



## Genetic issues



### Carrier detection tests and prenatal diagnosis

There are several types of muscular dystrophy and about 50 neuromuscular conditions, all of which fall under the umbrella of the Muscular Dystrophy Campaign. If you have a relative with one of these conditions and are hoping to start a family, you may want to know the answers to two important questions:

- **Am I a carrier of the condition?**
- **Will my children be affected?**

The answers will vary according to the type of muscular dystrophy or related condition, its inheritance pattern, and how much we know about its genetic causes. You can find out if carrier and prenatal testing are available for the condition in which you are interested by contacting the Muscular Dystrophy Campaign or your local Genetics Centre where a geneticist will be able to talk over your particular circumstances and how they might affect the possibility and accuracy of testing.

This factsheet is a reference guide to some of the general techniques and genetic tests which can be used in carrier detection and prenatal diagnosis.

Remember - Genetic tests may take several weeks or even months to complete, which is why they should preferably be done before a pregnancy is started.

Once the results are known, you will then have time to think through the various options open to you, and to discuss these with specialists at a genetic counselling centre.

#### **Carrier detection tests**

##### **What is a carrier?**

A carrier is a person who usually shows no symptoms of a condition but who carries the faulty gene which causes it; or a person who has very mild symptoms of a condition (but who may not have been diagnosed as having it), and carries the faulty gene which causes it.

There is a risk that a 'carrier' will pass the faulty gene on to his or her children, and that they might be affected by the condition or be carriers themselves. The level of that risk depends on the inheritance pattern of the condition (this is described in the factsheet relating to the particular condition in which you are interested, or you can discuss it with your geneticist).

##### **What are carrier detection tests?**

If someone actually has a particular condition, this will usually be evident on clinical examination. Genetic carrier tests are designed to discover whether a person who has no symptoms of a condition nevertheless carries the faulty gene which causes it.

##### **Direct genetic tests**

These are done on the part of a person's genetic code (DNA) which, when disrupted, causes a particular condition. Once scientists have identified the genetic cause of a condition they know where to look for the disruption among the thousands of genes that make up our genetic code (DNA). This disruption may take the form of a repeated piece of genetic coding (called a 'duplication' or 'expansion'), a missing chunk (called a 'deletion'), or a tiny alteration in the genetic code (called a 'point mutation'), depending on the condition. Different types of disruption are found in different disorders, or sometimes in different families with the same disorder, so it is important always to find

the specific genetic 'mistake' responsible for the disorder in a particular family before it can be used to test other members of that family. The larger the disruption, the easier it is to locate it. It is not always technically possible to identify a point mutation, even when it is present.

The DNA is obtained by taking a blood sample. If the relative who is affected by a particular condition is alive, he or she may be asked to give a blood sample which will then be compared directly with one from the person who is being tested for carrier or prenatal status. This can help scientists to make the diagnosis and speed up the process.

### **Linked genetic markers or 'family studies'**

Sometimes, in the absence of an obvious gene alteration (a duplication, deletion or point mutation) in an affected person, direct genetic tests cannot be done. In these cases, 'markers' are used to find out whether someone has inherited the crucial part of the genetic code which carries the genetic defect. They are pieces of DNA, situated close to the affected person's faulty gene, which can be used to distinguish it: they are said to be 'linked' to the gene. If the person being tested is found to have inherited the same markers as the affected person, then he or she is likely also to have inherited the faulty gene.

