IDPH
ILLINOIS DEPARTMENT OF PUBLIC HEALTH

**NEWBORN SCREENING**
**OFFICE OF HEALTH PROMOTION**
535 W. Jefferson St., 2nd Floor
Springfield, IL 62761
Phone: 217-785-8101
Fax: 217-557-5396

# Phenylketonuria
## Information for Physicians and Other Health Care Professionals

**Definition** Phenylketonuria (PKU) is a disorder of amino acid metabolism that results in excess levels of phenylalanine in body fluids. Elevated levels of phenylalanine can become neurotoxic; early detection and treatment of hyperphenylalaninemia is necessary to prevent mental retardation.

**Clinical Symptoms** Although infants with PKU usually appear normal at birth, early symptoms may include skin rash, seizures, excessive restlessness, irritable behavior and a musty odor of the body or urine. Later signs include developmental delays, gait disturbances and mental retardation.

**Newborn Screening and Definitive Diagnosis** Recently in Illinois, tandem mass spectrometry (MS/MS) has been implemented to provide newborn screening for PKU and hyperphenylalaninemia. This new laboratory technology has replaced the fluorometric analysis previously utilized for PKU screening. Although false positive and false negative results are possible with this screening, MS/MS should provide a more reliable screening method for the detection of elevated phenylalanine levels in dried blood samples, even in infants who have not been fed. As with all newborn screening, specimen collection should occur as soon as possible, but after the first 24 hours of life. **When receiving a presumptive positive result (elevated phenylalanine level), the clinician should *immediately* check on the clinical status of the baby and refer the infant to a metabolic disease specialist.**

**Treatment** Early diagnosis and treatment is essential to prevent developmental delays. Phenylalanine is an essential amino acid, and individuals with PKU require careful dietary management and monitoring for life. Individuals with PKU require a low phenylalanine diet, which consists of a specialized medical formula in combination with regular foods that are low in phenylalanine. There are several low phenylalanine products available for use as formula for infants and as dietary supplements for older children and adults. Illinois provides low phenylalanine formula at no cost to state residents who are under comprehensive medical management by an authorized PKU consultant. Women of childbearing age who are diagnosed with PKU or hyperphenylalaninemia require strict dietary control prior to conception and throughout pregnancy to reduce their risk of complications, including miscarriage or of having an infant with severe birth defects due to high maternal levels of phenylalanine. The National Institutes of Health recommends lifetime low phenylalanine diet for individuals with PKU.

**Incidence** PKU and hyperphenylalaninemia occur in one of every 12,000 births. Since 1965, Illinois has identified more than 600 cases of PKU and related disorders through the Newborn Screening Program.

**Inheritance Pattern** These disorders are inherited in an autosomal recessive pattern. As an autosomal recessive disorder, the parents of a child with PKU are unaffected, healthy carriers of the condition and have one normal and one abnormal gene. With each pregnancy, carrier parents have a 25 percent chance of having a child with two copies of the abnormal gene, resulting in PKU. Carrier parents have a 50 percent chance of having a child who is an unaffected carrier and a 25 percent chance of having an unaffected, non-carrier child. These risks hold true for each pregnancy. All siblings of infants diagnosed with PKU or hyperphenylalaninemia should be tested; genetic counseling services should be offered to the family.

**Physiology** Classical PKU is due to a deficiency of the liver enzyme, phenylalanine hydroxylase. In some cases, hyperphenylalaninemia also may result from impaired synthesis of biopterin factor. These inborn errors of phenylalanine metabolism result in the accumulation of excess levels of phenylalanine in body fluids and the clinical manifestations of the disorder.

**Key Points for Parents** Avoid overly alarming the child's parents if the diagnosis has not yet been confirmed. If the child needs additional testing or diagnostic evaluation, make certain the parents understand the importance of following the pediatrician's and/or the specialist's recommendations for additional testing and referrals.

**Follow-up After Confirmation of Diagnosis** These guidelines should be followed after a diagnosis of PKU has been confirmed:

1. Parents should understand that treatment is lifelong and that compliance with dietary management is imperative to the child's health, growth and development.

2. Infants and children with PKU or hyperphenylalaninemia should have regular follow-up appointments with a metabolic disease specialist.

3. Parents should understand that treatment is not curative and that all morbidity cannot necessarily be prevented. Long-term management, monitoring and compliance with treatment recommendations are essential to the child's well-being. A multidisciplinary approach is recommended and should include the following specialties: pediatrics, genetics and nutrition.

4. Genetic counseling services may be indicated. A list of counselors and geneticists, whose services are available through the Illinois Department of Public Health, should be given to the parents if they have not already seen a geneticist.

5. Provide a list of support services available within the community, such as the local health department, Early Intervention service providers and the University of Illinois at Chicago, Division of Specialized Care for Children (DSCC).

6. Parents should not feel responsible for causing the child's disorder or be overly fearful for the child's future. With proper medical care and lifelong dietary management, children with PKU can enjoy healthy, productive lives.

7. Additional information about newborn screening can be found at:
   - Baby's First Test: http://www.babysfirsttest.org/
     Health Resource and Service Administration (HRSA), Grant no. U36MC16509, Quality Assessment of the Newborn Screening System.

   - National Center for Biotechnology Information: http://www.ncbi.nlm.nih.gov/gtr/
     National Center for Biotechnology Information, U.S. National Library of Medicine, 8600 Rockville Pike, Bethesda MD, 20894 USA.

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