Feidhmeannacht na Seirbhíse Sláinte
Health Service Executive

Cork University Maternity Hospital,
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CUMH prenatal screening : Non-Invasive Prenatal Testing (NIPT)

This leaflet has been provided to help answer some of the questions you may have about NON-INVASIVE PRENATAL TESTING (HARMONY TEST)

Non-invasive prenatal testing (NIPT) analyses cell-free DNA circulating in the pregnant mother's blood. It is a new option in prenatal screening for Down syndrome (Trisomy 21) and other fetal chromosomal conditions Trisomy 13, Trisomy 18 as well as X and Y chromosomal abnormalities. This test can be requested for any singleton pregnancy, including IVF pregnancies, as well as for twin pregnancies.

About the Ariosa Harmony™ Non-Invasive Prenatal Test

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 chromosomal abnormality. The most common type of abnormality is called a trisomy which occurs when there are three copies of a particular chromosome instead of the expected two. This test can detect the following chromosomal abnormalities:

Trisomy 21 is the most common chromosomal abnormality at the time of birth. Also called Down syndrome, it is associated with moderate to severe intellectual disabilities and may also lead to digestive disease, congenital heart defects and other malformations.

Trisomy 18 (Edwards syndrome) and **Trisomy 13 (Patau syndrome)** are associated with a high rate of miscarriage. These babies are born with severe brain abnormalities and often have congenital heart defects as well as other birth defects. Most affected individuals die before or soon after birth, and very few survive beyond the first year of life.

Sex chromosome abnormalities. The sex chromosomes (X and Y) determine whether we are male or female. X and Y chromosomal abnormalities occur when there is a missing, extra, or incomplete copy of one of the sex chromosomes. The Harmony with X, Y test can assess risk for XXX, XYY, XXYY, XXY (Klinefelter Syndrome), and a missing X chromosome in a girl (Turner Syndrome). There is significant variability in the severity of these conditions, but most individuals have mild, if any, physical or behavioural features. If the mother is interested in having this optional testing, she should talk with her healthcare provider to determine if it is right for her.

What are the risks associated with this test?

The testing is non-invasive: it involves taking a blood sample from the mother. The pregnancy is not put at risk of miscarriage, or from other adverse outcomes that are associated with invasive testing procedures such as amniocentesis.

How accurate is this test?

Clinical studies have shown that the *Ariosa* Harmony™ Prenatal Test has exceptional accuracy for assessing fetal trisomy risk.

A "high risk" result is indicative of a high risk for a trisomy. In singleton pregnancies, the test identifies more than 99% of fetuses with trisomy 21, 98% of fetuses with trisomy 18, 80% of fetuses with Trisomy 13 and 96% of fetuses with Turner Syndrome. This test is also >99% accurate for fetal sex.

It is important to note that if the test results show there is a high risk that the fetus has trisomy 21, 18, 13 or sex chromosome conditions, it does not mean that the fetus definitely has one of these conditions, although it is highly likely. For this reason, in the event of a "high risk" (or positive) result, follow-up testing by an invasive procedure is recommended. After the test, the number of women required to have invasive prenatal testing such as CVS or Amniocentesis is less than 1%.

In the same way if the test results show that there is a "low risk" that the fetus has trisomy 21, 18, 13 or sex chromosome conditions, it is unlikely that the fetus has one of these conditions. However, there is a very small risk that not all trisomy fetuses will be detected.

Who can have the test?

Ariosa Harmony™ Prenatal Test can be ordered for women with pregnancies of at least 12 weeks gestational age. The Harmony™ Prenatal Test can now be ordered for all IVF Singleton pregnancies, including those with egg donors. Samples from pregnant women with twins naturally conceived, or those conceived using the patient's own egg, are also accepted. This test does not assess risk for mosaicism, partial trisomies or translocations.

The results will be ready in approximately two weeks. On the basis of the NIPT result and the ultrasound findings, a patient can decide whether or not she wants to have an invasive procedure such as amniocentesis or CVS.

Is there ever a need for a repeat sample?

There needs to be enough fetal DNA in the maternal blood sample to be able to provide a result. If there is insufficient fetal DNA in the sample (occurring in 3% of cases), another blood sample from the mother may be required. This will be processed in the laboratory at no extra charge.

How is the sample obtained?

Once a mother has taken a personal decision that she wants to have NIPT performed, she will be asked to sign a consent form and her blood sample can be taken from a vein in her arm.

Who carries out the analysis of the test?

The sample and completed request form are sent to TDL Genetics in London, after which they will be referred to Ariosa Diagnostics Inc, in the USA. Ariosa performs the Harmony™ Prenatal Test on the DNA extracted from the blood sample.

Will the mother need to have any other test?

The Ariosa Harmony™ Prenatal Test does not provide information on other rare chromosomal abnormalities. If the ultrasound scan shows an increased nuchal translucency in the fetus, or other major physical defects such as brain abnormalities, the risk for some rare chromosomal defects may be high. In such cases, the mother may choose to have a CVS or Amniocentesis directly.

The non-invasive prenatal test does not provide information on other physical defects such as spina bifida, or information on fetal growth.

How do I get the results?

If the result is low risk then no further tests will be offered. You will receive the results in the post usually within 16-18 working days.

If the result is high risk, we will contact you by phone with the high risk result within 14-16 working days of the blood test. You will be given an appointment with a Fetal Medicine Specialist to discuss the results. You will be offered a diagnostic test called an amniocentesis. Amniocentesis will give a definite 'yes' or 'no' answer about Down syndrome or other major chromosome abnormalities, but is associated with approximately a 1% (1 in 100) risk of causing a miscarriage.

It is recommended that high-risk Harmony test results are confirmed by amniocentesis.

How do I make an appointment?

This screening test is not available at your routine booking visit at 12 weeks or at your dating ultrasound between 10-14 weeks. It is a separate clinic that you can book if you are interested in prenatal screening. This test is performed on Monday afternoons in the Aislinn Suite.

Please contact our Harmony clinic at CUMH on (021) 4920550 for an appointment. You can make an appointment by ringing this number between 2-4pm on Monday-Thursday. There are a limited number of appointments available for this clinic.

You must have your 10-14 week dating scan done before we can offer you the Harmony test in CUMH. However, the test is then available to you throughout your pregnancy.

What are the costs?

This test is not funded by the Health Service Executive or by CUMH. It is being made available to you on a cost basis. The charge is €400 for the NIPT (Harmony) test. This includes administration costs, the laboratory charges for the blood tests and data analysis, as well as the courier charges to the laboratories in London and the USA.

How do I pay?

Once the laboratory has received your Harmony test they will invoice you directly for payment at the beginning of the following month.

Who can I contact with questions?

If you have any questions about the Harmony prenatal test or your test results, please contact the Aislinn Suite from Monday to Thursday (2-4pm) and ask to speak to one of the midwives working in the unit.