

## **DUCHENNE MUSCULAR DYSTROPHY**

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### **What is Duchenne Muscular Dystrophy?**

Duchenne muscular dystrophy (DMD) is the most common of nine muscular dystrophy disorders, and is characterized by progressive difficulty in walking and performing everyday activities. This lack of mobility is due to an absence of the protein dystrophin, causing muscles to deteriorate and break down.

First described in the late 19<sup>th</sup> Century by French neurologist Guillaume Duchenne, there have been ongoing advancements in understanding the aetiology and prognosis of DMD, and significant research is being undertaken to discover a cure, or at least an intervention to mitigate the rapid progression of DMD. Although there is no effective cure as yet, there are ways to help DMD patients enjoy the quality of life that others may take for granted.

### **What are the features of Duchenne Muscular Dystrophy?**

The following characteristics of DMD are frequently but not always displayed:

- Muscle weakness
- Fatigue
- Mild mental retardation
- Delayed walking age
- Frequent falls
- Difficulty in running and climbing stairs
- 'Waddling' gait
- Toe-walking
- Muscle deformities – pseudohypertrophy of calf
- Skeletal deformities
- Gower's manoeuvre
- Ability to walk lost between ages 8-12

Symptoms will generally be noticed by school age, but may appear as early as infancy. Some children with DMD will experience further complications:

- Although the majority (about 65%) of DMD people have normal intellectual capabilities and show average or above average intelligence, a minority will display intellectual problems or learning difficulties. Unlike the muscle weakness, however, it is not progressive. Whatever intelligence an affected boy has at birth, he retains unless it is affected by something else.
- There is the possibility behavioural difficulties may arise, affecting the DMD boy's social interactions at home, at school and in other

areas of his life, and for which he and his family will require support and assistance.

- In many cases of muscular dystrophy the heart tissue is also mildly affected, causing cardiomyopathy. Cardiomyopathy will not usually cause any trouble, but needs to be monitored through electrocardiogram (ECG) tests and medical assessments.
- Joints tend to become limited in their range of movement (contracture). The ankles are usually affected first, followed by the knees, hips, and joints of the upper body.
- Curvature of the spine is a serious problem in DMD, and is called scoliosis. Scoliosis is a curvature to the side, accompanied by rotation of the spine. Scoliosis worsens most rapidly in the latter stages of puberty, during the growth spurt. If severe, scoliosis can be extremely uncomfortable, and limits the function of the lungs and the upper limbs. It is also disfiguring, causing the chest wall to become more prominent on one side.
- As the muscles involved in breathing become very weak, lung function becomes inadequate, causing a reduction of oxygen and an increase of carbon dioxide in the blood. This results in headaches, drowsiness and feelings of poor health.

### **What causes Duchenne Muscular Dystrophy?**

DMD is caused by a defect in the gene located on the X chromosome, passed on from a carrier female at conception. The faulty gene results in a deficiency of the protein dystrophin, causing muscles to deteriorate and break down.

Since women have two X chromosomes, if one X chromosome has the defective gene, the second X chromosome will usually predominate and function to produce enough dystrophin for normal muscle function. Males on the other hand have one X chromosome, and one Y chromosome. Because they don't have another X chromosome to compensate for the defective gene, they will develop symptoms if they inherit the defective gene. Two-thirds of DMD cases are inherited this way.

Spontaneous mutations are responsible for the other one-third of DMD cases, with the genetic fault arising in the affected boy himself. This happens when the mutation in the dystrophin gene happens by chance in the formation of the egg or sperm. With a spontaneous mutation, the affected boy will be the first in his family to have DMD.

For further information on genetics and how disorders are inherited, please refer to the *Muscular Dystrophy Association Genetics Fact sheet*.

