BEING A CARRIER FOR DUCHENNE MUSCULAR DYSTROPHY

ACTION DUCHENNE

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This leaflet is mainly for women who know they are, or who think they may be, a carrier for Duchenne Muscular Dystrophy (DMD) or the milder form of the condition Becker muscular dystrophy (BMD). If you have a relative, for example, brother or an uncle with DMD or BMD, or because you mother is a carrier you may find this useful. DMD is a progressive, life-limiting muscular disease that begins in childhood. BMD has a later onset and milder presentation. For more information about the signs symptoms of DM, or BMD and available treatments and research, there are leaflets on the sites in the 'links' section. This leaflet mainly aims to answer questions specific to carriers.

HOW IS DMD INHERITED?

DMD and BMD primarily affect boys. They are both caused by an alteration (also called a mutation) in a gene called the *dystrophin* gene. In each family the exact mutation may be in a different place in the dystrophin gene.

Genes are the instructions that tell our bodies how to grow and work properly and we inherit them in the egg and sperm from which we are made. They are present in nearly all of the cells in our bodies. Genes are packaged into chromosomes and we have 23 pairs of chromosomes as we get one of each in the egg and one of each in the sperm from our parents. One pair of chromosomes is called the sex chromosomes (fig. 1). Women have two X chromosomes, whereas, men have one X and one Y. While the X is large and has many genes along it, the Y chromosome is very small and has very few. The *dystrophin* gene is on the X chromosome and NOT on the Y chromosome. This means that boys only have 1 copy of the *dystrophin* gene whereas girls have 2. When boys have a mutation in their *dystrophin* gene they have DMD. If girls have a mutation in one *dystrophin* gene they still have another good copy of the gene in all of their cells. For this reason they don't usually have symptoms of DMD but are 'carriers' of the condition.

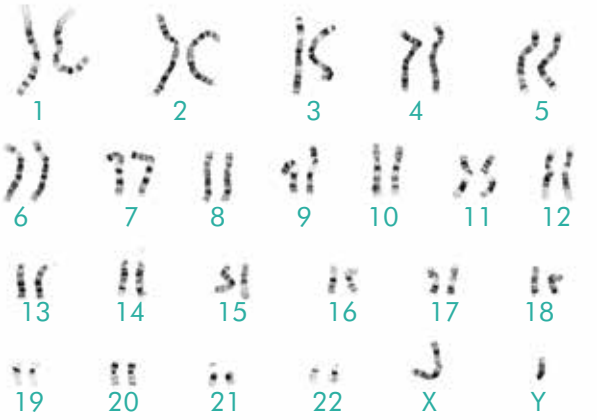


Fig 1: A male set of chromosomes

We inherit one of each chromosome from Mum and one from Dad, which means we always get an X chromosome from Mum and either an X or a Y from Dad. If we get a Y we are male. Girls always get an X from their Dad and one from their Mum. If Mum is a carrier then a daughter might inherit the X with the good *dystrophin* gene or the X with the mutation. This means they have a 1 in 2, or 50%, chance of also being a carrier. If they are pregnant, someone who is a carrier has a 1 out of 4 (i.e. 25%) chance that their baby will be a boy that is affected by DMD. This called X-linked inheritance (fig. 2). This is the same risk in each pregnancy.

