Antenatal Screening

Antenatal Screening for Down's Syndrome, Edwards Syndrome and Patau Syndrome

The Reflex DNA 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 their screening test – we hope you find it helpful. You are welcome to discuss the test with your midwife or consultant 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 (trisomy 21) is defined by the presence of an extra chromosome number 21 in the cells of the fetus or affected person. In an unscreened population about 1 in every 500 babies is 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 Edwards and Patau syndrome?

Edwards syndrome (trisomy 18) is defined by the presence of an extra chromosome number 18 in the cells of the fetus or affected person while Patau syndrome (trisomy 13) is defined by an extra chromosome number 13 in the cells of the fetus or affected person. Both syndromes affect multiple organs with a high risk of fetal death.

At 12 weeks of pregnancy Edwards syndrome has a prevalence of about 1 in 1,500 and Patau syndrome has a prevalence of about 1 in 3,500.

Babies born with either condition, on average, live for around two weeks with only 1 in 12 surviving for one year or more. Babies born with Edwards or Patau syndrome typically have severe structural defects (including defects of the heart, kidney, brain, skeleton and face) as well as severe learning disability.

What is DNA?

DNA (Deoxyribonucleic Acid) is the molecule that is the basis for defining every person's genetic make up.

What is the screening test procedure?

The **Reflex DNA test** involves taking two blood samples in the 11th, 12th or 13th week of pregnancy.

One sample is used straight away to carry out a **Combined test** while the other sample is retained and only used for a **DNA test** if this is indicated by the result of the Combined test.

The Combined test involves:

i) performing 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)** and free ß human chorionic gonadotrophin **(free ß-hCG).**

In pregnancies with Down's syndrome, the PAPP-A level *tends* to be low and NT measurement and the free ß-hCG level *tend* to be raised.

In pregnancies with Edwards or Patau syndrome the NT measurement *tends* to be raised while the PAPP-A and free ß-hCG levels *tend* to be low.

The DNA test involves:

i) analysing cell free DNA in your blood which contains a small amount of your baby's DNA as well as your own. In pregnancies with Down's, Edwards or Patau syndrome there will be a little bit more DNA from chromosomes 21, 18 or 13 respectively. The test depends on measuring this extra amount.

Why is the test called a 'Reflex' DNA test?

One blood sample is used to determine your risk of having a baby affected with Down's, Edwards or Patau syndrome using the Combined test. If this is greater than or equal to 1 in 300 the additional sample taken for DNA analysis is automatically tested without reporting a result and avoiding the need to recall you for your DNA test. This automatic testing strategy is called **reflex testing**.

About 1 in 20 women will have their DNA sample tested in this way. The flow diagram on page 7 sets out the screening pathway.

Is the DNA test always successful?

No, in about 1% of cases the result fails, usually because there is not enough DNA from the baby present in your blood. If your DNA test fails you will be asked to attend your antenatal clinic at around 14 or 15 weeks of pregnancy and have two more blood samples taken for a repeat DNA test and an Integrated test which we report should the DNA test fail again.The Integrated test involves measuring the concentration of three screening markers and using this information together with your Combined test result. If this happens your midwife will discuss the arrangements and the test with you.

Antenatal Screening

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 screening result be available?

For most women the result of the test is usually ready within 10 working days of the samples being taken. Results are sent to your antenatal clinic and a letter is sent to you to let you know that the result is ready.

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

What does a DNA screen-positive result mean?

A DNA screen-positive result means that you are in a high risk group (equal to or greater than 1 in 150) for having a baby with Down's, Edwards or Patau syndrome. If you are in this group, you will be offered a diagnostic amniocentesis or possibly a chorionic villus sampling (CVS). Most women with screen-positive DNA results will have a pregnancy with Down's, Edwards or Patau syndrome.

What does a screen-negative result mean?

If the risk of Down's, Edwards and Patau syndrome based on the Combined test is lower than 1 in 300 then the result is called screen-negative and the DNA sample is not tested and a diagnostic test is usually not offered. If the risk is greater than or equal to 1 in 300 the sample is retrieved and sent for the DNA test.

If the risk of Down's, Edwards and Patau syndrome based on the DNA test is less than 1 in 150 then the result is called screen-negative and no further testing is needed.

The different risk cut-offs are test specific and that is why they are different for the two tests.

Although a screen-negative result indicates that your risk of having a baby with Down's, Edwards or Patau syndrome is low it cannot rule out the possibility of a pregnancy with these disorders (false-negative result).

Does the Reflex DNA test detect all pregnancies with Down's, Edwards or Patau syndrome?

About 9 out of 10 cases of Down's syndrome are detected (screen-positive). This means that 1 out of 10 pregnancies with Down's syndrome is missed (screen-negative).

About 4 out of 5 cases of Edwards and Patau syndrome are detected. About 1 out of 5 cases are missed.

Is my age taken into account?

Yes, any woman may have a baby with Down's, Edwards or Patau 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 any of these disorders.