## **Diagnosis of Duchenne Muscular Dystrophy**

There are often difficulties in diagnosing DMD, as signs and symptoms of the disease vary. Where there is no family history, DMD may not even be suspected straight away. Once DMD is suspected, diagnostic tests will be offered to establish a definite diagnosis. These may include:

- **CK Testing**

Due to the lack of dystrophin in the muscle fibers, DMD patients have high levels of a muscle enzyme called creatine phosphokinase (CPK, or CK). A blood test will show elevated levels of CK in the blood serum of a boy with DMD, often 50-100 times greater than normal.

- **DNA Studies**

In some cases DNA studies are able to give definite information about the genetic abnormality responsible for the faulty DMD gene, whilst in others the abnormality will not be able to be exactly defined. Abnormalities may be of three types: deletions (missing parts), duplications (additional parts) or point mutations (changed parts).

- **Muscle Biopsy**

When DNA studies do not present a clear diagnosis, the child with suspected DMD may require a muscle biopsy. While under local anesthetic, a small piece of muscle is taken with a needle, usually from the thigh. Using special staining techniques in the laboratory, the muscle tissue is examined microscopically for dystrophin. The test is positive for DMD if dystrophin is shown to be absent.

Each son of a carrier female has a 1 in 2 (50%) chance of inheriting DMD through his mother's faulty X chromosome, and similarly, each daughter has a 1 in 2 (50%) chance of being a carrier of DMD in the same way.

Soon after the diagnosis of a DMD boy, it is essential that genetic counselling is arranged, for one or both of two issues. The first is the probability that the mother is a carrier of the mutation, and the second is whether testing for the condition in pregnancy can be offered and with what degree of reliability.

The probability of being a DMD carrier is first assessed by examining the family tree. If a woman has an affected son and an affected brother, uncle or cousin, it is certain that the faulty gene has passed through her to her son and she is called an obligate genetic carrier. If she has an affected son and no other affected relatives she is a possible genetic carrier, because the mutation may have occurred for the first time in a single egg from her. A woman who has passed a mutation to two offspring, and who has no other relevant family history, is a probable genetic carrier.

Sometimes a woman or man has mutations in the DMD gene of his or her sperm or eggs, but not in the other cells of his or her body. The mutation may even be in some sperm and/or eggs but not in others. This situation is called *germline mosaicism*. Germline cells are the egg and sperm cells. A woman or man with germline mosaicism may have more than one affected son even though genetic studies of his or her blood show that he or she is not a carrier. Genetic tests can estimate the risk that a person has germline mosaicism, and provide information regarding the risk for a person with germline mosaicism to have a child with Duchenne muscular dystrophy.

Genetic counselling can provide diagnostic information without invasive muscle-biopsies. These may include DNA analysis and Linkage Testing. If a woman knows she is a carrier, prenatal and pre-implantation diagnoses are possible.

Clinical genetic services are available in NZ and a referral can be made by your GP or the Muscular Dystrophy Association.

### **Management of Duchenne Muscular Dystrophy**

As yet, there is no treatment that can overcome the progressive muscle weakness of DMD. It is possible, however, to minimize complications by adhering to a management programme specially designed by a team of medical professionals. This team is headed by a paediatric specialist, and includes a physiotherapist, occupational therapist, together with specialists in other areas as required.

- **Exercise**

Both passive and active exercises play an important role in DMD management. The small boy, up to the age of around eight years, will participate in normal playground activities as far as he is able, but must be careful to avoid fatigue. From approximately six to eight years of age, he will require a manual wheelchair, followed by a power wheelchair to move longer distances and for speed. There is a range of organized wheelchair sports which some DMD boys choose to participate in. Swimming (in a heated pool) is an ideal activity that some DMD boys enjoy well into their twenties.

Passive exercise, or assisted stretching, should be established as early as possible. Physiotherapists will be able to assist in the development of an exercise programme to delay the shortening of muscles, known as contracture, which causes limitations in the range of motion of joints. These exercises should be undertaken on a daily basis and require assistance from parents and/ or caregivers.

- **Supportive Equipment**

When restriction of movement develops in the ankle joints (contractures), a type of orthosis may be offered to the DMD boy to be worn at night. These ankle splints will help to maintain the joint in a normal position, thereby assisting in the prevention of contractures.

