What is guanidinoacetate methyltransferase deficiency?

Guanidinoacetate methyltransferase deficiency is an inherited disease with early age of onset.\(^1,2\) Individuals with guanidinoacetate methyltransferase deficiency have a deficiency of the guanidinoacetate methyltransferase enzyme needed for making creatine, which is used by the body to store and use energy.\(^3\) The symptoms of guanidinoacetate methyltransferase deficiency are due the shortage of the enzyme and consequent effects on parts of the body that need energy, especially the nervous system.\(^1\) Guanidinoacetate methyltransferase deficiency belongs to a group of disorders called creatine deficiency syndromes.\(^2\)

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

Symptoms are usually evident between three months and three years of age and may include\(^1,2\):

- Intellectual disability
- Limited speech development
- Seizures
- Involuntary movements
- Developmental delay
- Hypotonia (poor muscle tone)
- Autistic behaviors including self-mutilation

Dietary treatment is most beneficial when started early and includes supplementation of creatine monohydrate and ornithine, and restriction of arginine or protein.\(^2\) Other treatments are supportive to manage symptoms and prevent complications.\(^2\)

How is guanidinoacetate methyltransferase deficiency inherited?

Guanidinoacetate methyltransferase deficiency is an autosomal recessive disease caused by mutations in the \textit{GAMT} gene.\(^1\) An individual who inherits one copy of a \textit{GAMT} gene mutation is a carrier. Carriers are not affected with guanidinoacetate methyltransferase deficiency. An individual who inherits two \textit{GAMT} mutations, one from each parent, is expected to be affected with guanidinoacetate methyltransferase 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.

Who is at risk for guanidinoacetate methyltransferase deficiency?

Guanidinoacetate methyltransferase deficiency is a rare condition that can occur in individuals of all races and ethnicities. It appears to be most common in individuals of Portuguese ancestry with a carrier frequency of 1 in 125.\(^4\)

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.
Guanidinoacetate methyltransferase deficiency

Where can I get more information?


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

References