

Ethylmalonic Encephalopathy

Subjects: Genetics & Heredity

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Ethylmalonic encephalopathy is an inherited disorder that affects several body systems, particularly the nervous system.

Keywords: genetic conditions

1. Introduction

Neurological signs and symptoms include delayed development and the loss of previously acquired skills (developmental regression), weak muscle tone (hypotonia), seizures, and abnormal movements. The body's network of blood vessels (the vascular system) is also affected. Children with this disorder often develop rashes of tiny red spots (petechiae) caused by bleeding under the skin and blue discoloration in the hands and feet due to reduced oxygen in the blood (acrocyanosis). Chronic diarrhea is another common feature of ethylmalonic encephalopathy.

The signs and symptoms of ethylmalonic encephalopathy are apparent at birth or begin in the first few months of life. Problems with the nervous system typically worsen over time, and most affected individuals survive only into early childhood.

2. Frequency

About 70 individuals with this condition have been identified worldwide, mostly in Mediterranean and Arab populations. Although ethylmalonic encephalopathy appears to be very rare, researchers suggest that some cases have been misdiagnosed as other neurological disorders.

3. Causes

Ethylmalonic encephalopathy results from mutations in the *ETHE1* gene. This gene provides instructions for making an enzyme that is active in mitochondria, which are the energy-producing centers in cells. The ETHE1 enzyme is part of a pathway that breaks down sulfide (H_2S), a molecule that is critical at very low levels for normal cell functioning but is toxic at high levels. Excess sulfide interferes with numerous cell activities, including mitochondrial energy production.

Mutations in the *ETHE1* gene lead to the production of a nonfunctional version of the enzyme or prevent any enzyme from being made. A shortage of functional ETHE1 enzyme prevents sulfide from being broken down, allowing this molecule to accumulate in cells. The buildup of sulfide interferes with the ability of mitochondria to produce energy and damages tissues and organs throughout the body. Researchers believe that the effects of excess sulfide in the brain, muscles, blood vessels, and lining of the intestines underlie most of the major features of ethylmalonic encephalopathy.

3.1. The Gene Associated with Ethylmalonic Encephalopathy

- ETHE1

4. Inheritance

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

5. Other Names for This Condition

- encephalopathy, petechiae, and ethylmalonic aciduria

- EPEMA syndrome

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