What happens if the ultrasound scan shows that I am too late for the Combined test?

The reflex DNA test would not be carried out but you could still be offered screening using the **Quadruple test.** This involves collecting a blood sample at around 15 weeks of pregnancy and measuring the concentrations of four screening markers and using this information to estimate your risk of having an affected pregnancy.

What are the diagnostic tests?

If your reflex DNA 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, Edwards and Patau syndrome are diagnosed using a technique called quantitative fluorescence polymerase chain reaction (QF-PCR). This provides a rapid diagnosis for Down's, Edwards and Patau syndrome, usually within 48 hours of the amniocentesis being performed.

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, Edwards and Patau syndrome usually within 48 hours. 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, Edwards and Patau syndrome.

Antenatal Screening

Is it safe to have a CVS or an amniocentesis?

CVS and amniocentesis have been offered for many years but the procedure is not without risk. It is estimated that about 1 in 100 women will have a miscarriage as a result of the procedure.

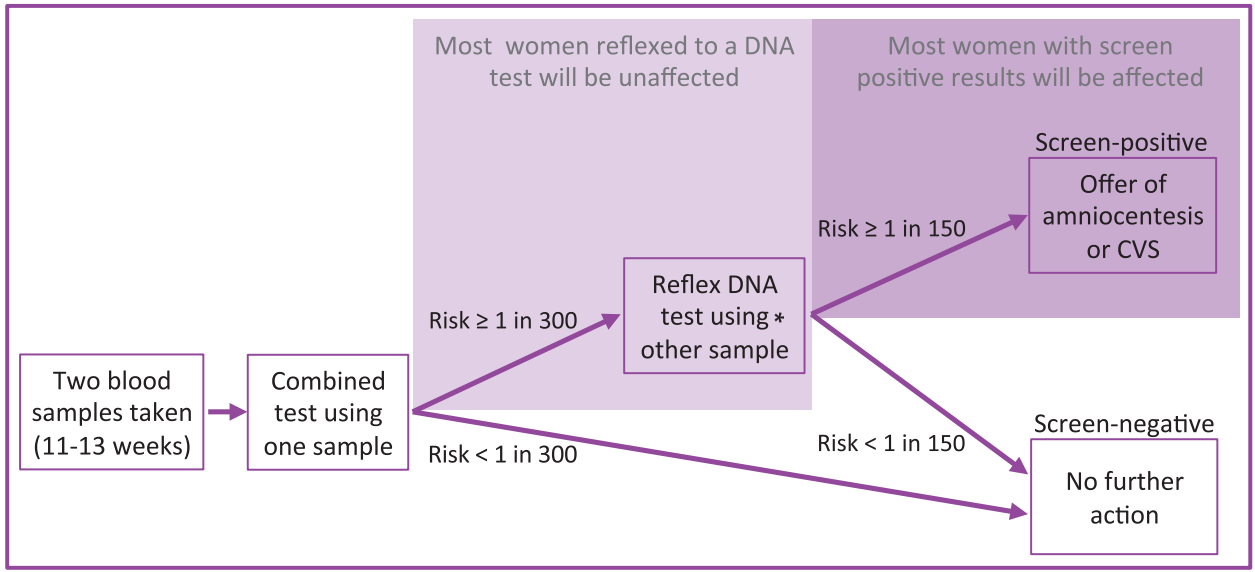
If the diagnostic test is negative and I do not have an affected pregnancy how could I have had a screen-positive result?

Most women with Reflex DNA screen-positive results will have an affected pregnancy. However some may have an unaffected pregnancy. This may be due to the DNA material collected reflecting the chromosomal make-up of the placenta but not the chromosomal make up of the baby. Although the screening test offered here discriminates well between women with affected and unaffected pregnancies it does not do so perfectly. Occassionally there are false-positive results (positive results with unaffected pregnancies) so that a diagnostic test is needed for women with screen-positive results.

What happens if my baby does have Down's, Edwards or Patau syndrome?

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 could discuss the support that is available with your consultant or midwife. If you decide to have a termination of pregnancy your consultant or midwife can make arrangements for this.

Reflex DNA screening pathway



* About 3% of DNA tests fail. Women with a failed DNA tests are invited for a repeat test. If it fails again an Integrated test is reported

Antenatal Screening

OTHER USEFUL ORGANISATIONS

Down's Syndrome Association
www.Downs-syndrome.org.uk 0333 1212 300

Antenatal Results and Choices (ARC)
www.arc-uk.org 0845 077 2290

Support Organisation For Trisomy 18/13(SOFT) UK
www.soft.org.uk 0121 351 3122

For further information, please contact:

Antenatal Screening
Wolfson Institute of Preventive Medicine
Barts and The London School of Medicine and Dentistry
Queen Mary, University of London
Charterhouse Square
London
EC1M 6BQ

Telephone: 020 7882 6293/4
e-mail: a.n.screening@qmul.ac.uk

or find us at:
www.wolfson.qmul.ac.uk/service-1/antenatal-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.

December 2016