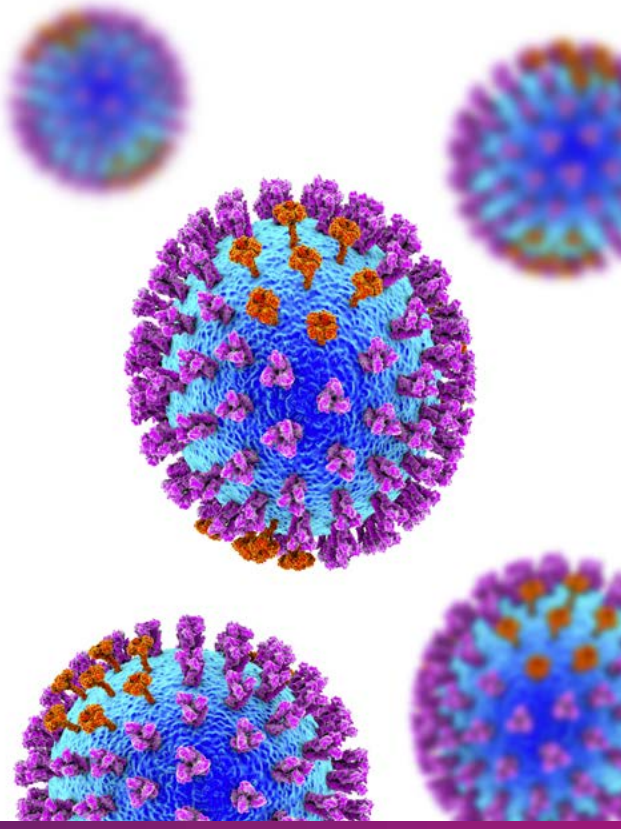
AUSTRALIAN Clinicallabs



PATHOLOGY FOCUS

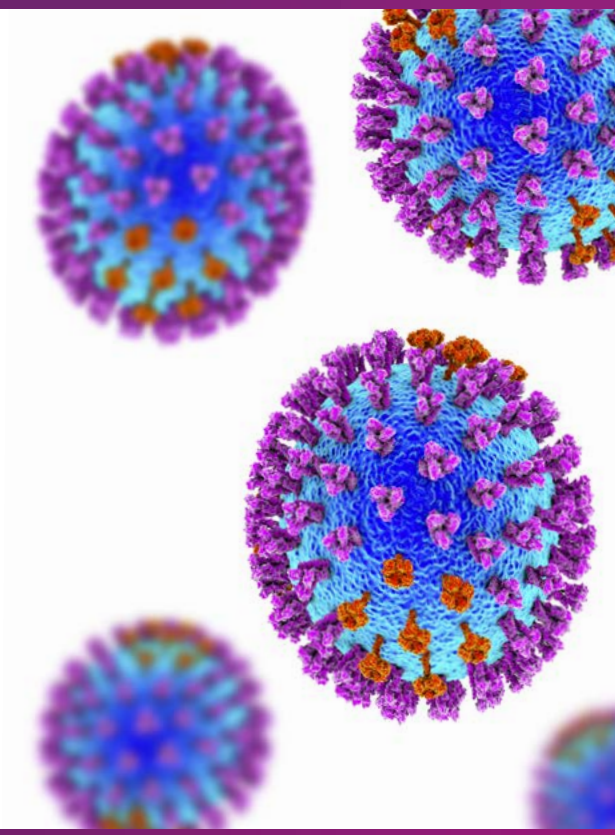
Medical Newsletter

July 2019 – Newsletter 6

Inside this Newsletter:

