

Muscular Dystrophy

Making a Difference Today

Muscular dystrophy (MD) describes a group of nine inherited, muscle-wasting diseases that progressively affect voluntary muscles. MD can appear at any stage of life, affect muscles in any part of the body, and progress slowly or rapidly. Sometimes cognitive delays also affect those with MD.

Duchenne MD, for example, affects boys almost exclusively, and typically is diagnosed between the ages of 3 and 5. A child may fall a lot, have trouble running or jumping, or be exceptionally tired. His calves may be unusually large, and he may no longer be able to walk by the time he is 12. Most boys with Duchenne MD do not live beyond their 20s. Myotonic MD, which affects adults, is the most common form of MD. Characteristically, hand, foot, and face muscles fail to relax after contraction. People with myotonic MD may have a mixture of other symptoms, including heart abnormalities, cataracts, diabetes, and gastrointestinal problems; typically, the progression of the disease is slow.

Together, the muscular dystrophies affect an estimated 80,000 people in the United States, according to the Muscular Dystrophy Association. A 1986 study calculated that the average yearly outpatient cost for these and other neuromuscular disorders is \$750 per patient; at \$1200, the annual per-person treatment cost for Duchenne patients is the highest.

Research Advances

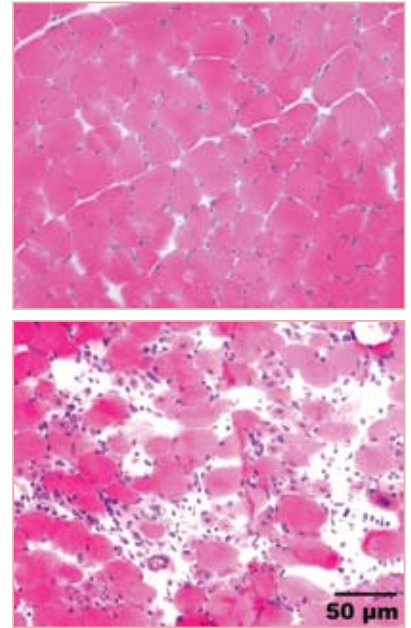
MD takes a toll on patients and families alike. Fortunately, with the backing of the National Institutes of Health (NIH), research institutes nationwide have made important advances in understanding this disease.

In particular, the development of genetic tools and techniques allowed government-funded researchers to identify the dystrophin gene, which, in its abnormal form fails to make the protein dystrophin, causing Duchenne MD and a related, milder form of the disease. This research made an important mouse model available for further study of MD and led to genetic testing and more precise, less invasive diagnoses.

It also led to the discovery of the dystrophin-associated protein complex, a group of proteins bound to each other at the membrane of muscle cells. As part of this complex, dystrophin is thought to stabilize muscle fibers and protect them from the stress of muscle contractions both by its structure and through signaling. Such advances in understanding have helped scientists define a common basis for a variety of muscular dystrophies and have spurred further genetic studies.

Promising Strategies

Unraveling the genetic and cellular level clues to MD sets the stage for treatments unimaginable in previous years. Currently, corticosteroid treatments may be used to delay muscle weakening, allowing patients to continue walking for several years. Yet only 60 percent of Duchenne patients take them, and many experience side effects. With continued funding, researchers can pursue promising treatments, including a variety of methods that use genes to repair protein deficiencies.



Muscle tissue breaks down through normal wear and tear, but for people with MD, a variation in their genes hasten the breakdown or block repair of that tissue. These slides show muscle tissue from a normal mouse, above, and from an MD model mouse, which does not make dystrophin protein. The dystrophic muscle fibers vary abnormally in size and show signs of inflammation and fibrosis, which are characteristic of the disease.

Continued funding for research could lead to:

- Treatments that encourage muscle growth in patients with MD.
- Gene-targeted therapies that correct deficiencies in dystrophin.
- Cell transplantation techniques to encourage muscle growth.

For more information please email brss@sfn.org.

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Muscular Dystrophy

Making a Difference Tomorrow

Despite significant advances in pinning down the biological basis for the progressive neuromuscular disorder muscular dystrophy (MD), few effective treatments are available and no cure exists.

Did you know that?

- The nine muscular dystrophies that exist appear in a variety of forms and affect people of all ages.
- An estimated 55,000 people in the United States have MD.
- Duchenne MD, which typically first appears in boys under 6, has the highest annual outpatient rehabilitation cost per person among neuromuscular disorders.

With continuing government support for MD research, scientists are hopeful that focused research will lead to more effective treatments for patients.

Research Brings Hope For The Future

Goals set out by a government-sponsored committee and federally funded centers of excellence are promoting focused research into potential new treatments for MD. In fact, more potential therapies are being studied now than ever before.

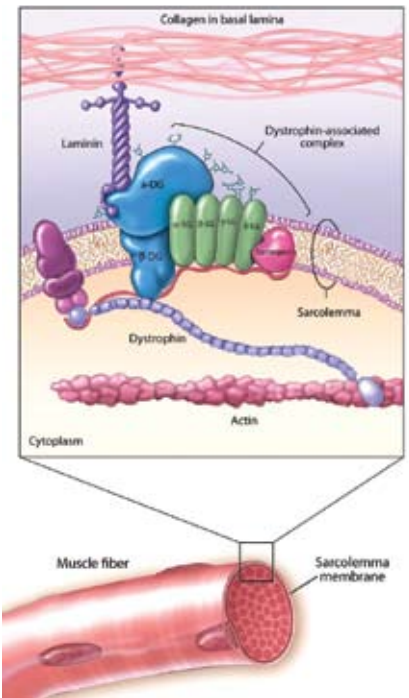
Scientists hope that years of research into the genes that cause MD and those that regulate how muscles develop can be harnessed and used to develop effective treatments. Researchers know, for example, that a protein known as myostatin keeps muscles from growing. Animal studies show that when scientists remove or block this protein, the size and strength of muscles increase. Clinical trials are now ongoing to test this therapy in three kinds of MD.

Other treatment approaches under study focus on the dystrophin gene. One technique studied in animals skips over abnormal sections of the gene, restoring cells' ability to make normal proteins.

Researchers are also looking at: encouraging the activity of growth factor in muscles, a treatment being tested in clinical trials; transplanting cells, such as undeveloped muscle cells that could encourage the growth of healthy new muscle fibers; and developing drug therapies.

Hope For Other Diseases

Scientists are hopeful that current genetic techniques and technologies for using cells in treatments could lead to new therapies for MD. Past advances in research into one form of MD has often advanced understanding of other forms. In addition, MD researchers can benefit from more general research into such areas as heart abnormalities and the mechanisms of muscle injury. Further funding for basic research could improve the lives of many Americans.



Variations in genes producing proteins that make up the dystrophin-associated protein complex, shown above, are indicated in a number of different forms of muscular dystrophy. The complex attaches to the cell membrane and provides structural support when muscles contract. Scientists hope that gene-targeted therapies will lead to effective treatments for the disease.

Already research has led to:

- The discovery of the *dystrophin* gene.
- Less invasive methods for diagnosing the disorder.
- A better understanding of the role of dystrophin and other proteins in muscle tissue structure, breakdown, and repair.

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