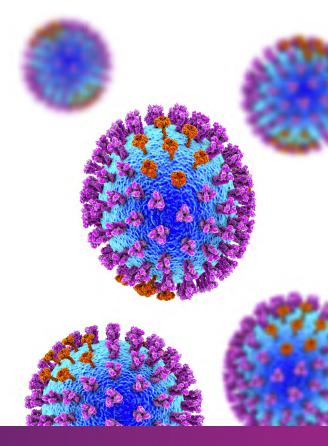


PATHOLOGY FOCUS

Medical Newsletter



July 2019 – Newsletter 6

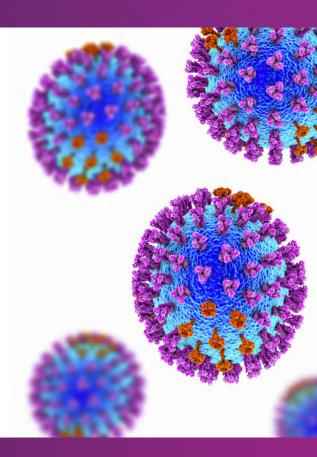
Inside this Newsletter:

- Influenza 2019 & Respiratory Pathogen PCR Testing
- H. pylori & Urea Breath Testing
- Screening for Early Onset Pre-Eclampsia

Confirmed flu cases in 2019 already greater than 2018

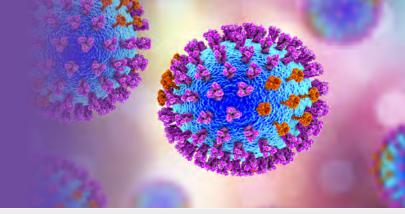
By Dr Linda Dreyer

Although influenza and influenza-like illnesses typically peak in August, Australia has experienced a higher than normal rate during the 2019 summer and autumn. Health experts are warning Australia is on track for a killer flu season, with numbers showing three times as many people have been diagnosed with the virus so far this year, compared to the same period in previous years.



WA

In March this year, more than 10,000 people were diagnosed with the flu. As of 5th June, there had already been a total of 69,380 laboratory confirmed notifications of influenza in 2019. Last year there were 58,570 confirmed influenza cases in Australia. Although we have already surpassed the total number for 2018, laboratory confirmed cases may not show the full extent of influenza as most people still do not get tested.



Who is at risk of complications?

- Elderly people
- Children under 6 months old
- Pregnant women including up to 2 weeks post-partum
- People with chronic conditions or immunosuppression

Why test for respiratory virus?

Other respiratory viruses such as respiratory syncytial virus (RSV), human metapneumovirus and parainfluenza

viruses have been associated with severe lower respiratory tract infection in children. There has also been a resurgence of RSV in the elderly due to waning immunity. It is not always easy to distinguish these infections based on a clinical picture.

The multiplex PCR to diagnose influenza and respiratory viral infections allows the clinician to have a quick and accurate diagnosis. This will enable the clinician to instigate earlier targeted treatment, avoiding inappropriate antibiotic therapy.

Respiratory Pathogen PCR Testing at Clinical Labs

Our rapid respiratory viral assay is performed daily, 7 days a week during flu season. Our increased assay specificity and sensitivity improves the accuracy and speed of diagnosis.

Turnaround Time	24hrs – Urgent	>24 hrs	
Tests included	 Influenza A & B RSV (A&B) Parainfluenza 1, 2, 3, & 4 Human Metapneumovirus Human Adenovirus Human Rhinovirus 	 Influenza A & B RSV (A&B) Parainfluenza 1, 2 & 3 Human Metapneumovirus Human Adenovirus Human Enterovirus/Rhinovirus Mycoplasma pneumoniae Bordetella pertussis Bordetella parapertussis 	
What to Request:	Respiratory Viral Screen/Multiplex PCR	Extended Multiplex PCR	

Flu A&B

99.3% Sensitivity

Specificity 98%

Additional clinical tests recommended based on relevant symptoms:

- If you suspect a lower respiratory infection then the appropriate sample is sputum for MCS
- If the patient presents with pharyngitis symptoms then obtain a swab from the throat for culture

How to Order PCR Tests:

- To assist the laboratory during flu outbreaks, please limit testing to suspected pathogens to ensure rapid result delivery (see table above)
- Samples required:
 - Nose/throat or nasopharyngeal swab(s) (must use dry flocked swab) or
 - o Nasopharyngeal/tracheal aspirates or
 - o Sputum
- Cost: Medicare bulk billing available and subject to Medicare guidelines and criteria



Dr Linda Dreyer

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Dr Linda Dreyer received her Master's degree in Clinical Microbiology (MMed (Path)) from the University of Pretoria in 2006. She worked as a consultant for the National Health Laboratory Services (NHLS) in Pretoria until January 2008 and also sat on the Infection Control Committee and the Antimicrobial Stewardship Committee of the Pretoria Academic Hospital. She came to Melbourne and joined Australian Clinical Labs (formerly Healthscope Pathology) in 2008 as a Senior Registrar and obtained Fellowship of The Royal College of Pathologists of Australasia (FRCPA) in 2010.

