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What is muscular dystrophy?

Muscular dystrophy (MD) refers to a group of more than 30 genetic diseases that cause progressive weakness and degeneration of skeletal muscles used during voluntary movement. These disorders vary in age of onset, severity, and pattern of affected muscles. All forms of MD grow worse as muscles progressively degenerate and weaken. Many individuals eventually lose the ability to walk.

Some types of MD also affect the:

- Heart
- Gastrointestinal system
- Endocrine glands
- Spine
- Eyes
- Brain
- Other organs

Respiratory and cardiac diseases may occur, and some people may develop a swallowing disorder. MD is not contagious and cannot be brought on by injury or activity.

How MD affects muscles

Muscles are made up of thousands of muscle fibers. Each fiber is actually a number of individual cells that have joined together during development and are encased by an outer membrane. Muscle fibers that make up individual muscles are bound together by connective tissue.

Muscles are activated when an impulse, or signal, is sent from the brain through the spinal cord and peripheral nerves (nerves that connect the central nervous system to sensory organs and muscles) to the neuromuscular junction (the space between the nerve fiber and the muscle it activates). There, the chemical acetylcholine triggers a series of events that cause the muscle to contract.

The muscle fiber membrane contains a group of proteins, or the dystrophin-glycoprotein complex, that prevent damage when muscle fibers contract and relax. When this protective membrane is damaged, muscle fibers begin to leak the protein creatine kinase, which is needed for the chemical reactions that produce energy for muscle contractions, and take on excess calcium that causes further harm. Affected muscle fibers eventually die from this damage, leading to progressive muscle degeneration.

Although MD can affect several body tissues and organs, it most prominently affects the integrity of muscle fibers. The disease causes:

- Muscle degeneration
- Progressive weakness

- Fiber death
- Fiber branching and splitting
- Phagocytosis (muscle fiber material is broken down and destroyed by scavenger cells)
- Chronic or permanent shortening of tendons and muscle

Also, overall muscle strength and tendon reflexes are usually lessened or lost due to replacement of muscle by connective tissue and fat.

Who is more likely to get muscular dystrophy?

MD occurs worldwide and affects all races. Its incidence varies as some forms are more common than others. Some types of MD are more prevalent in certain countries and regions of the world. Many muscular dystrophies are familial, meaning there is some family history of the disease.

All of the muscular dystrophies are inherited and involve a gene mutation (defect). The body's cells don't work properly when a protein is altered or produced in insufficient quantity (or sometimes missing completely). Many cases of MD occur from spontaneous mutations that are not found in the genes of either parent, and this can be passed to the next generation.

Genes are like blueprints; they contain coded messages that determine a person's characteristics or traits. They are arranged along 23 rod-like pairs of chromosomes with one half of each pair being inherited from each parent. Each half of a chromosome pair is similar to the other, except for one pair, which determines the sex of the individual. Muscular dystrophies can be inherited in three ways:

1. Autosomal dominant inheritance occurs when a child receives a "normal" gene from one parent and a defective gene from the other parent. Autosomal means the genetic mutation can occur on any of the 22 non-sex chromosomes in each of the body's cells. Dominant means only one parent needs to pass along the abnormal gene in order to produce the disorder. In families where one parent carries a defective gene, each child has a 50 percent chance of inheriting the gene and therefore the disorder. Males and females are equally at risk and the severity of the disorder can differ from person to person.
2. Autosomal recessive inheritance means that both parents must carry and pass on the faulty gene. The parents each have one defective gene but are not affected by the disorder. Children in these families have a 25 percent chance of inheriting both copies of the defective gene and a 50 percent chance of inheriting one gene and therefore becoming a carrier, able to pass along the defect to their children. Children of either sex can be affected by this pattern of inheritance.
3. X-linked (or sex-linked) recessive inheritance occurs when the female parent carries the affected gene on one of two X chromosomes and passes it to the male child (males always inherit an X chromosome from their female parent and a Y chromosome from their male parent, while females inherit an X chromosome from each parent). Male children of carrier female parents have a 50 percent chance of inheriting the disorder. Female children also have a 50 percent chance of inheriting the defective gene but usually are not affected, since the healthy X chromosome they receive from their male parent can offset the faulty one received from their female parent. Affected male parents

cannot pass an X-linked disorder to their male children but their female children will be carriers of that disorder. Carrier females occasionally can exhibit milder symptoms of MD.

Similar conditions

There are many other heritable diseases that affect muscles, nerves, or the neuromuscular junction. Diseases like inflammatory myopathy, progressive muscle weakness, and cardiomyopathy (heart muscle weakness that interferes with pumping ability) may produce symptoms that are very similar to those found in some forms of MD, but they are caused by different genetic defects. Disorders with symptoms similar to MD include:

- Congenital myopathy
- Spinal muscular atrophy
- Congenital myasthenic syndromes

The sharing of symptoms among multiple neuromuscular diseases, and the prevalence of sporadic cases in families not previously affected by MD, often makes it difficult for people with MD to obtain a quick diagnosis. Some individuals may have signs of MD but carry none of the currently recognized genetic mutations.

