

MANIFESTING CARRIERS OF DUCHENNE OR BECKER MUSCULAR DYSTROPHY

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What is a Manifesting Carrier?

A Manifesting Carrier is a female "carrier of Duchenne or Becker Muscular Dystrophy (DMD or BMD) genetic mutation and displays symptoms of that muscle disorder. The severity can vary from mild generalised weakness to an inability to walk, differing from individual to individual.

Only females can become Manifesting Carriers and onset of symptoms usually occurs between 16 to 48 years of age. It affects approximately 5-10% of all female carriers of DMD or BMD.

What are the Features of Manifesting Carriers of Duchenne or Becker Muscular Dystrophy?

Just as symptoms vary in DMD and BMD, there are a wide variety of presentations in Manifesting Carriers ranging from mild symptoms right through to a severe muscular dystrophy. There may be a slow progression of symptoms.

The first symptoms tend to be aching muscles (myalgia) or cramps and are later accompanied by muscle weakness, most commonly affecting the upper arms and upper legs. A clumsiness or lack of co-ordination may be apparent, particularly in playing sport at school. Muscle weakness is not always symmetrical, and this can result in an unusual pattern of walking and a tendency to trip and fall. Individuals may experience exhaustion and difficulty rising from sitting or climbing stairs. Enlarged calf muscles are also common, known as pseudohypertrophy. Despite their appearance, these muscles are also weak.

The heart muscle may also be affected, and this results in an abnormally fast heart rate (tachycardia). There may also be unexplained abdominal or chest pain.

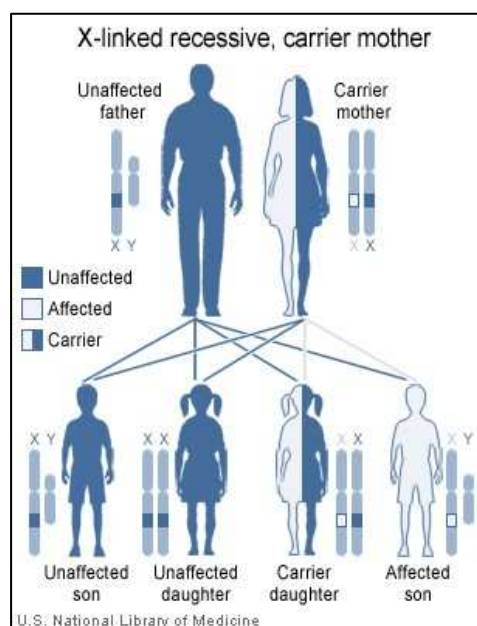
Intellectual ability may also be compromised to some degree.

What Causes a Manifesting Carrier?

DMD and BMD are both X-linked recessive disorders, and Manifesting Carriers arise in a few of the female carriers. One third of DMD and BMD cases are spontaneous, so it is possible to be a Manifesting Carrier without

a family history. For further information on genetics and how disorders are inherited, please refer to the *Genetics Factsheet*. Additionally, the *Muscular Dystrophy Association Becker Muscular Dystrophy* and *Duchenne Muscular Dystrophy Factsheets* give a more in depth look into these disorders.

It is commonly believed that carriers merely pass on the disorder and are unaffected, however this is not always the case. Women have two X chromosomes and are often unaffected in X-linked disorders due to the ability of one X chromosome to mask the defect in the other. On rare occasions, a female may lack a second X chromosome entirely, or it may have been damaged during development and therefore is unable to mask the effects of DMD or BMD. Alternatively, via a mechanism called "skewed X-inactivation", the body's cells rely on the X chromosome carrying the defect, so these females also develop the symptoms of DMD or BMD.



In DMD and BMD, there is a defect on the dystrophin gene that results in faulty production of the dystrophin protein. This protein ordinarily aids in the stabilization of the muscle cell membrane. Without dystrophin, the muscle cells are prone to damage and leads to increased cell death. Eventually, degeneration occurs faster than muscle cell regeneration, leading to decreased muscle size and strength.

Diagnosis of Manifesting Carriers of Duchenne or Becker Muscular Dystrophy

Diagnosis usually commences after the identification of key early symptoms of Manifesting Carriers of DMD or BMD.

