

*A Centre for Infectious Diseases and Microbiology - Public Health (CIDM-PH), and
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The Broad Street Pump

Point-Of-Care Testing

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Point-of-care (POC) testing is the fastest growing sector in the clinical *in vitro* diagnostic market, and is increasingly being used to improve patient outcomes by providing better access to diagnostic testing and faster turnaround times. Traditional POC testing methods using immunochromatography and wire-guided droplet microfluidics for physiological measurements have been further augmented by multicore processors, microchips, high-resolution cameras and wireless communication to advance POC testing in areas of life-threatening infectious diseases, cancer and cardiac care.

POC devices have the advantage of not requiring specialized laboratory equipment or expertise to operate, making them suitable for near patient deployment to provide rapid results in “real-time” which translates to improved clinical decision-making, quality of care and potentially, lower healthcare costs. Confirmation of a clinical diagnosis by POC testing further obviates unnecessary testing and allows the timely provision of targeted therapies. POC tests have also had a major positive impact in diagnostic testing and public health in low resource settings.



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In Australia, POC tests have been used by patients in their homes, hospital outpatient clinics, emergency departments and clinical laboratories. By contrast, such tests are also available over the counter or in general practices in other countries. Similar to tests performed in clinical diagnostic laboratories, internal quality control procedures and participation in external quality assurance programs are paramount to ensure that results of POC tests are accurate. At present, POC tests are not eligible for Medicare rebates when performed at sites not accredited for such testing. This limits the potential uptake of POC testing in the general practice or community setting, where costs are generally borne by the end-user.

Within the discipline of microbiology, POC testing has been available for many different pathogens including bacteria, viruses, fungi and parasites. Examples of POC tests that are in currently in clinical use include those detecting group A *Streptococcus*, *Legionella pneumophila* serogroup 1, *Clostridium difficile*, human influenza viruses, respiratory syncytial virus, dengue virus, human immunodeficiency virus (HIV), Ebolavirus, *Cryptococcus* species and malaria.

Users of these POC tests should be familiar with the performance and limitations of such tests. For example, the sensitivity of influenza POC tests can be affected by sample type, elapsed time between symptom onset and sample collection, the age of the person tested and the subtype of influenza virus. The positive and negative predictive values of influenza POC tests are also affected by the prevalence of influenza activity in the population tested. False positive results are more likely to occur when the prevalence of influenza is low in the community; by contrast, false negative results are more likely to occur when the community prevalence of influenza is high.

In December 2012, the first HIV POC test was registered on the Therapeutics Good Administration Australian Register of Therapeutic Goods (1). The New South Wales (NSW) Framework and Standard Operating Procedure for HIV POC testing was developed in January 2015 to guide service delivery of HIV POC testing (2). Such frameworks aim to ensure that these tests are used in the appropriate context (gay men and other men who have sex with men) and that proficiency standards and quality assurance requirements are met. Similar to influenza POC tests, false reactive results are more likely to occur when there is a low pre-test probability, although the test may still be used in specific populations where access to conventional laboratory testing is limited. The framework also stipulates that HIV POC tests should be used as a screening rather than a diagnostic test, and reactive results should be followed up and confirmed appropriately.

Several guidelines and policy documents are available to guide implementation and specify key requirements of POC testing. The international standard ISO 22870:2006 (Point-of-care testing –

Requirements for quality and competence) outlines the requirements that need to be applied when performing POC testing (3). Internal quality control and external quality assessments are required to ensure reliable results. Guidelines issued by National Association of Testing Authorities (NATA), Australia, require that appropriate quality control samples in the pathological range be run with every new batch of consumables and once per month (4). Where no quality control material is available, patient specimens must be substituted, and results compared to those from another NATA accredited laboratory. Other important issues that need to be considered include pre-implementation validation of the POC device, oversight of the clinical governance, and maintaining good laboratory practice and operation of the devices.

NPAAC Guidelines for POC testing were also developed in 2015, and sets out best practice guidelines for the governance and quality requirements of POC tests (5). The NPAAC guidelines also set out training requirements for test operators, occupational health and safety and environmental issues. Allowable limits of performance are also published in the guidelines for some biochemical POC tests. Where the allowable limits of performance have not been specified, the evaluation of POC devices against an established reference method requires the testing of at least 40 samples covering a clinically meaningful range of the measurand, construction of a Bland-Altman plot and performance of a regression analysis of the results (6).

