

What are Duchenne and Becker Muscular Dystrophies?

Muscular dystrophies are genetic disorders characterised by progressive muscle wasting and weakness that begin with microscopic changes in the muscle. As muscles degenerate over time, the person's muscle strength declines.

Duchenne muscular dystrophy (DMD) was first described by the French neurologist Guillaume Benjamin Amand Duchenne in the 1860s. Becker muscular dystrophy (BMD) is named after the German doctor Peter Emil Becker, who first described this variant of DMD in the 1950s.

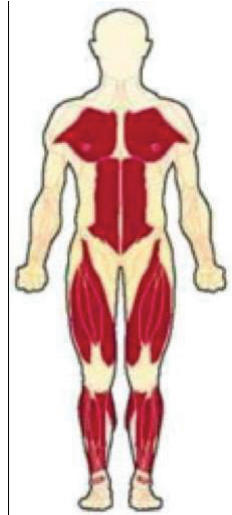
In DMD, boys begin to show signs of muscle weakness as early as age 3. The disease gradually weakens the skeletal or voluntary muscles, those in the arms, legs and trunk. By the early teens or even earlier, the boy's heart and respiratory muscles may also be affected.

BMD is a much milder version of DMD. Its onset is usually in the teens or early adulthood, and the course is slower and far less predictable than that of DMD. (Though DMD and BMD affect boys almost exclusively, in rare cases they can affect girls. See "Does It Run in the Family?")

What causes Duchenne and Becker Muscular Dystrophies?

Until the 1980s, little was known about the cause of any kind of muscular dystrophy. In 1986, researchers identified the gene that, when flawed - a problem known as a mutation - causes DMD. In 1987, the protein associated with this gene was identified and named dystrophin.

Genes contain codes, or recipes, for proteins, which are very important biological components in all forms of life. DMD occurs when a particular gene on the X chromosome fails to make the protein dystrophin. BMD results from different mutations in the same gene. People with BMD have some dystrophin, but it's not enough or it's poor in quality. Having some dystrophin protects the muscles of those with Becker from degenerating as badly or as quickly as those of people with Duchenne.



In the early stages, Duchenne and Becker MD affect the upper and lower legs, the trunk and the pectoral muscles (which draw back the shoulders).

These weaknesses lead to difficulty in rising, climbing stairs and maintaining balance.

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By the way, eating or not eating food with protein can't replace lost dystrophin. or more about the way gene mutations cause Duchenne and Becker dystrophies, see " Does It Run in the Family? "

What happens to the voluntary muscles of someone with DMD or BMD?

Duchenne

The course of DMD is fairly predictable. Children with the disorder are often late in learning to walk. In toddlers, parents may notice enlarged calf muscles, or pseudohypertrophy. A preschooler with DMD may seem clumsy and fall often. Soon, he has trouble climbing stairs, getting up from the floor or running.

By school age, the child may walk on his toes or the balls of his feet, with a slightly rolling gait. He has a waddling and unsteady gait and can easily fall over. To try to keep his balance, he sticks his belly out and puts his shoulders back. He also has difficulty raising his arms.

Nearly all children with DMD lose the ability to walk sometime between ages 7 and 12. In the teen years, activities involving the arms, legs or trunk require assistance or mechanical support.

Becker

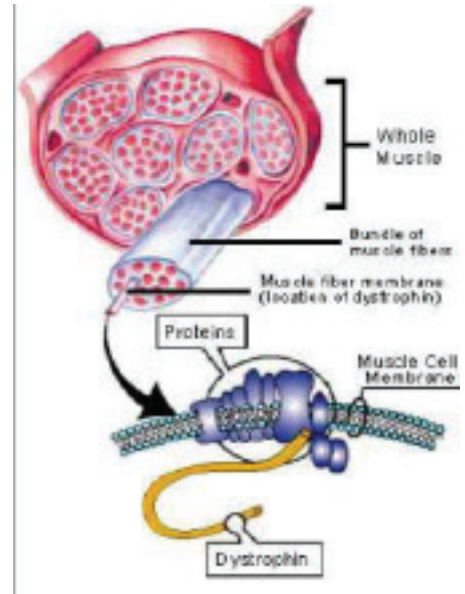
Often, the diagnosis of Becker muscular dystrophy isn't made until adolescence or even adulthood, possibly when a young man finds he can't keep up in physical education classes or military training. To compensate for his weakening muscles, the young man begins walking with a waddling gait, walking on his toes or sticking out his abdomen.

