

## Central core disease

### Description

Central core disease is a disorder that affects muscles used for movement (skeletal muscles). This condition causes muscle weakness that ranges from barely noticeable to very severe. The severity of muscle weakness may differ even among affected members of the same family.

Most people with central core disease experience persistent, mild muscle weakness that does not worsen with time. This weakness affects the muscles near the center of the body (proximal muscles), particularly muscles in the shoulders, upper legs, and hips. Muscle weakness in affected infants can delay the development of motor skills such as sitting, standing, and walking; most people with this condition are able to walk independently. Affected individuals may experience muscle pain (myalgia) or extreme fatigue in response to physical activity (exercise intolerance). Central core disease is also associated with eyes that do not look in the same direction (strabismus), a rounded upper back that also curves to the side (kyphoscoliosis), foot deformities, hip dislocation, and joint deformities called contractures that restrict the movement of certain joints. In severe cases, affected infants experience weakness in the muscles of the face, profound low muscle tone (hypotonia), and serious or life-threatening breathing problems.

Many people with central core disease also have an increased risk of developing a severe reaction to certain drugs used during surgery and other invasive procedures. This reaction is called malignant hyperthermia. Malignant hyperthermia occurs in response to some anesthetic gases, which are used to block the sensation of pain, either given alone or in combination with a muscle relaxant that is used to temporarily paralyze a person during a surgical procedure. If given these drugs, people at risk of malignant hyperthermia may experience a rapid increase in heart rate (tachycardia) and body temperature (hyperthermia), abnormally fast breathing (tachypnea), muscle rigidity, breakdown of muscle fibers (rhabdomyolysis), and increased acid levels in the blood and other tissues (acidosis). The complications of malignant hyperthermia can be life-threatening unless they are treated promptly.

Central core disease gets its name from disorganized areas called central cores, which are typically found in the center of skeletal muscle cells, but can be at the edges or span the length of the cell, in many affected individuals. These abnormal regions can only be seen when muscle tissue is viewed under a microscope. These central cores are often present in cells with few or no mitochondria, which produce energy within cells.

Although the presence of central cores can help doctors diagnose central core disease, it is unclear how they are related to muscle weakness and the other features of this condition.

## Frequency

The exact prevalence of central core disease is unknown. However, it is thought to be the most common of the congenital myopathies, which are a group of muscle disorders that cause weakness very early in life. As a group, congenital myopathies affect 6 per 100,00 newborns.

## Causes

Mutations in the *RYR1* gene cause central core disease. The *RYR1* gene provides instructions for making a protein called ryanodine receptor 1. This protein plays an essential role in skeletal muscles. For the body to move normally, these muscles must tense (contract) and relax in a coordinated way. Muscle contractions are triggered by the flow of charged atoms (ions) into muscle cells. The ryanodine receptor 1 protein forms a channel that releases calcium ions stored within muscle cells. The resulting increase in calcium ion concentration inside muscle cells stimulates muscle fibers to contract, allowing the body to move.

Mutations in the *RYR1* gene change the structure of ryanodine receptor 1 and the calcium channel that it forms. The abnormal calcium channel alters the normal flow of stored calcium ions within muscle cells. Specifically, calcium ions "leak" slowly but continually through the abnormal channel or calcium ions cannot pass through the channel when they are needed. This disruption in calcium ion transport prevents muscles from contracting normally, leading to the muscle weakness characteristic of central core disease.

[Learn more about the gene associated with Central core disease](#)

- RYR1

## Inheritance

Central core disease is most often 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 may result from new mutations in the gene. These cases occur in people with no history of the disorder in their family.

Less commonly, central core disease is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. Most often, the parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but typically do not show signs and symptoms of the condition. People who carry one *RYR1* gene mutation, however, may be at increased risk for

malignant hyperthermia.

## **Other Names for This Condition**

- CCD
- CCO
- Central core myopathy
- Myopathy, central core
- Shy's disease
- Shy-Magee syndrome

## **Additional Information & Resources**

### Genetic and Rare Diseases Information Center

- Central core disease (<https://rarediseases.info.nih.gov/diseases/6014/index>)

### Patient Support and Advocacy Resources

- National Organization for Rare Disorders (NORD) (<https://rarediseases.org/>)

### Clinical Trials

- ClinicalTrials.gov ([https://clinicaltrials.gov/search?cond=%22Central core disease%22](https://clinicaltrials.gov/search?cond=%22Central+core+disease%22))

### Catalog of Genes and Diseases from OMIM

- CONGENITAL MYOPATHY 1A, AUTOSOMAL DOMINANT, WITH SUSCEPTIBILITY TO MALIGNANT HYPERTHERMIA; CMYP1A (<https://omim.org/entry/117000>)

### Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28Myopathy,+Central+Core%5BMAJR%5D%29+AND+%28%28central+core+disease%5BTIAB%5D%29+OR+%28central+core+myopathy%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D>)

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