Classifying muscular dystrophy

There are nine major groups of the muscular dystrophies. The disorders are classified by the:

- Extent and distribution of muscle weakness
- Age of onset
- Rate of progression
- Severity of symptoms
- Family history (including any pattern of inheritance)

Although some forms of MD become apparent in infancy or childhood, others may not appear until middle age or later. Overall, incidence rates and severity vary, but each of the dystrophies causes progressive skeletal muscle deterioration, and some types affect cardiac muscle.

Duchenne muscular dystrophy is the most common childhood form of MD, as well as the most common of the muscular dystrophies overall, accounting for approximately 50 percent of all cases. Because inheritance is X-linked recessive (caused by a mutation on the X chromosome), Duchenne MD primarily affects males, although females who carry the defective gene may show some symptoms. About one-third of the cases reflect new mutations and the rest run in families. Female siblings of male children with Duchenne MD have a 50 percent chance of carrying the defective gene. The disorder gets its name from the French neurologist Guillaume Duchenne. Duchenne MD results from an absence of the muscle protein dystrophin. Dystrophin is a protein found in muscle that helps muscles stay healthy and strong. Blood tests of children with Duchenne MD show an abnormally high level of creatine kinase; this finding is apparent from birth. Duchenne MD usually becomes apparent during the toddler years, sometimes soon after an affected child begins to walk. Progressive weakness and muscle wasting (a decrease in muscle strength and size) caused by degenerating muscle fibers begins in the upper legs and pelvis before spreading into the upper arms. Other symptoms include:

- Loss of some reflexes
- A waddling gait
- Frequent falls and clumsiness (especially when running)
- Difficulty when getting up from a sitting position or when climbing stairs
- Changes to overall posture
- Impaired breathing
- Lung weakness
- Cardiomyopathy

Many children are unable to run or jump. The wasting muscles, in particular the calf muscles, and less commonly, muscles in the buttocks, shoulders, and arms, may be enlarged by an accumulation of fat and connective tissue, causing them to look larger and healthier than they actually are (pseudohypertrophy). As the disease progresses, the muscles in the diaphragm that assist in breathing and coughing may weaken. Individuals may experience breathing difficulties, respiratory infections, and swallowing problems. Bone thinning and scoliosis (curving of the spine) are common. Some children have varying degrees of cognitive and behavioral impairments.

Between ages 3 and 6, children may show brief periods of physical improvement followed by progressive muscle degeneration later. Children with Duchenne MD typically lose the ability to walk by early adolescence. Improvements in multidisciplinary care have extended the life expectancy and improved the quality of life significantly for children with Duchenne MD. Numerous individuals survive into their 30s, and some even into their 40s.

Becker muscular dystrophy is less severe than but closely related to Duchenne MD. People with Becker MD have partial but insufficient function of the protein dystrophin. The disorder usually appears around age 11 but may occur as late as age 25, and affected individuals generally live into middle age or later. The rate of progressive, symmetric (on both sides of the body) muscle atrophy and weakness varies greatly among affected individuals. Many individuals are able to walk until they are in their mid-30s or later, while others are unable to walk past their teens. Some affected individuals never need to use a wheelchair. As in Duchenne MD, muscle weakness in Becker MD is typically noticed first in the upper arms and shoulders, upper legs, and pelvis.

Early symptoms of Becker MD include:

- Walking on one's toes
- Frequent falls
- Difficulty rising from the floor

Calf muscles may appear large and healthy as deteriorating muscle fibers are replaced by fat, and muscle activity may cause cramps in some people. Cardiac complications are not as consistently present in Becker MD compared to Duchenne MD, but may be as severe in some cases. Cognitive and behavioral impairments are not as common or severe as in Duchenne MD, but they do occur.

Congenital muscular dystrophy refers to a group of autosomal recessive muscular dystrophies that are either present at birth or become evident before age 2. The degree and progression of muscle weakness and degeneration vary with the type of disorder. Weakness may be first noted when children fail to meet landmarks in motor function and muscle control. Muscle degeneration may be mild or severe and is restricted primarily to skeletal muscle. The

majority of individuals are unable to sit or stand without support, and some affected children may never learn to walk. There are three groups of congenital MD:

1. Merosin-negative disorders, in which the protein merosin (found in the connective tissue that surrounds muscle fibers) is missing
2. Merosin-positive disorders, in which merosin is present but other necessary proteins are missing
3. Neuronal migration disorders, in which very early in the development of the fetal nervous system the migration of nerve cells (neurons) to their proper location is disrupted

Defects in the protein merosin cause nearly half of all cases of congenital MD.

