Non Invasive Prenatal Testing (NIPT)

Harmony™ and Panorama™

Patient Information

The vast majority of babies are normal. However, all women, irrespective of their age, have a small chance of delivering a baby with a physical and/or learning disability. In some cases this disability is caused by a chromosomal abnormality. The most common chromosome abnormalities are Down syndrome (trisomy 21), Edwards syndrome (trisomy 18) and Patau syndrome (trisomy 13).

The Portland Hospital is offering a new approach to provide the most accurate way of estimating the risk of the fetus having these conditions by using a simple non invasive blood test that analyses genetic material of the baby in the mothers blood.

About the test:

DNA is the genetic material found in each and every cell in our body. The pattern of DNA makes up the genes that code for our characteristics, such as hair and eye colour, and any genetic conditions we may have or carry.

Fetal genetic material can be found in the maternal circulation, raising the possibility of using maternal blood to diagnose fetal disease. Intact fetal cells can be identified in maternal blood, but are not a reliable source of fetal genetic material because these cells are extremely rare and may persist for years after prior pregnancies. By comparison, fetal "cell-free" nucleic acids (DNA and RNA) are more plentiful in the maternal circulation and are unique to the current pregnancy.

DNA from the fetus circulates in the mother’s blood. Cell-free DNA (cfDNA) results from the natural breakdown of fetal cells (presumed to be mostly placental) and clears from the maternal system within hours of giving birth. During a pregnancy, cfDNA can be tested to give the most accurate screening approach in estimating the risk of a fetus having a common chromosome condition sometimes called a trisomy.
What is a Trisomy?

Humans have 23 pairs of chromosomes, which are strands of DNA and proteins that carry genetic information. A trisomy is a chromosomal condition that occurs when there are three copies of a particular chromosome instead of the expected two. The risk of having a baby with a trisomy increases with maternal age.

**Trisomy 21** is due to an extra chromosome 21 and is the most common trisomy at the time of birth. 

**Trisomy 21**, also called Down syndrome, is associated with mild to severe intellectual disabilities and may also lead to digestive disease and congenital heart defects. It is estimated that trisomy 21 is present in 1 out of every 700 newborns.(1)

**Trisomy 18** is due to an extra chromosome 18. Trisomy 18, also called Edwards syndrome, is associated with a high rate of miscarriage. Infants born with trisomy 18 often have congenital heart defects as well as various other medical conditions, shortening their lifespan. It is estimated that trisomy 18 is present in approximately 1 out of every 5,000 newborns.(2)

**Trisomy 13** is due to an extra chromosome 13. Trisomy 13, also called Patau syndrome, is associated with a high rate of miscarriage. Infants born with trisomy 13 usually have severe congenital heart defects and other medical conditions. Survival beyond the first year is rare. It is estimated that trisomy 13 is present in approximately 1 out of every 16,000 newborns.(3)

**Other chromosome conditions that can be screened for**

**Triploidy** is a chromosome condition caused by an extra set of chromosomes. Usually humans have 46 chromosomes that come in 23 pairs. Children with triploidy have 3 copies of every chromosome pair instead of two, resulting in a total of 69 chromosomes. Most pregnancies with triploidy miscarry. The few babies that are born with triploidy have problems affecting the brain, heart, kidneys, and other internal organs. In addition, there can also be birth defects of the face and limbs.

Triploidy is different than other chromosome conditions since it can also cause medical problems for the pregnant mother due to an abnormal placenta. Problems in the mother can include bleeding, extremely high blood pressure, and possibly other medical conditions, including choriocarcinoma in the case of paternal triploidy.

At 10 weeks of pregnancy, about 1 in 1,000 pregnancies are affected with triploidy. Babies born with this condition usually do not live past a few days of life according to the National Institutes of Health (www.nih.gov). Panorama is the only NIPT available in the market that can detect triploidy and is available at The Portland Hospital.

**Monosomy X, also called Turner syndrome**, is a chromosome condition caused by the absence of the second X chromosome in a female. Females usually have two X chromosomes and males have one X chromosome and one Y chromosome. Females who have Monosomy X have one X chromosome instead of two. Monosomy X is associated with a high rate of miscarriage.

The features of Monosomy X can vary from mild to more severe problems. Girls with Monosomy X may have heart defects and kidney problems. Most girls will be shorter than average height and some may have learning problems in school and hearing loss as they get older. Babies born with Monosomy X can have a normal lifespan. It is estimated by the National Institutes of Health that Monosomy X is present in approximately 1 out of every 2,500 newborns. (www.nih.gov).
How are trisomies diagnosed?

The only way to know for sure whether or not a baby has a chromosomal abnormality is to have an invasive test such as Chorionic Villus Sampling (CVS) or Amniocentesis.