The World Health Organization developed the ASSURED criteria (affordable, sensitive, specific, user-friendly, rapid and robust, equipment-free and deliverable), features that should be included when developing and evaluating POC testing devices. As such, POC tests based on lateral flow strips remain the dominant technology despite obvious limitations of limited sensitivity and the inability for multiplexing. Although “lab on a chip” technologies have yet to be fully translated into clinical practice, they are likely to become more common in the future. POC nucleic acid tests are also being developed with the availability of isothermal amplification and rolling circle amplification.

Irrespective of the type of POC device, the ultimate aim of these tests is to facilitate near-patient testing so that the provision of appropriate therapy can be expedited, and the provision of inappropriate therapies avoided. Several platforms are being calibrated for samples collected by patients themselves. Improvements in technologies including miniaturization and increases in the menu of tests available in a POC format is likely to shift common tests away from the traditional diagnostic laboratory. Pathology providers, clinicians and public health professionals should be prepared for this inevitable and impending paradigm shift.

Point-Of-Care Testing *(continued from page 2)*

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3. International Organization for Standardization. ISO 22870:2006 Point-of-care testing care (POCT) – Requirements for quality and competence. 2006 (Available at http://www.iso.org/iso/catalogue_detail.htm?csnumber=35173, Accessed January 28, 2016).
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6. Australasian Association of Clinical Biochemists. Guidelines for the evaluation of PoCT instruments. April 2012 (Available at <http://www.aacb.asn.au/documents/item/244>, Accessed January 28, 2016).

Point-Of-Care Testing Symposium

In October 2015, the “Point-Of-Care Symposium” was jointly presented by the Centre for Infectious Diseases and Microbiology – Public Health and Institute of Clinical Pathology and Medical Research, Pathology West at Westmead Hospital. The aim of the symposium was to explore point-of-care testing for infectious diseases, the rollout of tests across New South Wales and the implications of point-of-care testing for routine pathology service delivery. The implementation of point-of-care testing in the diagnosis and management of HIV infection and other significant bacterial, viral, fungal and parasitic pathogens was discussed. Selected presentations from the symposium can be found on the ‘News & Events page’ at: www.wslhd.health.nsw.gov.au/CIDM-PH



POINT-OF-CARE TESTING SYMPOSIUM ABSTRACTS

Roll out of POC in NSW

Chant, Kerry¹, Duck Tim¹, Holden Jo¹, Selvey Christine²

¹ NSW Ministry of Health, ² Health Protection NSW

Rapid HIV testing (RHT) is part of a mix of HIV testing services offered across NSW to encourage people from high risk populations to be tested regularly for HIV, in particular men who have sex with men who report high risk behaviours and/or not engaging in routine testing. The first RHT was registered for use in the Australian in December 2012. A range of conditions were imposed by the TGA before the tests could be used, highlighting the need for a framework to outline quality and safety standards for RHT in NSW health services outside the context of a research study.

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Point of Care Testing in Medical Mycology – have we arrived?

Sharon Chen^{1,2}, Catriona Halliday¹, Sue Sleiman¹, Tania Sorrell^{2,3}

¹ Centre for Infectious Diseases and Microbiology Laboratory Services, ICPMR – Pathology West, NSW; ² Sydney Medical School, University of Sydney, NSW; ³ Marie Bashir Institute for Infectious Diseases and Biosecurity, University of Sydney, NSW.

Point of care testing (POCT), or testing at or near the site of patient care, for invasive fungal infections (IFIs) has lagged behind POCT for other infectious diseases. Yet POCT devices for IFIs are coming into its time. These include rapid, robust, and simple lateral flow assays (LFAs) for cryptococcosis and invasive aspergillosis, two IFIs that are significant in Australia. Cryptococcal meningitis is the commonest cause of fungal meningitis whilst aspergillosis complicates immunocompromised patients, patients in ICU and those with chronic lung disease. Novel potential POCTs comprise rapid bedside detection of fungal volatile compounds (VOCs) in a patient's breath for *Aspergillus* and other mould pathogens.

