Fact Sheet

Confirmatory Prenatal Diagnosis following Preimplantation Genetic Testing

MONASH IVF GROUP

Key points:

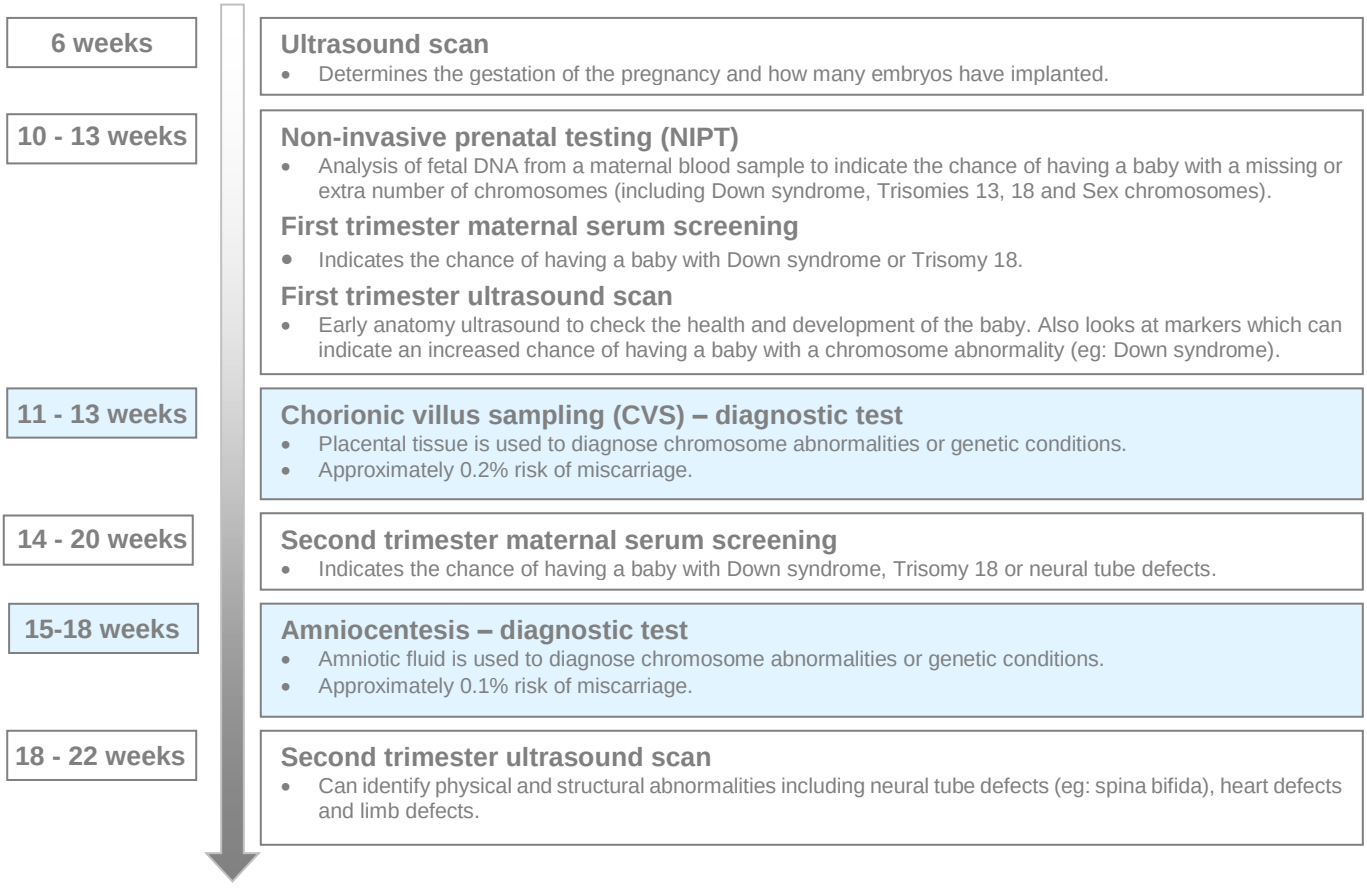
- Preimplantation Genetic Testing (PGT) is a screening test and **is not** 100% accurate. If a pregnancy is achieved following PGT, prenatal diagnosis during pregnancy is recommended to confirm the PGT result.
- There are a number of different prenatal tests available to assess the development of the baby during the pregnancy. Some of these prenatal tests are screening tests (eg: ultrasound, maternal serum screening, non-invasive prenatal testing), while others are diagnostic tests (eg: Chorionic Villus Sampling and Amniocentesis).
- Your IVF specialist and/or obstetrician will be able to advise you which of these prenatal testing option/s are the most appropriate for you.

What is confirmatory prenatal diagnosis following PGT?

Preimplantation Genetic Testing (PGT) is a technique that enables IVF embryos to undergo genetic screening before a pregnancy is established. The results obtained from PGT are not 100% accurate. The accuracy of the result can range from 90% to 99% depending on the type of test being performed, the quality of the sample being tested and the clarity of results obtained. Consequently, there may be up to a 10% error rate associated with any test. It is recommended that all patients who achieve a pregnancy following PGT undergo prenatal testing to confirm the PGT result.