Local pathologist near you



Dr Sudha Pottumarthy-Boddu

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Dr Sudha Pottumarthy-Boddu completed her Pathology/ Microbiology Fellowship training with the Royal College of Pathologists of Australasia. She comes to us from Houston, Texas, where she was Assistant Professor in the Department of Pathology and Laboratory Medicine at the University of Texas, School of Medicine. She was also the Technical Director of the Clinical Laboratory Services at the Houston Department of Health and Human Services.

harmony®

Pregnancy screening for chromosomal abnormalities



Non-invasive prenatal testing (NIPT) based on cell-free DNA analysis is not diagnostic: results should be confirmed by diagnostic testing. Before making any treatment decisions, all women should discuss their results with their healthcare provider, who can recommend confirmatory, diagnostic testing where appropriate. The Harmony Prenatal Test was developed by Ariosa Diagnostics. The Harmony Prenatal Test is performed in Australia. HARMONY PRENATAL TEST and HARMONY are trademarks of Roche. All other trademarks are the property of their respective owners.

AVAILABLE NOW AT CLINICAL LABS

NOW OFFERING 22q11.2 Microdeletion

Patients are asking — and clinicians need to be equipped with the right knowledge.

Harmony® is the most broadly studied non-invasive prenatal test (NIPT) for Down syndrome (trisomy 21), Edwards syndrome (trisomy 18), and Patau syndrome (trisomy 13) ¹⁻⁵. The Harmony Prenatal Test uses a proprietary, targeted DNA-based technology to provide you and your patients a greater level of assurance—simply requiring a maternal blood sample.

Harmony can be ordered for expectant mothers as early as 10 weeks 1.

While traditional screening can miss as many as 15% of pregnancies with trisomy 21, Harmony's DNA-based technology accurately identifies more than 99% of cases ¹. Clinicians in more than 100 countries have trusted Harmony ⁶.

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Clinical Labs Educational Modules

Prenatal Screening for 22q11.2 Microdeletion

Tune in to our next educational video presented by Associate Professor Mirette Saad on 22q11.2 Microdeletion.

The video is approximately 17 minutes long. You can access the module at this link below:

clinicallabs.com.au/doctor/educational-modules





Alternatively, scan the QR code with your device to go directly to the video.

Prenatal Screening for 22q11.2 Microdeletion



Dr Mirette Saad
Chemical Pathologist
Clinical Director of Molecular Genetics
MBBS (Hons), MAACB, FRCPA, PhD
Australian Clinical Labs

Placental Growth Factor (PIGF) for Early Onset Pre-Eclampsia (EO-PE) Screening

By Associate Professor Mirette Saad

As part of our Antenatal Screening offerings and in alignment with the new guidelines, Australian Clinical Labs is now offering Placental Growth Factor (PIGF 1-2-3™ assay-DELFIA Xpress®) blood test from PerkinElmer. Along with the combined First Trimester Screening (cFTS) and Harmony Non-Invasive Prenatal Testing (NIPT), PIGF is an additional first trimester screening marker. PIGF can be used to screen for Early-Onset Pre-Eclampsia (EO-PE) in pregnancy.

Pre-Eclampsia (PE)

Pre-Eclampsia (PE) is a multi-system disorder previously identified by the onset of hypertension accompanied by significant proteinuria after 20 weeks of gestation. In 2014, the definition of PE was broadened by the International Society for the Study of Hypertension in Pregnancy (ISSHP) (Table 1) and adopted by the Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) ²⁵ as it is considered a major cause of death and morbidity for the mother and perinatal death and long-term handicap for the baby. In the absence of proteinuria, the finding of maternal organ dysfunction is sufficient to make the diagnosis of PE ¹.

