Mitochondrial acetoacetyl-CoA thiolase deficiency

What is mitochondrial acetoacetyl-CoA thiolase deficiency?

Mitochondrial acetoacetyl-CoA thiolase deficiency is an inherited metabolic disease. Individuals with mitochondrial acetoacetyl-CoA thiolase deficiency have a defect in production of the acetyl-CoA acetyltransferase 1 enzyme, which plays a role in breaking down dietary protein and fats. Symptoms of the disease are due to the buildup of organic acids in the blood, which can damage the body’s tissues and organs. Mitochondrial acetoacetyl-CoA thiolase deficiency is characterized by intermittent ketoacidotic episodes that may include vomiting, dehydration, difficulty breathing, lethargy, and seizures. It is also known as beta-ketothiolase deficiency and alpha-methylacetoacetic aciduria.

What are the symptoms of mitochondrial acetoacetyl-CoA thiolase deficiency and what treatment is available?

Mitochondrial acetoacetyl-CoA thiolase deficiency is a disease that varies in age at onset and severity. Signs and symptoms may include:

- Vomiting
- Dehydration
- Polypnea and/or dyspnea (rapid and/or labored breathing)
- Hypotonic (muscle weakness)
- Lethargy (lack of energy)
- Coma
- Seizures
- Neurological problems
- Cardiomyopathy (abnormal heart muscle)
- Abnormal white blood cell counts
- Poor weight gain
- Kidney failure
- Short stature

Affected individuals usually have normal development with no clinical symptoms in early infancy, and may have later progressive loss of mental and motor skills. The first ketoacidotic episode usually occurs between 6 and 24 months of age. Ketoacidotic episodes can be triggered by illness, fasting, or other stressors. Affected individuals may have no clinical symptoms between episodes.

There is no cure for mitochondrial acetoacetyl-CoA thiolase deficiency. Treatment is focused on preventing ketoacidotic episodes and includes long-term dietary modifications and avoidance of triggers. With early diagnosis and appropriate management, affected individuals may develop normally; however, ketoacidotic episodes may be life-threatening or result in developmental delays.

Mitochondrial acetoacetyl-CoA thiolase deficiency is included in newborn screening panels in all 50 states.

How is mitochondrial acetoacetyl-CoA thiolase deficiency inherited?

Mitochondrial acetoacetyl-CoA thiolase deficiency is an autosomal recessive disease caused by mutations in the ACAT1 gene. An individual who inherits one copy of the ACAT1 gene mutation is a carrier and is not expected to have related health problems. An individual who inherits two ACAT1 mutations, one from each parent, is expected to be affected with mitochondrial acetoacetyl-CoA thiolase 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.
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Who is at risk for mitochondrial acetoacetyl-CoA thiolase deficiency?

Mitochondrial acetoacetyl-CoA thiolase deficiency is a rare condition that can occur in individuals of all races and ethnicities. Its prevalence is unknown.

Having a relative who is a carrier or who is affected can increase an individual's risk to be 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?


The Screening, Technology And Research in Genetics (STAR-G):
http://www.newbornscreening.info/Parents/organicaciddisorders/BKD.html

Children Living with Inherited Metabolic Diseases: http://www.climb.org.uk/

References