

**Disease Name:**

**MEDIUM CHAIN ACYL-CoA DEHYDROGENASE  
DEFICIENCY**  
(ACADM DEFICIENCY; MCAD DEFICIENCY; MCADD DEFICIENCY)

**Classification:** Fatty Acid Oxidation Disorder

**Genetic  
Information:**

**Inheritance:** Autosomal recessive

**Population Incidence:** 1/12,000

**Ethnic Incidence:** Approximately 1/70 carrier rate; incidence higher in Northern Europeans and US Caucasians.

**Gene & Location:** ACADM, 1p31

**Common Mutation:** 80% carry A985G; most are heterozygous for the A985G mutation and another private mutation.

**OMIM #** #201450; \*607008

**Disease  
Information:**

**Symptom Onset:** Typically 3-24 months, variable even within family member with identical gene mutations and can range from neonatal to adult. MCADD may account for about 3% of SIDS deaths.

**Symptoms:** Episodes of hypoketotic hypoglycemia, encephalopathy, coma or SIDS triggered by a common illness and/or a period of fasting. In 18% of cases, sudden death is the initial presenting manifestation and up to 50% of patients die during their first episode. Survivors may have significant developmental disability, muscle weakness, failure to thrive and cerebral palsy.

**Physical Findings:** No particular physical findings or dysmorphisms.

**Treatment:** Treatment is simple and effective: avoid fasting for more than 4 hrs as infant or 12 hours in older patients. It is imperative that glucose supplementation and hydration be provided during times of illness. A tangible clinical benefit of carnitine supplementation in patients with MCADD deficiency has not been proven, but several authors recommend oral supplementation with 100mg/kg/day to correct the observed secondary carnitine deficiency and to enhance the elimination of toxic metabolites.

**Natural History without treatment:** Mortality rate of up to 50% when untreated. Metabolic episodes can cause developmental and physical delays from hypoglycemia and liver insult.

**Natural History with treatment:**

Most physicians familiar with MCADD presume that patients will develop normally if diagnosed early and treated in order to avoid hypoglycemia and liver dysfunction. However, this has not been proven. Death on the other hand, has not been reported once the diagnosis is made and treatment carried out. Of survivors, diagnosed by clinical symptoms, 37% have neurodevelopment problems.

**Metabolic Information:**

**Missing Enzyme & Location:**

Medium chain acyl-CoA dehydrogenase is found in the liver, heart, muscle and fibroblasts. Located in mitochondria and involved in fatty acid B-oxidation. These patients are unable to metabolize C6-C10 length fatty acids.

**MS/MS profile:**

C6 (hexanoyl carnitine)- elevated  
C8 (octanoyl carnitine)- elevated  
C10 (decanoyl carnitine)- elevated  
C10:1 (decenoyl carnitine)- elevated  
C8/C10 ratio >3

**Prenatal testing:**

Yes, DNA and enzymatic

**Miscellaneous Information:**

With borderline C8 elevations, it is possible to detect carriers of MCADD

Prepared for the NW Regional Newborn Screening Program by Sara Copeland MD, Judith Tuerck RN MS and Lorinda Paradise at OHSU in Portland, OR.

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