As with Duchenne, the pattern of muscle loss in BMD usually begins with the hips and pelvic area, the thighs and the shoulders. But in BMD, the rate of muscle degeneration varies a great deal from one person to another. Some men require wheelchairs by their 30s or later, while some manage for many years with minor aids, such as canes.

What tests are used to diagnose DMD and BMD?

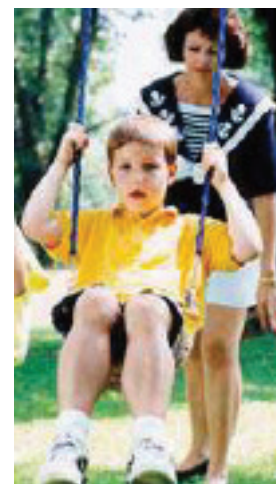
In diagnosing any form of muscular dystrophy, a doctor usually begins by taking a patient and family history and performing a physical examination. Much can be learned from these, including the pattern of weakness. The history and physical go a long way toward making the diagnosis, even before any complicated diagnostic tests are done.

It's important to get a formal diagnosis because other diseases have some of the same symptoms as DMD and BMD. Becker MD has often been overlooked or misdiagnosed as limb-girdle muscular dystrophy or spinal muscular atrophy. For this reason, it's important to have both genetic testing and a muscle biopsy before assuming that the problem is actually BMD.



Muscles are made up of bundles of fibres (cells). A group of independent proteins along the membrane surrounding each fibre helps to keep muscle cells working properly.

When one of these proteins, dystrophin, is absent, the result is Duchenne muscular dystrophy; poor or inadequate dystrophin results in Becker muscular dystrophy.



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The doctor also wants to determine whether the patient's weakness results from a problem in the muscles themselves or in the nerves that control them. Muscle-controlling nerves, or motor neurons, originating in the spinal cord and brain and reaching out to all the muscles, can cause weakness that looks like a muscle problem but really isn't.

Early in the diagnostic process doctors often order a special blood test called a CK level.

CK stands for creatine kinase, an enzyme that leaks out of damaged muscle. When elevated CK levels are found in a blood sample, it usually means muscle is being destroyed by some abnormal process, such as a muscular dystrophy or an inflammation. Therefore, a high CK level suggests that the muscles themselves are the likely cause of the weakness, but it doesn't tell exactly what the muscle disorder might be.

The availability of DNA diagnostic tests, using either blood cells or muscle cells to get precise genetic information, has expanded. You can ask your Neuromuscular clinic physician or genetic counselor what tests are available. Since many men with BMD (and some with DMD) become fathers, it's important to know for certain which inherited disease an individual has. Sisters of people with DMD or BMD can also be tested to find out whether they're carriers of the disease, meaning they could have children with the disorder.

To determine which disorder is causing a problem, a doctor may order a muscle biopsy, the surgical removal of a small sample of muscle from the patient. By examining this sample, doctors can tell a great deal about what's actually happening inside the muscles. Modern techniques can use the biopsy to distinguish muscular dystrophies from inflammatory and other disorders as well as between different forms of dystrophy.

Other tests on the biopsy sample can provide information about which muscle proteins are present in the muscle cells, and whether they're present in the normal amounts and in the right locations. This can determine whether the disease is DMD (with no dystrophin) or BMD (with some dystrophin).