International Society for the Study of Hypertension in Pregnancy (ISSHP) revised definition of PE, 2014

The revised ISSHP definition of pre-eclampsia (2014) is;

Hypertension developing after 20 weeks gestation and the coexistence of one or more of the following new onset conditions:

- 1. Proteinuria
- 2 Other maternal organ dysfunction:
- renal insufficiency (creatine >90 umol/L)
- liver involvement (elevated transaminases and/or severe right upper quadrant or epigastric pain)
- neurological complications (examples inlcude eclampsia, altered mental status, blindness, stroke, or more commonly hyperreflexia when accompanied by clonus, sever headaches when accompanied by hyperreflexia, persistent visual scotomata)
- haematological complications (thrombocytopenia, DIC, haemolysis)
- 3. Uteroplacental dysfunction
- foetal growth restrictions

Table 1: Quoted from Tranquilli AL et al. 2014 1

Pre-Eclampsia is a Spectrum Disorder 2,3,4

PE Can Be Sub-Classified Into:

- Early-Onset PE (with delivery at <34+0 weeks of gestation)
- Pre-Term PE (with delivery at <37+0 weeks of gestation)
- Late-Onset PE (with delivery at ≥34+0 weeks of gestation)
- Term PE (with delivery at ≥37+0 weeks of gestation)

These sub-classifications are not mutually exclusive. Early Onset PE (EO-PE) is associated with a much higher risk of short and long term maternal and perinatal morbidity and mortality ^{2,3,4}.

Pre-Eclampsia is More Common than Aneuploidies 5,6,7,8

The prevalence of PE and related conditions (fetal growth-restriction and pre-term birth) is much higher than that of Down syndrome. PE affects 2-8% of pregnancies globally ⁷. The incidence is increasing with the global increase in maternal age, obesity and the use of assisted reproductive techniques. It also follows the rising incidence of diabetes, hypertension, and renal disease – all are known co-morbidities that predispose sufferers to PE during pregnancy.

Unlike Down syndrome, PE is a major cause of maternal and perinatal morbidity and mortality. Thus, preventing PE would bring substantial improvements to maternal and perinatal health 5,6,7,8.

Pre-Eclampsia and Early Assessment 9,10,11,12

Screening for PE can be performed at 11-13+6 weeks' gestation by a combination of maternal demographic characteristics and medical history with some biophysical markers including mean arterial blood pressure (MAP) and the mean uterine artery pulsatility index (UTPI) along with measurements of biochemical markers 9,10,11,12. NHMRC recommend an assessment to all women for clinical risk factors for PE early in pregnancy ²⁶.

Pre-Eclampsia (PE) Screening and New Guidelines FIGO Guidelines, 2019 ⁴

In June 2019, the International Federation of Gynecology and Obstetricians (FIGO) released new guidelines to combat PE.

- FIGO adopts and supports the Fetal Medicine Foundation (FMF) position that all pregnant women should be screened for pre-term PE by the first-trimester combined test with maternal risk factors, MPAP, UTPI, and PIGF as a one-step procedure.
- FIGO adopts and supports the FMF position that in high-risk women, defined by the first-trimester combined test, aspirin ~150 mg/night should be commenced at 11–14+6 weeks of gestation until either 36 weeks of gestation, when delivery occurs, or when PE is diagnosed.
- FIGO encourages all countries and its member associations to adapt and promote strategies to improve access to prenatal services and encourage early booking.

FIGO encourages all countries and its member associations to ensure that risk assessment and resource-appropriate testing for pre-term PE become an integral part of routine first-trimester evaluation protocol offered at all maternal health services.

Biochemical Markers in Pre-Eclampsia 9,10

Biochemical markers that reflect placental function, such as Placental Growth Factor (PIGF) and pregnancy associated plasma protein-A (PAPP-A), are significantly reduced in the first trimester, and throughout the pregnancy, in patients that will later present with pre-term PE with delivery <37 weeks' gestation.

Of these two markers PIGF is a better PE screening marker than PAPP-A (i.e. it has higher sensitivity) 9,10.

Placental Growth Factor (PIGF) for Early Onset Pre-Eclampsia (EO-PE) Screening 13,14,15

PIGF is a glycoprotein that belongs to the vascular endothelial growth factor (VEGF) subfamily. It is a potent angiogenic factor. It is expressed in the villous syncytiotrophoblast and in the media of larger stem vessels in the human placenta. PIGF, together with VEGF, regulates the development of the placental vasculature, and the result depends on intra-placental oxygen pressure 13,14,15.

PIGF concentrations increase throughout pregnancy, peaking during the third trimester, and falling thereafter, probably as a consequence of placental maturation. In PE or intrauterine growth restriction (IUGR), changes in expression or function of PIGF, as well as some other angiogenic factors, may interrupt the function of the utero-placental unit, and thus contribute to many adverse obstetric outcomes 13,14,15.

