

# Duchenne Muscular Dystrophy Fact Sheet

## About Duchenne Muscular Dystrophy

- Duchenne muscular dystrophy (DMD), is a rare genetic disorder that causes progressive deterioration of muscle tissue, resulting in severe disability and eventually death.<sup>1</sup>
- DMD primarily affects boys, and occurs across all races and cultures, because the Duchenne gene is found on the X-chromosome. <sup>1</sup>
- Duchenne is both the most common childhood form and one of the most severe form of muscular dystrophy, affecting 1 in every 3,500 boys.<sup>2</sup>
- Children born with DMD do not produce enough dystrophin, an important structural component of muscle, causing muscle cells to break down and die.<sup>1</sup>
- Duchenne can be passed from mother to child, but approximately 35% of cases occur because of a random spontaneous mutation, which means it isn't inherited and can affect anyone.<sup>4</sup>
- Some cases of DMD are caused by "nonsense mutations," which are errors in the genetic code that prematurely stop the production of dystrophin.<sup>2</sup> Approximately 13% of boys with Duchenne muscular dystrophy have a nonsense mutation, resulting in a non-functional protein.<sup>3</sup>
- The symptoms of DMD usually appear in early childhood, as the muscles begin to weaken. Children with Duchenne usually have difficulty going up stairs and jumping. The child may walk on their tiptoes, or stumble, and may have difficulty getting up from a lying or sitting position.<sup>4</sup>
- Although there are supportive therapies that may help slow decline in muscle strength and motor function, there is currently no cure for Duchenne.<sup>5</sup>
- Doctors diagnose DMD by measuring a muscle enzyme called creatine kinase (CK), and doing a muscle biopsy. Boys with DMD have very high levels of this CK, which is released when muscle cells break down, and have dystrophin deficiency in muscle tissue.<sup>4</sup>
- Genetic testing can determine the boy's specific genetic mutation. Benefits of testing include diagnosis DMD, proving information about risk in the family and determining treatment study eligibility. <sup>6</sup>

## Symptoms and Progression of DMD

- Symptoms of DMD vary greatly, but can include: fatigue, learning disabilities, intellectual disability, muscle weakness and issues with motor skills, progressive difficulty walking, issues with heart and lung function.<sup>5</sup>
- While the progression and severity of DMD varies from person to person, there are distinct stages of degeneration that each boy with DMD will experience.

***Stage 1: Pre-symptomatic***

- In the early stages of development, there may be no distinct signs of DMD.
- If there is a family history, pre-symptomatic testing may be done to determine if the boy has DMD.

***Stage 2: Early ambulatory***

- DMD is typically diagnosed around age five, but symptoms may appear earlier.<sup>6</sup>
- Delays in early developmental milestones such as sitting, walking, and/or talking are often apparent.<sup>8</sup>
- Boys tend to move slower or with more difficulty than their peers, may fall frequently, and have difficulty walking, running or playing with friends.<sup>4</sup>

***Stage 3: Late ambulatory***

- Boys increasingly have difficulty walking as muscles in the legs weaken and cause balance issues.<sup>7</sup> Between ages 8 and 10 years, walking may require the use of braces.<sup>4</sup> Fatigue is common and they may need help from an assistive device such as a stroller, wheelchair or scooter.
- Most boys at this age have use of their hands and arms, but they may have difficulty carrying objects.<sup>9</sup>
- Heart problems requiring medication may begin to appear.

***Stage 4: Early non-ambulatory***

- Muscles further weaken, and by age 12, most boys with DMD are wheelchair dependent.<sup>4</sup>
- Weakness in the arms can make daily activities difficult. Most young men at this stage are still able to use their fingers, write, and use a computer.<sup>9</sup>
- Weak back muscles combined with sitting all day can lead to scoliosis (curvature of the spine) which, along with muscle cramps, can cause discomfort and pain.

***Stage 5: Late non-ambulatory***

- As the disorder progresses, life-threatening heart and respiratory conditions become more prevalent. Major symptoms of heart and lung complications include shortness of breath, fluid in the lungs, and swelling in the feet and lower legs.<sup>9</sup>
- By age 16–18, patients are predisposed to serious, sometimes fatal pulmonary infections.<sup>4</sup>
- Young men with Duchenne usually pass away in their 20s or early 30s due to cardiac and respiratory complications.<sup>9</sup>

**Symptom Management and Treatment | *Current state of DMD management:***

While there is currently no cure for Duchenne, researchers are making great advances in slowing the progression of the disease. Two promising treatments – **Eteplirsen** developed by Sarepta Therapeutics and **Translarna™ (ataluren)** discovered and developed by PTC Therapeutics Inc. are currently being studied, are undergoing regulatory review and becoming available in some parts of the world.