People with congenital MD may develop:

- Contractures (chronic shortening of muscles or tendons around joints, preventing them from moving freely)
- Scoliosis (curved spine)
- Breathing and swallowing difficulties
- Feet problems

The intellectual development of some children progresses as expected, while others become severely impaired. Weakness in diaphragm muscles may lead to respiratory failure. Congenital MD may also affect the central nervous system, causing vision and speech problems, seizures, and structural changes in the brain.

Distal muscular dystrophy (also known as distal myopathy) describes a group of at least six specific muscle diseases that primarily affect distal muscles (those farthest away from the shoulders and hips) in the forearms, hands, lower legs, and feet. Distal dystrophies are typically less severe, progress more slowly, and involve fewer muscles than other forms of MD, although they can spread to other muscles, including the proximal ones later in the course of the disease. Distal MD can affect the heart and respiratory muscles, and individuals may eventually require the use of a ventilator. They may not be able to perform fine hand movement and have difficulty extending the fingers. As leg muscles become affected, walking and climbing stairs become difficult and some people may be unable to hop or stand on their heels.

Onset of distal MD, which affects both males and females, is typically between the ages of 40 and 60 years. In one form of distal MD, a muscle membrane protein complex called dysferlin is known to be lacking.

Although distal MD is primarily an autosomal dominant disorder, autosomal recessive forms have been reported in young adults. Symptoms are similar to those of Duchenne MD but with a different pattern of muscle damage. An infantile-onset form of autosomal recessive distal MD has also been reported. Slow but progressive weakness is often first noticed around age 1, when the child begins to walk, and continues to progress very slowly throughout adult life.

Emery-Dreifuss muscular dystrophy primarily affects male children. The disorder has two forms: One is X-linked recessive and the other is autosomal dominant.

Onset of Emery-Dreifuss MD is usually apparent by age 10, but symptoms can appear as late as the mid-20s. This disease causes slow yet progressive wasting of the upper arm and lower leg muscles and symmetric weakness. Contractures in the spine, ankles, knees, elbows, and back of the neck usually precede significant muscle weakness, which is less severe than in Duchenne MD. Contractures may cause elbows to become locked in a flexed position. The entire spine may become rigid as the disease progresses. Other symptoms include:

- Shoulder deterioration
- Walking on one's toes
- Mild facial weakness

Serum creatine kinase levels may be moderately elevated. Nearly all people with Emery-Dreifuss MD have some form of heart problem by age 30, often requiring a pacemaker or other assistive device. Female carriers of the disorder often have cardiac complications without muscle weakness. In some cases, the cardiac symptoms may be the earliest and most significant symptom of the disease, and may appear years before muscle weakness does.

Facioscapulohumeral muscular dystrophy (FSHD) initially affects muscles of the face (facio), shoulders (scapulo), and upper arms (humera) with progressive weakness. Also known as Landouzy-Dejerine disease, this is the third most common form of MD and is characterized as an autosomal dominant disorder. Most people have a normal life span, but some become severely disabled.

Disease progression is typically very slow, with intermittent spurts of rapid muscle deterioration. Onset is usually in the teens but may occur as early as childhood or as late as age 40. One hallmark of FSHD is that it commonly causes asymmetric weakness. Muscles around the eyes and mouth are often affected first, followed by weakness around the shoulders, chest, and upper arms. A particular pattern of muscle wasting causes the shoulders to appear to be slanted and the shoulder blades to appear winged. Muscles in the lower extremities may also become weakened. Reflexes are diminished, typically in the same distribution as the weakness. Changes in facial appearance may include the development of a crooked smile, a pouting look, flattened facial features, or a mask-like appearance. Some individuals cannot pucker their lips or whistle and may have difficulty swallowing, chewing, or speaking. Muscle weakness can also spread to the diaphragm, causing respiratory problems.

Other symptoms may include:

- Hearing loss (particularly at high frequencies)
- Lordosis (inward curve of the lumbar spine)

Contractures are rare. Some people with FSHD feel severe pain in the affected limb. Cardiac muscles are not usually affected, and significant weakness of the pelvis is less common than in other forms of MD. An infant-onset form of FSHD can cause retinal disease and some hearing loss.

Limb-girdle muscular dystrophy (LGMD) refers to more than 20 inherited conditions marked by progressive loss of muscle bulk and symmetrical weakening of voluntary muscles, primarily those in the shoulders and around the hips. At least five forms of autosomal dominant limb-girdle MD (known as type 1) and 17 forms of autosomal recessive limb-girdle MD (known as

type 2) have been identified. Some autosomal recessive forms of the disorder are now known to be due to a deficiency of any of four dystrophin-glycoprotein complex proteins called the sarcoglycans. Deficiencies in dystroglycan, classically associated with congenital muscular dystrophies, may also cause LGMD.

