Manifesting carriers of Duchenne and Becker muscular dystrophy

What causes Duchenne and Becker muscular dystrophy?

Duchenne and Becker muscular dystrophy are genetic, muscle-wasting conditions caused by the complete or partial lack of a protein called dystrophin. Dystrophin is an important component of the muscles and when it is missing or not fully functional, muscle fibres break down and are replaced by fibrous and or fatty tissue causing the muscles to weaken gradually.

Duchenne and Becker muscular dystrophy are genetic conditions. They are caused by a mistake or mutation in the genetic code (DNA). In these conditions, the mutation occurs in a gene which is located on the X-chromosome. This genetic fault causes a complete lack of dystrophin in Duchenne muscular dystrophy, or the absence of a fully-functional dystrophin in Becker muscular dystrophy.

Duchenne and Becker muscular dystrophy usually affect only boys. However some girls and women can also be affected as manifesting carriers.

What is a manifesting carrier of Duchenne or Becker muscular dystrophy?

Girls have two X-chromosomes and boys have only one. Therefore, if boys have a mutation in the dystrophin gene they will be affected by Duchenne or Becker muscular dystrophy. Most commonly, if a female carries the mutation in the dystrophin gene on one of the two X-chromosomes, the second X-chromosome usually 'protects' her from developing the symptoms of the condition because the second X-chromosome produces a normal dystrophin protein.

These girls are referred to as 'carriers'. However, some carriers do show symptoms of the condition, because the second X-chromosome does not produce the dystrophin protein as it should. These carriers are called 'manifesting carriers'.

Each son of a carrier mother has a 50:50 chance of being affected and each daughter has a 50:50 chance of being a carrier herself, although she might be an asymptomatic – rather than a manifesting – carrier.

It is important that carriers, and other family members at risk, receive genetic counselling and advice with regard to testing future pregnancies. Your clinician or GP can arrange this for you.

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Do all manifesting carriers come from families where people are known to have Duchenne or Becker muscular dystrophy?

No. It is very important to note that the diagnosis of 'manifesting carrier' may be made in someone who has absolutely no family history of Duchenne or Becker muscular dystrophy.

It is an important diagnosis to make in these cases because the risk of having a child who may be affected with Duchenne or Becker muscular dystrophy is relatively high.

All carriers of Duchenne or Becker muscular dystrophy – both asymptomatic and manifesting – have a one in two chance of having an affected son in any pregnancy. There is no clear evidence to suggest that being a manifesting carrier tends to run in families. So, if one carrier in any family has muscle problems, this does not seem to make it any more likely that other female members of the family will also manifest any symptoms relating to being a carrier.

How is the condition diagnosed?

If there is a family history of Duchenne or Becker muscular dystrophy, female members of the family might already know their carrier status. In these cases, the diagnosis of 'manifesting carrier' is based on a physical examination by an expert clinician to confirm the signs of muscle weakness. If the carrier status is not known but there is a family history of Duchenne or Becker muscular dystrophy, the diagnosis can easily be confirmed by genetic testing, usually on a blood sample.

The diagnosis might be more difficult in the absence of a family history of Duchenne or Becker muscular dystrophy. As carriers of Duchenne and Becker muscular dystrophy do not usually have any muscle problems, other diagnoses are often considered.
If a blood test is done, high levels of a protein called creatine kinase (CK) might be seen. CK is normally found in muscle, but when muscles are damaged, such as in Duchenne and Becker muscular dystrophy, it leaks into the bloodstream. The liver enzymes (aminotransferases, ALT and AST) are also often found to be high but this is a consequence of the muscle damage and not of a liver problem. However, normal CK levels do not completely exclude a diagnosis of 'manifesting carrier'.

A muscle biopsy is often required to reach the diagnosis in a person without a family history of the condition. The muscle biopsy can show an abnormal expression of the protein dystrophin and it is very useful in excluding other forms of muscular dystrophy.

