



**NEWBORN SCREENING
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Organic Acid Disorders Information for Physicians and Other Health Care Professionals

Definition Organic acid disorders are a group of inherited metabolic conditions. Each organic acid disorder is associated with a specific enzyme deficiency that causes the accumulation of organic acids in blood and urine. The accumulated compounds or their metabolites are toxic, resulting in the clinical features of these disorders.

Newborn screening in Illinois includes testing for a panel of acylcarnitines. In some cases, an elevated level of a particular acylcarnitine may indicate the possibility of one of several different organic acid disorders; the specific disorder cannot be determined without further testing. It has been demonstrated that the following organic acid disorders may be detected using this panel:

Beta-ketothiolase deficiency (BKT)
Glutaric aciduria type I (GAI)
Isovaleric acidemia (IVA)
Propionic acidemia (PA)
Malonic aciduria (MA)
Methylmalonic acidemia (MMA)
Multiple carboxylase deficiency (MCD)
2-methylbutyryl-CoA dehydrogenase deficiency (2MBCD)
3-methylcrotonyl-CoA carboxylase deficiency (3MCC)
3-hydroxy-3-methylglutaryl-CoA lyase deficiency (HMG)
3-methylglutaconic aciduria (3MGA)

Clinical Symptoms Many organic acid disorders present in the neonatal period. Typically, an affected newborn appears normal for the first days of life, but then may develop vomiting, poor feeding, failure to thrive, hypoglycemia, hyperammonemia, seizures, hypotonia and lethargy, progressing to coma. Common findings include ketosis, metabolic acidosis and, in some cases, an unusual odor. Many individuals affected with organic acid disorders have a significant risk of death during infancy.

Newborn Screening and Definitive Diagnosis In Illinois, newborn screening for organic acid disorders is performed using tandem mass spectrometry to detect elevated acylcarnitine levels. False positive and false negative results are possible with this screening. Early specimen collection (after first 24 hours of age) may enhance the detection of these disorders, as acylcarnitine levels may decrease with infant age. **Infants with 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 For many organic acid disorders, early diagnosis and treatment can significantly change the outcome of the disease. Improved outcome is noted in most cases when the infant is provided a low- protein diet and carnitine supplementation. For some organic acid disorders, additional dietary supplements are recommended. Prevention of ketoacidotic episodes improves prognosis, and aggressive treatment during such episodes, including glucose administration, is warranted.

Incidence Estimates vary widely for the incidence of each organic acid disorder and for many, the actual incidence is not yet known. Most of these disorders are rare and incidence for individual organic acid disorders may vary from one in 20,000 births to less than one in 200,000 births.

Inheritance Pattern All of these disorders are 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 and the resulting organic acid defect. 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 an organic acid disorder should be tested; and genetic counseling services should be offered to the family.

Physiology In the normal degradation of many amino acids, the intermediate metabolites are organic acids. Each organic acid disorder is caused by a deficiency in a specific enzyme necessary to this degradation process. The organic acids accumulate in body fluids and are excreted in the urine. Severe metabolic acidosis can ensue.

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 an organic acid disorder 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 an organic acid disorder should have regular follow-up appointments with a metabolic disease specialist.
3. **Parents should be warned that if the infant shows early signs of the condition, such as vomiting or lethargy, they should immediately seek medical attention for the child.** A medical plan created by the metabolic specialist and the primary care provider should be developed for these acute episodes.
4. 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.
5. 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.
6. 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).
7. 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.