MDA Muscular Dystrophy Association

# Duchenne Muscular Dystrophy (DMD)

**Duchenne Muscular Dystrophy (DMD)** is the most common childhood form of muscular dystrophy. It is a genetic disorder characterized by progressive weakness and degeneration of skeletal muscles that control movement as well as the muscles that control breathing and heart function.

DMD affects approximately **1 in 3,600 live male births**. It is estimated that about **20,000** children are diagnosed with DMD globally each year.

DMD is classified as a **dystrophinopathy**, a muscle disease that results from the **deficiency of a protein called dystrophin**.

In DMD, **mutations in the dystrophin (*DMD*) gene** interferes with the production of the dystrophin protein, which is needed to form and maintain healthy muscle. Lack of the dystrophin protein in muscle cells causes them to be fragile and easily damaged.

Because the DMD gene is located on the X-chromosome, it **primarily affects males, while females typically are carriers**. However, some females can experience varying degrees of physical or cardiac DMD symptoms and are therefore called manifesting carriers.

DMD typically is **inherited through the mother**; however, in about 25% of cases, the disease occurs spontaneously in people who do not have a family history of DMD.

There is no cure for DMD, but a combination of established **care guidelines** and **approved treatments** can help to manage DMD symptoms and slow disease progression.

To learn more about DMD, visit **MDA.org** or contact the MDA Resource Center at **1-833-ASK-MDA1** (275-6321) or **ResourceCenter@mdausa.org.**

# What Are the Signs and Symptoms of DMD?

## Nervous system

- Developmental delay
- Motor delay
- Autism spectrum disorder
- Attention-deficit/ Hyperactivity disorder
- Anxiety
- Obsessive-compulsive disorder

## Cognition

- Learning disability

## Skeleton and muscle

- Muscle weakness
- Fatigue
- Muscle cramps
- Difficulty walking
- Difficulty climbing stairs
- Gait abnormalities
- Contractures
- Muscle pseudo hypertrophy
- Lordosis
- Scoliosis

## Gastrointestinal

- Dysphagia
- Constipation
- Reflux
- Gastroparesis

## Heart

- Cardiomyopathy
- Arrythmias

## Respiratory

- Breathing difficulties
- Respiratory infections
- Sleep apnea

## Endocrine

- Short stature
- Osteoporosis
- Delayed puberty

# What Should I Know About DMD?

**Diagnosis and Symptom Onset:** DMD symptom onset occurs in early childhood, by ages 2-5 years old, but may also be associated with earlier delays in achieving gross motor milestones like walking.

**Early Signs:** Children with DMD may exhibit a delayed ability to sit, stand, or walk. They typically have difficulty running, jumping, and climbing stairs as well as have frequent falls. Some will have problems getting up from the floor and may use a distinctive method known as Gowers' maneuver or Gowers' sign to push hands off the ground and off the legs to rise from the floor to standing

**Progressive Nature:** Muscle weakness usually begins in the hips, pelvic area, upper legs, neck flexors, and shoulders. The calves may be enlarged. Muscle weakness worsens with age and progresses to the arms, legs, and trunk. While disease progression varies, boys, on average, lose their ability to walk, and transition to full-time wheelchair use in their teenage years.

**Cognitive Effects:** DMD may also affect learning and memory, as well as communication and certain emotional skills. Other involvement may include: autism spectrum disorder (ASD), obsessive-compulsive disorder (OCD), anxiety, and attention-deficit hyperactivity disorder (ADHD), and learning disability.

**Cardiac Problems:** Most individuals with DMD will develop heart problems by their teen years. Signs of heart involvement can include fatigue, faster heart rate, shortness of breath, chest pain, palpitations, or swelling in the legs, and can lead to serious complications.

**Respiratory Involvement:** Beginning at about 10 years of age, the diaphragm and other muscles that operate on the lungs may weaken, making the lungs less effective at moving air in and out. Signs of poor respiratory function can include headaches and difficulty concentrating or staying awake. Weakened respiratory muscles also make it difficult to cough, leading to an increased risk of serious respiratory infection.

**Multidisciplinary Care is Critical:** Neurologists, cardiologists, pulmonologists, and physical therapists all play a role in managing disease progression. Other specialists may include orthopedists, endocrinologists, physical medicine and rehabilitation, dieticians, and neuropsychologists.
Thanks to advances in treatments, gene therapy, cardiac and respiratory care, life expectancy for individuals with DMD is increasing. Survival into the early 30s is becoming more common, and there are cases of men with DMD living into their 40s and 50s

# How is DMD Treated?

Treatment for DMD includes supportive interventions, such as physical and occupational therapy, along with emerging disease-modifying therapies that target the underlying cause of the disease.

Comprehensive **multidisciplinary care** can prolong life, improve quality of life, and slow disease progression.

**Physical therapy** through exercise helps to restore and maintain muscle strength and function. Stretching helps to maintain range of motion.

**Ankle-foot orthoses (AFOs)** are sometimes prescribed for night wear to keep the foot from pointing downward and keep the Achilles tendon stretched while a child is sleeping.

