DUCHENNE MUSCULAR DYSTROPHY

Duchenne muscular dystrophy (DMD) is the most common form of muscular dystrophy. It is a genetic disorder characterized by progressive weakness and degeneration of the skeletal muscles that control movement.

DMD affects approximately **1 in 5,000 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, a **mutation 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 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 medications and therapy can help manage some symptoms and potentially slow the course of the disease.

WHAT SHOULD I KNOW ABOUT DMD

1. DMD symptom onset occurs in early childhood, usually between the ages of 3 and 5 years.

2. Early signs of DMD may include delayed ability to sit, stand, or walk and difficulties learning to speak. Muscle weakness usually begins in the hips, pelvic area, upper legs, and shoulders. The calves may be enlarged.

3. Children with DMD typically develop an unusual walk and difficulty running and climbing stairs. Some will have problems getting up from the floor and may use a distinctive method known as Gower's maneuver or Gower's sign to "walk" their hands up their thighs in order to stand up. DMD may also affect learning and memory, as well as communication and certain emotional skills.

4. A small percentage of boys with DMD have some degree of learning disability, including problems in three general areas: attention focusing, verbal learning and memory, and emotional interaction.

5. Muscle weakness worsens with age and progresses to the arms, legs, and trunk.

6. While disease progression varies, boys, on average, lose their ability to walk, and transition to full-time wheelchair use at age 12.

7. Beginning at about 10 years of age, the diaphragm and other muscles that operate the lungs may weaken, making the lungs less effective at moving air in and out. Signs of poor respiratory function can include headaches, difficulty concentrating or staying awake, and nightmares.

8. Heart and respiratory muscle problems begin in the teen years and can lead to serious complications.

9. Weakened respiratory muscles make it difficult to cough, leading to increased risk of serious respiratory infection. A simple cold can quickly progress to pneumonia.

10. Thanks to advances in cardiac and respiratory care, life expectancy for individuals with DMD is increasing and many young adults with DMD attend college, have careers, get married, and have children.

11. 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?

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

Braces, also called orthoses, support the ankle and foot or may extend up over the knee. **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 can help treat respiratory muscle weakness.

Educational and psychological interventions can help with learning disabilities.

Corrective orthopedic surgery, including spine-straightening surgery, may help make sitting, sleeping, and breathing more comfortable.

Treatment with angiotensin converting enzyme (ACE) inhibitors and beta blockers may be used to slow the course of cardiac muscle deterioration in DMD.

The US Food and Drug Administration (FDA) has approved steroid treatment, exon skipping, and gene therapies for the treatment of DMD.

Steroids

Corticosteroids (such as prednisone) are commonly used in DMD to help preserve muscle strength and function, to prevent scoliosis, and to prolong the time that people with DMD can walk. It's thought that steroids work, at least in part, by reducing inflammation. However, corticosteroids also cause unwanted side effects such as increased appetite, weight gain, loss of bone mass, and cataracts.

Prednisone* is a corticosteroid available in tablet, liquid, or concentrated form which is encouraged to be taken for life.

Emflaza* is the first corticosteroid to be approved by the FDA for the treatment of DMD in individuals ages 2 and older.

Agamree* is a structurally unique steroidal anti-inflammatory drug to treat children ages 2 and older. This drug is administered through an oral suspension. Data from clinical trials suggests a reduction in adverse events, notably related to bone health, growth trajectory, and behavior.

Emflaza and prednisone/prednisolone are the current standard of care for patients with DMD. Corticostreoids improve muscle strength and function, delay loss of ambulation, improve pulmonary function, reduce the need for scoliosis surgery, and delay onset of cardiomyopathy. Both have been used off-label for many years (choice dependent on patient preference, cost, and geographic location) before the FDA approval of deflazacort for DMD in 2017. They are both available in liquid and tablet forms.

Exon Skipping Therapy

Amondys 45* is designed to treat a third subset of patients with DMD, specifically those with a mutation amenable to skipping of exon 45. Approval of Amondys 45 represents another significant step forward in the development of therapies for DMD that target the root

Exondys 51* 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.