The recessive LGMDs occur more frequently than the dominant forms, usually starting in childhood or the teens, and show dramatically increased levels of serum creatine kinase. The dominant LGMDs usually begin in adulthood. In general, the earlier the clinical signs appear, the more rapid the rate of disease progression. Limb-girdle MD affects both males and females. Some forms of the disease progress rapidly, resulting in serious muscle damage and loss of the ability to walk, while others advance very slowly over many years and cause minimal disability, allowing a normal life expectancy. In some cases, the disorder appears to halt temporarily, but progression then resumes.

The pattern of muscle weakness is similar to that of Duchenne MD and Becker MD. Weakness is typically noticed first around the hips before spreading to the shoulders, legs, and neck. Individuals develop a waddling gait and have difficulty when rising from chairs, climbing stairs, or carrying heavy objects. They fall frequently and are unable to run. Contractures at the elbows and knees are rare but individuals may develop contractures in the back muscles, which gives them the appearance of a rigid spine. Proximal reflexes (closest to the center of the body) are often impaired. Some individuals also experience cardiomyopathy and respiratory complications, depending in part on the specific subtype. Intelligence remains in most cases, though exceptions do occur. Many individuals with limb-girdle MD become severely disabled within 20 years of disease onset.

Myotonic dystrophy (DM1), also known as Steinert's disease and dystrophia myotonica, is another common form of MD. Myotonia, or the inability to relax muscles following a sudden contraction, is found only in this form of MD, but is also found in other non-dystrophic muscle diseases. People with DM1 can live a long life, with variable but slowly progressive disability. Typical disease onset is between ages 20 and 30, but childhood onset and congenital onset are well-documented. Muscles in the face and the front of the neck are usually first to show weakness and may produce a hollow temples, drooping facial skin, and a thin neck. Wasting and weakness noticeably affect forearm muscles. DM1 affects the central nervous system and other body systems, including the heart, adrenal glands and thyroid, eyes, and gastrointestinal tract.

Other symptoms include:

- Cardiac complications
- Difficulty swallowing
- Droopy eyelids (ptosis)
- Cataracts
- Poor vision
- Early frontal baldness
- Weight loss
- Impotence
- Testicular atrophy
- Mild mental impairment
- Increased sweating

Individuals may feel drowsy and have an excessive need for sleep. There is a second form known as myotonic dystrophy type 2 (DM2) that is similar to the classic form, but usually affects proximal muscles more significantly.

This autosomal dominant disease affects both males and females. Females may have irregular menstrual periods and are sometimes infertile. The disease may occur earlier and be more severe in successive generations. A childhood-onset form of myotonic MD may become apparent between ages 5 and 10. Symptoms include:

- General muscle weakness (particularly in the face and muscles farthest away from center of body)
- Lack of muscle tone
- Cognitive impairment

A female with DM1 can give birth to an infant with a rare congenital form of the disorder. Symptoms at birth may include:

- Difficulty swallowing or sucking
- Impaired breathing
- Absence of reflexes
- Skeletal deformities and contractures (club feet)
- Muscle weakness, especially in the face

Children with congenital myotonic MD may also experience cognitive impairment and delayed motor development. This severe infantile form of myotonic MD occurs almost exclusively in children who have inherited the defective gene from their female parent, whose symptoms may be so mild that they are sometimes not aware of the disease.

The inherited gene defect that causes DM1 is an abnormally long repetition of a three-letter "word" in the genetic code. In unaffected people, the word is repeated a number of times, but in people with DM1, it is repeated many more times. This triplet repeat gets longer with each successive generation. The triplet repeat mechanism has now been implicated in at least 15 other disorders, including Huntington's disease and the spinocerebellar ataxias.

Oculopharyngeal muscular dystrophy (OPMD) generally begins in the 40s and 50s and affects both males and females. In the U.S., the disease is most common in families of French-Canadian descent as well as among Hispanic residents of northern New Mexico. People first report drooping eyelids, followed by weakness in the facial muscles and pharyngeal muscles in the throat that cause problems with swallowing. The tongue may atrophy and changes to the voice may occur. Eyelids may droop so dramatically that some individuals compensate by tilting back their heads. Affected individuals may have:

- Double vision
- Problems with upper gaze
- Retinitis pigmentosa (progressive degeneration of the retina that affects night vision and peripheral vision)
- Cardiac irregularities

Muscle weakness and wasting in the neck and shoulder region is common. Limb muscles may also be affected. People with OPMD may find it difficult to walk, climb stairs, kneel, or bend. The most severely affected will eventually lose the ability to walk.

How is muscular dystrophy diagnosed and treated?