An MR (magnetic resonance) scan may also be ordered. These painless scans allow doctors to visualise what's going on inside weakening muscles.





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Does it run in the family?

On being told their child has a genetic disorder such as DMD or BMD, bewildered parents often ask, "But it doesn't run in the family, so how could it be genetic?" DMD can run in a family, even if only one person in the biological family has it. This is because of the ways in which genetic diseases are inherited.

Both DMD and BMD are inherited in an X-linked pattern. That means the gene that sometimes contains a mutation causing these diseases is on the X chromosome. Every boy inherits an X chromosome from his mother and a Y chromosome from his father, which is what makes him male. Girls get two X chromosomes, one from each parent.

Each son born to a woman with a dystrophin mutation on one of her two X chromosomes has a 50 percent chance of inheriting the abnormal gene and having DMD or BMD. Each of her daughters has a 50 percent chance of inheriting the mutation and being a carrier. Carriers usually have no disease

symptoms but can have a child with the mutation or the disease. DMD and BMD carriers are at risk for cardiomyopathy (see "The Heart").

How can a family with no history of DMD or BMD suddenly produce a son with the disease?

There are two possible explanations:

The genetic mutation leading to DMD or BMD may have existed in the females of a family for some generations without anyone knowing it. Perhaps no male children were born with the disease, or, even if a boy in an earlier generation was affected, relatives may not have known what disease he had.

The second possibility is that the child with DMD or BMD has a new genetic mutation that arose in one of his mother's egg cells. (Since this mutation isn't in the mother's blood cells, it's impossible to detect by standard carrier testing.)

Once a mother gives birth to a child with DMD or BMD, there's always the possibility that more than one of her egg cells has a dystrophin gene mutation, putting her at higher than average risk for passing the mutation to another child.

Once the new mutation has been passed to a son or daughter, he or she can pass it to the next generation.

A man with DMD or BMD can't pass the abnormal gene to his sons because he gives a son a Y chromosome, not an X. But he'll certainly pass it to his daughters, because each daughter inherits her father's only X chromosome. They'll then be carriers, and each of their sons will have a 50 percent chance of developing the disease, and so on.

A good way to find out more about the inheritance pattern in your family is to talk to your doctor or a genetic counselor.



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Females and DMD

Why don't girls get DMD or BMD? When a girl inherits the DMD gene from her mother, she usually also gets a healthy dystrophin gene from her father, giving her enough of the protein to protect her from the disease. Males who inherit the mutation get the disease because they have no second dystrophin gene to make up for the faulty one.

However, although girls don't usually get the full effects of DMD or BMD, some females with the gene mutation are somewhat affected. A minority of females with the mutation are manifesting carriers, who have a mild form of the disorder.

For these women, the dystrophin deficiency may result in weaker muscles in the back, legs and arms that fatigue easily. Manifesting carriers may have heart problems, which can be manifested as shortness of breath or inability to do moderate exercise. The heart problems, if untreated, can be quite serious, even life-threatening.

It's wise for any potential female carrier of DMD or BMD to get a full range of diagnostic tests to find out her status. Then, if she is a carrier, regular strength evaluations and close cardiac monitoring can help her manage any symptoms that may arise.

What can be done to treat DMD or BMD?

- Contractures
- Spinal curvatures
- Medications
- Splints, Standing Frames and Wheelchairs

Thanks to advances in many areas of medicine, there are very good therapies available to assist with all the effects of Duchenne and Becker muscular dystrophies.

These interventions are being improved all the time. Your doctor can provide referrals to specialists and therapists for these forms of care. By using all available therapies, patients can prolong their comfort, function and life expectancy.

Contractures

The impact of DMD and BMD can be minimised significantly by keeping the body as flexible, upright and mobile as possible. There are several ways to do this.

