hyperphenylalaninemia and PKU. The reported figures for PKU in the United States is 1 case per 15,000 live births. The disease has a wide variation of incidence by ethnic groups. In Europe, the incidence is 1 in 10,000 births; in Asia and Africa, the prevalence is quite low (Blau, van Spronsen, and Levy, 2010).

Clinical manifestations in untreated PKU include failure to thrive (growth failure); frequent vomiting; irritability; hyperactivity; and unpredictable, erratic behavior. Cognitive impairment is thought to be caused by the accumulation of phenylalanine and presumably by decreased levels of the neurotransmitters dopamine and tryptophan, which affect the normal development of the brain and CNS, resulting in defective myelinization, cystic degeneration of the gray and white matter, and disturbances in cortical lamination. Older children commonly display bizarre or schizoid behavior patterns such as fright reactions, screaming episodes, head banging, arm biting, disorientation, failure to respond to strong stimuli, and catatonia-like positions.

Diagnostic Evaluation*

The objective in diagnosing and treating the disorder is to prevent cognitive impairment. Every newborn should be screened for PKU. The most commonly used test for screening newborns is the **Guthrie blood test**, a bacterial inhibition assay for phenylalanine in the blood. *Bacillus subtilis,* present in the culture medium, grows if the blood contains an excessive amount of phenylalanine. If performed properly, this test detects serum phenylalanine levels greater than 4 mg/dl (normal value, 1.6 mg/dl), but it will not quantify the results. Other methods for testing include quantitative fluorometric assay and tandem mass spectrometry, which will give an absolute value. Only fresh heel blood, not cord blood, can be used for the test.

Avoid "layering" the blood specimen on the special Guthrie paper. Layering is placing one drop of blood on top of the other or overlapping the specimen. This practice results in a falsely high reading, or false positive, which will lead the newborn screening department to call the family and physician to arrange for a diagnostic blood phenylalanine test to determine whether the newborn truly has PKU. Best results are obtained by collecting the specimen with a pipette from the heel stick and spreading the blood