Diagnosing MD

Doctors review an individual's medical history and a complete family history to determine if the muscle disease is secondary to a disease affecting other tissues or organs or is an inherited condition. It is also important to rule out any muscle weakness resulting from prior surgery, exposure to toxins, or current medications that may affect the person's functional status. Thorough clinical and neurological exams can help doctors do the following:

- Rule out disorders of the central and/or peripheral nervous systems
- Identify any patterns of muscle weakness and atrophy
- Test reflex responses and coordination
- Look for contractions

Various laboratory tests may be used to confirm the diagnosis of MD, including:

- Blood and urine tests to detect defective genes and help identify specific neuromuscular disorders.
- Exercise tests to detect elevated rates of certain chemicals following exercise and are used to determine the nature of the MD or other muscle disorder.
- Genetic testing to look for genes known to either cause or be associated with inherited muscle disease. DNA analysis and enzyme assays can confirm the diagnosis of certain neuromuscular diseases, including MD. Genetic linkage studies can identify whether a specific genetic marker on a chromosome and a disease are inherited together. They are particularly useful in studying families with members in different generations who are affected. Advances in genetic testing include whole exome and whole genome sequencing, which will enable people to have all of their genes screened at once for disease-causing mutations, rather than have just one gene or several genes tested at a time.
- Genetic counseling to help parents who have a family history of MD determine if they are carrying one of the mutated genes that cause the disorder. Two tests can be used to help expectant parents find out if their child is affected.
- Amniocentesis at 14-16 weeks of pregnancy to test a sample of the amniotic fluid in the womb for genetic defects (the fluid and the fetus have the same DNA).
- Chorionic villus sampling (CVS) to test a very small sample of the placenta during early pregnancy.
- Diagnostic imaging can help determine the specific nature of a disease or condition. Magnetic resonance imaging (MRI) is used to examine muscle quality, any atrophy, or abnormalities in size, and fatty replacement of muscle tissue, as well as to monitor disease progression. Other forms of diagnostic imaging for MD include:
 - Phosphorus magnetic resonance spectroscopy measures cellular response to exercise and the amount of energy available to muscle fiber
 - Ultrasound imaging (also known as sonography) uses high-frequency sound waves to obtain images inside the body.
- Muscle biopsies to monitor the course of disease and treatment effectiveness. Muscle biopsies can sometimes also assist in carrier testing.

- Immunofluorescence testing to detect specific proteins such as dystrophin within muscle fibers.
- Electron microscopy to identify changes in subcellular components of muscle fibers. Electron microscopy also can identify changes that characterize cell death, mutations in muscle cell mitochondria, and an increase in connective tissue seen in muscle diseases such as MD.
- Neurophysiology studies to identify physical and/or chemical changes in the nervous system.
- Nerve conduction velocity to measure the speed and strength with which an electrical signal travels along a nerve and can help determine whether nerve damage is present.
- Repetitive stimulation to assess the function of the neuromuscular junction by electrically stimulating a motor nerve several times in a row.
- Electromyography (EMG) to record muscle fiber and motor unit activity. Results may reveal electrical activity characteristic of MD or other neuromuscular disorders.

Treating MD

Available treatments are aimed at keeping people independent for as long as possible and to prevent complications that can arise from weakness, reduced mobility, and cardiac and respiratory difficulties. Treatment may involve a combination of approaches, including physical therapy, drug therapy, and surgery.

- Assisted ventilation is often needed to treat respiratory muscle weakness that accompanies many forms of MD, especially in the later stages.
- Drug therapy may be prescribed to delay muscle degeneration.
 - The U.S. Food and Drug Administration (FDA) has approved injections of the drugs golodirsen and viltolarsen to treat individuals with Duchenne muscular dystrophy (DMD) who have a confirmed mutation of the dystrophin gene that is amenable to exon 53 skipping. The FDA approved injection of the drug casimersen to treat individuals who have a confirmed mutation of the DMD gene that is amenable to exon 45 skipping.
 - The FDA also approved three applications of fingolimod (Gilenya) to treat the relapsing form of MS in adults. Corticosteroids, such as prednisone, can slow the rate of muscle deterioration in Duchenne MD and help children retain strength to prolong independent walking by as much as several years. However, these medicines have side effects such as weight gain, facial changes, loss of linear (height) growth, and bone fragility that can be especially troubling in children.
 - Immunosuppressive drugs such as cyclosporine and azathioprine can delay some damage to dying muscle cells.
 - Drugs that may provide short-term relief from myotonia (muscle spasms and weakness) include mexiletine, phenytoin, and baclofen as they are known to block signals sent from the spinal cord to contract the muscles. Dantrolene interferes with the process of muscle contraction. And quinine is another option.
 - The FDA granted accelerated approval of the drug Exondys 51 to treat individuals who have a confirmed mutation of the dystrophin gene amenable to exon 15 skipping. The accelerated approval means the drug can be administered to people who meet the rare disease criteria while the company works on additional trials to learn more about the effectiveness of the drug. (Drugs for myotonia may not be effective in myotonic MD but work well for myotonia congenita, a genetic neuromuscular disorder characterized by the slow relaxation of the muscles.) Respiratory infections may be treated with antibiotics.

