

Understanding Diagnostic Tests in the
 6th Edition
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Childbearing Year

24 hours of birth. Ketoacids appear in the urine within a few days, causing it to have a distinct odor of burnt sugar or maple syrup. As with other disorders, there are less severe variants as well. The mildest form may go undetected for months until some illness reveals clinical and biochemical abnormalities.

Tests should be done as soon as this condition is suspected. Detection depends on protein ingestion or endogenous protein catabolism. Elevation of leucine is detected by a bacterial inhibition assay; normal levels are <2 mg/dl (<53 μmol/L). Even a transient elevation of plasma leucine is unusual unless the baby is premature and/or receiving IV amino acid preparations. Any baby whose plasma leucine is 4 mg/dl (305 μmol/L) or more should be considered to have MSUD until proven otherwise. *This constitutes a medical emergency as death can occur rapidly.* Dietary treatment must start immediately and continue for life.

Symptoms appear rapidly during the first days of life in untreated infants. They include high-pitched cry, irritability, spasticity, central nervous system depression leading to coma, vomiting, severe metabolic acidosis, hypoglycemia, and convulsions leading to death in 2 to 4 weeks. However, normal growth and development can be achieved if treatment begins before 10 days of age. Dietary management is necessary for life and must be extremely precise. Small dietary imbalances lead to rapid degeneration.

Muscular dystrophy is screened in some areas using an assay that identifies increased creatine phosphokinase (CPK) activity. Muscular dystrophy usually presents at 2 to 6 years of age with progressive degeneration of the muscle fibers and an overgrowth of connective tissue. Ten percent of those affected have nonprogressive mental retardation. Death is usually from pneumonia about 15 years after the onset of symptoms; most of those affected die by age 20. There is no bio-technical therapy available; as a result many feel it is not cost-effective to screen when nothing can be done to alter the disease progression.

Phenylketonuria (PKU) is an inborn metabolic disorder affecting about one in every 10,000 to 15,000 Caucasian infants. It appears to be less common among other races, but racial frequency is not well-known. The problem stems from an inability to metabolize phenylalanine, an essential amino acid (protein); therefore symptoms do not appear until sufficient milk feedings have been ingested. In fact, some infants with PKU may appear to be normal for months even though problems are developing. These include severe mental retardation, microcephaly, eczematous or oily skin, cerebral palsy, convulsions, dysplasia, projectile vomiting, hyperactivity with purposeless movements, and an abnormal EEG. Unprocessed phenylalanine builds up in the brain, causing damage and severe retardation. The disorder also blocks normal pigmentation. This can cause the baby to be fair, blonde, and blue-eyed among Caucasians or much lighter than other family members in dark-skinned Caucasian families or families of color. The urine of PKU babies has a characteristic musty or mousey odor. The phenylalanine level

is over 20 mg/dl (121 μmol/L). Normal phenylalanine values at one month of age range from 0.9 to 2.0 mg/dl (54.5-121 μmol/L). There are several intermediate forms of PKU in which plasma levels range between 3 and 20 mg/dl (182-1211 μmol/L). In these cases, mental retardation is variable and may, in some cases, be completely absent. Mothers whose babies have transient phenylalanine elevations should be tested to determine if PKU is a factor, particularly if the baby was tested within the first 24 hours of life.

Defects of bioprotein metabolism can also cause variable levels of phenylalanine. There will be progressive neurological damage with seizures and steady deterioration which becomes noticeable around 6 to 20 months of age despite a therapeutic diet. Because of this, all babies with persistently elevated levels of phenylalanine should have blood and urine tests for bioprotein.

Urine tests for phenylalanine were developed in the 1940s. Their use for screening purposes has been discontinued, because abnormal urinary levels are not apparent until 4 to 6 weeks of age, after brain damage has already begun. Blood testing using a bacterial inhibition assay (Guthrie test) determines if abnormally high levels of phenylalanine are present much earlier. The test is abnormal within 24 hours in 90% of cases and almost always by 48 hours of birth if the baby has ingested adequate dietary protein. In a breastfed baby, the test should be done after the milk has been in for 48 hours to allow for sufficient buildup of protein. Breast milk contains less phenylalanine than formula, so it is important to test after the milk supply and nursing are well-established. Variant or mild forms of PKU require longer feeding to produce abnormal results.

RESULTS	LIKELY REASONS:	WHAT HAPPENS NEXT
>6 mg/dl (≥363 μmol/L) (any age, no other abnormal tests)	PKU or variant forms of PKU likely	Retest
4 mg/dl (242 μmol/L) (infant <48 hrs old)	PKU or variant form possible; mother has PKU; false positive	Retest, consider screening mother
≥4 mg/dl (≥242 μmol/L) (infant ≥48 hrs old)	PKU or variant form possible; false positive	Retest

The baby will need a special low phenylalanine diet if phenylalanine levels are 6 mg/dl (363 μmol/L) or more. The diet is maintained until the myelin sheath of the nervous system is fully formed, usually 8 to 10 years and possibly longer, especially in girls. Some breastfeeding may be possible, depending on the level of phenylalanine tolerance in the baby. Frequent monitoring is required, especially in the first weeks of life, as variant forms may be indistinguishable from true PKU and improper nutritional therapy can be fatal. Untreated children have nasty dispositions, skin rashes, frequent tantrums and severe retardation. If the diet is started early, most children have normal intelligence and behavioral problems are minimized, but not necessarily avoided entirely. Results vary if dietary therapy is

3 days for milk to come in
 + 2 days for latching
 5 days
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