As muscle deteriorates, a person with muscular dystrophy often develops fixations of the joints, known as contractures. If not treated, these will become severe, causing discomfort and restricting mobility and flexibility. Contractures can affect the knees, hips, feet, elbows, wrists and fingers.

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However, there are many ways to minimise and postpone contractures. Range of motion exercises, performed on a regular schedule, help delay contractures by keeping tendons from shortening prematurely. It's important that a physical therapist show you how to do range-of-motion exercises correctly.

Splints on the hands and lower legs can also help keep the limbs stretched and flexible, delaying the onset of contractures. When contractures have advanced, surgery may be performed to relieve them.

Spinal Curvatures

In young men with DMD, the spine can be gradually pulled into a curved shape. The spine may curve from side to side (scoliosis) or forward in a "hunchback"; shape (kyphosis). The "swayback" curvature sometimes seen in those who are still walking is called lordosis.

Severe scoliosis can interfere with sitting, sleeping and even breathing, so it should be prevented. Exercises to keep the back as straight as possible and advice about sitting and sleeping positions can be obtained from a physical therapist.

Spine-straightening surgery involves inserting metal rods with hooks into the spine. Surgery for youngsters with DMD is usually performed in adolescence.

Medications

Medications belonging to a group known as corticosteroids have been found effective in slowing the course of DMD. (Data for or against corticosteroids in BMD are lacking.)

In 2005 the American Academy of Neurology released recommendations about the use of these drugs in DMD. It concluded that:

- Prednisone (available in Australia) and deflazacort (not usually available in Australia) are beneficial in the treatment of DMD. Seven high-quality studies showed a significant increase, with these medications, in strength, timed muscle function (such as time it took a boy to climb stairs) and pulmonary function.
- The dose should be reduced if excessive side effects, such as significant weight gain, cataracts, thinning of the bones (osteoporosis) or behavioural problems, occur. The most frequent side effects are weight gain and the development of a rounded, puffy face.
- Researchers don't yet know whether deflazacort has fewer side effects than prednisone.

The optimal age to begin treatment with corticosteroids has not been determined.

Some physicians believe corticosteroids should be started as soon as the diagnosis is made, while others prefer to wait until a boy is little older. Before starting treatment with corticosteroids, the physician and the family should have a balanced discussion about anticipated benefits and potential side effects.

Calcium supplements and vitamin D are often prescribed with prednisone to counteract the effects on the bones.





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A low-calorie diet may be recommended to help offset the weight gain seen with corticosteroids.

Medications that lessen the workload on the heart are sometimes prescribed for DMD or BMD. See “The Heart”

Splints, Standing Frames and Wheelchairs

Splints, also called orthoses, support the ankle and foot. Ankle-foot orthoses are sometimes prescribed for night wear to keep the foot from pointing downward while the child is sleeping.

Standing for a few hours each day, even with minimal weight bearing, promotes better circulation, healthier bones and a straight spine. A standing walker or standing frame can assist people with DMD and BMD to stand. Some wheelchairs will tilt into a standing position.

Sooner or later, all boys with DMD need wheelchairs. Many at first use wheelchairs at school or the mall, continuing to walk some at home. In Duchenne, it's typical for a child to be using a wheelchair full-time by about age 12. Although the child and parents may dread the wheelchair as a symbol of disability, most users find they are actually more mobile, energetic and independent than when trying to walk on very weak legs.

Other mobility and positioning aids can help those who care for people with DMD or BMD. Among the simplest is a transfer board for helping the person move in and out of the wheelchair. Mechanical (usually hydraulic) lifts, shower chairs and electronic beds may also be used.

In what other ways do DMD and BMD affect the body?

- Pain and Sensation
- The Heart
- Respiratory Function
- Intellectual Effects
- Diet
- Exercise
- Physical and Occupational Therapy
- How do Families Adjust to DMD or BMD?

Pain and Sensation

You may be relieved to know that the muscle deterioration in Duchenne and Becker isn't usually painful in itself. Some people report muscle cramps at times; these can usually be treated with over-the-counter pain relievers.