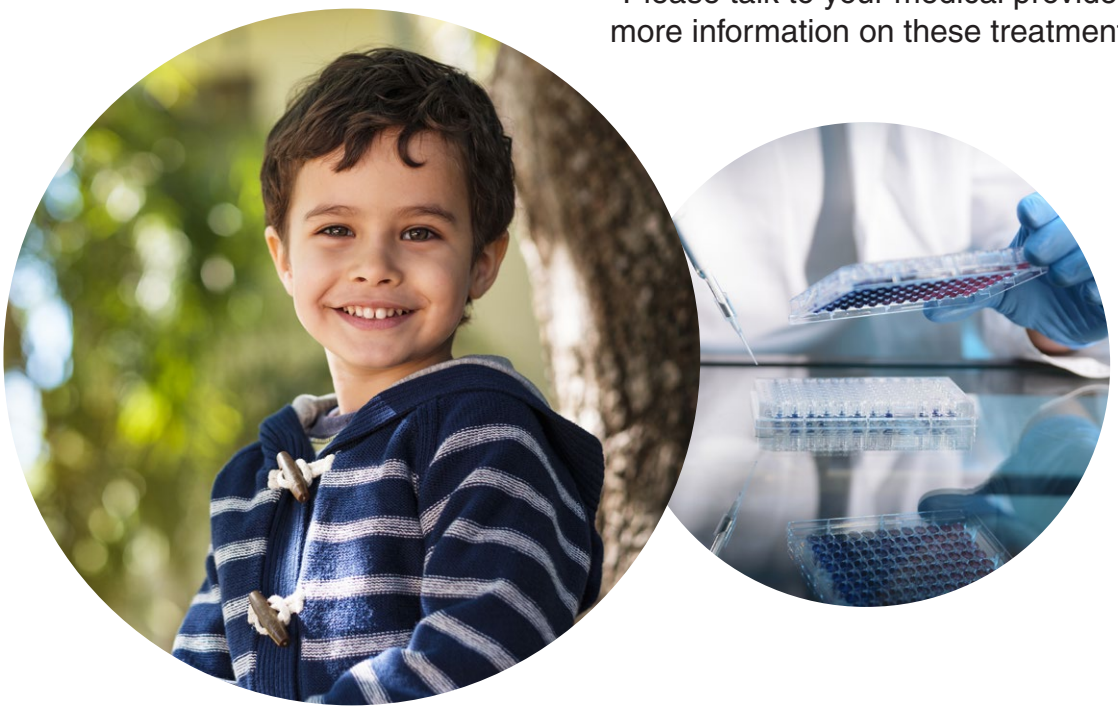
Viltepso* is an “exon skipping” drug that targets a section of DNA called exon 53. It is approved by the FDA for treatment of individuals who have a confirmed mutation of the DMD gene that is amenable to a therapeutic strategy called exon 53 skipping and may help up to 8% of individuals with DMD.

Vyondys 53* 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.

Gene Therapy

Elevidys* is the first FDA approved gene therapy to treat DMD. Elevidys is a one time IV infusion to treat children 4 to 5 years old who can walk and have a confirmed mutation in the dystrophin gene. Elevidys uses an adeno-associated virus to deliver a gene that introduces a shortened form of dystrophin (micro-dystrophin) to muscle cells. The FDA granted accelerated approval of Elevidys on June 22, 2023. As a condition of the approval, the FDA requires the completion of the clinical study to confirm the drug’s clinical benefit. The FDA may take a further action to revise the indication of Elevidys.

*Please talk to your medical provider to obtain more information on these treatments.



WHAT ARE THE SIGNS AND SYMPTOMS OF DMD?

Nervous system
- Developmental delay
- Motor delay

Cognition
- Learning disability

Gastrointestinal
- Dysphagia
- Constipation
- Reflux
- Gastroparesis

Heart
- Cardiomyopathy

Skeleton and muscle
- Muscle weakness
- Fatigue
- Muscle cramps
- Difficulty walking
- Difficulty climbing stairs
- Gait abnormalities
- Contractures
- Pseudohypertrophy
- Lordosis
- Scoliosis

Lungs
- Breathing difficulties
- Respiratory infections
- Sleep apnea

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

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

Gower's 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

Pseudohypertrophy
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

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