FIRST TRIMESTER SCREENING FOR FETAL ABNORMALITY AND PREGNANCY COMPLICATIONS

Women can be screened for increased risk of the following conditions in the first trimester of pregnancy:

<table>
<thead>
<tr>
<th>Condition</th>
<th>Prevalence per 1000 pregnancies</th>
<th>Test</th>
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<tbody>
<tr>
<td>Down Syndrome (Trisomy 21)</td>
<td>2 per 1000</td>
<td>NIPT or cFTS</td>
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<tr>
<td>Trisomy 13 and 18</td>
<td>&lt; 1 per 1000</td>
<td>NIPT or cFTS</td>
</tr>
<tr>
<td>Other genetic abnormalities</td>
<td>1 per 1000</td>
<td>cFTS and US</td>
</tr>
<tr>
<td>Early preeclampsia (&lt;34w)</td>
<td>4 per 1000</td>
<td>Biochemistry and US</td>
</tr>
<tr>
<td>Major structural abnormality</td>
<td>20 per 1000</td>
<td>US</td>
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<tr>
<td>Congenital cardiac disease</td>
<td>8 per 1000</td>
<td>US</td>
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The Combined First Trimester Screen calculates the chance that a woman is carrying a fetus with Down Syndrome, combining maternal age, biochemistry (PAPP-A and BHCG), and the ultrasound measurement of the nuchal translucency. In most studies, the cFTS is able to detect approximately 90% of fetuses with Down Syndrome, for a false positive rate of 5%. At Women’s Imaging, we would expect our detection rates to be higher (around 95%), and false positive rates to be lower, as we are one of the few centres in Australia to incorporate the additional features of nasal bone and ductus venosus into our calculation of the likelihood of Down Syndrome. Women having cFTS at Women’s Imaging can be simultaneously screened for all of the other complications listed above.

Non-invasive prenatal testing (NIPT) evaluates fragments of placental DNA in the maternal circulation, specifically targeting chromosomes 13, 18, 21, X and Y. It is more accurate than cFTS in screening for Trisomy 21, 13 and 18, with reported sensitivity and specificity of over 99%. However, it is still a screening test, and false positives and negatives do occur. NIPT may also be used to screen for a limited number of single gene disorders, but the positive predictive value is low. Up to 5% of women will have a failed test, and will be offered a redraw or cFTS. When women with failed tests are taken into account, the performance of NIPT is similar to cFTS.

NIPT may not be a suitable test for women with a history of recent treatment for cancer, organ transplant, treatment with low molecular weight heparin, autoimmune conditions, or early demise of a twin.

NIPT may be used as first line screening for Trisomy 13, 18 and 21, or as a second line screen for women who are given a high likelihood result after cFTS. NIPT does not screen for any of the other conditions listed above, and, as a minimum, it is recommended that women choosing to have NIPT as first line screening should also have an early anatomy scan with nuchal translucency assessment around 13 weeks. Women having first line NIPT may also choose to have biochemistry performed to screen for preeclampsia and atypical genetic conditions.

Screening for increased risk of early preeclampsia involves assessment of demographic and historical factors, maternal blood pressure, biochemistry, and uterine artery blood flow. This method of prediction is more sensitive and specific than using historical risk factors alone, and allows better targeting of preventative measures such as low dose aspirin and calcium supplementation.

Increasing expertise in first trimester ultrasound now allows us to identify or suspect around 80% of major structural abnormalities at the time of the first trimester scan. Assessment of nuchal translucency and the ductus venosus (also used in cFTS) also screens for an increased risk of structural heart malformation and other syndromes.

Abnormalities of anatomy, nuchal translucency, or biochemistry may occasional lead to the identification of an atypical genetic syndrome. This refers to any genetic abnormality other than the common conditions listed above, and encompasses a wide range of disorders.
Suggested approach:

7-9 weeks: discuss screening options, evaluate need for dating scan

Dating scan at 7 – 9 weeks for women if:
- Uncertain dates
- Concern for pregnancy viability or location
- Choosing NIPT as first line screen

Screening for Trisomy declined

NIPT as first line screen

Blood for NIPT at 10-11 weeks

Screening by cFTS

Biochemistry at 10-11 weeks optional for preeclampsia screening

Ultrasound scan at 11 – 13+6 weeks (12-13 weeks ideal)

Biochemistry at 10-11 weeks

16 week early morphology scan recommended for women at increased risk of structural malformation eg previous history, suspicion of abnormality on first trimester scan, abnormal biochemistry, nuchal translucency or ductus venosus

20 week morphology scan