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Will my Baby be Normal? - Options for Prenatal Diagnosis

One overwhelming concern of mothers and parents during a pregnancy is whether or not their baby will be normal at birth. This concern is not unrealistic because about one baby in 50 will eventually be shown to have some form of disability that dates from the pregnancy period. Unfortunately there is no sure way of guaranteeing a perfect outcome from every pregnancy and worry is as much a part of parenthood as is nappies and wind. Moreover, it does not end when the baby is born.

However, modern antenatal care can provide considerable reassurance about the health of a developing baby. A large part of such care in the 21st century is directed toward the identification of abnormalities in sufficient time to provide parents with the option of either terminating the pregnancy or preparing themselves for a particular problem.

This is a rapidly changing area of medical practice and the range of tests available is both extensive and confusing. This web page aims to help you to understand your options with respect to the prenatal diagnosis of fetal abnormalities. Further information is always available should it be required. In some instances a referral for specific genetic counselling may be required.

What Types of Abnormalities Can Occur?

In general there are two major groups of birth defects that we can look for during a pregnancy. The first is chromosomal disorder, the most important of which is Down syndrome. Other types of chromosomal disorder can occur but they are either less common or so severe that the pregnancy does not result in a live-birth. Miscarriage prior to 12 weeks is the most common outcome of a chromosomal disorder. Most chromosomal disorders result in severe problems and disability but there are some chromosomal variations that result in no visible problems or disability. This can provide dilemmas for parents if a chromosome analysis is done on a developing baby.

Indeed, a recurring theme in the subject of testing for fetal abnormalities is that it can provide information that is not always helpful but merely serves to increase worry!

The second group of abnormalities we refer to as structural defects. These range from the innocent (such as an extra toe or finger), through the more serious but treatable abnormalities such as cleft lip or palate and on to those that can result in severe disability such as spina bifida. Some babies with chromosomal disorders have structural defects and this may be the means by which the existence of a chromosomal problem is identified.

The third major group of abnormalities consists of all those things that can't be tested for, for example, most cases of cerebral palsy, learning disorders or an undesirable characteristic of personality. I have warned you that parenthood is a worry!

What Types of Tests are Available?

In general we refer to two types of tests. The first are what we refer to as "Screening Tests". This is because they do not provide a "yes" and "no" answer but they help us to decide whether more extensive testing is desirable.

The second type of tests are referred to as "Diagnostic Tests" because they are more certain in their prediction. Diagnostic tests may involve sampling tissues or fluids from the developing pregnancy in much the same way that we take blood tests from adults and children to diagnose certain disorders.

An intermediate group of tests arise from imaging that is most commonly done with ultrasound during pregnancy. Just as X-rays can be diagnostic of something as important as a fractured bone, ultrasound during pregnancy can be as certain of some problems with a pregnancy. However, in other instances, the ultrasound appearance may not be diagnostic and other tests are required.

What Can Ultrasound Show?

The capacity for ultrasound to detect and diagnose a problem depends on many factors. They include the stage to which the pregnancy has developed, the resolution capacity of the machine used, the expertise of the person using that machine and such individual factors as the amount of mother between the imaging probe and the baby (i.e. how much fat!) and/or the position of the baby and the amount of fluid around it.

Obvious things such as twins and signs of fetal life should be readily diagnosed with ultrasound from very early in pregnancy.

In general the more advanced is the pregnancy then the easier it is to pick structural abnormalities. For example, heart defects i.e. holes between the major chambers of the heart or other structural defects that require corrective surgery soon after birth, are some of the abnormalities sought with ultrasound.

Some structural defects can be very difficult to detect before 18 - 22 weeks of pregnancy and that is why it is recommended that the scan for this purpose be delayed until that date.

When Can Abnormalities be Detected?

If we are looking for those abnormalities that cannot be corrected or would result in severe disability then it is best that this is done as early as possible so that termination of the pregnancy is both a safe and acceptable alternative. Ideally that would all happen before 12 - 14 weeks of pregnancy when it is reasonably safe and simple to terminate a pregnancy.

Unfortunately, it is not always possible to detect severe abnormalities early and any sequence of tests i.e. a screening test followed by a diagnostic test is sometimes a "race against the clock".

If an abnormality is diagnosed after 14 weeks of pregnancy then most specialists would prefer to terminate a pregnancy by induction of a labour process. This involves the "stillbirth" of a baby - not a pleasant process for anyone to contemplate but sometimes preferable to the live-birth of a baby with major disability. If the diagnosis is made after 22 - 24 weeks of pregnancy then termination sometimes involves major ethical dilemmas. In general therefore medical science is looking for ways and means of detecting major abnormalities as early as possible with certainty and safety.

The Best Screening Test

The most common screening test for Down syndrome and related chromosomal abnormalities in Australia is a combination of an ultrasound measure of nuchal translucency (the NT test – *see below*) and a blood test of the mother performed between 10 and 13 weeks of pregnancy. A hormone and a protein specific to the pregnancy is measured in the blood sample and all the information, including the mother's age, ethnicity etc. is then used to produce an estimate of risk or chance of chromosomal abnormality. An arbitrary cut off of 1:300 is chosen as "screen positive".

