Saint Mary's Hospital
Manchester Centre for Genomic Medicine

Information for Patients

Duchenne Muscular Dystrophy (DMD)
Genetic Aspects

This leaflet is designed to give further information about the genetic aspects of Duchenne muscular dystrophy (DMD) and how it can be inherited.

What causes DMD?

DMD is a genetic condition caused by a change or mistake in the dystrophin gene which promotes muscle health. This mistake means that the gene no longer works properly. Genes are inherited from parents to children through chromosomes. Most genes come in pairs but the dystrophin gene is on the X chromosome and males only have one X chromosome in each of the cells in their body. As a result, they have only one copy of the dystrophin gene. Therefore if they have a change or mistake in this gene, they do not have another working copy and so will develop the muscle weakness associated with DMD.

Inheritance

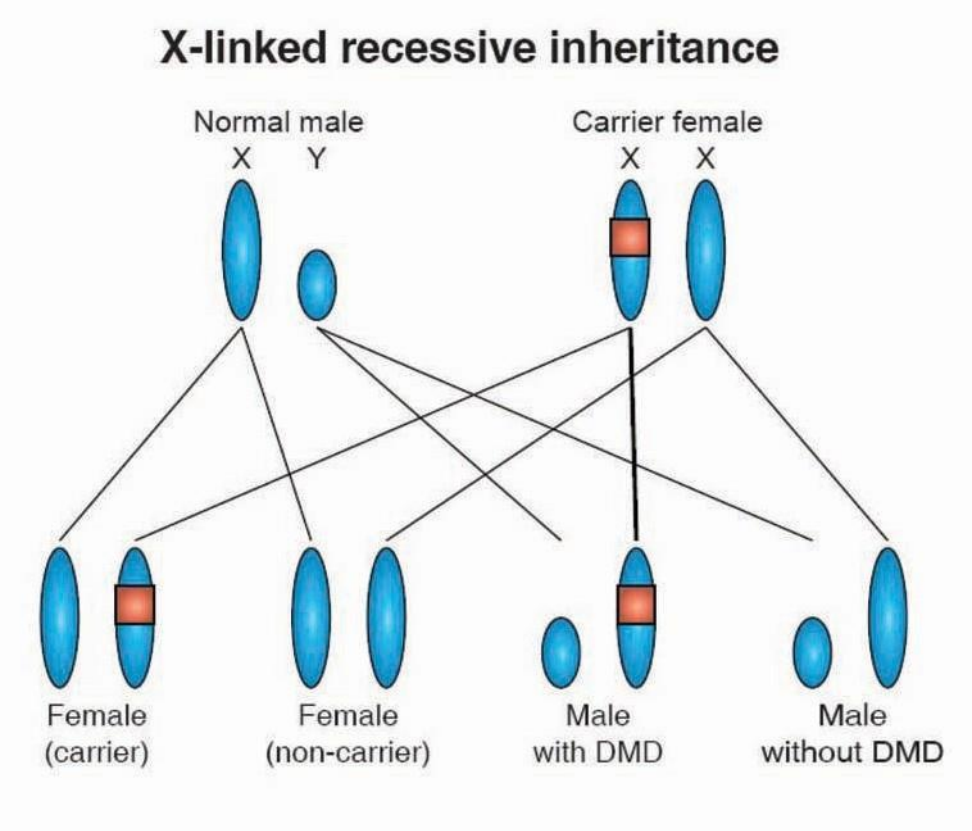
In around two thirds of cases, the DMD gene change has been inherited from the mother. A woman who has the gene change is known as a carrier of DMD. She is not likely to show symptoms because she has a working copy of the dystrophin gene on her other X chromosome. If a female carrier has a boy, there is a 50% (1 in 2) chance the boy will be affected by DMD. If a female carrier has a girl, there is a 50% (1 in 2) chance the girl will inherit the altered gene. If this happens, she will be a carrier, like her mother.

In around one third of boys with DMD, the genetic change started for the first time in the boy, occurring around the time of conception, or very early in development of the embryo. In these cases, no one else in the family will carry the DMD gene change, and therefore there is no increased chance of them having a child with DMD.

In some cases, women who have not been identified as carriers have a small number of cells in their ovaries that carry the DMD gene change. This is known as mosaicism. Blood tests are not able to detect this. Therefore, mothers of boys with DMD who are not found

to be carriers still have a chance of passing the DMD gene change to other children even if their own blood test is clear. This chance is lower, at around 10%.

The inheritance pattern of DMD is known as X-linked recessive. There are four possible outcomes in each pregnancy for a female carrier, which are outlined in the diagram below:



Carrier tests

In most boys with DMD, genetic tests can now identify the precise gene change that has caused DMD. If this is the case, other people in the family can be tested to see if they also carry the gene change. This test can be done on a small blood sample. Female relatives can be referred to the genetics service to discuss the inheritance of DMD and the option to have carrier testing. For young girls, this is normally offered from the age of 15, although they can be seen earlier if they wish. There is no rush for testing but if a woman is concerned about the possibility of having an affected boy it is usually preferable to have a consultation before starting a pregnancy.

Even if the precise gene change cannot be identified, muscle enzyme and other genetic tests can be done to determine the likelihood that someone in the family carries the gene change.

It is important to remember that the decision whether or not to have a carrier test is a personal choice. For some people, the results of a carrier test can raise unexpected emotions or issues. The genetic service can provide information and help you decide what the best option is for you.

Female DMD carriers

Females have two copies of the dystrophin gene in each of their cells because they have two X chromosomes, so even if one gene carries a DMD change, the other normal gene is usually enough to compensate. In rare cases, female DMD carriers do develop muscle weakness. This is usually milder and occurs later in life than in males with DMD.

It is now recommended that female carriers of DMD have cardiac screening, every five years, as a precaution from 16 years. This is because research has shown that although the majority of female carriers do not have any health problems associated with DMD, a small number do have muscle weakness which can involve the heart.

Prenatal tests

There are a number of tests that are available before, or during pregnancy.

It is possible to test the mother's blood from around 9 weeks' gestation, which can determine with greater than 97% accuracy whether the pregnancy is male or female. No further action is normally taken if the pregnancy if female.

If the exact gene change has been identified in the family, direct tests on a pregnancy to check for DMD are available from 11 and 15 weeks gestation. They are called chorionic villus sampling and amniocentesis. The prenatal test will indicate whether the baby is male and if so, whether he would have DMD. Deciding whether to go ahead with an affected pregnancy is a very personal choice and we will support you in your decision.

An alternative technique, called Pre-implantation Genetic Diagnosis (PGD). This uses IVF (in vitro fertilisation) technology. Embryos are tested for the DMD gene change soon after fertilisation, and only unaffected embryos are transferred to the womb. As this technique involves all the limitations of IVF, and is only available in a few specialised centres, it requires careful consideration.

There are separate pages regarding all these tests on this website. The genetics department can provide further details if you would like more information.

For more information

If you need more advice about any aspect of Duchenne Muscular Dystrophy, you are welcome to contact:

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Consultant: _____

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