The accuracy of all this depends on how near the marker is to the faulty gene. Sometimes, a reliable marker is not available, and so the test does not give any useful information. In order to use linked markers, a DNA sample from an affected person should be available, plus samples from as many other family members as possible, so that it can be established which 'markers' are linked to the faulty gene in your particular family

### **Creatine kinase (CK) estimation**

Creatine kinase (CK) is normally found in healthy muscles, but if the muscles are diseased or damaged (e.g. in Duchenne and Becker muscular dystrophy, and some other disorders such as polymyositis and other dystrophies), large amounts of CK also leak into the blood, and can be measured. Usually, three blood samples are taken from a person who might be a carrier of Duchenne or Becker muscular dystrophy, over a period of several weeks (either by their GP or at a hospital) and the CK level is analysed and averaged to give a result. These blood samples should not be taken immediately after exercise, or after any form of injury, since this may raise the CK further, and give a 'false' result. CK estimations are not reliable during pregnancy. CK estimation is usually not reliable enough to use as a test in its own right, and is generally carried out in conjunction with other tests.

### **Muscle biopsy**

Muscle biopsies (removing a sliver of muscle under local anaesthetic, and studying it) are often used to diagnose the different neuromuscular disorders, as they can, for instance, detect people who are very mildly affected (e.g. by Becker or Facioscapulohumeral muscular dystrophy). Sometimes they are also used to assist in carrier testing, but nowadays this is more often done by DNA tests.

Other special tests are occasionally used in particular situations.

## **Prenatal Diagnosis**

### **What is prenatal diagnosis?**

If one or both parents are 'carriers' of a particular condition, there is a risk that their unborn child will be affected by that condition. 'Prenatal tests' are carried out during pregnancy, to try to find out if the fetus (unborn child) is affected. The tests are only available for some neuromuscular disorders. You can check on availability by contacting your geneticist, or the Muscular Dystrophy Campaign.

A couple may want to consider whether or not to continue the pregnancy if the fetus is affected. Alternatively, they may wish to know if the fetus is affected so that they can carry on with the pregnancy armed with knowledge that will help them to prepare and plan for the future.

Different types of prenatal tests can be carried out after about 10 weeks of pregnancy. Chorion villus sampling (CVS) can be done at 10-12 weeks, and amniocentesis at about 14-16 weeks, while placental biopsy and fetal blood sampling can be done at about 18 weeks.

Women/couples need to consider carefully which test to have and to discuss this with their genetic counsellor. Earlier testing would allow early termination which would probably be less traumatic for the couple, but it carries a slightly higher risk of miscarriage than later testing (about 2%, as opposed to 0.5%).

To get the maximum benefit from these tests, it is very important that investigations into carrier status should commence BEFORE a pregnancy is started. For this reason, many people arrange to be carrier tested in their late teens.

The two most usual prenatal tests are:

### **Chorion villus sampling (CVS) and Amniocentesis**

These are used to obtain a DNA sample from the fetus (unborn child). Results from both tests can take some weeks to come through. The DNA is studied by scientists to try and discover whether or not the fetus has inherited the disrupted part of the genetic code. They will use 'Direct genetic tests' or 'Linked genetic markers' (see previous pages). The parents will be told the results, and will then decide for themselves whether to continue with the pregnancy.

### **Chorionic Villus Sampling (CVS)**

The chorion is the tissue which surrounds the fetus during early pregnancy, part of which later becomes the placenta (afterbirth). It contains the same sort of DNA as the fetus. A tiny sample of the chorion is obtained at a very early stage of pregnancy. From this tissue fragment, enough DNA can be extracted to perform the test, which involves looking for the same genetic change as the one already identified in an affected person in the family.

#### **What does the test involve?**

The test can be performed at about 10 -12 weeks of pregnancy. An ultrasound scan is performed first, to check how far advanced the pregnancy is, and to determine the position of the placenta. The test involves passing a needle through the abdomen in a similar way to an amniocentesis (see page 6); to obtain a small piece from the chorion. The test usually takes about 20 to 30 minutes, and can be done in a hospital outpatient department. The woman being tested is awake and aware of what is happening during the test.

#### **Is the test painful?**

Most women describe it as being uncomfortable rather than painful. Local anaesthetic is usually used but most women say that they are aware of a 'pushing' feeling; they may feel some soreness over the area afterwards.