It is important to understand several points about this test (and these are much the same for each of the screening tests described in more detail below):

1. Careful timing of the tests is required.

   It is very important therefore to accurately date the pregnancy. This will be checked either before or during the test by an ultrasound measure of embryo size.

2. Approximately one woman in 20 will be "screen positive.

   These women will be offered further diagnostic testing using chorion villus sampling or amniocentesis (see below). The majority of these women (in fact some 80 – 90%) will NOT have a baby with a chromosomal abnormality. A few will have other abnormalities but most will have a healthy and normal baby.

3. Almost 90% of babies with a major chromosomal abnormality are detected by the combined NT ultrasound and maternal blood test

   However, this means that there is a small possibility that a "screen negative" result will include a baby with Down syndrome. Furthermore, other abnormalities such as spina bifida are not detected with this test.

An attractive but expensive alternative being offered by some private laboratories is the Non-invasive Prenatal Test (NIPT) which requires a sample of blood from the mother at not less than 10 weeks gestation. About 2 in every 100 samples will be unsuitable for further processing (especially from women who are overweight >160 Kg) but this test, which involves analysis of fragmented maternal and fetal DNA in the sample, will detect 99.5% of babies with Down Syndrome. The test currently costs $800 - $1400. Its disadvantage is that it will not provide all of the information that arises from the combined tests of ultrasound and measures of maternal hormones and proteins.

The Nuchal Translucency (NT) Screening Test

The baby's skin early in pregnancy is very thin and fluid builds up in the space between the skin and the tissue at the back of the baby's neck. This area can be seen and the nuchal thickness can be measured using ultrasound. It is known that there is a relationship between that measurement and the chance that the baby has a chromosomal abnormality.

Nuchal translucency measurement is a specialised test that needs to be performed at centres by staff who have had specific training. Experience elsewhere suggests that the NT test alone can detect up to 80% of cases of Down syndrome and up to 75% of other major chromosomal abnormalities.

To be valid this test must be done between 11.5 and 14 weeks of pregnancy i.e. from the first day of the last period or 9.5 - 12 weeks from the date of conception.

The principal advantage of the test is that the result is immediately available and there is still a reasonable time to consider all of the further options for diagnostic testing or termination of pregnancy should it become necessary.

One further point about this test: At present Medicare does not support the cost of ultrasound scans performed at this stage of pregnancy unless some other indication or risk factor is present. You may therefore be asked to pay for the full cost of this scan. If you think that this is not right then you may write a letter to your Member of Parliament or the Federal Minister for Health.

Maternal Serum Hormone and Protein Tests

This is best performed between 10 and 13 completed weeks of pregnancy (8 - 12 weeks from conception) as a part of the combined test described above.

A later test can be taken between 15 and 17 completed weeks since the last menstrual period (13 - 15 weeks from conception). It is sometimes called the "Triple Test" because three different proteins and hormones unique to that pregnancy are measured in a mother's blood. Again a computer program is used to correct for other factors including the mother's age and weight.

In terms of test accuracy a maternal serum test alone is similar to the Nuchal Translucency test alone i.e. between 60 and 75% of the cases of Down syndrome will be detected.

This test may be misleading if the dates have not been accurately determined by the time it is taken. The results of these tests require modification in twin pregnancies or if the mother has insulin dependent diabetes.

On advantage of a 15-week Triple Test is that it also screens for neural tube defects including spina bifida because one of the proteins measured, alpha-fetoprotein (AFP), is elevated with this condition. However, not all cases of spina bifida are detected by the test and, as in the detection of Down syndrome, most pregnancies that are "screen positive" will not have a neural tube defect. Ultrasound at 18-22 weeks alone should be sufficient for the diagnosis of most cases of severe spina bifida.

Each of these tests are covered by Medicare but a special "collection fee" may be charged by some Pathologists. The Non-invasive Prenatal Test (NIPT) of fetal and maternal DNA fragments is not covered by Medicare.

Diagnostic Tests

At present three diagnostic tests are available for the detection of fetal abnormalities:

Diagnostic Ultrasound

This is an ultrasound scan performed at any stage during pregnancy with the purpose of making a specific diagnosis. It often follows a screening ultrasound that has highlighted a possible problem with the baby. In general it will be performed in a Fetal Medicine Unit in a tertiary referral hospital or specialist clinic by a medical practitioner with appropriate and "state of the art" equipment.

Chorion Villus Sampling (CVS)

This test takes a small sample of placental tissue (10-20 mg) under ultrasound guidance and via an abdominal or vaginal approach. It is most commonly performed between 10 and 12 weeks from the last menstrual period but can be

undertaken at any stage during the pregnancy.

The tissue removed is usually cultured (the cells are dispersed and allowed to grow in a laboratory) for a number days or weeks before an analysis of chromosomes can be made. Rapid results using a technique called Fast FISH or DNA can detect a number of chromosomal problems including Down syndrome but this involves extra cost.