Why PIGF?

Several studies have shown that women who subsequently develop PE have significantly lower maternal PIGF concentrations in the first trimester than those with normal pregnancies 22,23.

A systematic review and meta- analysis demonstrated that PIGF is superior to the other biomarkers for predicting PE 24. Serum PIGF biomarker can identify up 75% of women who develop pre-term PE with delivery at <37 weeks' gestation and 90% of those with early PE at <32 weeks, at a screen-positive rate of 10%.

The COMPARE ¹⁶ Study states that the high negative predictive values (NPV) support the role of PIGF-based tests as 'rule-out' tests for PE. Among the tests compared, the DELFIA Xpress® PIGF 1-2-3™ assay has the highest NPV.

ASPRE Study ¹⁷: Using PIGF 1-2-3[™] assay (PerkinElmer) in PE screening, ASPRE was the biggest prospective, randomised, placebo controlled trial that showed that use of aspirin was associated with a significant 62% reduction in the incidence of pre-term PE (<37 weeks GA) and an 82% reduction in the incidence of EO-PE (<34 weeks GA).

Recently, studies 15,18,19,20 showed that the administration of aspirin in pregnancies at high risk of PE reduces the length of stay in the neonatal intensive care unit (NICU) by about 70% mainly through the prevention of EO-PE.

When to offer?

The optimal time for screening is 11-13+6 weeks of gestation.

Who to offer?

Patients with high blood pressure, advanced age pregnancy, high BMI, positive history of pre-eclampsia or eclampsia, diabetes or kidney disease, multiple pregnancies or IVF assisted pregnancies.

The PIGF test can be offered to pregnant women of any age or risk category. It can be ordered for all naturally conceived or in vitro fertilisation (IVF) singleton or twin pregnancies, including those with egg donors. PIGF test is currently viewed as a screening test and clinical interpretation is always recommended 13,14.

Can it be offered with cFTS?

Yes, the same blood sample can be used for the measurement of biochemical markers for both pre-eclampsia screening and aneuploidy Down syndrome screening.

Specimen Requirements:

Plain tube or serum gel 7 ml

- The Placental Growth Factor (PIGF) costs \$50
- Blood samples can be collected at any of our **Australian Clinical Labs pathology collection centres**

For assistance please call Biochem Dep. on (03) 9538 6790 or FTS (MSS) service on 0429116049

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About the author



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Urea Breath Testing in General Practice

By Dr Wessel Jenner

Diagnosing H. pylori

Helicobacter Pylori (H. pylori) is a spiral shaped gram-negative bacteria that colonises the mucous layer of the stomach.

H. pylori causes a chronic inflammatory reaction in the mucous layer and can lead to an increased risk of developing peptic ulcers, duodenal ulcers or some cancers of the stomach.

Infection appears to be acquired during childhood and persists lifelong unless treated. It is postulated that one can become infected by contact with saliva, vomit or stools of an infected person. It's unusual to catch the infection as an adult.

The urea breath test is an accurate, safe and quick way to diagnose H. pylori.

¹⁴C-Urea Breath Testing - Clinical Recommendations

- People with duodenal or stomach ulcers.
- People with non-ulcer dyspepsia.
- Monitoring the success of eradication of H. pylori
- In some cases, family members of infected people.

How does the test work?

The H. pylori bacteria is very effective in breaking down urea into CO, and ammonia to create an environment in the stomach for it to survive. During the urea breath test, the patient is given a capsule that contains urea labelled with ¹⁴C. The H. pylori, if present, will break down the urea quickly and release the $^{\rm 14}{\rm C}$ in the form of $^{\rm 14}{\rm CO_2}$ that is exhaled. The $^{\rm 14}{\rm CO_2}$ is collected in a balloon and sent to a laboratory where the ¹⁴CO₂ content is measured.

If the bacteria is not present, the labelled urea will not be broken down and the breath will not contain ¹⁴CO_a.

How safe is this test?

¹⁴C is a rare, naturally occurring radioactive form of carbon, as opposed to the more common occurring ¹²C. The radiation exposure during the test is far less than that of a standard X-ray. Studies have not been done to determine safety in pregnancy, or for breast feeding mothers and children so use in these groups is not recommended unless there are special circumstances.

As an alternative in these cases a stool antigen test can be ordered.



Helicobacter pylori bacteria colonising the stomach.

