



# Antenatal Screening

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

## The Integrated 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 and 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 (NTD) are spina bifida and anencephaly.

Babies born 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 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 integrated test involve?

The integrated test is performed in two stages. The first stage is best performed at 11 weeks of pregnancy, but any time between 10 and 13 weeks of pregnancy is acceptable. The second stage is best performed at 15 or 16 weeks of pregnancy and no later than 22 weeks.



### The first stage involves:

- i) An ultrasound scan examination to precisely determine the gestational age of the pregnancy and to measure the nuchal translucency (**NT**) thickness, a space at the back of the baby's neck.
- ii) Taking a sample of your blood to measure the concentration of pregnancy associated plasma protein-A (**PAPP-A**).
- iii) Providing you with a blood sample kit and a recommended date for taking a second blood sample for the second stage of the test.

### The second stage involves:

- i) Taking a second blood sample to measure the concentration of the following four markers:
  - alpha-fetoprotein (**AFP**)
  - free  $\beta$ -human chorionic gonadotrophin (**free  $\beta$ -hCG**)
  - unconjugated oestriol (**uE<sub>3</sub>**)
  - **inhibin-A**
- ii) Integrating the measurements from the first and second stages into a single screening result. The NT measurement and the levels of the five markers in your blood are used, together with your age, to estimate your risk of a Down's syndrome pregnancy.

In pregnancies with Down's syndrome, PAPP-A, AFP and uE<sub>3</sub> levels *tend* to be low and nuchal translucency measurement, inhibin and free  $\beta$ -hCG levels *tend* to be raised.

The level of AFP in the second blood sample is also used to determine if there is an increased risk of spina bifida or anencephaly.

### Why wait until the second stage to have a risk estimate?

Because by using information from both stages the test is safer and more effective than a test using information from the first stage alone. It will distinguish affected from unaffected pregnancies more effectively, reducing the chance that a Down's syndrome pregnancy is missed as well as reducing the chance that you will need an invasive diagnostic test, such as amniocentesis or chorionic villus sampling (CVS).

### 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 risk, we expect that 1 of these women will have a baby with Down's syndrome and that 99 will 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?

The results of the test are usually ready within three working days of the second blood sample being taken. Results are sent to your antenatal clinic or GP and a letter is sent to you to let you know that the result is ready.

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Your screening result is either screen-positive or screen-negative.

Screen-positive results are telephoned and faxed to a named person in the antenatal clinic or your GP. If you do not receive your result or have further questions please telephone the Wolfson Institute (020 7882 6293).

## 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 65 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 6 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 screen-positive you will be offered an ultrasound scan examination at 18 to

20 weeks of pregnancy, and possibly an amniocentesis. This is organised by your hospital or GP.

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 integrated 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 integrated test detect all pregnancies with Down's syndrome or an open neural tube defect?

No. About 9 out of 10 cases of Down's syndrome are detected (classified as screen-positive). This means that 1 out of 10 pregnancies with Down's syndrome is 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 estimate, the test cannot completely rule out the possibility of

the baby having Down's syndrome or an open neural tube defect.

**Why do you take my age into account?**

Any woman may have a baby with Down's syndrome but the chance of this happening increases as a woman gets older and so we use age as one of the factors when working out your risk of having a pregnancy with Down's syndrome. It 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.

<b>Maternal age group (years)</b>	<b>Probability of a screen-positive result</b>	<b>Proportion of Down's syndrome pregnancies detected (%)</b>
Under 25	1 in 100	85
25-29	1 in 90	86
30-34	1 in 50	89
35-39	1 in 20	94
40-44	1 in 8	97
45 and over	1 in 5	98
<b>All</b>	<b>1 in 65</b>	<b>90</b>

(early mid-trimester estimates, first stage performed at 11 completed weeks of pregnancy)

**Can any other abnormalities be identified?**

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

Edwards' syndrome is a rare (birth prevalence about 1 in 7000) 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 are offered another ultrasound examination and amniocentesis. The integrated test detects about 6 out of 10 pregnancies affected with Edwards' syndrome.

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## What happens if I cannot attend for the second blood test?

An integrated test result can only be given if you provide a blood sample at both stages. If a second blood sample is not received by the end of your 16th week a reminder will be sent to you or your GP or antenatal clinic. If the second sample is not received by the end of your 20th week the risk of Down's syndrome will be estimated using information from the first stage of the test only. This test is less effective than the integrated test.

If you know that you will not be able to attend for the second blood test please discuss this with your midwife or doctor. You could have the screening test based on the first blood test and the ultrasound examination alone (the combined test) but this test is less effective than the integrated test.

## What happens if the ultrasound scan shows that I am too late for the first stage of the test?

We cannot report a screening result for the integrated test. You could have a screening test based on the second stage alone (the quadruple test) and that can usually be performed immediately.

## 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

## 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 a CVS or an amniocentesis?**

CVS and amniocentesis 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 a CVS or amniocentesis will have a miscarriage as a result of the procedure.

**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 and ultrasound marker levels. You are therefore more likely to have a screen-positive result if you are older, if your PAPP-A, AFP

or uE<sub>3</sub> levels are low, and if your NT, β-hCG or Inhibin levels are high. However, since the six 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 an open 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 integrated 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**

Antenatal Screening Service .....	020 7882 6293
Down's Syndrome Association .....	020 8682 4001
Antenatal Results and Choices (ARC) .....	020 7631 0285
Association for Spina Bifida and Hydrocephalus.....	01733 555988

# Antenatal Screening

For further information, please contact:

Antenatal Screening  
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or find us at: [www.wolfson.qmul.ac.uk/epm/screening](http://www.wolfson.qmul.ac.uk/epm/screening)

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.