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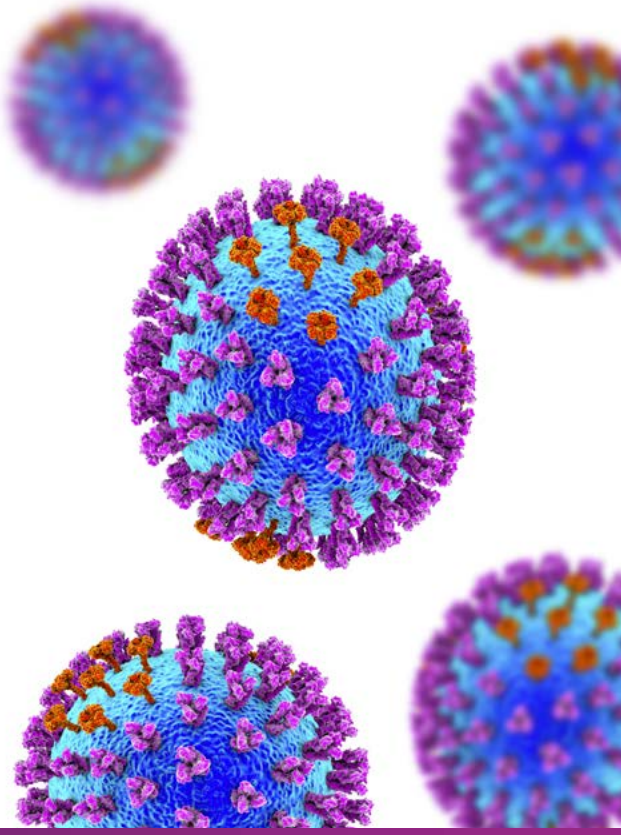
Medical Newsletter



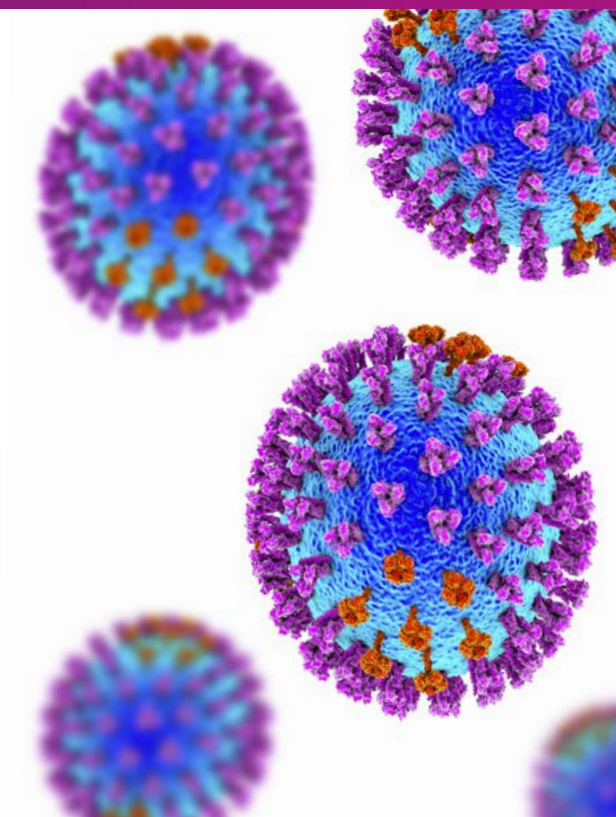
July 2019 – Newsletter 6

VIC

Inside this Newsletter:

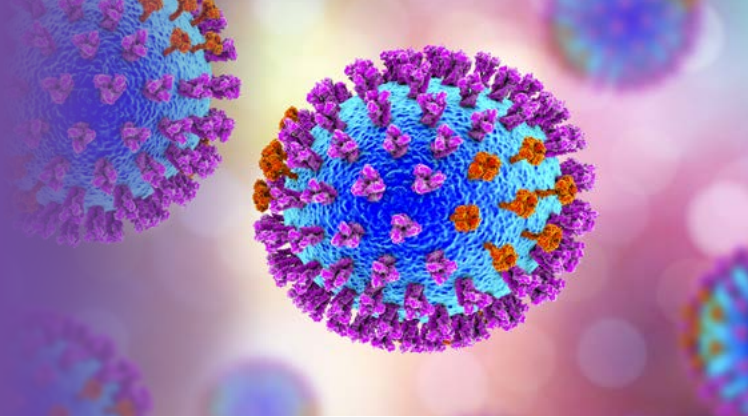
Confirmed flu cases in 2019 already greater than 2018

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.

