



**NEWBORN SCREENING
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MCAD and Other Fatty Acid Oxidation Disorders Information for Physicians and Other Health Care Providers

Definition Fatty acid oxidation disorders are a group of inherited metabolic conditions that lead to an accumulation of fatty acids, and a decrease in cell energy metabolism. Each fatty acid oxidation disorder is associated with a specific enzyme defect in the fatty acid metabolic pathway and affects utilization of dietary and stored fat.

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 fatty acid oxidation disorders; the specific disorder cannot be determined without diagnostic testing. It has been demonstrated that the following fatty acid oxidation disorders may be detected in newborn dried blood spot samples.

Carnitine/acylcarnitine translocase deficiency (CACT) - early onset types, extremely rare
Carnitine palmitoyl transferase deficiency type II (CPT II)
Carnitine palmitoyl transferase deficiency type 1A (CPT1A) - may not be reliably detected in first few days of life
Carnitine Uptake Defect (CUD) - may not be reliably detected in first few days of life
Glutaric aciduria type II (GA II)/Multiple acyl-CoA dehydrogenase deficiency (MADD)
Isobutyryl-CoA dehydrogenase deficiency (IBCD)
Medium chain acyl-CoA dehydrogenase deficiency (MCAD)
Long chain 3-hydroxyacyl-CoA dehydrogenase deficiency (LCHAD)
Short chain acyl-CoA dehydrogenase deficiency (SCAD)
Medium/Short chain L-3-hydroxyacyl-CoA dehydrogenase deficiency (M/SCHAD)
Trifunctional protein deficiency (TFPD)
Very long chain acyl-CoA dehydrogenase deficiency (VLCAD)

Clinical Symptoms Affected infants can be diagnosed in the neonatal period. Children with MCAD have a significant risk of death during the first, or subsequent clinical episode of hypoglycemia. In the past, these deaths were sometimes attributed to sudden infant death syndrome (SIDS). In most cases, the first episode arises following illness or fasting, and occurs in infancy or early childhood. Fatty acid oxidation disorders can cause recurrent episodes of hypoglycemia. Clinical findings may include lethargy, hypotonia, failure to thrive, persistent vomiting, hepatomegaly, rhabdomyolysis and Reye syndrome-like episodes.

Newborn Screening and Definitive Diagnosis In Illinois, newborn screening for fatty acid oxidation defects is performed using tandem mass spectrometry to detect elevated acylcarnitine levels. Early specimen collection (after first 24 hours of age) may enhance the detection of these disorders, as acylcarnitine levels may decrease with infant age. False positive and false negative results are possible with this screening. **Infants with a presumptive positive screening test 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. The attending physician should also advise the parents to avoid any significant time gap in feedings.**

Treatment Early diagnosis and treatment is essential for an improved prognosis. If left untreated, these conditions may result in significant disability and, ultimately, death. Most of these conditions are chronic, with life-long episodes of hypoglycemia. In some of the more severe infantile forms, there is a very poor prognosis. For most fatty acid oxidation disorders, including MCAD, management involves avoidance of fasting and aggressive medical management during illness, especially if the child is vomiting or is not receiving adequate nutritional intake. At the time of intercurrent illness, the infant/child should be admitted for medical care, including administration of intravenous dextrose to prevent hypoglycemia. Supplemental carnitine, a low-fat diet and home glucose monitoring, may be prescribed depending on the specific disorder.

Incidence MCAD is the most common of the fatty acid oxidation disorders with an incidence of approximately one in 10,000 to 20,000 births. LCHAD and VLCAD are rare disorders with an estimated incidence of one in 100,000 births. There is a mild form of SCAD deficiency that appears to be quite common, but the clinical significance of this condition is unclear.

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 fatty acid oxidation 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 a fatty acid oxidation disorder should be tested and genetic counseling services should be offered to the family.

Physiology Fatty acid oxidation is essential for energy production. This metabolic pathway is complex and comprises as many as 20 individual steps including uptake and activation of fatty acids by cells, the carnitine cycle and the beta-oxidation spiral, with various enzymes required for the oxidation of unsaturated fatty acids. Inherited enzymatic defects in the pathway lead to accumulation of fatty acids or a decrease in cell energy metabolism and result in the clinical manifestations of the disorder.

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 a fatty acid oxidation disorder has been confirmed:

1. Parents should understand that treatment is lifelong and that compliance with dietary management and awareness of and prompt attention to episode triggers, including illness and fasting, are imperative to the child's health, growth and development.
2. Infants and children with a fatty acid oxidation defect should have regular follow-up appointments with a metabolic disease specialist.
3. **Parents should be warned that if an infant shows warning signs of the disorder, such as lethargy or vomiting, they should immediately seek medical attention.** A medical plan created by the metabolic specialist and the primary care provider should be developed for these acute episodes.
4. Long-term management and treatment compliance 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.