- Physical therapy can help prevent malformation, improve movement, and keep the muscles as flexible and strong as possible.
 - Passive stretching can increase joint flexibility and prevent contractures that restrict movement and cause loss of function.
 - Regular, moderate exercise can help people with MD maintain range of motion and muscle strength, prevent muscle atrophy, and delay the development of contractures. Individuals with a weakened diaphragm can learn coughing and deep breathing exercises that are designed to keep the lungs fully expanded.
 - Postural correction is used to counter the muscle weakness, contractures, and spinal irregularities that force individuals with MD into uncomfortable positions.
 - Support aids such as wheelchairs, splints and braces, other orthopedic appliances, and overhead bed bars (trapezes) can help maintain mobility. Spinal supports can help delay scoliosis. Orthotic devices such as standing frames and swivel walkers can help people remain standing or walking.
 - Repeated low-frequency bursts of electrical stimulation to the thigh muscles may produce a slight increase in strength in some male children with Duchenne MD, though this therapy has not been proven to be effective.
- Occupational therapy may help some with progressive weakness and loss of mobility. Some individuals may need to learn new job skills or new ways to perform tasks while other people may need to change careers altogether. Assistive technology may include modifications to home and workplace settings and the use of motorized wheelchairs, wheelchair accessories, and adaptive utensils.
- Speech therapy may help individuals whose facial and throat muscles have weakened. They can learn to use special communication devices, such as a computer with voice synthesizer.
- Dietary changes have not been shown to slow the progression of MD. Proper nutrition is essential, however, for overall health. Feeding techniques may help people with MD who have a swallowing disorder.
- Corrective surgery is often performed to ease complications from MD.
 - Tendon or muscle-release surgery is recommended when a contracture becomes severe enough to lock a joint or greatly impair movement.
 - Individuals with either Emery-Dreifuss or myotonic dystrophy may require a pacemaker at some point to treat cardiac problems.
 - Surgery to reduce the pain and postural imbalance caused by scoliosis may help some individuals. Scoliosis occurs when the muscles that support the spine begin to weaken and can no longer keep the spine straight.
 - People with myotonic dystrophy often develop cataracts, a clouding of the lens of the eye that blocks light, and may need cataract surgery.

What are the latest updates on muscular dystrophy?

The National Institute of Neurological Disorders and Stroke (NINDS), a part of the National Institutes of Health (NIH), supports a broad program of research on muscular dystrophy. NINDS and the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), the National Institute of Child Health and Human Development (NICHD), and the National Heart, Blood, and Lung Institute (NHLBI), lead the MD research efforts conducted at the NIH and at grantee institutions across the country.

The NIH supports a broad range of basic, translational, and clinical research in the muscular dystrophies. Advances in basic research are essential to the basic understanding of each type of MD. While many genes that cause muscular dystrophy still remain to be identified, advances

in gene sequencing has aided the identification of genes that may be involved for most types of muscular dystrophy. In turn, new knowledge of specific disease mechanisms is identifying potential targets for therapy development. Research into the underlying disease mechanisms has created new opportunities for therapy development in nearly all types of MD. For example, advances in targeted therapy have led to promising efforts in myotonic dystrophy and facioscapulohumeral muscular dystrophy.

Federal funding, through the NIH and other agencies, as well as the venture philanthropy programs supported by patient advocacy groups, have attracted biotechnology and pharmaceutical firm investments into therapies for the MDs. A variety of strategies are employed in developing new drug and biologic therapies for the range of MDs. Strategies being explored are either specific to a particular type of MD or may address disease progression that may apply to multiple types of MD.

Gene replacement therapy

Gene therapy has the potential to address the primary cause of MD by providing for the production of the missing protein. For muscular dystrophies with central nervous system consequences (congenital muscular dystrophy and myotonic dystrophy), researchers are developing and fine-tuning gene therapy vectors (a way to deliver genetic materials to cells) that can cross the protective blood-brain barrier. Progress in delivery of replacement genes in MD includes considerable refinement of the viral vector types that improve the targeting to skeletal muscle and vascular approaches to deliver replacement gene to most or all skeletal muscles.

Clinical testing of gene therapy strategies in MD has been underway for Duchenne and limb-girdle muscular dystrophy. Injections of gene therapy vectors into single muscles of participants were the first step to establishing safety of the approach. With the support of extensive studies in animal models, clinical trials are now moving toward testing of gene therapy of all muscles of entire limbs, using an isolated vascular delivery approach. If isolated limb delivery approaches prove safe and effective, research will move to systemic delivery of gene therapy vectors so all muscles can be treated simultaneously.

