

## Medium Chain acyl Coenzyme A Dehydrogenase (MCAD) deficiency

### Why is Medium Chain acyl Coenzyme A Dehydrogenase (MCAD) deficiency an emerging public health issue?

Medium Chain acyl Coenzyme A Dehydrogenase (MCAD) deficiency is the most common inborn error of [fatty acid](#) metabolism. Although MCAD deficiency is detectable and treatable, there are currently only a few states that screen for MCAD through [newborn screening \(NBS\) programs](#). Deaths resulting from an undiagnosed MCAD deficiency may be mistakenly declared cases of Sudden Infant Death Syndrome (SIDS) and [Reye Syndrome](#).

MCAD occurs in approximately 1 in 6,500 to 1 in 20,000 live births and primarily occurs in Caucasians of northern European descent. The carrier frequency of the primary [gene](#) change in this population is estimated at 1 in 40 to 1 in 100. MCAD deficiency related deaths accounts for ~1% of SIDS.

If not detected and treated, MCAD deficiency can result in death. Undiagnosed, MCAD deficiency has a mortality rate of 20-25%. One fifth of children with MCAD die with their first illness, before MCAD deficiency is known. Untreated MCAD deficiency can lead to developmental and behavioral disability, failure to thrive, chronic muscle weakness, and cerebral palsy. However, people with treated MCAD will lead virtually normal, productive lives. Suggested Reading: Keppen LD, Randall B (1999) Inborn Defects of Fatty Acid Oxidation: A Preventable Cause of SIDS. *S D J Med* 52:187-8 discussion 188-9 [[Medline](#)]

### What is MCAD deficiency?

MCAD deficiency is a [metabolic](#) disorder. MCAD is an [enzyme](#) found in the [mitochondria](#) that is responsible for the metabolism of medium chain fatty acids. When this enzyme is missing, the body is unable to convert these fatty acids to energy during times of decreased food intake. Individuals who are MCAD deficient are not able to fast for extended periods of time because of the inability to convert the body's fat to energy when the food store has run out. When individuals with MCAD do fast, they experience a range of serious life threatening symptoms or even death.

### What are the symptoms of MCAD deficiency?

There are no symptoms of MCAD at birth. Symptoms of MCAD deficiency generally begin to occur between the second month and second year of life. Symptoms occur when in a fasting state, often due to illness, and include hypoglycemia, vomiting, lethargy, liver dysfunction, seizures, and coma. Affected individuals are usually symptom free between episodes. If left untreated, brain damage, cardiac arrest, serious illness, and death can occur.

### What causes MCAD deficiency?

MCAD deficiency is [inherited](#) in an [autosomal recessive](#) fashion. A single gene change, K304E, accounts for 90% of MCAD deficiency cases. This gene is located on [chromosome](#) 1. Eighty-one percent of individuals with MCAD deficiency are [homozygous](#) for this [mutation](#). Individuals who are [heterozygous](#) (carriers) have no symptoms.

When two carriers (heterozygotes) have children, the risk is 1 in 4 or 25% their children will have MCAD deficiency: 25% their children will have no changed MCAD genes; and 50% their children will be carriers like themselves and have no MCAD deficiency symptoms.

### **How is MCAD deficiency detected?**

In order to distinguish MCAD from other fatty acid metabolic disorders, multiple tests must be performed which include the clinical status of the patient at the time of the test. Initial laboratory testing for MCAD should include the analyses of plasma acylcarnitines, plasma-free fatty acids, urine organic acids, and urine acylglycines. Tandem mass spectrometry is the most recently developed test for population-based screening of MCAD. This test is usually followed by confirmatory DNA (genetic) studies.

Testing should be initiated in individuals with the following indications:

- Prenatal diagnosis for carrier couples
- Carrier screening in families of affected individuals
- Intermittent hypoglycemia
- Carnitine deficiency
- Urinary excretion of medium chain fatty acids and decreased ketones
- Vomiting, lethargy, and/or coma following fasting

Risk factors include finding fatty infiltration of the liver, family history of sudden death, Reye's Syndrome, myopathy, and decreased caloric intake before death. All siblings of individuals with MCAD should be tested even if they are without symptoms.

### **Tandem mass spectrometry (MS/MS)**

[Tandem mass spectrometry \(MS/MS\)](#) can be used to first detect MCAD in NBS programs using blood spots. MS/MS can be performed on either blood or urine samples.

### **DNA testing**

[Polymerase chain reaction \(PCR\)](#) can be performed on blood spots from newborns to detect the K304E gene change. However, approximately 1% of MCAD deficient patients will remain undetected if diagnosis is based on K304E DNA analysis. Currently, testing for non-K304E mutations is on a research basis.

In at risk pregnancies where both parents carry the gene change, prenatal diagnosis is possible through [amniocentesis](#) and [chorionic villus](#) testing (CVS).

### **How is MCAD treated?**

Treatment for MCAD deficiency is simple and allows for a good prognosis. Treatment consists of avoiding fasting for more than 2-6 hours in an infant. After infancy, overnight fasts of longer than 12 hours should be avoided. These values may vary from person to person. A high carbohydrate diet with restriction of fats and supplemental carnitine is recommended, especially during illness. The treatment regimen must be followed throughout the lifetime of the affected individual. Fasting should especially be avoided during times of illness. If an individual is unable to keep down fluids, has diarrhea or a fever, he or she should be evaluated promptly and given intravenous glucose immediately following blood chemistry sampling.

Some doctors may prescribe a drug called L-Carnitine to children. This drug helps the child's blood sugar from getting low when they have infections or don't eat. L-Carnitine is a substance made by the body that carries wastes out of body cells and into the urine. Individuals with MCAD make more toxic wastes than normal individuals so they need more L-Carnitine to carry out this process.

### **Information and Support Resources**

- CDC: HuGE Net Reviews MCAD Deficiency
  - [Medium chain acyl-coA dehydrogenase deficiency](#)
  - [MCAD deficiency fact sheet](#)
- [GeneClinics](#)
- [Fatty Oxidation Disorder Communication Network \(FOD\):](#)
- Medium Chain Acyl-CoA Dehydrogenase Deficiency: MCAD-A Guide For Parents (temporarily unavailable)