Patient preparation

To avoid inaccurate results, the following precautions should be taken:

- Patient should fast for at least 4 hours before the test (including water).
- The following medication should be discontinued to prevent false negative results:

Antibiotics and bismuth containing products	4 weeks before test
Cytoprotectives, e.g. Sucralfate	2 weeks before test
Proton pump inhibitors	1 week before test
H2-antagonists and antacids	During fasting and during test

Cost:

Bulk billed subject to Medicare criteria.

- ces:
 Tietz Textbook of Clinical Chemistry and Molecular Diagnostics, Fourth Edition.
 Gastroenterology Society of Australia, Information leaflet, Third Edition 2010.
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Dr Wessel Jenner

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Dr Jenner completed his studies in chemistry and biochemistry in 1992 followed by a Bachelor's degree in Medicine and Surgery (MBChB) from the Faculty of Health Sciences, University of Pretoria, South Africa in 1997. Following three years of clinical practice, he commenced training in Chemical Pathology in 2001 and obtained the Fellowship from the Colleges of Medicine of South Africa in 2004 and a Master's degree in Chemical Pathology from the University of Pretoria in 2005. Dr Jenner obtained his Fellowship from the Royal College of Pathologists of Australasia in 2013 and joined Australian Clinical Labs (formerly Healthscope Pathology) in early 2014.

Local pathologist near you



Dr Damon Bell
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cardiovascular disease

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Dr Damon Bell received his undergraduate medical education in New Zealand graduating from the University of Otago. He completed his physician training in Endocrinology (FRCPA) and subsequently chemical pathology training (FRCPA) at Wellington Hospital. Dr Bell is also a sessional Chemical Pathologist for PathWest and Physician in the School of Medicine & Pharmacology, UWA based at Royal Perth Hospital. His current research interests relate to screening strategies for familial hypercholesterolaemia (FH) which complements his clinical practice in the Lipid Disorders Clinic.



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Practice Suburb	Post Code
Please tick one of the below:	
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○ Specialist	
Medical Centre / Practice Manager	

Thank you

T:41~

Updates From The Lab

Clinical Labs WA have recently welcomed the highly-trained expertise of four new pathologists. Based in Subiaco & Osbourne Park their specialities cover the fields of anatomical pathology, oral and maxillofacial pathology, chemical pathology and toxicology.



Dr Louisa Dunk
Qualifications: MB ChB, FRCPath (UK)
Anatomical Pathology, Subiaco

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Dr Dunk graduated from The University of Birmingham Medical School in 1991. She trained in pathology at The University Hospitals of Leicester (UK) and obtained Fellowship of the Royal College of Pathologists (UK) in 2010. She then worked at The University Hospitals of Leicester as a consultant histopathologist, specialising primarily in breast pathology and became Head of Service for the Cellular Pathology Department. Dr Dunk started teaching pathology at the University of Leicester where she was awarded the title of Lecturer and then Senior Lecturer in Medical Education. Her areas of professional interest include breast and cutaneous pathology and cytology.



Professor Camile Farah

Qualifications: BDSc, MDSc (OralMed OralPath), PhD, GCEd (HE), GCExLead, FRACDS (OralMed), MAICD, AFCHSM, FOMAA, FIAOO, FICD, FPFA, FAIM

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Professor Farah is a dual registered specialist in Oral Medicine and Oral Pathology with sub-specialty training in Oral Oncology. Camile obtained his dental degree from the University of Western Australia, followed by a PhD in Oral Pathology & Immunology and specialist training in Oral Medicine and Oral Pathology from the University of Queensland. He gained further experience at the Eastman Dental Institute, UCL, UK. Camile has 23 years' experience with particular interest in oral mucosal pathology, salivary gland pathology and bone pathology. He has authored 175 peer reviewed papers and book chapters, and is senior editor and author of the authoritative textbook "Contemporary Oral Medicine".



Dr Jonathan Grasko

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Dr Grasko is a consultant Chemical Pathologist and Toxicologist. He has sixteen years of local and international medical experience and has provided State-wide services for paediatric, metabolic, newborn screening and clinical toxicology. He has reported over 40 forensic toxicology and coronial cases in the magistrate, civil and supreme courts. He is currently completing a PhD in breast cancer genetics and is a Fellow of the Royal College of Pathologists of Australasia.



Dr Zena Slim

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Dr Slim studied medicine at the University of Southampton (UK), and trained in anatomical pathology in the UK and New Zealand. She is a Fellow of the Royal College of Pathologists of Australasia and is keen on developing her expertise in Molecular Pathology and recently gained a Postgraduate Certificate in Cancer, Molecular Pathology and Genomics from Barts Cancer Institute at the University of London. Her particular areas of interest are dermatopathology and gastrointestinal pathology.