

# Antenatal Screening

Antenatal Screening for Down's Syndrome

## The Combined 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 does the Combined test involve?

The combined test is best performed at 11 weeks of pregnancy, but anytime between 10 and 13 completed weeks is acceptable. A sample of your blood is taken and at the same time an ultrasound scan is performed.

The two substances in your blood which are markers of Down's syndrome and an ultrasound marker will be measured.

The two blood markers are:

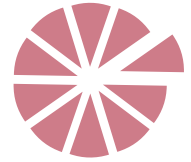
- (i) pregnancy associated plasma protein-A (**PAPP-A**);
  - (ii) free  $\beta$ -human chorionic gonadotrophin (**free  $\beta$ -hCG**);
- and the ultrasound marker is:
- (iii) nuchal translucency (**NT**).

In pregnancies with Down's syndrome, PAPP-A *tends* to be low, NT and free  $\beta$ -hCG levels *tend* to be raised.

The values of these three markers are used together with your age to estimate the risk of Down's syndrome in your pregnancy.

## 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 two 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 mean?

A screen-positive result means that you are **in a higher risk group** for having a baby with Down's syndrome. If your result is in this group, you will be offered a diagnostic test.

The result is called screen-positive if your risk of Down's syndrome based on maternal age, PAPP-A, free  $\beta$ -hCG and NT is 1 in 150 or greater. About 1 in every 40 women screened will be in this risk group.

**Most women with screen-positive results do not have a pregnancy with Down's syndrome.** For example, of 10 women with screen-positive results for Down's syndrome, only one would actually have a pregnancy with Down's syndrome.

#### What does a screen-negative result mean?

If the risk of Down's syndrome based on your age and the levels of the three markers is lower than 1 in 150, then the result is called 'screen-negative' and a diagnostic test would

not usually be offered.

Although a screen-negative result means that you are **not at high risk** of having a baby with Down's syndrome, **a screen-negative result does not rule out the possibility of a pregnancy with Down's syndrome.**

#### Does the Combined test detect all pregnancies with Down's syndrome?

No. About 8 - 9 out of 10 cases of Down's syndrome are detected (classified as screen-positive). Therefore about 1 - 2 out of 10 pregnancies with Down's syndrome will have a screen-negative result and so will be missed by the Combined test.

#### Why do women with screen-negative results occasionally have babies with Down's syndrome?

It is unusual for a woman to have a baby with Down's syndrome, 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 screening test cannot rule out the possibility of the baby having Down's syndrome.

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## Why do you take 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 a having 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.

## Can any other abnormalities be identified?

Yes, measurements used as part of the combined 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 combined test detects about 6 out of 10 pregnancies affected with Edwards' syndrome.

Maternal age group (years)	Probability of a screen-positive result	Proportion of Down's syndrome pregnancies detected (%)
Under 25	1 in 120	71
25-29	1 in 100	72
30-34	1 in 50	78
35-39	1 in 20	86
40-44	1 in 7	93
45 and over	1 in 4	95
<b>All</b>	<b>1 in 40</b>	<b>84</b>

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



### What are the diagnostic tests?

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

#### Chorionic Villus Sampling (CVS)

A CVS is offered early in pregnancy (about 11 weeks) and usually takes only a few minutes to perform. CVS involves taking a sample of placental tissue (using local anaesthetic) usually by inserting a needle through the abdominal wall. The needle will be inserted under the guidance of an ultrasound scan.

Down's syndrome is diagnosed using a technique called quantitative fluorescence polymerase chain reaction (QF-PCR). This provides a rapid diagnosis of Down's syndrome, usually within 48 hours of the CVS being performed. It also detects trisomy 18, 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.

#### Amniocentesis

An amniocentesis 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. As with CVS 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.

#### 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 CVS or amniocentesis 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.

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## **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 PAPP-A is low, and if your NT or  $\beta$ -hCG levels are high. However, since the three 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?**

Remember that it is more likely that your baby does not have Down's syndrome even if your combined test result is screen-positive. If your baby does have Down's syndrome 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, Barts and The London School of Medicine and Dentistry .....	020 7882 6293
Down's Syndrome Association .....	020 8682 4001
Antenatal Results and Choices (ARC) .....	020 7631 0285



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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.