There are many different prenatal testing options available during pregnancy (Figure 1). Some of these prenatal tests are classified as screening tests (which indicate whether or not there is an increased chance that the baby will have a genetic condition), while others are classified as diagnostic tests (which provide a definitive diagnostic result, for example after a screening test has indicated an increased chance of an abnormality).

Figure 1: Prenatal testing options available during pregnancy. The white boxes represent screening tests; the shaded boxes represent diagnostic tests. Your doctor will advise which of tests are recommended.



How are different prenatal tests done?

Ultrasound scans and maternal serum screening

Ultrasound scans are performed during pregnancy to examine the anatomy of the developing baby. During these scans, the sonographer will check for structural abnormalities in the developing baby. Some of these structural abnormalities may indicate an increased chance that the baby will have a chromosome condition, such as Down syndrome.

Results of the first trimester ultrasound scan are often assessed in conjunction with maternal age and maternal serum screening results (ie: results from a blood test that is performed on the mother). This is referred to as the 'first trimester combined screening test' and is used to determine if there is an increased chance that the baby will have Down syndrome or other chromosome abnormalities. The accuracy of detecting Down syndrome is approximately 85-90% using this screening test. Women with an "increased probability" result will be offered a prenatal diagnostic test (ie: CVS or amniocentesis).

Non-invasive prenatal testing

Non-invasive prenatal testing (NIPT) is usually performed from 10 weeks of gestation and involves collecting a blood sample from the mother. This blood sample contains genetic material (DNA) from both the mother and the baby. By screening the genetic material from the mother's blood sample, it is possible to determine whether the baby has an increased chance of having some of the most common chromosomal conditions, including Down syndrome (Trisomy 21), Edward syndrome (Trisomy 18) or Patau syndrome (Trisomy 13). If requested, NIPT can also be used to determine fetal sex and screen for sex chromosome conditions. Following testing, NIPT results will be reported as either "low probability" or "high probability". A "low probability" result indicates that the expected number of chromosomes were detected, while a "high probability" result indicates that too many or too few copies of one of the chromosomes has been identified. If a "high probability" result is returned, follow up diagnostic testing is recommended (ie: CVS or amniocentesis).

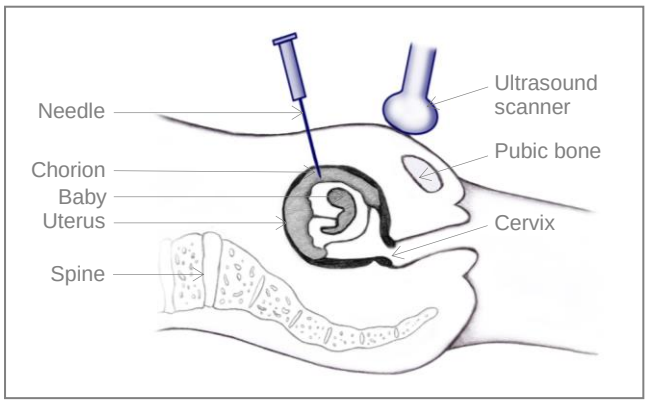
Chorionic villus sampling

CVS is performed between 11 and 13 weeks of gestation (Figure 2). This testing is usually offered to patients with:

- Increased probability first trimester screening or NIPT results
- Increased nuchal translucency or other abnormal ultrasound findings
- A family history of a chromosome abnormality or other genetic disorder
- Increased risk for a genetic disease due to known carrier status
- Advanced maternal age (ie: above 37 years) and desire for definitive exclusion of chromosomal abnormality

The skin of the lower abdominal wall is cleansed with an antiseptic alcohol solution. A local anaesthetic is used to numb the skin where the sampling needle will be inserted. A thin needle is inserted through the abdomen and into the uterus (womb). The needle is observed at all times during the procedure using ultrasound to ensure that it does not go near the baby. A small sample of the placental tissue (chorionic villi) is removed for genetic analysis. Cells from the placental tissue usually have the same genetic makeup as the baby and can therefore be used for genetic testing. In rare cases, the CVS result may be difficult to interpret or a result may not be provided. In these cases an amniocentesis is offered to clarify the results. There is a 1 in 500 (0.2%) risk of miscarriage following CVS. This is usually related to infection introduced at the time of the procedure. Antiseptic precautions are taken to minimise this risk.