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
    - Nasopharyngeal/tracheal aspirates or
    - Sputum
- Cost: Medicare bulk billing available and subject to Medicare guidelines and criteria

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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.

Placental Growth Factor (PlGF) 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 (PlGF 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), PlGF is an additional first trimester screening marker. PlGF 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 PlGF 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 (PlGF) 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 PlGF is a better PE screening marker than PAPP-A (i.e. it has higher sensitivity) [9,10].

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

PlGF 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. PlGF, together with VEGF, regulates the development of the placental vasculature, and the result depends on intra-placental oxygen pressure [13,14,15].

PlGF 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 PlGF, 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 PlGF?

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

A systematic review and meta- analysis demonstrated that PlGF is superior to the other biomarkers for predicting PE [24]. Serum PlGF 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 PlGF-based tests as 'rule-out' tests for PE. Among the tests compared, the DELFIA Xpress® PlGF 1-2-3™ assay has the highest NPV.

ASPRE Study [17]: Using PlGF 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 PlGF 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. PlGF 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 is used for the measurement of biochemical markers for both pre-eclampsia screening and aneuploidy Down syndrome screening using the same instrument at Australian Clinical Labs [21].

Specimen Requirements:

Plain tube or serum gel 7 ml

- **The Placental Growth Factor (PlGF) 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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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.*

^{14}C-Urea Breath Testing - Clinical Recommendations

- People with duodenal or stomach ulcers.
- People with non-ulcer dyspepsia.
- Monitoring the success of eradication of *H. pylori* infection.
- 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_2 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 ^{14}C. The *H. pylori*, if present, will break down the urea quickly and release the ^{14}C in the form of $^{14}CO_2$ that is exhaled. The $^{14}CO_2$ is collected in a balloon and sent to a laboratory where the $^{14}CO_2$ content is measured.

If the bacteria is not present, the labelled urea will not be broken down and the breath will not contain $^{14}CO_2$.

How safe is this test?

^{14}C is a rare, naturally occurring radioactive form of carbon, as opposed to the more common occurring ^{12}C. 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.

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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

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Dr Deam graduated with Honours in Medicine from Monash University in 1978 and obtained his FRCPA in 1985 following postgraduate training in Biochemistry at the Royal Melbourne Hospital. He joined Gribbles Pathology (now Australian Clinical Labs) in 1998. Dr Deam has played an active role in teaching scientific, nursing and medical staff at both undergraduate and postgraduate levels and has been an examiner for the Australasian Association of Clinical Biochemists as well as the Royal College of Pathologists of Australasia.

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- ◯ Medical Centre / Practice Manager

Thank you

Clinical Labs Warfarin Dosing Program Update

At Clinical Labs we pride ourselves on the level of care we provide patients who are registered in our Warfarin Dosing Program.

As you may be aware, apart from the collection fee, Medicare does not fund the cost of providing Warfarin dosing services. Furthermore, the funding we receive as part of the Medical Benefits Scheme has not increased in 20 years and in 2009, government rebates per collection were reduced from $14.80 to $5.10. Over the same period, our business costs have risen exponentially: collector and courier salaries, consumables, collection centre rents, vehicles and petrol, and the IT people and systems required to report results to doctors.

In regards to Warfarin dosing, once a collection is complete and the sample is couriered to the lab, we invest significant resources managing the patient's needs and protecting their safety. This includes specialist GP and pathologist monitoring of patients; specially trained contact centre staff; dosing and reminder correspondence: both paper and electronic; and telephone follow-up when a patient requires urgent dosing changes. None of these additional services are funded by Medicare.

It is in the context of rising service provision costs that we have introduced an annual registration fee for access to our Warfarin Dosing Program.

The annual fee will vary, depending on whether the patient receives their Warfarin dosing levels in writing via SMS or over the telephone. We believe that all patients should receive their dose in writing as this reduces the risk of misunderstanding dosing instructions. On the 30th June 2019, all patients, both new and existing, were invoiced the annual registration fee, with the full amount payable within 30 days. The fees are as follows:

Concession card holder
$55 annual registration fee, only available to patients: • With concession cards receiving dosing in writing via SMS
Non concession card holder
$105 annual registration fee, for patients: • Receiving dose by SMS • With a concession card and not using our SMS service

Patients who elect to receive dosing in writing via our SMS notification service will be registered when we next call them about their dosing. From that moment, the patient will receive all dosing information via SMS.

If you have any questions about our Warfarin Dosing Program please call **(03) 9538 6711.**

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