The use of standing frames during parts of the school day can be beneficial for a DMD child once he is wheelchair bound.

Seating systems can offer individualized support to maintain an upright position in the wheelchair, and to ensure maximum comfort.

Other types of supportive equipment will be available as the need arises, and usually caters to individual need. Advice concerning these will be offered by the physiotherapist, the occupational therapist, or by the MDA.

It is wise to consider suitability of the home environment at an early stage, so that future adjustments can be made over time. For example, multi-storied housing can compromise accessibility, and the installation of a lift may bring further problems. When a powered wheelchair becomes necessary, a suitable vehicle for transportation, as well as access and adjacent parking space will be required. Space for a ramp will be necessary up steps, as well as doorways wide enough to allow a wheelchair through.

- **Medical Treatment**

Many medicines and dietary supplements have been tried over the years to treat the symptoms of DMD. Some have shown promise, and are still being investigated. But so far there is only one group of drugs – the catabolic steroids – that have shown any significant benefit. In many clinical trials, Prednisone and deflazacort have been shown to slow the loss of muscle function, or even to increase strength, possibly allowing the DMD boy to delay full wheelchair reliance. If the child's paediatrician, after discussion with the child and his parents and/ or caregivers, considers this form of treatment to be suitable, he or she will decide what the appropriate treatment programme should be, and at what age it should commence. Possible side effects will be made clear. The most common side effects of Prednisone are weight gain, raised blood pressure and sugars, and also psychological distress.

- **Nutrition**

Excessive weight gain leading to obesity can occur not only as a side effect of steroid treatment, but also from reduced physical activity produced by the muscle weakness. Obesity can further complicate the difficulties a DMD boy will experience with his heart and bowel function, and also with breathing. It is therefore imperative that weight is monitored and that a well-balanced diet is followed. Family and friends can assist the DMD boy adhere to his diet by offering him healthy foods

such as fruit and vegetables, and restricting foods containing high levels of sugar and fat.

- **Surgery**

If contractures develop at the ankle joints, these can be surgically treated by release of the Achilles tendon. This procedure is usually done once the child is wheelchair dependent, and helps improve their foot position. Having a comfortable foot position may help prolong mobility for some DMD boys.

Spinal fusion surgery is performed to correct scoliosis. The medical team, including an Orthopaedic Surgeon and headed by the paediatrician, will discuss this option with the DMD boy and his family well before the surgery becomes necessary. It is advisable that scoliosis is surgically corrected at the ideal time during a 'window of opportunity' which takes into account the boy's stage of adolescent growth. Duchenne boys who undergo this 'spinal fusion' are usually very pleased with the outcome.

- **Respiration**

Respiratory function usually remains adequate until the boy with DMD is about 10 years old. Between the ages of 10 and 14 years, respiratory muscle function starts to decline enough to produce changes in the way the lungs pull air in and push it out. The early treatment of sniffles and sore throats, and the prevention of chest infections is important. The normal defenses people use to rid themselves of excessive secretions do not function effectively in DMD boys, and a common cold can quickly turn into a life-threatening pneumonia. People with DMD should try to preserve their lung function by avoiding second hand smoking, and in no circumstance should he be an active smoker.

Family and caregivers must watch carefully for signs of disrupted sleep due to respiratory problems. Signs include morning drowsiness, lack of concentration, headaches, confusion, sleepiness during the day and wakefulness at night with an increased need to be turned. When respiratory problems become apparent, ventilation machines are available to assist with ventilation during the night.