Figure 2: Chorionic villus sampling



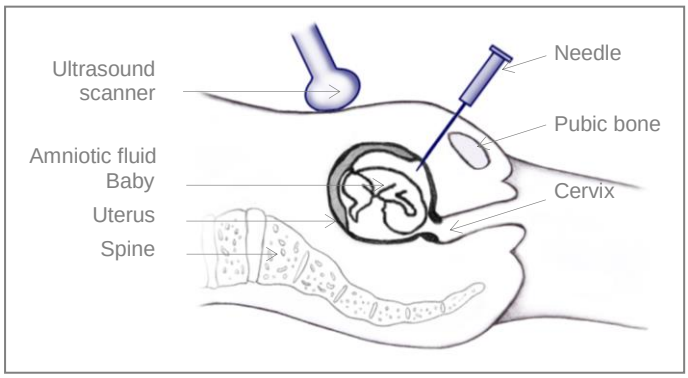
Amniocentesis

Amniocentesis is usually performed between 15 and 18 weeks of gestation (Figure 3), but can be performed at any time throughout the remainder of the pregnancy. This testing is usually offered to patients with:

- Increased probability first trimester screening or NIPT results
- Increased nuchal translucency or other abnormal ultrasound findings
- A family history of a chromosome abnormality or other genetic disorder
- Increased risk for a genetic disease due to known carrier status
- Advanced maternal age (ie: above 37 years) and desire for definitive exclusion of chromosomal abnormality

An ultrasound examination is performed to confirm gestation, assess the position of the placenta and assess the baby. The skin of the lower abdominal wall is cleansed with an antiseptic alcohol solution. A thin needle is inserted through the abdomen and into the uterus (womb). The needle is observed at all times during the procedure using ultrasound to ensure that it does not go near the baby. A small sample of amniotic fluid (which contains cells shed by the fetus) is removed for genetic analysis. Results are typically available in 10 – 21 days. Amniocentesis is one of the most reliable prenatal tests and provides results with an accuracy of 99.9%. In rare cases, a result may not be obtained and a repeat sample may need to be taken. There is an approximate 1 in 1000 (0.1%) risk of miscarriage following amniocentesis. This is usually related to infection introduced at the time of the procedure. Antiseptic precautions are taken to minimise this risk.

Figure 3: Amniocentesis



What to do next?

Your IVF specialist and/or obstetrician will be able to advise which prenatal testing option/s are the most appropriate for you. The type of prenatal testing that is recommended will often be related to the initial indication for PGT. Table 1 outlines common prenatal testing pathways based on the different indications for PGT. Please note that these prenatal testing pathways are given as a guideline only. You should follow the advice of your IVF specialist and/or obstetrician who will have more detailed information regarding your reproductive history and personal circumstances.

Table 1: Common prenatal pathways based on the different indications for PGT

Indication for PGT	**Possible prenatal testing pathway**
PGT-A *Testing for chromosome copy number*	Undertake non-invasive prenatal testing (NIPT) - If a "low probability" result is returned, further prenatal testing may not be warranted. - If a "high probability" result is returned, consider undertaking a diagnostic test (ie: CVS or Amniocentesis) to clarify the result.
PGT- Sex Selection *Approved sex selection to avoid/reduce the risk of X-linked genetic conditions*	Undertake non-invasive prenatal testing (NIPT) - If the NIPT result confirms the desired sex and is "low probability" for chromosome abnormalities, further prenatal testing may not be warranted. Correlation of fetal sex with ultrasound is recommended. - If the NIPT result indicates the undesired sex and/or is "high probability" for chromosome abnormalities, consider undertaking a diagnostic test (ie: CVS or Amniocentesis) to clarify the result.

PGT-SR *Testing to avoid unbalanced forms of a structural chromosome rearrangement (eg: translocation)*	Undertake CVS or Amniocentesis to confirm the PGT result. Some NIPT providers offer translocation analysis. There is insufficient evidence to recommend this screening for translocation carriers, and false positive and false negative results occur.
PGT-M *Testing for a specific monogenic disorder due to a family history of genetic disease*	Undertake CVS or Amniocentesis to confirm the PGT result.

You may like to contact your local Genetic Counselling Service (using the details provided below) to discuss these prenatal diagnostic testing in more detail. This will help ensure you are fully informed about your prenatal testing options and the associated benefits, risks and limitations.

Genetic counselling service contact details

Victoria	
Metropolitan Services	
Monash Ultrasound for Women	(03) 9427 7610
Clayton (Monash Medical Centre)	(03) 9594 2026
Parkville (The Royal Women's Hospital)	(03) 8345 2180
Mercy Hospital for Women	(03) 8458 4346
Regional Services	(03) 8341 6297 Ballarat, Bendigo, Geelong, Mildura, Warrnambool (03) 8341 6332 Gippsland

New South Wales	
Sydney Ultrasound for Women	1300 557 226
The Children's Hospital at Westmead	(02) 9845 3273
Albury/Wodonga	(02) 6041 3545

Australian Capital Territory	(02) 6244 2133

Queensland	(07) 3636 1686

South Australia	
Repromed (Dulwich)	(08) 8333 8111
SA Clinical Genetics Service (Women's and Children's Hospital)	(08) 8161 7375

Tasmania	(03) 6222 8296

Western Australia	(08) 9340 1525

New Zealand		
Auckland	(09) 307 4949 Extn: 25870	Toll Free: 0800 476 123
Wellington	(04) 385 5310	Toll Free: 0508 364 436
Christchurch	Ph: (03) 378 6574	Toll Free: 0508 364 436