Inheritest® CARRIER SCREEN

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.[3,4] Symptoms of the disease are due to the buildup of organic acids in the blood, which can damage the body's tissues and organs.[3,4] Mitochondrial acetoacetyl-CoA thiolase deficiency is characterized by intermittent ketoacidotic episodes that may include vomiting, dehydration, difficulty breathing, lethargy, and seizures.[2] It is also known as beta-ketothiolase deficiency and alpha-methylacetoacetic aciduria.[5]

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:[2,3,4,5]

- Vomiting
- Dehydration
- Polypnea and/or dyspnea (rapid and/or labored breathing)
- Hypotonus (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.[2] The first ketoacidotic episode usually occurs between 6 and 24 months of age.[2,3] Ketoacidotic episodes can be triggered by illness, fasting, or other stressors.[2] Affected individuals may have no clinical symptoms between episodes.[2]

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.[2] With early diagnosis and appropriate management, affected individuals may develop normally; however, ketoacidotic episodes may be life-threatening or result in developmental delays.[1]

Mitochondrial acetoacetyl-CoA thiolase deficiency is included in newborn screening panels in all 50 states.[6]

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.[3,4] 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?

Genetics Home Reference: http://ghr.nlm.nih.gov/condition/beta-ketothiolase-deficiency

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

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