In addition to chromosomal disorders it may be possible to test for a wide range of genetic disorders including, for example, cystic fibrosis. *However, such tests are not routinely done but reserved for specific instances where there is a particular risk of such conditions.*

The principal advantage of an early CVS is that it provides a diagnosis in sufficient time for a pregnancy to be terminated safely by curettage. However, you need to be aware that sometimes the test will fail for technical reasons, there is a small chance of a misleading or confusing report, and there is a small risk of losing the pregnancy (perhaps as many as one chance in 50 or as few as one loss in every 100 procedures).

CVS does not test for spina bifida and other structural defects and, like amniocentesis, it may diagnose minor chromosomal abnormalities that will provide ethical dilemmas for parents.

CVS is only performed in specialist centres by skilled operators who perform sufficient numbers of the procedure to maintain expertise.

Any woman can elect to have a CVS (or amniocentesis) but it is particularly recommended for those with special risk factors or after a positive screening test (Nuchal Translucency or Combined Test).

Amniocentesis

This test is usually performed between the 15th and 18th weeks of pregnancy although it can be done later as well. With ultrasound guidance a fine needle is passed through the mother's abdominal wall and into the fluid sac (amniotic cavity) surrounding the baby. Discomfort is minimal. About 15 ml of fluid is removed and this will contain cells shed from the developing baby. These cells are allowed to grow in culture in a laboratory and thereafter the test proceeds as for CVS.

The same range of abnormalities can be tested for as for CVS with similar problems and limitations. On extra advantage of this test is that AFP is measured in this fluid and this can alert to the presence of a spina bifida.

In general, the risk of a miscarriage from the procedure is less than 1% i.e. one in 100 procedures but this does depend on the degree of technical difficulty involved. Leakage of amniotic fluid sometimes follows after amniocentesis but this does not always continue nor does it always result in an adverse outcome for the pregnancy.

You need to be aware that, by the time a diagnosis is reached after amniocentesis, the pregnancy as usually advanced to the stage where termination of the pregnancy is neither simple nor pleasant. Fortunately, for most women that will not be an issue after this diagnostic test, particularly if the only reason for doing the test was a positive screening test.

Who Should have a Screening Test Done?

This is a question that is quite controversial in medical circles. In my opinion, it comes down to the wishes of the individual mother who needs certain information about the test in order to make that choice. Here are the questions that you need to understand before you undertake a test:

- What is the test for i.e. what can it detect?

- What is the chance that I have a baby with that or those problems?
- Will it pick up all the babies with that problem? If not, how many will it miss?
- What does it mean if the test is positive?
- What will I do if the test is positive?
- What will I do if the baby has that particular problem?

Unfortunately, in some instances, doctors may be hedging with some answers because some of the techniques are still new and not all of the information is in. In other instances it is reasonable for you to say that you cannot answer the question before you have the result of the test. However, I recommend that you give it serious thought to the questions before embarking on any testing.

Who Needs these Tests?

The most common risk factor for having a baby with a chromosomal disorder is advancing age of a mother. Overall the chance of having a live-born baby with Down syndrome is one in 846 (1:846) but, at 35 years of age for a mother, the risk is 1:384, at 40 years of age it is 1:112 and at 45 years of age it is 1:28. The risk of a live-born baby with any form of chromosomal abnormality at 35 years is 1:179, at 40 years it is 1:64 and at 45 years it is 1:19 (see also table below).

Because many more women less than 35 years of age have babies than those beyond this age, and because it is possible to have a baby at any age with Down syndrome, there are actually more Down syndrome babies in our community that were born to younger women. This is the reason why many doctors recommend or simply perform screening tests on all pregnant women.

I regard every woman as an individual and it is important that you make an individual decision on this important matter.

A few popular myths need to be set aside. While it is true that women who have had one baby with a chromosomal problem (and some with other anomalies as well) have a greater risk of another baby with a chromosomal or other problem, the converse is not necessarily true. That is to say the fact that you have had several healthy babies does not reduce the risk associated with advancing age. Nor does a negative family history for Down syndrome and other problems. And the age of the father has very little, if any influence on the risk of chromosomal problems.

One scientific fact is certain: Screening tests work better for women who are of high risk than it does for women of low risk. This is a statistical phenomenon that may not affect you as an individual but it is the reason that I recommend the test for women of high risk.

Of course one alternative always is to skip the screening tests (Nuchal Translucency or the serum Triple Test) and go straight to diagnostic testing by chorion villus sampling or amniocentesis.

Risk of Baby with Chromosomal Abnormality by Maternal Age		
Mother's Age at expected date of delivery (Years)	Chance of live-born baby with Down's Syndrome *Chance of Down 's at 10-20 wks	Chance of live-born baby a chromosomal abnormality
20 - 24	1:1420	1:500
25 - 30	1:1250	1:480
31 - 34	1:1140	1:420
35	1:355*	1:179
36	1:300*	1:149
37	1:220*	1:124
38	1:165*	1:105
39	1:125*	1:81
40	1:90*	1:64
41	1:70*	1:49
42	1:50*	1:39
43	1:40*	1:31
44	1:35*	1:24
45	1:25*	1:21
46	1:20*	1:16
47	1:18*	1:13
48	1:14*	1:10
49	1:11*	1:8

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