- Currently available treatment aims to control symptoms to improve quality of life, but do not address the underlying cause of the disease.
- Corticosteroids, including prednisone and deflazacort, can slow the loss of muscle strength and help retain motor function longer.
  - Corticosteroids may be started when the child is diagnosed, or when muscle strength begins to decline.
  - Side effects are common with these drugs, and can include: weight gain, stunted growth low bone density, cataracts, cushingoid (“moon face”) appearance, hair growth, acne, behavioral changes consisting of irritability and hyperactivity, osteonecrosis (loss of blood to the bone, causing bone death and collapse), and hypertension.<sup>8</sup>
  - Physical therapy may be helpful to maintain muscle strength and function. Speech therapy is often needed.
- As the disease progresses, a variety of assistive devices may be used including:<sup>9</sup>
  - Assisted ventilation;
  - Drugs to help heart function, such as angiotensin-converting-enzyme inhibitors, beta-blockers, and diuretics;
  - Orthopedic appliances to assist mobility, including braces and wheelchairs; and
  - Proton pump inhibitors to control gastroesophageal reflux.

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- <sup>1</sup> National Institute of Neurological Disorders and Stroke, "Muscular Dystrophy: Hope Through Research." Available at: [http://www.ninds.nih.gov/disorders/md/detail\\_md.htm](http://www.ninds.nih.gov/disorders/md/detail_md.htm). Accessed June 25, 2015.
- <sup>2</sup> Duchenne Connect, "About Duchenne and Becker Muscular Dystrophies." Available at: <https://www.duchenneconnect.org/about-dmd-bmd.html>. Accessed June 25, 2015.
- <sup>3</sup> Finkel R, Flanigan K, Wong B, Bönnemann C, Sampson J, Sweeney HL, et al. "Phase 2a study of ataluren-mediated dystrophin production in patients with nonsense mutation muscular dystrophy." *Plos One* 2013;8:e81302. Available at: <http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0081302#s1>. Accessed June 25, 2015.
- <sup>4</sup> Parent Project Muscular Dystrophy, "About Duchenne." Available at: [http://www.parentprojectmd.org/site/PageServer?pagename=understand\\_about](http://www.parentprojectmd.org/site/PageServer?pagename=understand_about). Accessed June 25, 2015.
- <sup>5</sup> Fauci AS, "Neurologic Disorders." *Harrison's Online Featuring the Complete Contents of Harrison's Principles of Internal Medicine*, 18th ed. New York: McGraw-Hill, Medical Pub. Division, 2012:3491-3495.
- <sup>6</sup> Duchenne Connect, "Understanding Genetic Testing." Available at: <https://www.duchenneconnect.org/understanding-genetic-testing.html>. Accessed August 18, 2016.
- <sup>7</sup> Canadian Stem Cell Foundation, "About Muscular Dystrophy." Available at: <http://stemcellfoundation.ca/en/diseases/muscular-dystrophy/>. Accessed June 25, 2015.
- <sup>8</sup> Bushby K, Finkel R, Birnkrant DJ, et al; DMD Care Considerations Working Group. "Diagnosis and management of Duchenne muscular dystrophy, part 1: diagnosis, and pharmacological and psychosocial management." *Lancet Neurology*, 2010;9(1):77-93.
- <sup>9</sup> Parent Project Muscular Dystrophy, "Stages of Duchenne." Available at: [http://www.parentprojectmd.org/site/PageServer?pagename=understand\\_stages](http://www.parentprojectmd.org/site/PageServer?pagename=understand_stages). Accessed June 25, 2015.
- <sup>10</sup> Sanzarelo I, Merlini L, et al. "Corticosteroid Treatment Impact on Spinal Deformity in Duchenne Muscular Dystrophy." *International Scholarly Research Notices*, 2014; 965235. Available at: <http://dx.doi.org/10.1155/2014/965235>. Accessed July 17, 2015.
- <sup>11</sup> Bushby K, Finkel R, Birnkrant DJ, et al; DMD Care Considerations Working Group. "Diagnosis and management of Duchenne muscular dystrophy, part 2: implementation of multidisciplinary care." *Lancet Neurology*, 2010;9(2):177-89.