Placental growth factor as a marker for pre-eclampsia

In the past, pre-eclampsia has been difficult to diagnose. However, a new test that measures serum placental growth factor (PLGF) is providing a high level of accuracy in identifying those women at risk of developing the condition later in their pregnancies.

Pre-eclampsia or pre-eclamptic toxaemia (PET) is defined as the new onset of hypertension and proteinuria after 20 weeks of gestation. It affects about 5% of pregnancies and is responsible for significant maternal and neonatal morbidity and mortality—eclampsia is responsible for around 12% of maternal deaths worldwide.

Although the exact cause is still uncertain, it is known that PET is associated with an imbalance in circulating pro- and anti-angiogenic proteins in the maternal circulation. Placental growth factor (PLGF) is an important pro-angiogenic factor belonging to the VEGF (vascular endothelial growth factor) family of proteins. In normal pregnancy, the concentration of PLGF increases progressively from week 12, reaching a peak during weeks 29–32 and decreasing thereafter. However, in early onset PET, anti-angiogenic factors such as sFlt1 (soluble FMS-like tyrosine kinase) and sEng (soluble endoglin) are released by an abnormal placenta into the blood. There they antagonize the effects of pro-angiogenic factors such as VEGF and PLGF.

Compared with controls, PLGF levels for women who later develop PET are significantly lower, and this difference can be measured as early as week 12. The consequence of these changes is incomplete invasion of fetal cytotrophoblasts into the maternal uterine wall, resulting in placental vessels with decreased capacity and increased resistance.

Normal pregnancy

Placenta and developing fetus are provided with sufficient maternal oxygen and nutrients:

- fetal cytotrophoblast cells invade the maternal uterine wall
- uterine spiral arteries are remodelled into large vessels with high capacity and low resistance

Pre-eclamptic pregnancy

Inadequate blood flow between placenta and uterus:

- invasion of cytotrophoblasts is incomplete—they can only be found in superficial layers of uterus
- uterine spiral arteries fail to be invaded, resulting in vessels with a decreased capacity and increased resistance
Changes to screening test for plasma catecholamines

From July 2014 plasma catecholamines and 24-hour urine catecholamines will no longer be used as the screening test for diagnosis of pheochromocytoma and paragangliomas. They will be replaced by the diagnostically more sensitive plasma-free metanephrines. A single sample for plasma-free metanephrines will be collected when 24 hour urine catecholamines are requested for SCREENING purposes.

Placental growth factor cont
The degree of adverse maternal and fetal consequences is inversely related to the gestational age at onset of pre-eclampsia. PET is classified into three categories:
- early onset at 20–34 weeks (severe pre-eclampsia)
- intermediate onset at 34–37 weeks (medium pre-eclampsia)
- late onset after 37 weeks (moderate pre-eclampsia)

Of course, such measurements would be relatively pointless without the potential to intervene in the progression of the disease. Fortunately, it has now been shown that treatment with low-dose aspirin will significantly reduce the prevalence of pre-eclampsia if started before 16 weeks gestation. In a recent study, PET prevalence in the treatment group was 9.3%, compared with 21.3% in controls. This dosage of aspirin also appears to be quite safe with respect to fetal development and maternal wellbeing.

This test is generally requested as part of the first trimester screen (11–13 weeks gestation), but it should be requested separately as it currently does not attract a Medicare rebate. The PLGF assay is performed on the Kryptor platform; the cost is $58. PLGF may be requested as a stand-alone test at any stage during pregnancy as required for PET screening.

For optimal sensitivity in screening for PET, PLGF is combined with a number of other parameters. In addition to PLGF, PAPP-A, mean arterial pressure (MAP), uterine Doppler (uA-PI) and maternal history are combined to give a final risk calculation. This is usually performed by standard screening software, such as that provided by the Fetal Medicine Foundation (FMF) or Viewpoint (Siemens). The combined test results in a detection rate for early PET of greater than 90%.

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<th>DR at 5% FPR</th>
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<tbody>
<tr>
<td>33</td>
<td>64</td>
<td>84</td>
<td>87</td>
<td>92</td>
<td>96</td>
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<td>88</td>
<td>93</td>
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Different studies with resulting detection rates by using different screening methods

- Detection rate
- False positive rate
- Maternal history
- Mean arterial blood pressure
- Uterine artery pulsatility index

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SNP Collection Centres Locator App now available

With our new App, it’s now easier than ever to locate Sullivan Nicolaides Pathology collection centres.
- using a built-in GPS feature and the device’s current location, surrounding SNP collection centres are displayed
- filter for opening days and procedural tests to find the most conveniently located SNP collection centre

Sullivan Nicolaides Pathology is now performing anti-phospholipase A2 receptor antibodies testing to aid in the diagnosis of idiopathic membranous nephropathy. We will be using the EUROIMMUN anti-PLA2 receptor indirect immunofluorescence test, which has excellent sensitivity and specificity.

Idiopathic membranous nephropathy is a chronic inflammatory disease of the kidneys resulting in proteinuria and progressive loss of renal function. Patients can present with proteinuria alone or with nephrotic syndrome. More recently, autoimmune damage to renal podocytes, has been suggested as the cause, with antibodies specifically targeting the M-type phospholipase A2 receptors expressed on renal podocytes.1

This test uses anti-PLA2R transfected HEK 293 cells; patient antibodies that are bound are then detected. The test result is expressed as a titre, with a 1:10 titre being considered positive. The utility of titre monitoring has yet to be established. The test result is expressed on renal podocytes, has been suggested as the cause, with antibodies specifically targeting the M-type phospholipase A2 receptors expressed on renal podocytes.

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Reference