Utrophin is a protein that is closely related to dystrophin and is not affected in the gene mutations that cause Duchenne MD. Targeting increased expression of utrophin may prove a useful approach in treating Duchenne MD. NIH supports both gene therapy and small molecule drug development programs to increase the muscle production of utrophin.

Finally, modifier genes—genes with activities that act to reduce the severity of MD—have been discovered by NIH-funded teams. These genes, including latent TGF binding protein 4 and osteopontin, represent new therapeutic targets to potentially reduce the severity of several types of muscular dystrophy.

Genetic modification therapy to bypass inherited mutations

Most individuals with Duchenne have mutations in the dystrophin gene that cause it to function improperly and stop producing the dystrophin protein. By manipulating the protein synthesis process, production of a gene that either "reads through" or "skips" the genetic mutation can result in at least partial functional dystrophin.

Two strategies are currently under study to bypass dystrophin mutations:

1. One of which is drugs that cause the protein synthesis machinery to ignore the premature stop signal and produce functional dystrophin. This strategy, which is potentially useful in about 15 percent of individuals with Duchenne MD, is currently in clinical trials.
2. Second, a more recent approach uses antisense oligonucleotides (short strands of nucleic acid designed to block the transfer of some genetic information into protein production) to alter splicing and produce nearly a full-length dystrophin gene, potentially converting an individual with Duchenne to a much milder Becker MD. Biotechnology companies are currently testing oligonucleotide drugs in advanced clinical trials for people who require skipping of exon 51 of dystrophin. (An exon is a coding sequence in a gene for a protein). NINDS and NIAMS are supporting preclinical work on oligonucleotide drugs for individuals with Duchenne MD who require skipping of exon 45. As many as 80 percent of affected individuals could benefit from this new technology.

Antisense oligonucleotide technology is also being evaluated for use in myotonic dystrophy, but by a different mechanism than in Duchenne MD. In myotonic dystrophy, long duplications of repetitive DNA sequences lead to production of a toxic RNA that sequesters a splicing regulator, Muscleblind, causing mis-splicing of many genes in muscle and brain. An NINDS and NIAMS-supported project is advancing an oligonucleotide therapeutic designed to degrade the toxic RNA and mitigate the splicing defects. This approach, in partnership with academic investigators and biotechnology and pharmaceutical companies, has the potential to address all people having myotonic dystrophy and is planned to be in clinical trials within the next few years.

Drug-based therapy to delay muscle wasting

Progressive loss of muscle mass is primarily responsible for reduced quality and length of life in MD. Drug treatment strategies designed to slow this muscle degeneration can have substantial impact on quality of life. Similarly, skeletal muscle has the ability to repair itself, but its regeneration and repair mechanisms are progressively depleted during the course of several types of MD. Understanding the repair mechanisms may provide new therapies to slow, and possibly stabilize, muscle degeneration.

Corticosteroids are known to extend the ability of people with Duchenne MD to walk by up to two years, but steroids have substantial side effects and their mechanism of action is unknown. A study funded by NINDS is evaluating drugs and their efficacy and tolerability at different doses in order to determine optimal clinical practice for their use in Duchenne MD. In addition, a biotechnology company supported by the NIH's National Center for Advancing Translational Sciences is developing a modified steroid to increase its efficacy in Duchenne while reducing the side effects that often limit individuals from using corticosteroid therapy.

Preclinical drug development efforts supported by NINDS and NIAMS are developing a peptide therapeutic that has dual activity in mitigating muscle damage due to inflammation and also enhancing muscle regeneration in animal models. Efforts to preserve muscle mass through inhibition of a negative regulator of muscle growth, myostatin, have encountered some roadblocks, including failed clinical trials, but are still under study.

Cell-based therapy

The muscle cells of people with MD often lack a critical protein, such as dystrophin in Duchenne MD or sarcoglycan in some of the limb-girdle MDs. Scientists are exploring the possibility that the missing protein can be replaced by introducing muscle stem cells capable of making the missing protein in new muscle cells. Such new cells would be protected from the progressive degeneration characteristic of MD and potentially restore muscle function in affected persons.

The natural regenerative capacity of muscle provides possibilities for treatment of MD. Researchers have shown that stem cells can be used to deliver a functional dystrophin gene to skeletal muscles of dystrophic mice and dogs. The focus of research has been on identifying the cell types with the highest potential for engraftment and growth of muscle and on strategies to deliver these muscle precursor cells to human skeletal muscles. Overall, cell-based therapeutic approaches are under consideration for multiple types of MD.

