

What is MCAD deficiency?

MCAD deficiency is an inherited metabolic disease characterized by lethargy, vomiting, and low blood sugar triggered by fasting or common illness. If untreated, it can quickly progress to liver problems, seizures, coma, and death. Individuals with MCAD deficiency have abnormalities in an enzyme involved in the breakdown of medium-chain fatty acids that are used for energy in the cells. Symptoms associated with MCAD deficiency are due to low levels of energy in cells and the toxic build-up of fatty acids, which causes damage to the cells, especially in the liver and brain.¹

What are the symptoms of MCAD deficiency and what treatment is available?

Individuals with MCAD deficiency may appear normal at birth. First signs usually appear before age two and are triggered by fasting or a common illness. Symptoms are episodic and may include:²

- Lethargy (lack of energy)
- Vomiting
- Hypoglycemia (low blood sugar)

If untreated, symptoms may worsen and can include:^{2,3}

- Breathing difficulties
- Hepatomegaly (enlarged liver) and liver disease
- Seizures
- Spasticity (abnormally tight muscles)
- Muscle weakness
- Coma and risk of sudden death

Early diagnosis is critical in treatment of MCAD deficiency. Treatment includes avoidance of fasting by ensuring frequent feedings or meals. A low fat, high carbohydrate diet with nutrition supplements is often recommended. When properly treated, individuals usually live healthy lives with typical growth and development.² If repeated episodes of symptoms occur, individuals may have permanent spasticity, chronic muscle weakness, and learning disabilities.³

MCAD deficiency is included in all state newborn screening profiles in the United States.^{2,5}

How is MCAD deficiency inherited?

MCAD deficiency is an autosomal recessive disease caused by mutations in the *ACADM* gene.¹ An individual who inherits one copy of an *ACADM* gene mutation is a carrier and is not expected to have related health problems.³ An individual who inherits two *ACADM* mutations, one from each parent, is expected to be affected with MCAD deficiency.

If both members of a couple are carriers of mutations in the same gene, the risk for an affected child is 25% in each pregnancy; therefore, it is especially important that the reproductive partner of a carrier be offered testing. Female carriers with an affected fetus may be at increased risk for a specific pregnancy complication called HELLP syndrome.²

Who is at risk for MCAD deficiency?

MCAD deficiency can occur in individuals of all races and ethnicities. It is most common in individuals of Northern European descent. The incidence of MCAD deficiency in the United States is approximately 1 in 15,700 with a carrier frequency of 1/63.⁴

Having a relative who is a carrier or is affected can increase an individual's risk of being a carrier. Consultation with a genetics health professional may be helpful in determining carrier risk and appropriate testing.

What does a positive test result mean?

If a gene mutation is identified, an individual should speak to a physician or genetics health professional about the implications of the result and appropriate testing for the reproductive partner and at-risk family members.

What does a negative test result mean?

A negative result reduces, but does not eliminate, the possibility that an individual carries a gene mutation. The likelihood of being a carrier is also influenced by family history, medical symptoms, and other relevant test results.

Where can I get more information?

Fatty Acid Oxidation Disorder Family Support Group (FOD): www.fodsupport.org

Genetic and Rare Disease Information Center: <https://rarediseases.info.nih.gov/gard/540/medium-chain-acyl-coenzyme-a-dehydrogenase-deficiency/resources/1>

References

1. Medium-chain acyl-CoA dehydrogenase deficiency. *Genetics Home Reference*. Available at: <http://ghr.nlm.nih.gov/condition/medium-chain-acyl-coa-dehydrogenase-deficiency>. Accessed on: April 25, 2012
2. Matern D, Rinaldo P. Medium-chain acyl-coenzyme A dehydrogenase deficiency. *GeneReviews*. Available at: <http://www.ncbi.nlm.nih.gov/books/NBK1424/>. Accessed on April 25, 2012
3. Medium-chain acyl-CoA dehydrogenase deficiency. *Screening, Technology and Research in Genetics*. Available at: <http://www.newbornscreening.info/Parents/fattyacid disorders/MCADD.html>. Accessed on April 25, 2012
4. Chace D *et al*. The application of tandem mass spectrometry to neonatal screening for inherited disorders of intermediary metabolism. *Annu Rev Genomics Hum Genet* 2002; 3:17-45
5. National Newborn Screening Status Report. November 2, 2014. Available at: <http://genes-r-us.uthscsa.edu/sites/genes-r-us/files/nbsdisorders.pdf>. Accessed January 6, 2016.