Detection of cryptococcal antigen (CRAG) in serum and cerebrospinal fluid is a sensitive and specific marker of disease. The cryptococcal LFA test, an immunological test akin to all LFA formats, detects cryptococcal polysaccharide with high accuracy. The LFA is more rapid than the latex agglutination test for CRAG (20 min vs. 2 h) with high sensitivity, specificity and detects both *C. neoformans* and *C. gattii* infection. However, titres obtained by the LFA cannot be compared with those by latex agglutination. The *Aspergillus* LFA strip test has been evaluated in vitro and in vivo and appears to perform with comparable sensitivity and specificity to *Aspergillus* galactomannan on serum and bronchoalveolar fluid.

e-Nose testing devices have become sophisticated yet simple. This technology is being translated to devising POCT instruments for detecting fungal VOCs in breath samples. Commercial in-kind kits are being trialed for diagnosing VOCs of *Aspergillus* in high risk haematology patients.

POCT approaches in diagnostic mycology are advancing. Prioritisation of needs and resource allocation are essential.

Point of Care Testing – Quality Assurance and Regulatory Aspects

Ms Susan Badman and A/Prof Tony Badrick

RCPA Quality Assurance Programs

It is estimated that pathology based tests and investigations feature in 70% of health care decisions affecting diagnosis or treatment. Therefore, maintaining the quality and safety of pathology is crucial to the efficient and effective delivery of health care. Generally pathology is carried out in the controlled and regulated environment of a recognised medical laboratory, however the use of point of care testing in Australia is increasing and will become more widespread in the future. The quality assurance and regulatory aspects of point of care testing in Australia include the Therapeutic Goods Administration *in vitro* diagnostic medical devices regulations, NPAAC guidelines and NSW Health Framework and Standard Operating Procedure for the provision of point of care testing for HIV in clinical and non-clinical settings.

POINT-OF-CARE TESTING SYMPOSIUM ABSTRACTS

POC- Pitfalls and impact on the routine diagnostic laboratory

Professor Joan Faoagali

University of Queensland and Infection Management Services Princess Alexandra Hospital

POCT offers huge promise to change clinical microbiology from “after” the event to “at the time” of the event. Information confirming the presence and identity of an infecting microbe at the time of sample collection holds promise in reducing the inappropriate use of antibiotics, allowing selection of an appropriate treatment and detection the presence of a virus to assist with appropriate patient isolation and therapy.

POCT in the diagnostic microbiology laboratory has a chequered history. The sensitivity and specificity of the tests may be poor. The tests are not cheap especially when they have to be confirmed by standard methods which may be in a central specialised laboratory far from the patient and satellite laboratory. Performing a POCT in the diagnostic laboratory when the test is sensitive and specific has huge advantages compared with satellite POC laboratory testing in clinics, ED or the home where non scientists, non trained personnel who are already overworked are expected to add this task to their scope of practice. The diagnostic microbiology laboratory staff are trained in quality management, use of controls and in date kits as well as sample and patient identification and safe waste control. Kits are stored appropriately to ensure their optimum performance and interpretation and reporting of the results is undertaken in a professional manner by competent staff who can ensure addition of the results to the laboratory information system ensuring reliable recording and commenting of the results, Public Health notification and expert commentary if required. But scientific staff are aging, traditional methods are being replaced by molecular methods, whole genome sequencing is not yet available at the bedside and laboratory centralisation is removing the opportunities for rapid turnaround times as this perceived cost saving attitude is implemented.

Microbiology POCT in the diagnostic laboratory can provide a clinical service for patients and doctors whereby rapid results performed by trained staff in an on-site facility has the potential to reduce patient length of stay, reduce costs and preserve the dwindling supply of effective antibiotics.

Point of Care testing for bacterial infections: implications for public health surveillance

Assoc Professor Vitali Sintchenko

Centre for Infectious Diseases and Microbiology – Public Health, Westmead Hospital and University of Sydney

Point-of-care testing (POCT) has improved diagnosis and management of bacterial sexually transmitted infections (STIs) and community-acquired pneumonia. Results provided by assays, which target *Legionella pneumophila* serotype 1 and pneumococcus, have demonstrated high sensitivity and reproducibility. These assays have allowed more timely diagnosis and more targeted use of antibiotics. Growing application of POCT in healthcare increases the number of diagnoses and underscores the role of co-infection with several pathogens in the natural history of communicable diseases. The POCT can be treated as a public health intervention. This presentation will examine the impact of POCT on the time-to-diagnosis, time-to-treatment and on interrupting disease transmission. POCT may offer the greatest benefits in the areas of high disease prevalence and high testing coverage. Rapid testing platforms support larger disease screening interventions that could reduce prevalence of STIs in hard-to-reach populations. The development and field evaluation of point-of-care sequencing instruments promise to transform the practice of outbreak investigations. The potential of POCT to reduce completeness of gonorrhoea and chlamydia notification data will be also discussed.

