

DMD and Duchenne/Becker Muscular Dystrophy

Description

Muscular dystrophies are a group of genetic conditions characterized by progressive muscle weakness and wasting (atrophy). **The Duchenne and Becker types of muscular dystrophy are two related conditions that primarily affect skeletal muscles which are used for movement, and heart or cardiac muscle. These forms of muscular dystrophy occur almost exclusively in males.**

Duchenne and Becker muscular dystrophies have similar signs and symptoms and are caused by different mutations in the same gene. Symptoms appear in early childhood and rapidly worsen. Children are typically wheelchair dependent by 12 years of age. Heart problems usually appear after age 18 years. A variable degree of intellectual disability is possible in affected males. **The two conditions differ in their severity, age of onset, and rate of progression.** In boys with Duchenne muscular dystrophy, muscle weakness tends to appear in early childhood and worsen rapidly. Affected children may have delayed motor skills, such as sitting, standing, and walking. They are usually wheelchair-dependent by adolescence. The signs and symptoms of Becker muscular dystrophy are usually milder and more varied. In most cases, muscle weakness becomes apparent later in childhood or in adolescence and worsens at a much slower rate.

Both the Duchenne and Becker forms of muscular dystrophy are associated with a heart condition called cardiomyopathy. This form of heart disease weakens the cardiac muscle, preventing the heart from pumping blood efficiently. In both Duchenne and Becker muscular dystrophy, cardiomyopathy typically begins in adolescence. Later, the heart muscle becomes enlarged, and the heart problems develop into a condition known as dilated cardiomyopathy. Signs and symptoms of dilated cardiomyopathy can include an irregular heartbeat (arrhythmia), shortness of breath, extreme tiredness (fatigue), and swelling of the legs and feet. These heart problems worsen rapidly and become life-threatening in most cases. Most males with Duchenne muscular dystrophy typically die before thirty years of age due to heart or respiratory failure, while males with Becker muscular dystrophy can survive into their forties or beyond.

A related condition called X-linked dilated cardiomyopathy is a form of heart disease caused by mutations in the same gene as Duchenne and Becker muscular dystrophy, and it is sometimes classified as subclinical Becker muscular dystrophy. People with X-linked dilated cardiomyopathy typically do not have any skeletal muscle weakness or wasting, although they may have subtle changes in their skeletal muscle cells that are detectable through laboratory testing.

DMD and BMD are caused by pathogenic variants in the DMD gene.

Frequency - How Often Does Duchenne/Becker Muscular Dystrophy Occur?

Duchenne and Becker muscular dystrophies together affect 1 in 3,500 to 5,000 newborn males worldwide. Between 400 and 600 boys in the United States are born with these conditions each year.

Normal Function of the DMD Gene And Genetic Changes

Mutations in the DMD gene cause the Duchenne and Becker forms of muscular dystrophy. The DMD gene provides instructions for making a protein called dystrophin. This protein is located primarily in skeletal and cardiac muscle, where it helps stabilize and protect muscle fibers. Dystrophin may also play a role in chemical signaling within cells. Mutations in the DMD gene alter the structure or function of dystrophin or prevent any functional dystrophin from being produced. Muscle cells without enough of this protein become damaged as muscles repeatedly contract and relax with use. The damaged fibers weaken and die over time, leading to the muscle weakness and heart problems characteristic of Duchenne

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and Becker muscular dystrophies. Mutations that lead to an abnormal version of dystrophin that retains some function usually cause Becker muscular dystrophy, while mutations that prevent the production of any functional dystrophin tend to cause Duchenne muscular dystrophy. Because Duchenne and Becker muscular dystrophies result from faulty or missing dystrophin, these conditions are classified as dystrophinopathies.

Pattern of Inheritance - How Is Duchenne/Becker Muscular Dystrophy Inherited?

This condition is inherited in an X-linked recessive pattern. The gene associated with this condition is located on the X chromosome, which is one of the two sex chromosomes. **Males have only one X chromosome therefore one altered copy of the gene in each cell is sufficient to cause the condition.** When the pathogenic variant is inherited from the unaffected carrier mother, the male child will have the genetic disease. There is a 50% chance that a baby will inherit the pathogenic variant from the mother; females who inherit the pathogenic variant will be carriers, males who inherit the pathogenic variant will be affected.

A characteristic of X-linked inheritance is that fathers cannot pass X-linked traits to their sons. In DMD, 2/3 of the cases are inherited pathogenic variants, the remaining 1/3 result from new pathogenic variants in the DMD gene in affected males and are not inherited. In BMD, 90% of mothers are carriers of a pathogenic variant.

Females have two X chromosomes thus a mutation would have to occur in both copies of the gene to cause the disorder. Because it is unlikely that females will have two altered copies of this gene, males are affected by X-linked recessive disorders much more frequently than females. In X-linked recessive inheritance, a female with one mutated copy of the gene in each cell is called a carrier. She can pass on the altered gene but usually does not experience signs and symptoms of the disorder. Occasionally, however, females who carry a DMD gene mutation may have muscle weakness and cramping. These symptoms are typically milder than the severe muscle weakness and atrophy seen in affected males. Females who carry a DMD gene mutation also have an increased risk of developing heart abnormalities including cardiomyopathy.

What Does It Mean To Be A Carrier?

Females who are carriers may develop a variable degree of muscle weakness and cramping, and are at risk to develop heart problems in adulthood. Routine cardiac evaluation is recommended.

Carrier Rates		
Ethnicity	Detection Rate	Carrier Frequency
General Population	>96%	Same for all ethnicities

Clinician References

OMIM [DMD:310200] (<http://www.ncbi.nlm.nih.gov/omim>)

Gene Reviews: Dystrophinopathies (<http://www.ncbi.nlm.nih.gov/books/NBK1116/>)

Patient and Family Resources

Genetics Home Reference: Duchenne Muscular Dystrophy (<http://ghr.nlm.nih.gov/>)

Muscular Dystrophy Association: Duchenne Muscular Dystrophy (<http://mda.org/disease/>)