**Chorionic villi sampling (CVS)** is a procedure that takes a small amount of tissue from the developing placenta. The tissue is then sent to a laboratory to test the chromosomes. CVS is typically performed between 11 and 14 weeks of pregnancy. CVS is associated with a small risk of miscarriage, 1-2%

**Amniocentesis** is a procedure that withdraws a small amount of fluid that surrounds the fetus. The fluid is then sent to the laboratory to test the chromosomes. An amniocentesis is usually performed around or after the 15 weeks of pregnancy. Amniocentesis is associated with a small risk of miscarriage, 1%

**Risk of having the NIPT:**

The NIPT is a simple safe blood test undertaken by the mother with absolutely no risk to mother or baby.

**NIPT offered at the Portland**

Here at the Portland hospital we offer two types of NIPT

1. Harmony test - Ariosa Diagnostics San Jose California
2. Panorama test – Natera San Carlos California

The differences between the tests are summarised on the following page.
<table>
<thead>
<tr>
<th>Condition</th>
<th>Sensitivity</th>
<th>False Positive rate</th>
<th>Sensitivity</th>
<th>False Positive rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Down’s syndrome (Trisomy 21)</td>
<td>&gt;99%</td>
<td>0.1%</td>
<td>&gt;99%</td>
<td>0%</td>
</tr>
<tr>
<td>Edwards syndrome (Trisomy 18)</td>
<td>98%</td>
<td>0.1%</td>
<td>&gt;99%</td>
<td>&lt;0.1%</td>
</tr>
<tr>
<td>Patau’s syndrome (Trisomy 13)</td>
<td>80%</td>
<td>0.05%</td>
<td>&gt;99%</td>
<td>0%</td>
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<tr>
<td>Turner’s syndrome (Monosomy X)</td>
<td>96.7%</td>
<td>Unreported</td>
<td>91.7%</td>
<td>&lt;0.1%</td>
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<tr>
<td>Triploidy (optional)</td>
<td>Unable to detect</td>
<td></td>
<td>&gt;99%</td>
<td></td>
</tr>
<tr>
<td>Gender (optional)</td>
<td>&gt;99%</td>
<td>Unreported</td>
<td>&gt;99%</td>
<td>0%</td>
</tr>
<tr>
<td>Redraw Rate</td>
<td>3-5%</td>
<td>Unreported</td>
<td>6%</td>
<td></td>
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<tr>
<td>Results available</td>
<td>10-14 working days</td>
<td></td>
<td>10-14 working days</td>
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<tr>
<td>Fetal Fraction reported</td>
<td>Yes</td>
<td>Yes</td>
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<td>Available for twins</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td></td>
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<tr>
<td>Available for Donor eggs</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>Available from</td>
<td>10 weeks gestation</td>
<td></td>
<td>9 weeks gestation</td>
<td></td>
</tr>
</tbody>
</table>

*Note: data on Panorama excludes 4 known mosaic cases: two Monosomy X, one T13, and one T18. Both cases of Monosomy X were called positive, the T18 was called negative and the T13 was no called. False positives and false negatives can occur on all chromosomes due to maternal, fetal and/or placental mosaicism or other causes.*
How will my test results be presented?

Your test result will be reported as low risk or high risk of a fetal trisomy. If the Harmony or Panorama test shows that there is a high risk that the baby has trisomy 21 or 18 or 13, it does not mean that the baby definitely has one of these conditions. You will be offered an invasive test (CVS or amniocentesis) which is the only way to know for sure whether or not an unborn baby has a chromosomal abnormality.

If the Harmony or Panorama test shows that there is a low risk that the baby has trisomy 21 or 18 or 13, it is highly unlikely that the baby has one of these conditions.

Do I need to have any other tests?

The NIPT prenatal test does not provide information on other rare chromosomal abnormalities. Depending on how many weeks pregnant you are it is important for you to have your 12 week scan. If the ultrasound scan shows a high nuchal translucency or other major physical defects such as brain abnormalities, heart abnormalities, the risk for some rare chromosomal defects may be high. In such cases, you may choose to have a CVS or an amniocentesis. The NIPT prenatal test does not provide information on other physical defects such as spina bifida, or information on fetal growth. It is therefore advisable that you have all the usual ultrasound scans during your pregnancy.

In addition to the NIPT and 12 week nuchal translucency scan we recommend that you have ultrasound scans at 20-22 weeks to examine the baby’s anatomy and at 30-34 weeks to examine the baby’s growth.

Transfer of your information outside the European Union

For the purposes of carrying out the Harmony and Panorama Prenatal test, your personal information will be transferred outside of the European Union, to the USA. Please be aware that the laws applicable to your personal data in the USA are different from those operating in the UK, where The Portland Hospital is established.

Who do I contact if I would like more information about the NIPT?

If you have any questions about the NIPT, please do not hesitate to contact a member of staff from the Ultrasound department at the Portland Hospital: 0207 390 6351 or email Dean Meredith, Sonography & Fetal Medicine Lead at dean.meredith@hcahealthcare.co.uk.

References


Websites

5. http://fetalanomaly.screening.nhs.uk/