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

SA/NT

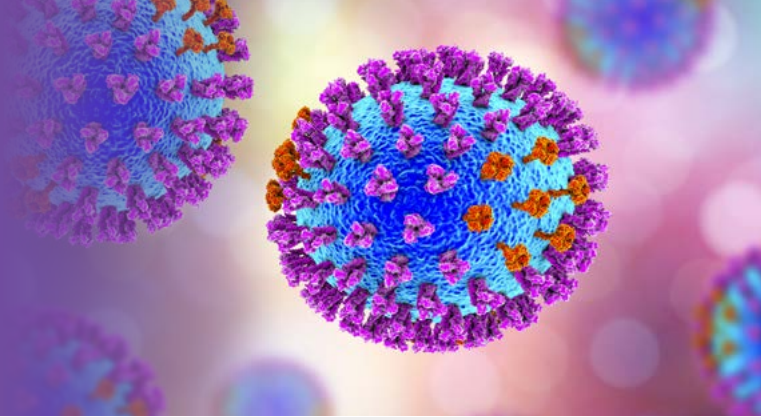


Confirmed flu cases in 2019 already greater than 2018

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	24hrs – Urgent	>24 hrs
Tests Included	• Influenza A & B • RSV (A&B)	• 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:	Rapid Flu	Respiratory Viral Screen	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

About the author

Dr Linda Dreyer

MBChB, MMED (Path) (South Africa), FRCPA

Lab: Clayton
Areas Of Interest: Antimicrobials, infection control and molecular diagnostic assays in contemporary clinical microbiology
Speciality: Infection Control, Microbiology
Phone: (03) 9538 6777
Email: Linda.Dreyer@clinicallabs.com.au

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 Travis Brown

B. COM/B. COMP, B. SCI (MED SCI), MBBS, FRCPA

Lab: Adelaide Airport
Areas Of Interest: Information Technology and Pathology informatics
Speciality: General Pathology
Phone: (08) 8205 5604
Email: Travis.Brown@clinicallabs.com.au

Dr Travis Brown obtained his MBBS from the Australian National University (ANU) in Canberra. After completing two years as a junior doctor at St Vincent Hospital in Melbourne, he undertook Anatomical Pathology training at Ballarat Base Hospital and the Royal Melbourne Hospital before transferring to General Pathology Specialty training with Healthscope Pathology (now Australian Clinical Labs) in Clayton, Melbourne. Dr Brown completed General Pathology Specialty training in November 2016 and now works at Australian Clinical Labs in Wayville, Adelaide.

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

References

1. Tranquilli AL et al. The classification, diagnosis and management of the hypertensive disorders of pregnancy: A revised statement from the ISSHP. Pregnancy Hypertens 2014;4:97-104.
2. Wright D et al. A competing risks model in early screening for preeclampsia. Fetal Diagn Ther. 2012;32(3):171-178.
3. Wright D et al. Competing risks model in screening for preeclampsia by maternal characteristics and medical history. Am J Obstet Gynecol 2015;213:62.e1-10.
4. Poon et al. The International Federation of Gynecology and Obstetricians (FIGO) Initiative on Pre-Eclampsia: A pragmatic Guide for First Trimester Screening and Prevention. Int J Gynecol Obstet 2019;145 (Suppl. 1): 1–33.
5. Parker S et.al. Updated National Birth Prevalence estimates for selected birth defects in the United States, 2004-2006. Birth Defects Res A Clin Mol Teratol. 2010.
6. WHO media centre, fact sheet 2016. http://www.who.int/mediacentre/factsheets/ fs363/en/
7. Duley L. The global impact of pre-eclampsia and eclampsia. Semin Perinatol. 2009.
8. Romo A et al. Intrauterine growth retardation (IUGR): epidemiology and etiology. Pediatr Endocrinol Rev. 2009.
9. Tsiakkas A et al. Serum placental growth factor in the three trimesters of pregnancy: effects of maternal characteristics and medical history. Ultrasound Obstet Gynecol 2015;45:591-598.
10. Wright A et al. Maternal serum PAPP-A and free β-hCG at 12, 22 and 32 weeks' gestation in screening for pre-eclampsia. Ultrasound Obstet Gynecol 2016;47:762-767.
11. Poon LC et al. Protocol for measurement of mean arterial pressure at 11-13 weeks' gestation. Fetal Diagn Ther 2012;31:42-48.
12. O'Gorman N et al. Uterine artery pulsatility index at 12, 22, 32 and 36 weeks' gestation in screening for pre-eclampsia. Ultrasound Obstet Gynecol 2016;47:565-567.
13. Royal College of Obstetricians and Gynaecologists patient information leaflet, Information for you: Pre-eclampsia. RCOG Patient Information Committee, London, UK, Aug 2012.
14. Rolnik DL et al. Nicolaides KH. ASPRE trial: performance of screening for preterm pre-eclampsia. Ultrasound Obstet Gynecol Jul 25, 2017.
15. Bujold E et al. Prevention of preeclampsia and intrauterine growth restriction with aspirin started in early pregnancy: a meta-analysis. Obstet Gynecol. 2010;116:402-414.
16. McCarthy FP et al. Comparison of three commercially available placental growth factor tests in women with suspected preterm pre-eclampsia: the COMPARE study. Ultrasound Obstet Gynecol 2019;53:62-67.
17. Rolnik DL et al. ASPRE trial; Aspirin versus Placebo in Pregnancies at High Risk for Preterm Preeclampsia.N Engl J Med. 2017 Aug 17;377(7):613-622.
18. Roberge S et al. Early administration of low-dose aspirin for the prevention of preterm and term preeclampsia: a systematic review and meta-analysis. Fetal Diagn Ther.2012;31(3):141-146. doi: 10.1159/000336662. Epub 2012 Mar 21.
19. Roberge S et al. The role of aspirin dose on the prevention of preeclampsia and fetal growth restriction: systematic review and meta-analysis. Am J Obstet Gynecol. 2017 Feb;216(2):110-120.e6.
20. Wright D et al. Secondary analysis of ASPRE trial. Am J Obstet Gynecol. 2018;612.e6.
21. PerkinElmer PlGF assay product inserts 13908271, 13907817.
22. Chau K et al. Placental growth factor and pre-eclampsia. J Hum Hypertens. 2017;31:782–786.
23. Wortelboer EJ et al. Longitudinal trends in feto-placental biochemical markers, uterine artery pulsatility index and maternal blood pressure during the first trimester of pregnancy. Ultrasound Obstet Gynecol. 2011;38:383–388.
24. Zhong Y et al. Serum screening in first trimester to predict pre-eclampsia, small for gestational age and preterm delivery: Systematic review and meta-analysis. BMC Pregnancy Childbirth. 2015;15:191.
25. https://www.ranzcog.edu.au/Womens-Health/Patient-Information-Resources/Pre-eclampsia-and-High-Blood-Pressure-During-Pregn
26. NHMRC National Health and Medical Research Council, October 2017. Evidence Based Recommendations

