Amino Acid Disorders
(aka Aminoacidopathies)

Amino acid disorders are caused by the body's inability to breakdown or metabolize certain amino acids in proteins, or by the inability to detoxify the by-product of amino acids (ammonia) through the urea cycle. The buildup of amino acids and/or by-products of amino acid metabolism in the blood cause severe medical complications. The presentation of the various aminoacidopathies varies from no obvious clinical symptoms for months (phenylketonuria), to acute encephalopathy (maple syrup urine disease, citrullinemia, argininosuccinic aciduria) within days following birth. In each of these disorders, the lack of early identification and treatment may result in serious medical consequences, including mental retardation, developmental delays, failure to thrive, and/or death. Amino acid disorders are autosomal recessive.

Missouri has been screening for phenylketonuria (PKU) since 1967, but as of July 1, 2005, we have been able to add several additional amino acid disorders to the screening panel using tandem mass spectrometry. Amino acids are stable in the dried blood spot samples and can be measured and compared to other amino acids present. Elevated (marker) amino acids act as an indication that the enzyme needed to metabolize them may be disabled or missing.

The list of amino acid disorders that we screen for are:

Argininemia (ARG, arginase deficiency)
Argininosuccinate acidemia (ASA, argininosuccinase)
Citrullinemia type I (CIT-I, argininosuccinate synthetase)
Citrullinemia type II (CIT-II, citrin deficiency)
Defects of biopterin cofactor biosynthesis (BIOPT-BS)
Defects of biopterin cofactor regeneration (BIOPT-RG)
Homocystinuria (HCY, cystathionine beta synthase)
Hyperphenylalaninemia (H-PHE)
Hypermethioninemia (MET)
Maple syrup urine disease (MSUD, branched-chain ketoacid dehydrogenase)
Phenylketonuria (PKU, phenylalanine hydroxylase)
Tyrosinemia type I (TYR-1, fumarylacetoacetate hydrolase) *****
Tyrosinemia type II (TYR-II, tyrosine aminotransferase)
Tyrosinemia type III (TYR-III, hydroxyphenylpyruvate dioxygenase)

***** There is a lower probability of detection of this disorder during the immediate newborn period.

Prevalence: 1: 8,000 (This is the projected, combined prevalence of all the amino acid disorders).

Analytes Measured: The list of amino acid markers and ratio of markers that we monitor in each dried blood spot specimen to screen for these disorders are:

Disorder	Marker	Abnormal Range
ARG	Arginine	> 100 umol/L
ASA	Argininosuccinic acid	> 4.0 umol/L
	ASA/Arg	> 0.75
CIT-I and CIT-II	Citrulline	> 60 umol/L
	Cit/Tyr	> 1.0
	Cit/Arg	> 6.0
HCY and MET	Methionine	> 70 umol/L
	Met/Phe	> 1.2
MSUD	Leucine	> 250 umol/L
	Valine	> 250 umol/L
	Leu/Phe	> 4.0
	Val/Phe	> 3.5
PKU, H-PHE BIOPT-BS and BIOPT-RG	Phenylalanine	> 130 umol/L
	Phe/Tyr	> 2.0
TYR-I, TYR-II, and TYR-III	Tyrosine	> 250 umol/L

Reported Abnormal Ranges may change slightly with reagent kit lot changes.

Feeding Effect: Protein feeding is helpful as it challenges the metabolic pathways involved and causes the identifying markers to elevate above the normal cutoff levels allowing detection of the disorder. The optimum collection time for the newborn screening sample is between 24 and 48 hours after birth, and sufficient protein feeding has taken place by then. This includes TPN feeding, which contains amino acids.

TPN feeding can elevate several of the amino acids above the designated cutoffs. If the infant is on TPN, we ask that it be noted on the requisition form to help us reduce the reporting of false positive results. Not all TPN fed infants will get abnormal results, but if they do, we ask that a repeat newborn screening sample be collected 48 hours after the TPN has been discontinued.

Timing Effect: The recommended sample collection time is between 24 and 48 hours after birth. If the sample is collected before 24 hours of age, then a second screening sample is required after 24 hours of age.

We have special sample collection guidelines for premature, sick, low birth-weight, and NICU infants in regards to minimizing interferences from factors causing false positives in that population; while at the same time upholding prompt identification of true disorders (see NICU guidelines on this web-site).

Confirmation: Screening results that indicate a low risk for an amino acid disorder require only a repeat newborn screening test. This means that only a slight elevation of one of the markers was detected on the initial screening test, and that specific diagnostic testing does not appear necessary. Our cutoffs are set low enough so that some normal infants (sometimes carriers of the disorder) will be flagged for retesting. If, however, the infant is sick or displays signs of metabolic distress, the physician may wish to conduct diagnostic testing instead of, or in addition to the repeat screen.

Screening results that indicate a moderate to high risk for an amino acid disorder are considered "presumptive positive" and are immediately phoned and faxed to the physician of record. The doctor is then referred to our contracted genetic referral centers for expert advice on the disorder in question and is informed on what confirmatory diagnostic testing should be done to rule out the disorder, and what precautionary measures should be taken until the confirmatory results are completed.

Treatment: Treatment of these disorders is accomplished with dietary restriction of the offending amino acid(s) and sometimes medication. Urea cycle disorders will require treatment with low protein diets and medications to prevent hyperammonemia and remove toxic compounds. Infants with neonatal presentations of a urea cycle disorders represent medical emergencies and outcomes may be variable. These patients typically require aggressive treatment with hemodialysis.