- > Muscle Biopsy – looks at individuals muscle cells for characteristic patterns of dystrophin
- > Blood Testing – look for non-random X-inactivation patterns and elevated levels of creatine phosphokinase (CPK)
- > Electromyography (EMG) – observes the electrical activity of muscles and its consistency with activity typical of Manifesting Carriers.
- > Electrocardiogram (ECG) – can identify abnormal heart rhythms
- > DNA Testing – can identify the presence of the abnormal gene in the individual

Individuals are sometimes misdiagnosed due to the similarity of symptoms in Manifesting Carriers to Limb Girdle Muscular Dystrophy. It is important to differentiate between the two.

Soon after a diagnosis is made in the family, it is essential that genetic counselling is arranged. Genetic services in NZ are available and a referral can be made by the NMA.

Management of Manifesting Carriers of Duchenne or Becker Muscular Dystrophy

As there is currently no cure for DMD or BMD, treatment for Manifesting Carriers focuses on the prevention and management of symptoms.

From an early stage, it is important to undergo regular exercise and stretching programmes, with the help of a physiotherapist, to maintain muscle strength and flexibility. Swimming is an excellent option to exercise and mobilize all muscles and joints. Resistance training has also been shown to be beneficial in decreasing falls and increasing strength.

A good diet with plenty of fresh fruit and vegetables is very important in ensuring excessive weight does not impede mobility. Contact with a physician and/or a nutritionist is valuable for this.

It is also helpful to have baseline and periodic evaluations on heart function to monitor any problems.

Anaesthesia can be risky, and it is important that anaesthetists and surgeons are aware of the condition if surgery is necessary.

Research on Duchenne Muscular Dystrophy and Becker Muscular Dystrophy

Research is continuously being carried out and as more discoveries are made about the underlying causes of DMD and BMD, it will be possible to develop treatments aimed more directly at these causes, rather than simply towards the management of its symptoms.

Research is looking into transferring new dystrophin genes to muscle cells and how to do so without causing an immune reaction.

There are also studies looking at stem cells therapy, which replaces cells containing the defective gene with undifferentiated cells to regenerate muscle cells.

Alternatively, experiments are researching how to use oligoribonucleotides to change the faulty genetic information and repair the mutation.

Utrophin is a protein very similar to dystrophin, and individuals who maintain utrophin have less severe symptoms than those without it. It is thought that this protein, if upregulated, could replace the function of dystrophin.

Support for Manifesting Carriers of Duchenne or Becker Muscular Dystrophy

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

There is no reason why individuals with a diagnosis of Manifesting Carrier should be disadvantaged in terms of receiving full education. For more information, request the Education Pack available from the NMA.

Disability should not hinder employment possibilities. Any individual has the right to equal pay and equal rights for employment. For more information contact the Employment Relations infoline on 0800 800 863 or visit www.ers.dol.govt.nz.

The government promotes equal employment opportunities in private sector and can be contacted on (09) 525 3023 or visit www.eeotrust.org.nz

Workbridge provides a professional employment service for people with all types of disabilities and administers support funding on behalf of Work and Income. Contact on 0508 858 858 or visit www.workbridge.co.nz

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.

The Muscular Dystrophy Association Website also contains information on services available within NZ, contacts, membership details, news and links to other sites - www.mda.org.nz

Further Resources

www.nzord.org.nz – the New Zealand Organisation for Rare Disorders website provides information on a number of rare disorders, a directory of support groups, practical advice, health and disability resources, research information, news and issues.

www.mdausa.org – the Muscular Dystrophy Association USA website has an extensive site with plenty of further information on any muscular dystrophy conditions as well as research news.

www.dfsg.org.uk – Duchenne Family Support Group is a UK website with further information on Manifesting Carriers and management.

Information in this fact sheet was primarily sourced from:

Muscular Dystrophy Campaign (2004) Manifesting Carriers of Duchenne Muscular Dystrophy <www.muscular-dystrophy.org>

Wikipedia (2006) Duchenne Muscular Dystrophy <http://en.wikipedia.org/wiki/Duchenne_muscular_dystrophy>