



**NEWBORN SCREENING
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Maple Syrup Urine Disease Information for Physicians and Other Health Care Professionals

Definition Maple syrup urine disease (MSUD) is an inherited disorder of amino acid metabolism, caused by a deficiency in an enzyme complex that results in defects in the catabolism of the amino acids leucine, isoleucine and valine.

Clinical Symptoms Onset of symptoms can be within the first week of life. Initial signs include poor feeding and vomiting. Additional clinical findings may include lethargy, irritability, muscular rigidity, seizures and eventual metabolic decompensation leading to coma and death. There is a life-long risk for episodes of ketoacidosis, and hypoglycemia is common. Mental and neurological deficits are common findings among individuals with MSUD, especially in patients diagnosed after symptoms have developed.

Newborn Screening and Definitive Diagnosis In Illinois, newborn screening for MSUD is performed using tandem mass spectrometry. False positive and false negative results are possible with this screening. **Infants with a presumptive positive screening tests require prompt follow-up and, when notified of these results, 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 prompt treatment can significantly affect prognosis. Individuals with MSUD need a life-long diet restricted in branched-chain amino acids, and supplemented with vitamin B1 (thiamine). During periods of metabolic decompensation, peritoneal dialysis and/or treatment with intra-venous hyperalimentation **without** branched-chain amino acids (leucine, isoleucine, valine) may be necessary.

Incidence MSUD has an estimated incidence between one in 100,000 to one in 300,000 births.

Inheritance Pattern MSUD is inherited in an autosomal recessive pattern. As an autosomal recessive disorder, the parents of a child with one of these conditions are unaffected, healthy carriers of the condition, and have one normal gene 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 MSUD. 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 would hold true for each pregnancy. All siblings of infants diagnosed with MSUD should be tested; and genetic counseling services should be offered to the family.

Physiology Decarboxylation of leucine, isoleucine and valine is accomplished by a multi-complex enzymatic system (branched-chain alpha ketoacid dehydrogenase). Deficiency of a component enzyme within this pathway causes accumulation of branched-chain amino acids and ketoacids in body fluids and tissues resulting in the clinical manifestations of MSUD.

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 that the parents understand the importance of following the pediatrician's and/or specialist's recommendations for additional testing and referrals.

Follow-up After Confirmation of Diagnosis These guidelines should be followed after a diagnosis of MSUD 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 MSUD should have regular follow-up appointments with a metabolic disease specialist.
3. Long-term management, monitoring and compliance with treatment recommendations are essential to the child's well-being. A multi-disciplinary approach including the following specialties is recommended: pediatrics, genetics and nutrition. Parents should understand that treatment is not curative and that all morbidity cannot necessarily be prevented.
4. Genetic counseling services are recommended. A list of genetic 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 available support services in 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. 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.