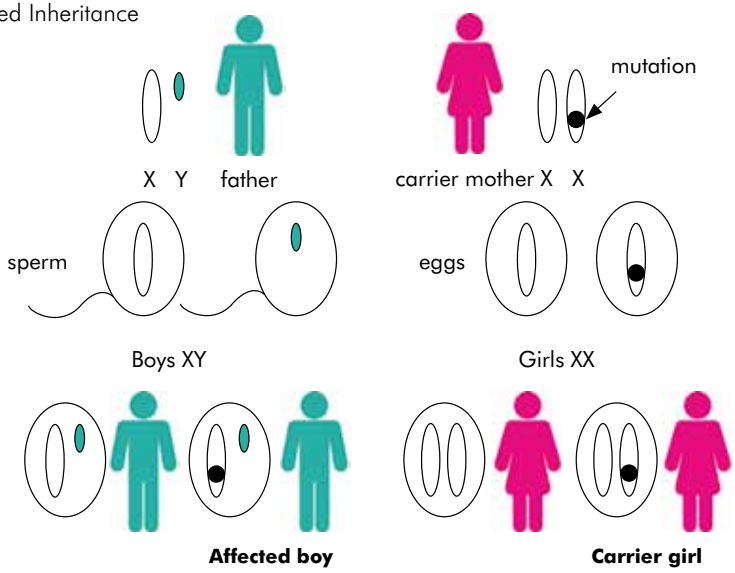
When a boy is diagnosed with DMD his *dystrophin* gene is carefully examined to find the particular mutation causing his disease. If this is identified his mother and sisters can be offered a test for that mutation.

When there is only one boy in the family with DMD, their mother is a carrier about 70% of the time. The rest of the time the mutation has most likely happened for the first time in the boy with the condition.

If your brother has DMD but your mother is not a carrier i.e. does not have the mutation, you still have a small chance of being a carrier. This is because your mother might have a cluster of eggs with the *dystrophin* mutation. This is called mosaicism. It means that you can still be offered a test to see if you are a carrier even if your mother is not.

All of this also applies to the inheritance of BMD. BMD tends to be caused by different mutations in the *dystrophin* gene than those that cause DMD. In any one family boys or men who have DMD or BMD will tend to be affected in a similar way.

Fig 2: X-linked Inheritance



HOW DO I KNOW IF I'M A CARRIER?

You can have a genetic test to find out if you are a carrier of DMD. Your GP can refer you to your local Genetics Service to discuss having a test with a Genetic Counsellor. They can arrange for you to have a small blood sample taken which can be tested for the mutation in the *dystrophin* gene that is in your family. You can discuss all aspects of being a carrier for DMD with your Genetic Counsellor, including whether there are any health issues and what options you have available when starting a family. Having an appointment with a Genetic Counsellor does not mean you have to have a test and your discussion is confidential. Genetic counsellors hold clinics in most major hospitals.

Some women, especially in the past, have had a different blood test called a CK test (creatine kinase test) to see how likely it is they are carriers. This test looks for a chemical in the blood that goes up in level when a woman is a carrier. Sometimes this test is difficult to interpret. A genetic test is more reliable.

The Genetics service will need information about the specific gene mutation in your family. It is therefore helpful to provide you GP with the name of the carrier, or relative affected by DMD, in your family and where in the country they were seen for genetic testing.

WHEN SHOULD I HAVE A TEST?

There is no fixed time for having a genetic test to see if you are a carrier. However, late teenage can be a good time as this is usually before planning a family and at a time when girls may learn about genetics at school and therefore have more understanding. Having a test before starting a pregnancy gives you and your partner time to consider all of your options.

WILL I HAVE ANY HEALTH PROBLEMS AS A RESULT OF BEING A CARRIER?

Occasionally, women who are carriers may show some signs or symptoms of muscle disease, such as muscle pain or fatigue but this is not usually severe. This can happen at any age and slowly worsen with time. Sometimes it is also very hard to know if this in connected to being a carrier. Overall, about 10% of carriers may show some signs of muscle problem, which is called being a 'manifesting carrier'.

Why do these women get any symptoms if they always have a good *dystrophin* gene? This is related to something called X-inactivation. When they are very small, female embryos stop using (switch off) one X chromosome in each cell. This means that their muscles have some groups of cells with one X 'active' and other groups with the other X 'active'. If there are too many muscle cells active with the X containing the mutated *dystrophin* gene this can explain muscle symptoms.

There is evidence that a small number of women who are carriers may develop a heart problem called cardiomyopathy. This is rarely severe. There is some debate about how frequently this occurs and how often it becomes a clinical problem. Some doctors advise carriers of DMD to have a heart scan called an ultrasound scan that looks at the structure of the heart. This involves having jelly on your chest and a monitor that looks through the chest wall. It is painless and does not involve any X-rays. Not all doctors believe this is necessary unless you are having any symptoms such as shortness of breath, dizziness or palpitations. It is important to report these symptoms to your GP.

