The Fragile X Society

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Prenatal Testing for Fragile X Syndrome

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Introduction

The information provided in this article is general. Most genetic centres, fetal medicine units or obstetric departments have produced leaflets explaining their own arrangements and you should ask if one is available.

Anyone considering having a prenatal test should have the opportunity to discuss things fully with a genetic counsellor ideally before a pregnancy is started. This is because there might be factors that will affect the risks of the accuracy of the test in a particular individual. If you have not been referred for genetic counselling, you should ask your family doctor (GP) for a referral.

Reading this article might raise questions in your mind and these should be discussed with your genetic counsellor.

This article is concerned with the facts of the tests and procedures. I have not addressed the emotional considerations which of course are also extremely important, and will affect individual decisions.

What tests are available?

The most usual prenatal test for fragile X syndrome is the chorionic villus sampling test (CVS for short). This test has been in use for many years, not just for fragile X syndrome and it is usually carried out from around 11 weeks of pregnancy. This test would be offered to women who already have a child with fragile X syndrome, or who have been identified as being carriers.

How is CVS performed?

The test involves taking a small sample of what is the developing placenta or “after birth” (the chorionic villi). It is usually performed from around 11 weeks of pregnancy as an outpatient test.

It is recommended that, before having a CVS a dating scan is performed on the pregnancy to ensure that the test is done at the right time. This scan can usually take place at your local hospital.

There are two ways of doing the test:

- Through the abdomen (transabdominal). The skin over the abdomen is cleaned with antiseptic solution and a local anaesthetic is given to numb the area. A fine needle is then passed through the wall of the womb into the chorionic tissue using ultrasound guidance and a small sample is removed through the needle.

- Through the neck of the womb (transcervical). Your vagina is cleaned with antiseptic solution. This feels similar to having a smear test. A fine pair of forceps is then passed through the cervix (neck of womb) while the ultrasound picture helps the doctor guide the forceps to the right place. A small piece of chorionic villi is removed and sent to the laboratory for testing.

Which method is chosen depends upon the individual practice of the doctor you are seeing and the position of the placenta and the womb on ultrasound scan.

What are the risks of CVS?
The test carries a small risk of causing a miscarriage. The hospital doing your test will give you their own risk figures. However, it is generally thought that around 1-2% of women who have the test will miscarry as a result of the procedure – in other words, for every 50 women having the test, one will have a miscarriage.

The possibility of injury to mother and baby other than miscarriage is extremely small. However, some reports have suggested that a very few babies have had problems with their limbs after mothers had CVS very early in pregnancy. It is still by no means clear that these findings are directly related to the CVS test but any such possibility needs to be taken seriously. In the great majority of cases when a limb abnormality has been reported the CVS was done before the 10^{th} week of pregnancy. For this reason CVS is usually performed at 11 weeks or later.

Is CVS painful?
Although you will be aware of what is happening, most women describe it as being uncomfortable rather than painful. Some say that the transcervical method feels like having a smear test.

If you have the test done through the abdomen, most women say that you are aware of a "pushing" feeling and you may feel some soreness over the area afterwards.

What happens after the CVS?
The test normally takes 20 to 30 minutes to do which includes the time taken for scanning. Afterwards, you stay in the clinic for about half an hour and then you can make your way home. You will be advised to have someone with you. You can use public transport but should not drive yourself. It is recommended that you take things easy for 24 hours. You will be given more information by the unit performing the test.

If your blood group is Rh (sometimes called rhesus) negative you will be advised to have an injection of anti-D immunoglobulin after the procedure to prevent you from developing antibodies against the baby's blood cells.

It is not unusual to have some "spotting" vaginally for a couple of days after the test. You may also feel a little bruised and experience some period type pains. These are usually nothing to worry about and resolve after a day or two.

How reliable are the tests?
No test is guaranteed to be 100% reliable but the chance of getting a completely wrong result is extremely small.

With fragile X syndrome, there can be some problems in interpreting a positive result. It is complicated to explain but the various possible results are discussed below, which might help to clarify things. It is **essential** that this be discussed with a genetic counsellor before the test is done so that you can clarify how much information you wish to have.

What do the different results mean?

1. Male baby, full mutation
   This result indicates that the child will have fragile X syndrome. The degree to which he will be affected can vary but is reasonably predictable.

