

Antenatal Screening

Antenatal Screening for Down's Syndrome
and Open Neural Tube Defects

The Quadruple Test

Questions and Answers for women
considering the test

The Wolfson Institute of Preventive Medicine
Barts and The London School of Medicine and Dentistry

Antenatal Screening

This leaflet answers some of the common questions women ask about the screening test – we hope you find it helpful. You are welcome to discuss the test with your midwife, consultant or GP before you decide whether you would like to be screened. If you have any further questions screening staff at the Wolfson Institute are available to talk to you on 020 7882 6293.

What is Down's syndrome?

Down's syndrome is defined by the presence of an extra chromosome number 21 in the cells of the fetus. In an unscreened population about 1 in every 500 babies are born with Down's syndrome. Usually it is not inherited and so a baby can be affected even if there is no history of Down's syndrome in the family.

Down's syndrome is the most common cause of severe learning disability and is often associated with physical problems such as heart defects or difficulties with sight and hearing. It is not possible to assess the degree of disability before the baby is born. About 9 out of 10 babies with Down's syndrome will survive their first year and nearly half of these will reach 60 years of age.

What are open neural tube defects?

The two main kinds of open neural tube defects (NTDs) are spina bifida and anencephaly.

Babies with spina bifida have an opening in the bones of the spine

which can result in damage to the nerves controlling the lower part of the body. This causes weakness and paralysis of the legs and sometimes bowel and bladder problems. Babies with spina bifida are also more likely to have a collection of fluid on the brain, called hydrocephalus, which can be treated surgically but may lead to learning disability.

Babies with anencephaly have a large part of the skull missing and the brain is not properly formed. They always die before or very soon after they are born.

In about 1 in every 5 babies with spina bifida the spinal opening is covered with skin or thick tissue. This is called closed spina bifida and will not be detected by the blood test. This condition is usually less severe than open spina bifida.

What does the quadruple test involve?

A sample of your blood is taken between 14 and 22 weeks of pregnancy (15 weeks is the earliest time to screen for open neural tube defects). **The stage of pregnancy is best estimated by an ultrasound**



dating scan. The levels of four substances in your blood will be measured and compared with the average levels for your stage of pregnancy. The substances are:

- (i) alpha-fetoprotein (**AFP**)
- (ii) unconjugated oestriol (**uE₃**)
- (iii) total human chorionic gonadotrophin (**hCG**).
- (iv) **inhibin-A**

The concentration of these four substances are used together with your age to estimate the risk of Down's syndrome in your pregnancy.

In pregnancies with Down's syndrome AFP and uE₃ levels *tend* to be low and hCG and inhibin levels *tend* to be raised.

The level of AFP is also used to determine if there is an increased risk of open spina bifida or anencephaly.

What is a 'risk'?

A risk is the chance of an event occurring. For example, a risk of Down's syndrome of 1 in 100 means that if 100 women have this test result, we would expect that 1 of these women would have a baby with Down's syndrome and that 99 would not. This is the same as a 1% chance that the baby has Down's syndrome and a 99% chance that the baby does not.

When will the result be available?

Your result will usually be ready within three working days of the laboratory receiving the sample and will be sent to your antenatal clinic or General Practitioner.

The result will be either screen-positive or screen-negative.

What does a screen positive result for Down's syndrome mean?

A screen-positive result means that you are in a higher risk group for having a baby with Down's syndrome. If you are in this group, you will be offered a diagnostic amniocentesis or possibly a chorionic villus sampling (CVS).

The result is screen positive if the risk of Down's syndrome is 1 in 150 or greater. About 1 in every 27 women screened will be in this group.

Most women with screen-positive results do not have a pregnancy with Down's syndrome. For example, of 16 women with screen-positive results for Down's syndrome, only one would have a pregnancy with Down's syndrome.

What does a screen positive result for open neural tube defects mean?

A screen-positive result means that you are in a group with an increased risk of having a baby with an open neural tube defect. If the result is

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screen positive you will be offered an ultrasound scan and examination at 18 to 22 weeks of pregnancy and possibly an amniocentesis.

The result is screen-positive when the AFP level is equal to or greater than two and a half times the normal level for your stage of pregnancy.

What does a screen-negative result mean?

If the risk of Down's syndrome based on the quadruple test is lower than 1 in 150 and the AFP level is less than two and a half times the normal level for your stage of pregnancy then the result is called screen-negative and a diagnostic test is usually not offered.

Although a screen-negative result means that your risk of having a baby with Down's syndrome or open neural tube defect is not high, **a screen-negative result cannot rule out the possibility of a pregnancy with either of these abnormalities.**

Does the screening test detect all affected pregnancies?

No. About 4 out of 5 cases of Down's syndrome are detected (classified as screen-positive). This means that about 1 out of 5 pregnancies with Down's syndrome are missed (classified as screen-negative).

About 4 out of 5 cases of open spina bifida are detected and 1 out of 5 is missed. Nearly all cases of anencephaly are detected.

Why do women with screen-negative results occasionally have babies with Down's syndrome or an open neural tube defect?

It is unusual for a woman to have a baby with either Down's syndrome or an open neural tube defect and it is even more unusual for a woman with a screen-negative result, but it does sometimes happen.

This is because the screening test cannot completely distinguish affected from unaffected pregnancies. However small the risk is, the test cannot completely rule out the possibility of the baby having Down's syndrome or an open neural tube defect.

Can any other abnormalities be identified?