#### **How accurate is the test?**

Sometimes it is important to know the sex of the fetus and this can be determined very quickly using this test. Identifying a genetic defect can depend on several factors such as the size of the disruption, and therefore how easy it is to find, or whether a sample from an affected relative has been obtained, or how accurate 'Linked genetic markers' are. Your geneticist will discuss all these factors with you before any test, and will explain whether there is a risk of error with the test result.

**Is the test safe?**

There is a risk of miscarriage of 1-2%, which is higher than for amniocentesis. As far as the mother's health is concerned, there are thought to be no serious complications, although she should avoid strenuous exercise for a few days. The test could be carried out at 8 weeks, but this may be associated with limb deformities, so it should not be done before 10-12 weeks.

**How long will the results take?**

The sex of the foetus can be determined within a week. Results from DNA tests may take from a few days up to two weeks (rarely, up to four weeks).

**Amniocentesis****What does the test involve?**

Amniocentesis is usually done around 14-16 weeks of pregnancy (but could be done earlier under some circumstances). First of all an ultrasound scan is done to check how far the pregnancy is advanced. The skin around the mother's abdomen is then cleaned with antiseptic lotion, and a fine needle is passed through the abdomen. A sample of about 20ml (4 teaspoons) of the amniotic fluid surrounding the fetus in the uterus (womb) is taken. This fluid sample contains the same DNA as the fetus. Amniocentesis can be done in a hospital outpatient department, and the woman being tested is awake and aware of what is happening during the test which usually takes only a few minutes.

**Is it painful?**

Women who have had the test generally say that it is no more painful than having a blood test or an injection.

**How accurate is the test?**

Amniocentesis is as accurate as CVS. The accuracy varies from one condition to another, and sometimes depends on the situation in an individual family. This will all be discussed with you by your geneticist before the test is taken.

**How quickly do results come through?**

The result can come through in a few days, but often takes about 1-2 weeks.

**Is the test harmful to the baby?**

There is a slight risk (about 0.5%) of miscarriage; otherwise it is not thought to harm the baby. Women are advised to avoid strenuous exercise for a few days.

**Where can I get advice about carrier detection and prenatal testing?**

You can find out if testing is available for the condition in which you are interested from the Muscular Dystrophy Campaign, or from your nearest Genetics Centre. If you want to be tested, your family doctor can refer you to the Genetics Centre. A list of such Centres is held by the Support Services Department at the Muscular Dystrophy Campaign Head Office. The Genetics Centre and your family doctor can then arrange for possible carriers and family members to visit the appropriate Centre, and/or to give blood samples for testing.

**The most important things to remember about the tests are:**

Sometimes the tests can be accomplished rapidly in an emergency (for example in the event of an unexpected pregnancy), but it is usually much more difficult to get reliable results from a 'rush job'. It can be hard to get blood samples from relevant family members at short notice, and in the case of a pregnancy it leaves parents much less time to consider what action to take.

The tests should involve as many relevant family members as possible to obtain a clear picture of the part of the gene responsible for the dystrophy, and for a more accurate estimation of the risk of being a carrier and of having an affected child. The tests can be arranged through any one of the specialist Genetics Centres.

This factsheet talks about the tests that are currently available. These do change and while some will be relevant to your situation, others will not, so do check with your local Genetics Centre as to what tests are best.

### **Support organisations**

ARC (Antenatal results and choices ) formerly Safta

A self-help charity for women and couples who discover that their unborn baby has an abnormality. The organisation can provide information on specific medical conditions, clinical research and genetic counselling, and can put women/couples in touch with a local ARC member who can offer regular contact and support.

The ARC Handbook is free of charge for parents and should be available at the time of diagnosis from the hospital or available from ARC.

There is a charge for this Handbook for Professionals.

ARC

73-75 Charlotte St

London

WIP 1LB

Helpline: 0207 631 0285 (10am – 5.30pm)

Administration: 020 7631 0280

Email: [info@arc-uk.org](mailto:info@arc-uk.org)

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