However, the diagnosis of a carrier has to be confirmed by genetic testing, usually on a blood sample. Different types of genetic tests can provide specific and more detailed information about the DNA mutation. A genetic diagnosis is important as it alerts the carrier to initiate adequate management, to seek genetic advice and to identify other family members who could be at risk of carrying the mutation.

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What symptoms does a manifesting carrier have?

There is a wide variety of symptoms presented by manifesting carriers of Duchenne and Becker muscular dystrophy. The majority of the female carriers do not have any sign of the condition at all, while a small number of carriers may have a muscular dystrophy that is almost as severe as boys with Duchenne muscular dystrophy. Between these two extremes, there is a variety of signs and symptoms.

Most manifesting carriers experience mild problems with muscle weakness late in adult life. Some get aches and pains in their muscles as their first complaint, and may notice enlargement of their calves and other muscles. Symptoms usually start in the legs but in time may also involve the shoulders and the arms. Muscle weakness may get worse over time, however the progression is usually slow.

Please note: it is important to be aware that some manifesting carriers of Duchenne and Becker muscular dystrophy may have problems with their heart (cardiomyopathy), which are independent of their muscle symptoms.

Heart problems in carriers of Duchenne and Becker muscular dystrophy often do not cause any symptoms, but they can often be treated, so it is important for carriers to be followed up by a specialist for monitoring over time.

The muscles of facial expression, speech and swallowing, and the involuntary muscles (for example those of the bowel and bladder), are not affected.

Some carriers of Duchenne or Becker muscular dystrophy can show learning and/or behavioural difficulties. As learning difficulties are not progressive, it is important they are identified and addressed promptly (e.g. at school), to offer the child the support she will need to reach her full potential to develop her skills. Family support is essential, and specialists may need to be consulted to address specific issues of learning and behaviour.

Is there a treatment or cure?

There is currently no cure available for manifesting carriers of Duchenne and Becker muscular dystrophy.

As symptoms, age of onset and severity can be significantly different from one person to another, the management of symptoms and recommended interventions strictly depend on how much the carriers are affected. Children with clear symptoms of muscle weakness will require close follow-up at a specialist clinic and a multi-disciplinary approach, with the input of specialists, including physiotherapists and occupational therapists.

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Women who experience muscle symptoms that affect their daily lives may also benefit from a multi-disciplinary approach in a specialist clinic, with input from a physiotherapist and family care advisor. However, adults with relatively minor problems may not need regular follow-up, providing their family doctor is aware of their problems and can refer them to the appropriate clinic should their symptoms become more severe.

For all carriers, it is important to keep as fit and active as possible. Regular daily exercise is better than occasional sudden bouts of exertion. Swimming is particularly recommended, as it provides gentle exercise to all body muscles without over-exertion.

Carriers of Duchenne and Becker muscular dystrophy should have a heart check, including an echocardiogram, at the time of diagnosis and possibly every three to five years thereafter. Early treatment of heart problems (with drugs called ACE inhibitors and/or beta-blockers) can be protective for the heart muscle.

If you wish to learn more about the latest research from our team, contact the research department at: 020 7803 4813 or research@musculardystrophyuk.org

We're here for you at the point of diagnosis and at every stage thereafter, and can:

- Give you accurate and up-to-date information about your or your child's muscle-wasting condition, and let you know of progress in research
- Give you tips and advice about day-to-day life, written by people who know exactly what it's like to live with a muscle-wasting condition
- Put you in touch with other families living with the same muscle-wasting condition, who can tell you about their experiences
- Tell you about – and help you get – the services, equipment and support you're entitled to.

If you would like your GP or other health professional to have more information about manifesting carriers of Duchenne and Becker muscular dystrophy, we have some relevant materials. We've developed an online training module for GPs, as well as one for physiotherapists working with adults with muscle-wasting conditions. Contact our helpline or email us to find out more.

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Here for you

The friendly staff in the care and support team at the Muscular Dystrophy UK's London office are available on **0800 652 6352** or **info@musculardystrophyuk**.org from 8.30am to 6pm Monday to Friday to offer free information and emotional support.

If they can't help you, they are more than happy to signpost you to specialist services close to you, or to other people who can help.

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