**Occupational therapy** can help improve daily living and work skills.

**Assisted ventilation (e.g., BiPAP)** can help manage lung function and respiratory muscle weakness.

**Cough assists** provide mechanical assistance to simulate a cough and help remove mucus and secretions from the lungs.

**Orthopedic care**, including corrective surgical interventions for scoliosis or joint contractures, may help make sitting, sleeping, and breathing more comfortable.

## Medications

**Corticosteroids:** These medications are used to reduce inflammation, which helps prevent muscle damage in DMD. Corticosteroids can slow disease progression and delay the loss of ambulation. Corticosteroids include:

- **Prednisone/Prednisolone:** The oldest, and most well studied corticosteroid that is used to treat DMD.
- **Emflaza (deflazacort)**: A derivative of prednisone. Available as a tablet or oral suspension for ages 2 and up.
- **Kymbee** is another tablet form of deflazacort.
- **Agamree (vamorolone):** A steroid-alternative that reduces inflammation and preserves muscle strength but works differently to reduce some unwanted side effects.

**Cardiac medications** such as angiotensin converting enzyme (ACE) inhibitors, beta blockers, aldosterone receptor antagonist, and others may be used to slow the course of cardiac muscle deterioration in DMD.

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**Duvyzat* (givinostat)**: A histone deacetylase (HDAC) enzyme inhibitor approved for the treatment of DMD in patients 6 years of age and older. By inhibiting HDACs, Duvyzat mitigates muscle inflammation and fibrosis, slowing DMD disease progression and potentially increasing muscle mass and reducing improper death of muscle tissue.

## Gene Replacement Therapy

Gene therapy is a new type of treatment that introduces specific genetic material into affected cells to treat or slow down the progression of a genetic disease. The process of receiving gene therapy treatment involves complex care that typically extends over several months, so patients and families need to understand each step well.

**Elevidys* (delandistrogene moxeparvovec)**: The first FDA-approved gene therapy to treat DMD. Elevidys is a one-time IV infusion to treat patients who have a confirmed mutation in the dystrophin gene. Elevidys uses an adeno-associated virus (AAV) to deliver a shortened version of the dystrophin gene (micro-dystrophin) to muscle cells.

Contact MDA's Gene Therapy Support Specialists to be connected with additional information and resources.
Phone: 1-833-275-6321
Email: resourcecenter@mdausa.org

**Please talk to your medical provider to obtain more information about these treatments for DMD.*

## Exon-skipping Therapies

These drugs promote skipping over a section of genetic code (known as an "exon") to avoid the DMD gene mutation, allowing the body to produce a shortened, but functional dystrophin protein. Exon skipping therapies are typically made of bits of genetic material, known as anti-sense oligonucleotides (ASOs).

**Amondys 45* (casimersen)** is an "exon skipping" drug that targets a section of DNA called exon 45 and may help up to 8% of patients with DMD.

**Exondys 51* (eteplirsen)** is an "exon skipping" drug that targets a section of DNA called exon 51. It is approved by the FDA for treatment of individuals who have a confirmed mutation of the DMD gene that is amenable to a therapeutic strategy called exon 51 skipping and may help up to 13% of individuals with DMD.

**Viltepso* (viltolarsen)** is an "exon skipping" drug that targets a section of DNA called exon 53. It is approved by the FDA for treatment of individuals who have a confirmed mutation of the DMD gene that is amenable to a therapeutic strategy called exon 53 skipping and may help up to 8% of individuals with DMD.

**Vyondys 53* (golodirsen)** is an "exon skipping" drug that targets a section of DNA called exon 53. It is approved by the FDA for treatment of individuals who have a confirmed mutation of the DMD gene that is amenable to a therapeutic strategy called exon 53 skipping and may help up to 8% of individuals with DMD.

# MDA Glossary

### Atrophy
A decrease in the size and mass of muscle tissue

### Cardiomyopathy
A condition in which the heart muscle is weakened, making it harder for the heart to pump blood to the body

### Contracture
A shortening of muscles or tendons around joints that can limit mobility

### Corticosteroids
A group of steroid hormones that have been shown to dampen the inflammatory response in damaged muscle

### Dysphagia
Difficulty swallowing

### Exon skipping
A treatment strategy in which sections of genetic code are "skipped," allowing cells to manufacture partially functional dystrophin, the muscle protein missing in DMD

### Gastroparesis
Also known as delayed gastric emptying; a condition that affects the ability of the stomach to empty its contents into the small intestine, even though there is no blockage

### Gene Therapy
A technique that modifies a person's genes to treat a disease

### Gowers' maneuver
A person's use of their hands and arms to "walk" up their own body in order to rise from a squatting position; this medical sign indicates weakness of the muscles in the hips and legs

### Lordosis
Posture characterized by an inward curving of the lower back

### Muscular dystrophy
A term that refers to a number of diseases that cause progressive loss of muscle mass, resulting in weakness and, sometimes, loss of mobility

### Mutation
A flaw in the DNA code

### Pseudo-hypertrophy
A condition in which muscles become enlarged with deposits of fat and fibrous tissue

### Scoliosis
An abnormal sideways curvature in the spine that occurs when weakened muscles are unable to hold the spine straight