

Amino Acid Disorders (NBS)

Use

Quantitative measurement of phenylalanine, arginine, citrulline, leucine, methionine, tyrosine, and valine in blood specimens dried on filter paper as an aid in screening newborns for phenylketonuria (PKU) and other amino acid disorders, including argininemia, argininosuccinic aciduria, citrullinemia type I, citrullinemia type II, homocystinuria, hypermethioninemia, maple syrup urine disease, benign hyperphenylalaninemia, bipterin defect in cofactor biosynthesis, bipterin defect in cofactor regeneration, tyrosinemia type I, tyrosinemia type II, tyrosinemia type III.

Clinical Significance

Elevated amino acids in newborn blood can be indicative of one or more of several metabolic disorders, collectively known as amino acidopathies. In amino acidopathies, enzymes necessary for the metabolism of certain amino acids are unavailable or have reduced activity. As a result, the concentration of the affected amino acids and alternative metabolites increases in the infant's body. These excesses can have severe deleterious effects on the infant's health, including death. Some commonly studied amino acidopathies are:

- *PKU* is a disorder of aromatic amino acid metabolism in which phenylalanine cannot be converted to tyrosine. If untreated, PKU leads to various degrees of mental retardation.
- *Hyperphenylalaninemia* leads to mental retardation and muscular rigidity.
- *Homocystinuria* leads to vascular occlusive disease, osteoporosis, accumulation of homocysteine and methionine, and variable developmental delays.
- *Maple Syrup Urine Disease* (MSUD) is caused by a disorder of branched- chain amino acid metabolism resulting in elevated levels of leucine, isoleucine and valine in the blood. If untreated, lethargy progressive to coma, developmental delay, and convulsions will develop.
- *Tyrosinemia type 1* (hereditary tyrosinemia) leads to acute hepatic failure or chronic cirrhosis and hepatocellular carcinoma.
- *Citrullinemia* leads to convulsions, anorexia, vomiting and lethargy, followed rapidly by potentially lethal coma.

Further information and ACT Sheets can be found at the OSDH Newborn Screening Program [website](#).

Methodology

Tandem mass spectrometry (MS/MS)

Specimen Type

See [Guidance for Collection of NBS Dried Blood Spots](#)

Minimum Volume/Size

See [Guidance for Collection of NBS Dried Blood Spots](#)

Collection Instructions

See [Guidance for Collection of NBS Dried Blood Spots](#)

Common Causes for Rejection

See [Guidance for Collection of NBS Dried Blood Spots](#)

Shipping

See [Guidance for Collection of NBS Dried Blood Spots](#)

Turn-around Time

Within 5 working days of receipt

Reference Range

- Phenylalanine < 150 µmol/L
- Arginine < 100 µmol/L
- Citrulline < 50 µmol/L if age is < 7 days
- Citrulline < 63 µmol/L if age is ≥ 7 days
- Leucine < 330 µmol/L
- Methionine < 75 µmol/L
- Succinylacetone < 1.30 µmol/L
- Tyrosine < 370 µmol/L
- Arginosuccinic Acid < 2.89
- Valine < 330 µmol/L
- Phe/Tyr ratio < 2.0
- Cit/Arg ratio < 5.0
- ASA/Arg < 0.2
- Leu/Phe ratio < 4.8
- Met/Phe ratio < 1.2

Reportable Results

- Within Normal Limits
- Outside Normal Limits

Interpretation

- Within Normal Limits
 - Not consistent with Amino Acid Disorders
- Outside Normal Limits
 - Elevated: Submit repeat specimen as soon as possible
 - High or Repeat Elevated: Consistent with <AA disorder>; immediate confirmatory testing recommended
 - Pattern of Multiple Elevated Analytes: Consistent with TPN; submit new specimen at 14 days of age

Limitations/Interferences

- This is a screening test only. A diagnostic procedure should be used for confirmation of presumptive abnormal amino acid profiles.
- False negative results for some amino acid disorders can be obtained from blood samples that have been collected too soon after birth, i.e., ≤ 24 hours post-partum; or that have been collected from infants who have not received an adequate protein-containing diet within the 24-hour period prior to sample collection.
- High nutritional intake of amino acids may interfere with the validity of amino acid concentrations.
- Variables such as hematocrit, prematurity, and age of infants may affect the interpretation of the values produced.
- Specimens improperly collected, processed or transported may result in erroneous results.

CPT Code

82139

Notes

This test is approved for *in vitro* diagnostic use by the U.S. Food and Drug Administration.