

Disease Name:

PHENYLKETONURIA

PHENYLALANINE HYDROXYLASE DEFICIENCY, PAH DEFICIENCY, OLIGOPHRENIA PHENYLPYRUVICA, HYPERPHENYLALANINEMIA, MILD

Classification: Amino Acid disorder

Genetic **Inheritance:** Autosomal recessive

Information: **Population Incidence:** 1:13,000

Ethnic Incidence: Northern European, Ireland (1:4,500)

Gene & Location: 12q24.1

Common Mutation: Several; 490 separate mutations

OMIM # 261600

Disease **Symptom Onset:** Usually around 6 months of age, but can this can be variable.

Information:

Symptoms: Mental retardation is insidious, beginning at birth, but not usually apparent until the sixth month of life, by astute parents or physician. Other symptoms may include a 'mousy' or old urine odor, eczema, seizures, lighter pigmentation than other family members and peculiarities of gait or posture. The extent of retardation is related to the degree of enzyme deficiency and the length of time the brain has been exposed to elevated phenylalanine.

Physical Findings: None particular, except de-pigmentation that may be subtle. Odor may not appear until phenylalanine is over 1500 mm/l

Treatment: Standard of care is to treat any person with a phenylalanine over 1000 mm/l with a phenylalanine restricted diet. Diet is recommended for life and the degree of compliance with the diet affects brain development. Phenylalanine ammonia lyase (PAL) combines with phenylalanine in the gut to prevent absorption. Large neutral amino acids (LNAA) block uptake of phenylalanine in the brain. Both are under study as possible treatments, but are not yet clinically available. Tetrahydrobiopterin, a cofactor of phenylalanine hydroxylase has been found to reduce phenylalanine significantly in children with milder forms of PKU. Unfortunately, it is not available in the U.S. Liver transplant cures PKU, but is seldom used due to the risks and ongoing need for medical care. Gene therapy is still being investigated.

Natural History without treatment: Generally severe mental retardation, white matter changes with phenylalanine levels above 1540 mm/l (normal = 58-62 mm/l); milder brain damage with intermediate levels (600-1540mm/l). In addition there may be seizures, eczema, and difficult explosive behavior or attention deficits. Discontinuation of a phenylalanine restricted diet may result in loss of IQ, disturbed executive functions, behavior and psychological problems as well as the appearance of eczema, odor and seizures. Females have a 95% chance of producing children damaged by phenylalanine prenatally unless they adhere to strict diet during pregnancy.

Natural History with treatment: Mental retardation can be completely prevented, although there may still be specific learning disabilities. Strict control of blood phenylalanine through out life is now recommended for all severe PKU patients.

Metabolic Information: **Missing Enzyme & Location:** Phenylalanine hydroxylase; liver
MS/MS profile: Elevated phenylalanine and abnormal Phenylalanin/Tyrosine ratio
Prenatal testing: Chorionic villus, amniocentesis, DNA mutation analysis

Miscellaneous Information: Diagnosis is made by amino acid analysis of phenylalanine and tyrosine and exclusion of bipterin defects (see Hyperphenylalaninemia, bioptern defects). DNA mutation analysis may be helpful in predicting severity of PKU.

Prepared for the NW Regional Newborn Screening Program by Judi Tuerck, RN MS.

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