Yes, measurements used as part of the quadruple test can also identify pregnancies at high risk of Edwards' syndrome (trisomy 18).

Edwards' syndrome is a rare (birth prevalence about 1 in 4,500) and usually fatal abnormality which arises from an extra copy of chromosome number 18 in the cells of the fetus. If your risk is 1 in 100 or higher you will be offered another ultrasound examination and amniocentesis. The quadruple test detects about 6 out of 10 pregnancies affected with Edwards' syndrome.



Why do you take age into account?

Any woman could have a baby with Down's syndrome, whatever her age, but the likelihood of this happening does increase as a woman gets older and so we use age as one of the

factors when working out your risk of a pregnancy with Down's syndrome. It also means that an older woman is more likely to have a result in the higher risk group (screen-positive) and so be offered a diagnostic test. This is shown in the table below.

Maternal age group (years)	Probability of a screen-positive result	Proportion of Down's syndrome pregnancies detected (%)
Under 25	1 in 80	60
25-29	1 in 60	62
30-34	1 in 35	70
35-39	1 in 10	85
40-44	1 in 5	93
45 and over	1 in 3	96
All	1 in 27	80

(early mid-trimester estimates)

What are the diagnostic tests?

If your result is screen-positive, you will be offered a diagnostic test, usually an amniocentesis or possibly chorionic villus sampling (CVS). The diagnostic test will determine whether or not the pregnancy is actually affected.

Amniocentesis

An amniocentesis is a simple and widely used procedure. It is performed at about 16 weeks of pregnancy and involves collecting a small sample of amniotic fluid from

around the baby by inserting a needle through the abdominal wall. This fluid contains cells from the baby.

Down's syndrome is diagnosed using a technique called quantitative fluorescence polymerase chain reaction (QF-PCR). This provides a rapid diagnosis for Down's syndrome, usually within 48 hours of the amniocentesis being performed. It also detects trisomy 18 and 13 and sometimes sex chromosome abnormalities. In some cases an examination of all chromosomes is carried out. The results of this can take up to two weeks

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Chorionic Villus Sampling (CVS)

This test can be offered as an alternative to amniocentesis. CVS involves taking a sample of placental tissue, by inserting a needle through the abdominal wall or a fine instrument through the cervix. As with amniocentesis QF-PCR is used to provide a rapid diagnosis for Down's syndrome, trisomy 18 and 13 and sometimes sex chromosome abnormalities. In some cases an examination of all chromosomes is carried out. The results of this can take up to two weeks.

There is a small chance (about 1 in 100) that the CVS will not provide a conclusive diagnosis. If this happens you will need to have an amniocentesis.

Will these diagnostic tests guarantee that my baby is free of all birth defects?

No test can guarantee that your baby will be free of all birth defects but if the result of the amniocentesis or CVS is negative it will almost certainly rule out Down's syndrome, trisomy 18, 13 and sex chromosome abnormalities.

Is it safe to have an amniocentesis or a CVS?

Amniocentesis and CVS are procedures that have been offered for many years. Their safety has been carefully studied and it is estimated that around 1 in 100 women who have an amniocentesis or CVS will have a miscarriage as a result of the procedure.

Detailed Ultrasound Scan

Anencephaly and Spina bifida

A detailed scan is used to detect anencephaly and open spina bifida.

Down's syndrome

It is not possible to make a diagnosis of Down's syndrome from an ultrasound scan. There are however certain physical features which may be associated with Down's syndrome and can be seen on the routine ultrasound scan between 18 and 22 weeks. If any of these features are seen this would be a further indication for a diagnostic test but the absence of these features could not rule out Down's syndrome.



If I do not have an affected pregnancy, how could I have a screen-positive result?

The screening result is based on your age and the blood marker levels. You are therefore more likely to have a screen-positive result if you are older, if your AFP or uE₃ are low, and if your inhibin or hCG levels are high. However, since the four markers also naturally vary between women, there is usually no apparent reason for women having either high or low levels and so most women with screen-positive results will not have an affected pregnancy. A screen-positive result only indicates who is in a higher risk group so that we know who should be offered a diagnostic test.

What happens if my baby does have Down's syndrome or a neural tube defect?

Remember that it is more likely that your baby does **not** have Down's syndrome or an open neural tube defect, even if your quadruple test result is screen-positive. If your baby does have one of these abnormalities you will be offered counselling to discuss the implications and your options. If you decide to continue with the pregnancy you can talk to someone about the special help and support that you would receive to help you look after your baby. If you decide to have a termination of pregnancy your consultant, GP or midwife can make arrangements for this.


USEFUL TELEPHONE NUMBERS AND WEBSITES

Antenatal Screening Service, Barts and The London
School of Medicine and Dentistry 020 7882 6293
www.wolfson.qmul.ac.uk/epm/screening

Down's Syndrome Association 0845 230 0372
www.downs-syndrome.org.uk

Antenatal Results and Choices (ARC) 020 7631 0285
www.arc-uk.org

Association for Spina Bifida and Hydrocephalus 0845 450 7755
www.asbah.org



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The Wolfson Institute of Preventive Medicine has played a leading role in the discovery, development and implementation of antenatal screening methods. It is committed to improving the efficacy and safety of screening. We use information collected as part of our screening programme, including measurements on stored blood samples, to audit our screening programme and ensure that it is meeting our expected quality standards. Such information may also be used to help discover and validate new tests that improve the quality of screening services.