Also, since muscular dystrophy doesn't affect nerves directly, those who have the disorders retain normal sensations of touch and other senses. They also usually have control over the smooth, or involuntary, muscles of the bladder and bowel, and have normal sexual functions.

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The Heart

Like muscles in the limbs, heart muscle also can be weakened by lack of dystrophin. By the teen years, the damage done by DMD to the heart can become life-threatening. This system should be monitored closely, usually by a pediatric cardiologist.

People with DMD and BMD often develop cardiomyopathy — heart muscle weakness — because of a deficiency of dystrophin. The muscle layer (myocardium) of the heart deteriorates, just as the skeletal muscles do, putting the person at risk of fatal heart failure.

Some people with BMD have mild skeletal muscle involvement but severe cardiac problems.

It is usually recommended that boys with DMD have a complete cardiac evaluation by a specialist beginning in early childhood and regularly until age 10. After that, the evaluations should be done every year or at the onset of symptoms of heart weakness, such as fluid retention or shortness of breath.

Similar evaluations are recommended for those with BMD.

Carriers of DMD and BMD are at higher than average risk of developing cardiomyopathy. The academy suggests that carriers should undergo a complete cardiac evaluation in late adolescence or early adulthood, or sooner if symptoms occur, and that they should be evaluated every five years starting at age 25 to 30.

There's some evidence that treatment with angiotensin converting enzyme (ACE) inhibitors and beta blockers can slow the course of cardiac muscle deterioration in DMD and BMD. This is effective if the medications are started as soon as abnormalities on an echocardiogram (ultrasound imaging of the heart) appear but before symptoms occur.

Some people with BMD who have severe heart problems but generally good health have been successfully treated with heart transplants.

Respiratory Function

After a boy with DMD is about 10 years old, the diaphragm and other muscles that operate the lungs may weaken, making them less effective in moving air in and out.

Problems that may indicate poor respiratory function include headaches, mental dullness, difficulty concentrating or staying awake, and nightmares. Anyone with a weakened respiratory system is also subject to more infections and difficulty in coughing. A simple cold can quickly progress to pneumonia in this person.

During infections, it's important to get prompt treatment before a respiratory emergency occurs.

At some point, assisted ventilation may be needed to help provide sufficient air flow into and out of the lungs. Boys will then be offered the option of assisted ventilation using a non-invasive device, earning one that doesn't require any surgical procedures. The person receives air under pressure through a mask, nosepiece or mouthpiece. Non-invasive ventilation may be helpful in improving the quality of life of young men with DMD, in terms of their levels of alertness and energy, and helping them to cope with infections.



Boys with DMD should have an electrocardiogram, to check for heart damage, every year beginning about age 10.



Noninvasive ventilation can improve sleep quality

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Intellectual Effects

About a third of boys with DMD have some degree of learning disability, although few are severely intellectually impaired. Doctors believe that dystrophin abnormalities in the brain may cause subtle cognitive and behavioral deficits. The learning problems seen in some people with DMD and BMD occur in three general areas: attention focusing, verbal learning and memory, and emotional interaction.

Children suspected of having a learning disability can be evaluated by a developmental or pediatric neuropsychologist through the school system's special education department or with a referral from your doctor. If a learning disability is diagnosed, educational and psychological interventions can begin right away. The specialist may prescribe exercises and ways to interact with your child that can help improve these deficits, and the school can also provide special help with learning.

Can special diets or exercises help In DMD and BMD?

Diet

Many people, when they hear the words "lack of a protein," logically ask, "Should I eat more protein?" Unfortunately, eating more protein has no effect on any of the proteins missing in muscular dystrophy.

No special dietary restrictions or additions are known to help in DMD or BMD. Most doctors recommend a diet similar to that for any growing boy, but with a few modifications.

