Screening for Chromosomal Abnormalities at the Harley Street Centre for Women

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 trisomy 21 (Down syndrome), trisomy 18 (Edwards syndrome) and trisomy 13 (Patau syndrome).

The Harley Street Centre for Women has introduced a new approach to provide the most accurate way of estimating the risk of a baby having Down syndrome and other chromosomal abnormalities. This approach combines an early abnormality scan / the Combined test with the new Harmony$_{TM}$ Prenatal Test.

What is trisomy 21, 18 or 13?

Most of us have a normal complement of chromosomes, this being 46 in total, made up of 23 pairs. In trisomy, there is an additional copy of a particular chromosome, resulting in a total of 47 chromosomes. The most frequently occurring trisomy is trisomy 21, more commonly known as Down syndrome. Other trisomies include trisomy 18 and trisomy 13, known more commonly as Edwards and Patau Syndrome, respectively.

- Trisomy 21 is found in around 1 in 700 births and the risk of having a baby affected by trisomy 21 increases with advancing maternal age. The condition is associated with learning disability and some structural problems within the baby's major organs, most commonly heart abnormalities. The life expectancy is around 60 years.
- Trisomies 18 and 13 are found in around 1 in 7,000 births and the risk of having a baby affected by one of these trisomies also increases with advancing maternal age. These conditions are associated with severe learning disability and multiple physical abnormalities. Most affected babies die before or soon after birth, and rarely survive beyond the first year of life.

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. Invasive testing gives very accurate results because genetic material obtained directly from the pregnancy is used for analysis. However, as these procedures involve inserting a needle into the womb to obtain this genetic material, they carry a small but significant risk of causing a miscarriage (1%).

What is the Combined test and the Early Anomaly Scan?

The Combined test is a traditional screening test for chromosomal abnormalities and can be undertaken between 11-14 weeks. It comprises an ultrasound scan and blood test. The ultrasound scan is used to confirm the number of weeks pregnant the woman is and to measure the nuchal translucency (the area at the back of the baby's neck). In addition, other structures within the baby are assessed as abnormalities within them are associated with chromosomal abnormalities; these include the nasal bone and blood flow through the heart and liver. A sample of the mother's blood is taken to measure two hormones produced by the placenta (free βhCG and PAPP-A). The findings from the scan and blood test are combined with the woman's age to calculate the risk for trisomies 21, 18 and 13. The Combined test

can detect up to 95% of babies with trisomy 21, 18 and 13, but it would be necessary for 3-5% of pregnant women to have invasive testing.

The Early Anomaly Scan is an ultrasound scan performed prior to 16 weeks' gestation which involves a detailed examination of the baby's anatomy. This includes examination of the baby's major organs, including the brain, heart, abdomen, stomach, bladder and limbs.

What is the Harmony$_{TM}$ Prenatal 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. Cell free DNA is genetic material which comes from the baby but can be detected in the mother's blood during pregnancy. The exact mechanism as to how the baby's DNA – the cell free DNA - finds its way into the maternal bloodstream is not clear. However, scientists have discovered that cell free DNA is present from early pregnancy and is undetectable 2 hours after the baby is born.

The Harmony$_{TM}$ Prenatal Test analyses cell free DNA in maternal blood and gives a strong indication of whether the baby is at high or low risk of having trisomies 21, 18 and 13.

The Harmony$_{TM}$ Prenatal Test identifies more than 99% of babies affected by trisomy 21, 98% of babies affected by trisomy 18 and 80% of babies affected by trisomy 13. The false positive rate of the Harmony$_{TM}$ Prenatal Test is 1%, i.e less than 1% of women will be required to have a CVS or amniocentesis. Traditional Down Syndrome screening tests have a detection rate of 75-95% for a false positive rate of 3-5%. This means that this novel screening test will detect a greater proportion of babies affected by chromosomal abnormalities, and women will be less likely to require an invasive test (which carries a 1% of causing a miscarriage) following screening.

Who can have the Early Anomaly Scan / Combined test and the Harmony$_{TM}$ Prenatal Test?

- The Combined test and Early Anomaly Scan can be performed in all pregnancies (singleton and multiple) at 11-14 weeks of pregnancy.
- The Harmony$_{TM}$ Prenatal Test can be performed in women carrying a single baby at or after 10 completed weeks of pregnancy, IVF singleton pregnancies including self-donor, unrelated egg donor and surrogate pregnancies.
- The test can also be performed in women carrying twins resulting from patient's own eggs or non-self egg donor.
- This test is not for use in multiple pregnancies other than twins (e.g. triplets) The Combined Test can still be offered in these situations.

