# Congenital Myasthenic Syndrome

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Contributor: Nicole Yin

Congenital myasthenic syndrome is a group of conditions characterized by muscle weakness (myasthenia) that worsens with physical exertion.

Keywords: genetic conditions

## 1. Introduction

The muscle weakness typically begins in early childhood but can also appear in adolescence or adulthood. Facial muscles, including muscles that control the eyelids, muscles that move the eyes, and muscles used for chewing and swallowing, are most commonly affected. However, any of the muscles used for movement (skeletal muscles) can be affected in this condition. Due to muscle weakness, affected infants may have feeding difficulties. Development of motor skills such as crawling or walking may be delayed. The severity of the myasthenia varies greatly, with some people experiencing minor weakness and others having such severe weakness that they are unable to walk.

Some individuals have episodes of breathing problems that may be triggered by fevers or infection. Severely affected individuals may also experience short pauses in breathing (apnea) that can lead to a bluish appearance of the skin or lips (cyanosis).

## 2. Frequency

The prevalence of congenital myasthenic syndrome is unknown. At least 600 families with affected individuals have been described in the scientific literature.

## 3. Causes

Mutations in many genes can cause congenital myasthenic syndrome. Mutations in the *CHRNE* gene are responsible for more than half of all cases. A large number of cases are also caused by mutations in the *RAPSN*, *CHAT*, *COLQ*, and *DOK7* genes. All of these genes provide instructions for producing proteins that are involved in the normal function of the neuromuscular junction. The neuromuscular junction is the area between the ends of nerve cells and muscle cells where signals are relayed to trigger muscle movement.

Gene mutations lead to changes in proteins that play a role in the function of the neuromuscular junction and disrupt signaling between the ends of nerve cells and muscle cells. Disrupted signaling between these cells results in an impaired ability to move skeletal muscles, muscle weakness, and delayed development of motor skills. The respiratory problems in congenital myasthenic syndrome result from impaired movement of the muscles of the chest wall and the muscle that separates the abdomen from the chest cavity (the diaphragm).

Mutations in other genes that provide instructions for proteins involved in neuromuscular signaling have been found to cause some cases of congenital myasthenic syndrome, although these mutations account for only a small number of cases. Some people with congenital myasthenic syndrome do not have an identified mutation in any of the genes known to be associated with this condition.

### 3.1. The Genes Associated with Congenital Myasthenic Syndrome

- CHAT
- CHRNE
- COLQ
- DOK7
- PLEC

- RAPSN
- SCN4A

## 4. Inheritance

This condition is most commonly 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.

Rarely, this condition is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder. In some cases, an affected person inherits the mutation from one affected parent. Other cases result from new mutations in the gene and occur in people with no history of the disorder in their family.

## 5. Other Names for This Condition

- CMS
- congenital myasthenia
- congenital myasthenic syndromes

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