a byproduct of phenylalanine metabolism called a phenylketone. Excretion of phenylketones in the urine is called phenylketonuria.

Disorders in which an amino acid cannot be metabolized correctly are known as “metabolic disorders” or “inborn errors of metabolism.” PKU is one of the most common metabolic disorders. Without treatment, most individuals with PKU develop severe to profound intellectual disability, seizures, and behavioral problems. However, the problems observed in individuals with PKU are variable. With prompt diagnosis and treatment (e.g., dietary restriction of phenylalanine), many of the problems observed in individuals with PKU can be helped if not avoided altogether.

Diagnosis/Testing

Most individuals with PKU have changes or mutations in a gene called PAH. This gene is responsible for making an enzyme called phenylalanine hydroxylase. This enzyme converts phenylalanine to another amino acid called tyrosine. Mutations in the PAH gene result in a deficiency of phenylalanine hydroxylase. As a result, levels of phenylalanine in the blood become much higher than normal and abnormal byproducts of phenylalanine metabolism accumulate in the body.

Management/Surveillance

Management of individuals with PKU includes placing them on a special diet in which the intake of phenylalanine is severely restricted. Since phenylalanine is an amino acid and therefore found in protein, this often means that the protein intake of individuals with phenylalanine is restricted. The restriction is maintained at least through adolescence, and individuals must be carefully monitored while on this diet to ensure appropriate growth and nutrition. Monitoring is done by measuring the level of phenylalanine in blood.

In women with PKU, the high levels of phenylalanine increase the risk that a baby could have problems such as heart defects, poor growth, small head size, and intellectual disability. Accordingly, women with PKU who are planning a pregnancy have to keep their phenylalanine levels very low, even lower than they would otherwise.

Mode of inheritance

PKU is inherited in an autosomal recessive pattern. This means that an individual has to inherit two PAH mutations (i.e., one from each parent) to be affected with PKU. If both parents are carriers of a PAH mutation, they have a 1 in 4 (25%) chance with each pregnancy of having a child with PKU. Babies born in the United States are screened for PKU by newborn screening.

Risk to family members

Parents of a child with PKU are carriers of PKU. If a sibling of a child with PKU is unaffected, he/she has a 2 in 3

(or 66%) chance of being a carrier of PKU.

Special considerations

None

Resources

National PKU Alliance
http://npkua.org/
Children's PKU Network
http://www.pkunetwork.org/
Genetics Home Reference: Phenylketonuria
http://ghr.nlm.nih.gov/condition/phenylketonuria
MayoClinic.com: Phenylketonuria
http://www.mayoclinic.com/health/phenylketonuria/DS00514
Medical Home Portal: Phenylketonuria (PKU) and Pterin defects
http://www.medicalhomeportal.org/diagnoses-and-conditions/phenylketonuria-and-pterin-defects/description

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