

Hereditary myopathy with early respiratory failure

Description

Hereditary myopathy with early respiratory failure (HMERF) is an inherited disease that affects muscles used for movement (skeletal muscles) and muscles that are needed for breathing (respiratory muscles).

The major signs and symptoms of HMERF usually appear in adulthood, often in the mid-thirties. Among the earliest signs of the condition are breathing problems and difficulty walking. Weakness of the respiratory muscles, particularly the diaphragm (the muscle that separates the organs in the abdomen from those in the chest), causes breathing problems. This weakness worsens over time and can lead to life-threatening respiratory failure. Some affected individuals have weakness of muscles of the lower leg and foot, which makes it difficult to lift the toes while walking, a condition known as foot drop. Other muscles that become weak in people with HMERF include those of the hips, thighs, upper arms, and neck.

When viewed under a microscope, muscle fibers from affected individuals contain abnormal structures called cytoplasmic bodies. In many cases, the cytoplasmic bodies are arranged side-by-side in a ring inside the muscle fiber, resembling a necklace (necklace cytoplasmic bodies).

Frequency

HMERF is a rare condition with an unknown prevalence. It has been found in populations worldwide.

Causes

HMERF is caused by mutations in the *TTN* gene. This gene provides instructions for making a protein called titin. Titin plays an important role in muscles the body uses for movement (skeletal muscles) and in heart (cardiac) muscle.

Within muscle cells, titin is an essential component of structures called sarcomeres. Sarcomeres are the basic units of muscle contraction; they are made of proteins that generate the mechanical force needed for muscles to contract. Titin has several functions within sarcomeres. One of its most important jobs is to act as a backbone in these structures, providing structure, flexibility, and stability. Titin also plays a role in chemical signaling and in assembling new sarcomeres.

The *TTN* gene mutations responsible for HMERF lead to the production of an altered version of the titin protein that cannot fold into its normal 3-dimensional shape. Researchers are studying how abnormally folded titin contributes to the muscle damage that underlies the signs and symptoms of HMERF. It is unclear why these effects are usually limited to skeletal muscles and respiratory muscles, and do not involve cardiac muscle.

Rarely, people with the characteristic features of HMERF do not have identified mutations in the *TTN* gene. In these cases, the genetic cause of the condition is unknown.

[Learn more about the gene associated with Hereditary myopathy with early respiratory failure](#)

- *TTN*

Inheritance

HMERF is typically inherited in an autosomal dominant pattern, which means one copy of the altered *TTN* gene in each cell is sufficient to cause the disorder. An affected person usually has one parent with the condition.

In rare cases, a specific mutation in one copy of the *TTN* gene leads to mild signs and symptoms of the condition, such as respiratory problems that begin later than is typical in HMERF with no other muscle weakness. However, family members who have the mutation in both copies of the gene have severe features of HMERF.

Other Names for This Condition

- Edstrom myopathy
- HMERF
- Myopathy, proximal, with early respiratory muscle involvement

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Myopathy, myofibrillar, 9, with early respiratory failure (<https://www.ncbi.nlm.nih.gov/gtr/conditions/C1863599/>)

Genetic and Rare Diseases Information Center

- Hereditary myopathy with early respiratory failure (<https://rarediseases.info.nih.gov/diseases/12591/index>)

Patient Support and Advocacy Resources

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

Catalog of Genes and Diseases from OMIM

- MYOPATHY, MYOFIBRILLAR, 9, WITH EARLY RESPIRATORY FAILURE; MFM9 (<https://omim.org/entry/603689>)

Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28hmerf%5BTIAB%5D%29+OR+%28%28dominant+myopathy%5BTIAB%5D%29+AND+%28early+respiratory+muscle%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D>)

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