Non-Invasive Prenatal Testing (NIPT)

Dr Glenn Gardener, Director, Mater Centre for Maternal Fetal Medicine

What is NIPT?

Non-invasive prenatal testing (NIPT) refers to testing of the fetal genome (DNA) through a sample of the mother's blood; hence it is 'non-invasive' and poses no risk to the pregnancy. The major benefit of NIPT is a significant reduction in the need to perform invasive testing eg chorionic villous sampling (CVS) or amniocentesis – procedures which carry a risk of fetal loss of up to 1%.

NIPT is a new technology that detects fragments of cell-free DNA (cfDNA) in the mother's blood. The mother's blood contains a combination of maternal and fetal cfDNA (the 'fetal fraction' of cfDNA within the maternal plasma can vary with gestation and maternal BMI but is around 10%). A minimum threshold of fetal DNA fraction must be detected in the maternal blood sample for reliable testing. The primary source of fetal cfDNA is from placental trophoblast. NIPT uses next generation DNA sequencing technology or single nucleotide polymorphism technology (SNP) to provide a risk for trisomy 21 (Down syndrome) and other specific conditions eg trisomies 18, 13 and monosomy X.

What are the limitations of NIPT?

NIPT does not screen for all fetal abnormalities. NIPT is very specific about the chromosomes it is testing (eg 21,18,13 and X). A negative NIPT test does not completely rule out the chromosomal abnormalities that it is testing for. Patients who themselves carry a chromosomal abnormality, who have had a bone marrow or organ transplant or stem cell therapy may not suitable for NIPT. IVF pregnancies with donor eggs and multiple pregnancies have specific restrictions with some NIPT tests. Neither Qld Health nor Medicare covers any costs of NIPT.

How accurate is NIPT?

Reported detection rates (DR) for trisomy 21 (Down syndrome) and 18 (Edward syndrome) using NIPT are >98% and false positive rates (FPR) are <1%, making NIPT the most accurate screening test currently available for trisomy 21. Detection rates for trisomy 13 (Patau syndrome) and XO (Turner syndrome) are generally less than the detection rates for trisomy 21. Whilst NIPT is a very good screening test, it is not a diagnostic test and invasive testing (amniocentesis) is recommended to confirm a positive NIPT result. Some NIPT providers are now offering additional screening for microdeletion syndromes (the commonest is Di George syndrome or 22q.11 deletion syndrome which occurs in approx. 1 in 3000-5000 pregnancies). Published test performance data for microdeletion screening using NIPT is still limited and professional bodies do not currently recommend NIPT screening for microdeletions.

How reliable is NIPT?

All companies offering NIPT have peer reviewed published data to support their individual claims of test performance. All report sensitivity and specificity for trisomies 21 and 18 at >98%. The rates of detection of trisomy 13 and some sex chromosome abnormalities varies between providers with detection rates from

80-99%. In up 3% of cases, NIPT testing will fail to give a result and if still not successful on repeat testing, these cases have an increased risk of chromosomal abnormality. Therefore if a NIPT test fails to report a result on repeat NIPT testing, referral is recommended to Mater Maternal Fetal Medicine.

When is NIPT performed?

The test can be done as early as 9 weeks gestation (Panorama only) but most NIPT providers offer testing from 10 weeks gestation. The fetal fraction is often higher with increasing gestation so doing the test closer to 12 weeks is recommended particularly in higher BMI women.

How can patients access testing?

Patient and doctor information, request forms, consent forms and information regarding blood collection and interpreting results are available online with each provider. The test is currently available through all the major Pathology providers. The turnaround time from blood sampling to result is 1-2 weeks. The 'no-call' rate or an indeterminate result occurs in 1-5% of samples and if this occurs a 2nd sample can be tested at no additional charge.

How does NIPT impact on other screening tests e.g. Combined First Trimester Screen (CFTS)?

If NIPT has already been performed in a pregnancy, the risk result for trisomy 21 will be more accurate than any other currently available screening test. Invasive karyotyping can still helpful in some circumstances (eg enlarged nuchal translucency) because it looks at all 23 pairs of chromosomes and additional testing may sometimes also be indicated e.g. chromosomal microarray. If the nuchal translucency measurement is increased (e.g. >3.5mm) or other structural anomalies are seen on scan, a negative NIPT result will be reassuring for trisomy 21 but other conditions such as atypical chromosomal abnormalities may not be detected e.g. an unbalanced chromosome rearrangement. For high risk first trimester screen results, some patients may prefer invasive testing (e.g. CVS) over NIPT to obtain an earlier, definitive and more comprehensive result that excludes more conditions than the common trisomies. Appropriate counselling is recommended before undertaking invasive tests and this is available through Mater MFM.

When should I refer to Mater Mothers Hospital Maternal Fetal Medicine?

Patients with positive/high risk NIPT results or who request invasive testing should be referred to the Mater Centre for Maternal Fetal Medicine for review, counselling and invasive testing if requested.

If inconclusive, indeterminate or no result from NIPT there is an increased risk of the fetus having a chromosomal abnormality. Further review and management is available through the Mater Centre for Maternal Fetal Medicine.

Is a CFTS required for Down syndrome screening if a NIPT has already been performed?

No. Calculating an individual risk result for trisomy 21 is not required if NIPT already been performed. The 12-13 week scan should still assess the nuchal translucency thickness and look for other major structural anomalies eg anencephaly, megacystis, body-stalk anomaly, holoprosencephaly and omphalocele. A 2nd trimester morphology scan is still recommended for evaluation of fetal structural abnormalities. Some ultrasound providers will specifically offer 1st trimester ultrasound assessment for structural abnormalities and risk assessment for early onset pre-eclampsia.

An MFM doctor can be contacted for advice during office hours Mon-Fri on (07) 3163 1597 or after hours through Mater switchboard (07) 31638111

***This field of prenatal testing is changing rapidly so please check that current information is correct with Provider (Feb 2017)**