- **Palliative Care**

The difficulty in facing the inevitability of death from DMD can sometimes prevent acceptance of this final outcome. It is unlikely that an affected male will live past his early 30s, and the average life expectancy is 18 years. Open communication between medical professionals, and also within the family, is vital when discussing these issues. Each member of the family is likely to deal with the impending death in an individual way, and on his own timetable. Some young men in the later stages of DMD welcome the end of their struggle, while others may insist on every last medical intervention, of which may give them an extra day or two of life. In some families, it may be the weary parents that are psychologically

ready for the end long before their sons are, and this should be no cause for guilt as long as it doesn't disrupt the family functionality. It is normal for attitudes to change from day to day, and waves of denial to filter through. The MDA can help guide and support families to cope with these feelings of grief and loss.

### **Research into Duchenne Muscular Dystrophy**

There are many promising results from ongoing research each year, but it is difficult to say whether that will translate into something we will see in the clinic in five years, 10 years, etc. Research has moved from trying to transfer sufficient amounts of dystrophin into the nuclei of dystrophic cells, to actually changing the faulty genetic information.

The USA, Canada, Belgium, Argentina, Australia and India are performing clinical studies on young men with substances that showed positive results in a screening program on dystrophic mice. Studies with creatine, glutamine, coQ10 and oxandralone are complete. Studies with Pentoxifylline are in progress.

### **Support for people with Duchenne Muscular Dystrophy**

Support is available from the MDA who can offer specialist assessment, information, support, advocacy and referrals to other providers. There is also a nationwide Support Network for those interested in meeting with others.

- **Education**

In New Zealand, every child has the right of equal access to all aspects of education. This means that all children with a neuromuscular condition have the right to attend a mainstream school. Many schools have special units attached which can provide any extra help needed, including an individualized education plan for appropriate assistance with physical and mental needs.

It is important that DMD children are not overprotected or patronized – they should be mentally stimulated and creative skills encouraged.

- **Employment**

There is no reason why a person with DMD should not expect to have the same employment opportunities as anybody else; however it is probably prudent to plan a career which will remain suitable even if physical ability declines.

Workbridge provides a professional employment service for all people with all types of disabilities and injuries, no matter what the disability or skill level. Workbridge also administers support funding on behalf of Work and

Income. Workbridge can be contacted on free phone: 0508 858 858 or through their website: [www.workbridge.co.nz](http://www.workbridge.co.nz)

More help on equal employment rights can be found on the Employment Relations website [www.ers.dol.govt.nz](http://www.ers.dol.govt.nz). Employment Relations also has an infoline: 0800 800 863.

The government promotes equal employment opportunities (EEO) in private sector employment through the EEO Trust. They can be contacted on (09) 523 3023, or by visiting their website [www.eeotrust.org.nz](http://www.eeotrust.org.nz)

Remember, it is illegal for employers to discriminate against people because of ethnicity, sexual orientation, gender, marital status, religious belief or disability. Equal rights are demanded by the Human Rights Act, 1993, and the Equal Pay Act, 1972.

### **More information**

Muscular Dystrophy Association can be contacted for further information, assistance, advice, support and referrals, on 0800 800 337 or by e-mail at [info@mda.org.nz](mailto:info@mda.org.nz).

The Muscular Dystrophy Association Website also contains information on services available within NZ, our quarterly magazine, contacts, membership details, news and links to other sites - [www.mda.org.nz](http://www.mda.org.nz)

### **Further resources**

[www.mdausa.org](http://www.mdausa.org) – the MDA USA website has an extensive site with plenty of further information on any muscular dystrophy conditions as well as research news.

[www.mda.org.au](http://www.mda.org.au) – the Australian MDA has an easy-to-read web site, with good information.

[www.muscular-dystrophy.org](http://www.muscular-dystrophy.org) – the UK muscular dystrophy site. It contains good general information on the condition.

NZ also has an excellent website dedicated to helping and informing those families with rare disorders – [www.nzord.org.nz](http://www.nzord.org.nz)

Parent Project Muscular Dystrophy <http://www.parentprojectmd.org>

#### *Information in this fact sheet was primarily sourced from:*

Parent Project Muscular Dystrophy <http://www.parentprojectmd.org>

MedlinePlus <http://www.nlm.nih.gov/medlineplus/ency/article/000705.htm>