Moving forward with research in MD

Until recently, most therapy development programs in MD were focused on Duchenne. With dramatic advances in understanding disease mechanisms, significant therapy development efforts are now being launched in many types of MD. NINDS funding supports teams working on the disease mechanisms in facioscapulohumeral muscular dystrophy, central nervous system involvement in myotonic dystrophy, and on the role of fibrosis in Duchenne MD. Similarly, NIAMS-supported projects are identifying novel therapy development targets that are attracting interest from biotechnology and pharmaceutical companies and will help move toward therapy development programs for all types of MD.

Parallel efforts need to be made in clinical trial readiness, so that clinical trials are feasible when a candidate reaches that stage. Patient registries, natural history studies, biomarker identification, development of clinical trial endpoint measures, and the emergence of standards of care are all essential in supporting clinical trials and are being advanced in several types of muscular dystrophy with the support of both public and private sector partners. The NIH has recently undertaken several new initiatives in training, career development, and research that are targeted toward MD. These advances, along with the NINDS focus on translational and clinical research, will lead to the growth of clinical trials and promising treatment strategies.

Federal commitment to muscular dystrophy

In December 2001, President George W. Bush signed into law the Muscular Dystrophy Community Assistance, Research, and Education Amendments Act of 2001 (the MD CARE Act, Public Law 107-84). The MD-CARE act was reauthorized in 2008.

In response to the MD CARE Act, the NIH formed the [Muscular Dystrophy Coordinating Committee](#) to help guide research on MD. The MD Coordinating Committee is made up of physicians, scientists, NIH professional staff, and representatives of other federal agencies and voluntary health organizations with a focus on MD. The purpose of the group is to help NIH add new capabilities to the national effort to understand and treat MD without duplicating existing programs.

The NIH is expanding and intensifying its research efforts on the muscular dystrophies and established the [The Wellstone Muscular Dystrophy Research Network](#) in honor of the late Senator Paul D. Wellstone of Minnesota. Established as part of the NIH enhancement and intensification of muscular dystrophy research associated with the MD-CARE Act, the centers

are supported by five-year, renewable grants. The following NIH Institutes participate in the Wellstone Centers Program:

- [National Institute of Arthritis and Musculoskeletal and Skin Diseases \(NIAMS\)](#)
- [Eunice Kennedy Shriver National Institute of Child Health & Human Development \(NICHD\)](#)
- [National Institute of Neurological Disorders and Stroke \(NINDS\)](#)
- [National Heart, Lung and Blood Institute \(NHLBI\)](#)

Research has led to the discovery of disease mechanisms and improved treatment for many forms of MD. Current research promises to generate further improvements. In the coming years, physicians and affected individuals can look forward to new forms of therapy developed through an understanding of the unique traits of MD.

Learn About Clinical Trials

Clinical trials are studies that allow us to learn more about disorders and improve care. They can help connect patients with new and upcoming treatment options.

How can I or my loved one help improve care for people with muscular dystrophy?

Consider participating in a clinical trial so clinicians and scientists can learn more about MD and related disorders. Clinical research uses human volunteers to help researchers learn more about a disorder and perhaps find better ways to safely detect, treat, or prevent disease.

All types of volunteers are needed—those who are healthy or may have an illness or disease—of all different ages, sexes, races, and ethnicities to ensure that study results apply to as many people as possible, and that treatments will be safe and effective for everyone who will use them.

For information about participating in clinical research visit [NIH Clinical Research Trials and You](#). Learn about clinical trials currently looking for people with MD at [Clinicaltrials.gov](#).

Where can I find more information about muscular dystrophy?

Information may be available from the following organizations and resources:

[Centers for Disease Control and Prevention \(CDC\)](#)

Phone: 800-311-3435 or 404-639-3311

[Coalition to Cure Calpain 3\(link is external\)](#)

Phone: 203-221-1611

[Cure CMD\(link is external\)](#)

Phone: 562-444-5656

[Facioscapulohumeral Muscular Dystrophy \(FSH\) Society\(link is external\)](#)

Phone: 562-444-5656

[Jain Foundation\(link is external\)](#)

Phone: 425-882-1440

[Muscular Dystrophy Association\(link is external\)](#)

Phone: 800-572-1717

[Myotonic Dystrophy Foundation\(link is external\)](#)

Phone: 866-968-6642; 415-800-7777

[National Institute of Arthritis and Musculoskeletal and Skin Diseases \(NIAMS\)](#)

Phone: 301-496-8190 or 877-226-4267

[National Institute of Child Health and Human Development \(NICHD\)](#)

Phone: 301-496-5133

[Parent Project Muscular Dystrophy \(PPMD\)\(link is external\)](#)

Phone: 800-714-5437

Order publications from the NINDS Catalog

The NINDS Publication Catalog offers printed materials on neurological disorders for patients, health professionals, and the general public. All materials are free of charge, and a downloadable PDF version is also available for most publications.