About the author

Assoc. Prof. Mirette Saad

Qualifications: MBBS (Hons), MD, MAACB, FRCPA, PhD.

Lab: Clayton

Areas Of Interest: Molecular Genetics, Cancer Genetics, Antenatal Screening, NIPT, Endocrine, Fertility Testing and Research, Medical Teaching

Speciality: Chemical Pathology

Phone: (03) 9538 6777

Email: Mirette.Saad@clinicallabs.com.au

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.

References:
1. Tietz Textbook of Clinical Chemistry and Molecular Diagnostics, Fourth Edition.
2. Gastroenterology Society of Australia, Information leaflet, Third Edition 2010.
3. PYtest Information for Users leaflet, Tri-Med Distributors (2015).
4. https://www.labtestsonline.org.au/learning/test-index/hpylori

About the author

Dr Wessel Jenner

Qualifications: BSc, MBChB, FRCPA

Lab: Bella Vista

Areas Of Interest: Chemical Pathology, Endocrinology and Proteins

Speciality: Biochemistry, Chemical Pathology

Phone: (02) 8887 9999

Email: Wessel.Jenner@clinicallabs.com.au

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 Travis Brown

Qualifications: B. COM/B. COMP, B. SCI (MED SCI), MBBS, FRCPA

Lab: Adelaide Airport

Areas Of Interest: Information Technology and Pathology informatics

Speciality: General Pathology

Phone: (08) 8205 5604

Email: Travis.Brown@clinicallabs.com.au

Dr Travis Brown obtained his MBBS from the Australian National University (ANU) in Canberra. After completing two years as a junior doctor at St Vincent Hospital in Melbourne, he undertook Anatomical Pathology training at Ballarat Base Hospital and the Royal Melbourne Hospital before transferring to General Pathology Specialty training with Healthscope Pathology (now Australian Clinical Labs) in Clayton, Melbourne. Dr Brown completed General Pathology Specialty training in November 2016 and now works at Australian Clinical Labs in Wayville, Adelaide.