A combination of immobility and weak abdominal muscles can lead to severe constipation, so the diet should be high in fluid and fiber, with fresh fruits and vegetables dominant.

For boys who use power wheelchairs, take prednisone or who aren't very active, caloric intake should probably be somewhat restricted to keep weight down. Obesity puts greater stress on already weakened skeletal muscles and the heart. Doctors have found that a low-calorie diet doesn't have any harmful effect on the muscles.

Exercise

Exercise can help build skeletal muscle, keep the cardiovascular system healthy, and contribute to feeling better. But in muscular dystrophy, too much exercise could damage muscle. Consult with your doctor about how much exercise is best. A person with DMD or BMD can exercise moderately but shouldn't go to the point of exhaustion.

Some experts recommend swimming and water exercises as a good way to keep muscles as toned as possible without causing undue stress on them. The buoyancy of the water helps protect against certain kinds of muscle strain and injury. Before undertaking any exercise program, make sure you've had a cardiac evaluation.

Physiotherapy and Occupational Therapy

A physiotherapy program is usually part of the treatment for DMD and BMD. Your doctor will refer you to a physiotherapist for an evaluation and a personal program.



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The primary goals of physiotherapy are to allow greater motion in the joints and to prevent contractures and scoliosis.

Occupational therapy focuses more on specific activities and functions, while physiotherapy emphasises mobility and, where possible, strengthening of large muscle groups. OT can help with tasks related to work, recreation or daily living, such as driving, dressing or using a computer.

How do families and children adjust to DMD or BMD?

When a family member has DMD or BMD, all members of the family are affected by caregiving demands and emotional reactions. Many people find help and support from religious sources, families with similar experiences, self-help books or professional counseling. These experts usually suggest the following:

For the Child

- Answer children's questions about the disease when they arise, with honesty and in language they understand.
- Always view the child as an individual, with the disease only one aspect of his life.
- Emphasise what the child can do and let him find ways to do things he wants. Children often find creative ways to participate in sports and other hobbies.
- Treat him as you would any other child, providing discipline, responsibility, hope and love. Don't overprotect him, and do help him become independent.
- Undertake normal family activities, including vacations and recreation. With imagination and patience, you can find ways to do almost anything.

For the Family

- Respect each other's emotions and stress levels; be kind and patient
- Schedule regular breaks from caregiving responsibilities.
- Deal with the disease one day at a time, one crisis at a time, one year at a time. Don't focus on future complications.
- Give yourself credit for the effort you expend and the difficulty of your task.
- Build a support team, and ask for help when you need it.
- Get information from every available source, your doctor and your local MDA



What are Duchenne and Becker Muscular Dystrophies?

Search for treatments and cures

Since 1986, when researchers identified the gene that, when altered, leads to DMD and BMD, scientists have built on that foundation to better understand the diseases. Researchers are pursuing several directions in search of a way to halt or reverse the muscle destruction of these disorders.

A working dystrophin gene without the DMD mutation has been created, and its safety is now being tested in a small clinical trial in boys with the disease.

In another approach, researchers at a biotechnology company are testing PTC124, a drug that changes the way muscle cells “read” genetic instructions, in boys with DMD.

In some 15 percent of boys with the disease, a molecular stop signal occurs too early in the DNA instructions for a complete dystrophin protein to be made. It’s this signal that PTC124 coaxes cells to ignore.

Other scientists are experimenting with antisense oligonucleotides (exon skipping), compounds designed to encourage cells to skip over any type of genetic error, not just a stop signal. These compounds are undergoing laboratory testing, and a pilot clinical trial began in Europe in 2006.

Still other teams of scientists are using stem cells generated from muscle and bone marrow to regenerate muscles in laboratory models of DMD.

In addition, some groups are testing strategies to increase production of the protein utrophin, which closely resembles dystrophin but is produced normally in people with DMD or BMD. Laboratory evidence shows that increasing utrophin levels can to some extent compensate for a dystrophin deficiency.