2. Male baby, premutation
   This shows a boy who will be unaffected by fragile X syndrome but he will pass the gene to all his daughters and none of his sons. His daughters will be unaffected, but will be at risk of having affected children themselves.

3. Male baby, "mosaic" result
   This is where some cells have the full mutation, and some the premutation. This can be particularly difficult to interpret, but it would usually be predicted that the baby would be affected by fragile X syndrome to some degree.

4. Female baby, full mutation
   This shows a girl who has about a 50/50 chance of being affected with fragile X. If she is affected it is difficult to predict how mild or severe her problems might be since fragile X is much more variable in girls than in boys. At the moment there is no way of predicting which girls with a full mutation will be affected and which will not. Girls with a full mutation can pass the gene to their sons or daughters.

5. Female baby, premutation
   This shows a girl who is unaffected by fragile X syndrome but who can pass the gene to her sons or daughters.

6. Male or female baby, no premutation or full mutation
   This means that the baby has not inherited the X chromosome with the gene mistake on it, but has the unaffected X chromosome. With this result there is no chance that the baby will have fragile X and it cannot pass it to any of his or her children.

As you can see, several different results are possible and the difficulty in predicting how much a child with a full mutation will be affected (especially when it is a girl) can make it particularly hard to decide how much information you wish to be told following the test.

Some parents decide that they only want to know if they have an affected male pregnancy as it is easier to predict that a boy will be affected. If it is a girl, parents may ask that no further testing is done on the sample. Parents might also choose not to know the sex of the baby, but simply that it is not an affected male.

Other parents decide that they wish to know only if the fragile X chromosome has been passed on or not, and do not wish to know whether the baby is a boy or a girl, nor whether it has a premutation or a full mutation. There are known to be some other clinical problems associated with having a premutation (some adult women have an early menopause and some adult males can develop neurological problems in later life), these are not usually major factors in prenatal testing but families should be aware of them.

Testing to look at whether the baby has inherited a full mutation or a premutation can take longer, and can be especially complicated with girls. This is because they have two X chromosomes and it can sometimes be difficult to be sure that both have been checked.

All these things require careful explanation and consideration. It is easier if you have had time to think things through before having the test.

How long does it take to get the results?
This will depend on how much information is required, whether there are any technical problems with the test, and what day of the week the test is carried out. A result giving the sex of the baby is usually available within 2 working days. Further testing will take longer, but a result should be available within 3 weeks. Your genetic counsellor will be able to advise you about this.

What happens if I decide to have a termination?
The arrangements should have been discussed with you before having the test. You should be clear about how and when the termination will be done and how long you are likely to have to stay in hospital. If the result is from a CVS and is available by around the 13^{th} week of pregnancy, a "surgical" termination can usually be carried out. The mother is given an anaesthetic and the contents of the womb are evacuated. It is often possible to go home on the same day. Some people consider this procedure less physically distressing than a later termination, but it is no less emotionally distressing.

If the result of the test is delayed, it might be necessary to undergo an induced labour in order to end the pregnancy. This is sometimes described as a "mini-labour" although most people would not consider this a suitable term. The labour is as painful and can last as long as a full-term labour. However you will be offered strong pain relief. It is also a very distressing procedure to have to endure in the circumstances.

Most parents who have the test do so with the intention of ending the pregnancy if it is affected. Some parents find that they change their mind when they are faced with making that decision after getting the result. No-one should pressurise you into having a termination if you have doubts, and if you need extra time to consider things you should say so. You should however bear in mind that a long delay might change the options available for termination of pregnancy.

Other tests

There is a relatively new test available called free fetal DNA testing. This test can identify the sex of the baby by testing a sample of the mother's blood from around 8 weeks of pregnancy. The test can detect the baby's DNA or genes in the mother's circulation and this can be used to identify the sex of the baby. The test is thought to be very accurate although it is still a relatively new test so experience is limited. Parents who do not want girls to be tested for fragile X may find this test useful as if the baby was identified as a girl the parents may decide against having an invasive test such as CVS. If you think you might be interested in this test you should discuss this with your genetic counsellor to see if it is available locally.

In conclusion

It is essential to discuss all aspects of the prenatal test with a genetic counsellor before proceeding. If it is a while since you have seen a genetic counsellor, you should check whether there have been any advances or improvements in the tests.

You should also discuss this information in the light of your own circumstances, both in terms of your genetic make-up (that is, whether you have a premutation or a full mutation), and in terms of your personal situation and beliefs.

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