WHAT ABOUT PREGNANCY?

If you are concerned about having a baby with DMD you can talk to your Genetic Counsellor about what your options are when you are planning a family. It is best to do this before you become pregnant and arrange to go with your partner. You don't have any obligation to do anything but it can be helpful to know what your choices are and talk them through.

PRE-NATAL DIAGNOSIS

If you become pregnant naturally you can be offered two types of test and your Genetic Counsellor can organise these for you. The first is called free fetal DNA (FFDNA) sexing. This uses a small blood sample from you to test if your pregnancy is male or female. It relies on being able to detect small amounts of Y chromosome material floating around in your blood stream. It can be done from around 8 weeks of pregnancy and takes about 5 days. If your pregnancy is female it will be highly unlikely to have symptoms of DMD. If it is male then it could have either the good or the mutated *dystrophin* gene and therefore has a 50% chance of having DMD.

If you do not want to have a baby affected by DMD you can be offered a second test called CVS (for chorionic villous sampling) at around 11-12 weeks. This involves having a needle through the tummy that takes a small sample of the placenta, the tissue that feeds the growing embryo. The placenta has the same 'genes' as the embryo. This can be tested in the laboratory, which takes up to a week. A similar procedure can be done from 16 weeks and is called amniocentesis. Because they use a needle these are called invasive procedures. They are done by specialised obstetricians and are available in all regions.

These procedures are very safe but have a small chance of causing a miscarriage (about 1 in 100 or less). If the pregnancy has DMD then termination of pregnancy can then be performed. Decisions about pregnancy can be difficult and throughout this you would have the advice and support of your Genetic Counsellor and midwives.

At the moment invasive procedures are the most reliable way of testing whether a pregnancy has DMD. However, there is new research to develop an accurate test just using a small blood sample from the pregnant mother. This is called non-invasive prenatal diagnosis (NIPD). You can ask your Genetic Counsellor more about whether this test is ready to use for DMD.

If you are a carrier but do not want to have an invasive test in pregnancy, your baby can have a genetic test after birth to see if they have DMD.

PRE-IMPLANTATION GENETIC DIAGNOSIS (PGD)

If prenatal diagnosis is not for you, you may want to consider PGD. This involves creating embryos in the laboratory with sperm and eggs from parents using the techniques of IVF (*in vitro* fertilisation). After a few days, each fertilised egg becomes a ball of cells (early embryo), which can be tested to see if it is male or female and whether it has inherited the DMD gene with a mutation. If a male embryo *without* the DMD mutation, or a female embryo, is identified, this can be placed into the mother's womb. So, providing the pregnancy becomes established there is no need to have any invasive tests as the baby will not be a boy with DMD.

This is only done at a few specialist centres in the UK. Women are eligible to be referred for this treatment on the NHS if they do not have a healthy child already, don't smoke, have a BMI (body mass index) between 19 and 30 and are under 40 at the time of treatment. There is about a 30% chance that this will succeed for each IVF cycle. Your Genetic Counsellor can tell you more about this and refer you to a local specialist centre for an initial discussion.

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Duchenne Muscular Dystrophy and Action Duchenne

WHERE CAN I FIND MORE INFORMATION?

There are a number of support groups and internet sites that have reliable information about DMD. Some of these have contact email or phone numbers where you can also speak to someone with your particular question. Genetic Alliance has a list of regional NHS Genetic services.

LINKS:

Action Duchenne	www.actionduchenne.org
Muscular Dystrophy Campaign (UK)	www.muscular-dystrophy.org
Parent Project Muscular Dystrophy	www.parentprojectmd.org
Contact a Family	www.cafamily.org.uk
Duchenne Family Support Group	dfsg.org.uk/understand-dmd
Genetic Alliance	www.geneticalliance.org
Antenatal Results and Choices	www.arc-uk.org

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