What will happen if I choose to have the Early Anomaly Scan / Combined Test and the Harmony$_{TM}$ Prenatal Test?

If you are less than 11 weeks:

You will have two visits to the Harley Street Centre for Women:

- The first visit will be between 10 weeks to 10 weeks and 6 days. of your pregnancy. During this visit, we will explain the test to you and answer any questions you may have. You will then have an ultrasound scan to confirm that you have singleton pregnancy (one baby), that the baby is alive and that the size of the baby agrees with the number of weeks pregnant you are. We will also take a sample of blood from you that will be used for the Harmony$_{TM}$ Prenatal test.
- The second visit will be two weeks later, at 12 weeks. At this visit we will discuss the results of the Harmony$_{TM}$ Prenatal test

and will also carry out an early abnormality scan for detailed examination of the baby's anatomy.

On the basis of the Harmony$_{TM}$ Prenatal test and the early anomaly scan you will be supported to decide whether you wish to have invasive testing or not.

If you are 11-14^{+1} weeks:
You will have one visit to the Harley Street Centre for Women

- During this visit, we will explain the test to you and answer any questions you may have. You will then have an ultrasound examination; this will comprise an early anomaly scan and the ultrasound component of the Combined test. We will also take a sample of blood from you that will be used for the Harmony$_{TM}$ Prenatal test and to measure two hormones in the blood that are produced by the placenta.

On the basis of the Harmony$_{TM}$ Prenatal test, the early anomaly scan and the Combined test results you will be supported to decide whether you wish to have invasive testing.

If you are more than 14^{+1} weeks:

You may have already had Down syndrome screening and an anomaly scan at 18-20 weeks. The Harmony$_{TM}$ Prenatal test for prediction of trisomies is still available to you. We would be happy to see you at the Harley Street Centre for Women to review the results of any previous examinations / tests and to perform a detailed ultrasound examination to examine the baby's anatomy and growth. We will then take a blood sample from you that will be used for the Harmony$_{TM}$ Prenatal test.

On the basis of the Harmony$_{TM}$ Prenatal test you will be supported to decide whether you wish to have invasive testing.

Who carries out the analysis of the Harmony$_{TM}$ Prenatal Test?

We will send your blood sample along with your personal information (including name, date of birth, gestational age) to a company called Ariosa Diagnostics, Inc., San Jose, CA in the USA, who will extract cell-free DNA from your blood and carry out the Harmony$_{TM}$ Prenatal test on the cell-free DNA.

There will be no further clinical testing on this blood and your blood sample will be discarded once we have confirmed the results with you. Ariosa Diagnostics Inc. will not use your blood sample or the extracted DNA samples for any other purpose.

When can I expect to get my results?

The results from the Harmony$_{TM}$ Prenatal Test will generally be available within two weeks and we will either give them to you at the time of the second visit to the Harley Street Centre for Women at 12 weeks or contact you by telephone and letter.
In around 5% of women, the test does not give a result. In this happens to you, we will discuss alternative traditional screening options available to you. If the test does not give a result the first time, Harmony$_{TM}$ may recommend that we send a second sample.

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$_{TM}$ Prenatal 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$_{TM}$ Prenatal 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. The test identifies more than 99%, but not all, of the babies with trisomy 21, 98% of babies with trisomy 18 and 80% of babies with trisomy 13.

Do I need to have any other tests?

The Harmony$_{TM}$ Prenatal Test does not provide information on other rare chromosomal abnormalities. If the Early Anomaly Scan detects a structural problem within the baby's major organs, the risk for some rare chromosomal defects may be high. In this situation you would be offered invasive testing.

In addition to the Early Anomaly Scan and the Harmony$_{TM}$ Prenatal Test we recommend that have ultrasound scans at 20-22 weeks to examine the baby's anatomy and at 30-32 weeks to examine the baby's growth.

What is the next step?

You are invited to take the time to ask all the questions you might have to enable you to make an independent personal decision as to whether you wish to take the Harmony$_{TM}$ Prenatal Test. You are under no obligation to make a decision immediately. If you decide you want to take the Harmony$_{TM}$ Prenatal Test, you will be asked to sign a consent form by one of our doctors.

Whom do I contact if I would like more information?

If you have any questions about the Harmony$_{TM}$ Prenatal Test, please do not hesitate to contact a member of staff from the Harley Street Centre for Women.

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Access to your information and correction

You have the right to request a copy of the information we hold about you. If you would like a copy of some or all of your personal information, please contact us at the address provided below. We want to make sure that your personal information is accurate and up to date. You may ask us to correct or remove information you think is inaccurate. You may contact the UK's data protection authority, the Information Commissioner's Office (www.ico.gov.uk), at any time if you feel we have not complied with your legal rights.