4 February 2014

Dear Doctor,

Re: Combined First Trimester Screening and Non-Invasive Prenatal Testing: Changes in risk assessment advice at Royal Prince Alfred Hospital.

I would like to make GPs involved in our obstetric shared care program aware of the fact that we will be making some changes to the Down syndrome screening program run through RPA Obstetric and Gynaecological Ultrasound.

These changes are designed to facilitate access to non-invasive prenatal testing (NIPT). NIPT, or molecular testing of cell free fetal DNA in the maternal circulation, is highly effective at screening for Downs with reported sensitivity of 99% and specificity >99%. The current cost of this test ($495 from 3 February 2014) makes it prohibitive for first line screening in a public health program. We are therefore providing access to this test as a second line screening tool, for women at high or intermediate levels of risk after combined first trimester screening. The NIPT test is not available through Medicare and women will have to fund this test themselves. The tests have reduced in price significantly over the last year and are currently retailing around $500.

The major change that GPs will see in our screening program will be in the manner in which risks from combined first trimester screening are reported. Risks are currently calculated from maternal age, nuchal translucency measurement, defining presence or absence of the nasal bone and from assessment of maternal serum BhCG and PAPP-A concentrations. This process will not change, but the counseling based on risk stratification (currently either described as a high or low risk for Down syndrome) will be different. Risks will now be defined in four groups:

**A risk of 1:2 to 1:50 will be defined as a “high risk” result.** Women who have a high risk result will be contacted by hospital staff and will be advised that invasive testing (a CVS or amniocentesis) would be the most appropriate way to obtain further information. Women who
wanted to avoid an invasive test could have NIPT, but have to recognize that NIPT does not detect all abnormalities seen through traditional routes of karyotyping.

**A risk of 1:50 to 1:300 will be defined as an “increased risk” result.** Women will be informed by hospital staff about both invasive testing (CVS or amniocentesis) and NIPT options. Invasive testing will continue to be performed with no out of pocket costs to the patient at the point of care. NIPT will have to be funded by the patient and payment for this test will be made directly to the company providing the NIPT service. We can facilitate this by ensuring adequate counseling and arranging phlebotomy and transport and there will be no out of pocket costs to the patient for facilitating testing.

**A risk of 1:300 to 1:1000 will be defined as a “low risk”**. These results will be reported back to the referring GP for dissemination to the patient. Women in this risk category are not currently advised to have an invasive test and, due to the risk of miscarriage from CVS or amniocentesis we do not propose to change this advice. NIPT does, however, offer a potential method of reassurance that does not expose the pregnancy to any risk and we recognize that women may want to take advantage of this new test for added reassurance. Information on the availability of NIPT will be included in the written report from combined first trimester screening. If, on discussion of this result, women in this risk category chose to have NIPT, we are happy to be contacted to arrange a further appointment where we can facilitate testing.

**NIPT tests can be arranged by contacting:**

Our genetics counselors:
Zara Richmond 02 9515 5015 / RPA pager 81213
Ron Fleischer 02 9515 6999 / RPA pager 88569

Our administration manager:
Kylie Wright 02 9515 8887 / pager 81668 / Fax 02 9515 3811

**Ultrasound appointments / troubleshooting – please contact:**

Obstetric / Gynaecology Ultrasound reception: 02 9515 6042
The ultrasound fellow (Dr Sumathi Rajendran): RPA pager 87253
The MFM fellow (Dr Wendy Carseldine): RPA pager 81645

**A risk less than 1:1000 will be defined as a “very low” risk result.** These results will be reported back to the referring GP for dissemination to the patient. We do not see any obvious value in advising these women to have NIPT. The report will not include a statement about the availability of NIPT. If, in the process of discussion of results, it becomes apparent that your patient would like to have NIPT, we would be happy to facilitate this.
This model of screening has been described as a 'contingent' model; the use of NIPT being contingent on the outcome of combined first trimester screening. This approach has the advantage that it potential allows higher sensitivity (projected to increase from 90 to 97% if all women with a risk between 1 in 300 and 1 in 1000 took up the option of NIPT) whilst reducing the false positive rate (currently 5%, with projected reduction to 1.5% by offering NIPT to women with a risk between 1 in 50 and 1 in 300). We see this as a major improvement in the screening process and will endeavor to demonstrate the value of this new test so that we can provide funding for this initiative in the future.

There is currently no on-shore provider of NIPT and we shall send samples to laboratories in the United States. The laboratories used are accredited to American pathology standards.

I have attached a copy of our patient information sheet for NIPT and an article describing the pros and cons of NIPT. The laboratory's also have comprehensive educational resources, for both clinicians and patients, on the internet. Examples include:

The Ariosa 'Harmony' test:
Patient information: [http://www.ariosadx.com/for-pregnant-women/](http://www.ariosadx.com/for-pregnant-women/)

The Natera 'Panorama' test:
Patient information: [http://www.panoramatest.com/prenatal_test_overview](http://www.panoramatest.com/prenatal_test_overview)
Information for healthcare providers: [http://www.panoramatest.com/welcome_clinicians](http://www.panoramatest.com/welcome_clinicians)

I am happy to answer any questions you may have about these changes to our screening process and can be contacted by email (jon.hyett@sswhs.nsw.gov.au). We are also able to arrange further counseling for any patient who has outstanding questions about this new test.

Best wishes,

Clinical Professor Jon Hyett
Head of High Risk Obstetrics
RPA Women and Babies