Subscribe to our electronic mailing list

Subscribe to the Clinical Labs mailing list and receive our bi-monthly clinical newsletter, important updates, educational resources and more, delivered directly to your inbox. Simply visit **clinicallabs.com.au/subscribe** and follow the instructions.

Alternatively, complete the form below, tear along the perforated edge and fax it to Clinical Labs Head Office on **(03) 9538 6733**

Title

Given Name

Surname

Email

Practice Name

Practice Address

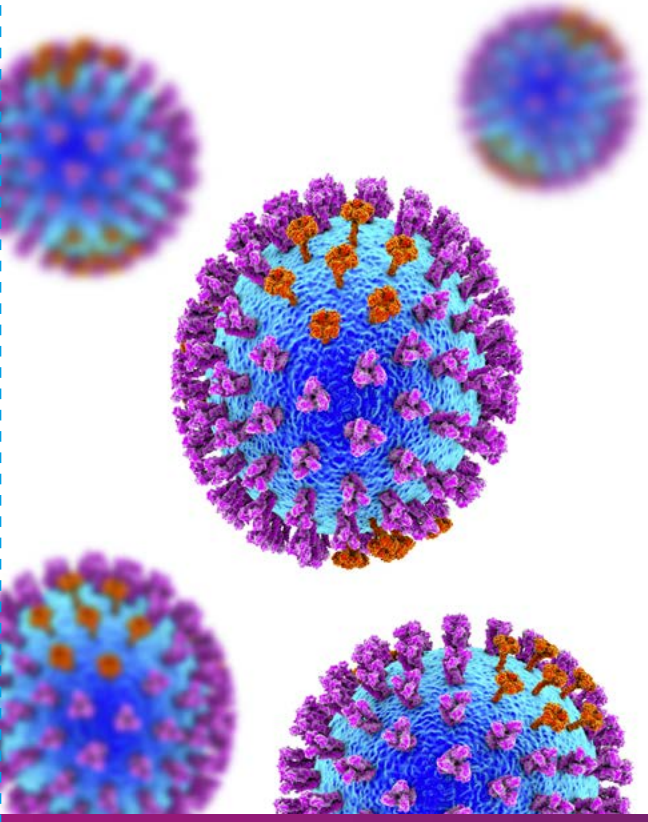
Practice Suburb

Post Code

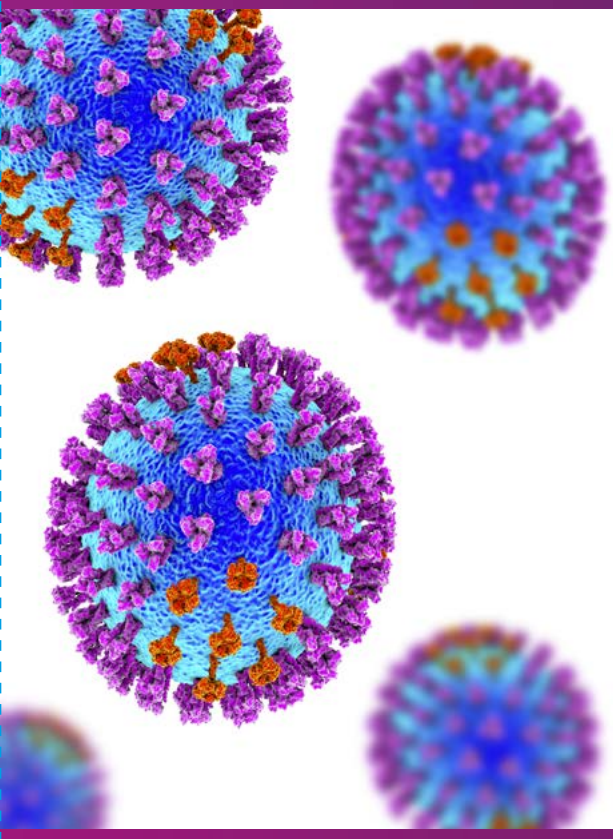
Please tick one of the below:

- ◯ General Practitioner
- ◯ Specialist
- ◯ Medical Centre / Practice Manager

Thank you



To receive our bi-monthly clinical newsletter, updates, educational resources and more, go to clinicallabs.com.au/subscribe and follow the instructions.



ACLMAR-NEWS-SA-0019.1 07/19

AUSTRALIAN Clinicallabs