POINT-OF-CARE TESTING SYMPOSIUM ABSTRACTS

Point of Care Testing in Emerging and Exotic Infections

Dr Matthew O'Sullivan

Centre for Infectious Diseases and Microbiology, Westmead Hospital

The outbreak of Ebola Virus Disease in West Africa is a key case study for the role of rapid point of care testing in containing outbreaks of infectious diseases. Clinical case definitions are often sacrifice specificity for sensitivity: as a result uninfected individuals may be cohorted with infected individuals while awaiting the results of laboratory testing. Rapid, accurate point of care testing could therefore play a key role in the termination of transmission. However, the current long lead time for developing and validating such assays for novel pathogens has so far limited their use in this setting.

Point of Care Testing in Parasitic Infections

Dr Rogan Lee

Centre for Infectious Diseases and Microbiology, ICPMR Pathology West, Westmead Hospital

Majority of point- of-care tests (POCT) are based on detection of parasite antigens. Some have also been designed to detect antibodies to recombinant antigens. The rapid result of tests and ease at which these tests can be done makes them useful in resource poor settings. However, these tests are becoming increasingly popular in Australian laboratories because they can be carried out at patient's bedside without the need for skilled laboratory staff. The main POCT used at Pathology West is for detection of malaria. This test can provide an early diagnosis when viral haemorrhagic fevers are also suspected in returned travellers. Variability in performance of these tests prompted WHO to conduct a global evaluation of 42 kits from 34 manufacturers. The results of this evaluation will be discussed. Other POCT for parasitic infections such as cryptosporidium and giardia and lymphatic filariasis are also used at ICPMR.

Applications of Point of Care testing for viral pathogens

Dr Jen Kok

Centre for Infectious Diseases and Microbiology, Westmead Hospital

Point-of-care (POC) testing is the fastest growing sector in the clinical *in vitro* diagnostic market, and is increasingly being used to improve patient outcomes by providing faster turnaround times. Technological advances, widescale manufacturing, miniaturization of testing devices and the integration of multiple pathogens into a single test have further improved testing availability and capability. In this presentation, I will discuss the performance of POC devices in the diagnosis of respiratory viruses, in particular influenza virus. I will also discuss the potential applications of POC devices for surveillance purposes.

Rapid diagnosis in septic shock

Professor Jon Iredell

Centre for Infectious Diseases and Microbiology, Westmead Hospital and CRE in Critical Infection, University of Sydney

- Recognition of sepsis using clinical indicators is insensitive and has performed poorly as a decision tool. Most biomarkers have been disappointing
- Recognition of bacteraemia at point of presentation is practical and potentially highly informative in the context of septic shock and it is possible to greatly improve diagnostic sensitivity by using culture-independent methods
- Identification of key prescribing decision thresholds is already well established for major Gram-positive pathogens but Gram-negative pathogens are very important in septic shock and their antibiotic resistance is drawn from a mobile resistance gene pool
- The natural ecology of the transmissible gene pool means that the relevant antibiotic resistance genes can be reliably predicted, with clear implications for surveillance / infection control strategies and for rapid diagnosis in the critically ill

Staff Profile



Name: Dr Rebecca Rockett

Position: Postdoctoral Fellow in Molecular Diagnostics,
Centre for Infectious Diseases and Microbiology -
Public Health, Westmead Hospital, Sydney

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After completing her undergraduate studies at the University of Queensland, Rebecca worked in numerous national and international virology reference laboratories, including the HIV Reference Laboratory, SydPath, Enteric Virus Unit, Public Health England and the South London Specialist Virology Centre, Kings College Hospital. Rebecca returned to Australia and commenced her PhD studies at the Queensland Paediatric Infectious Diseases Laboratory, characterising the biology and pathogenesis of newly described human polyomaviruses. These emerging viruses were uncovered using Next Generation Sequencing techniques which lead to Rebecca's keen interest in pathogen genomics, particularly optimising methodologies to characterise fastidious agents.

Currently the use of genomics to characterise pathogens is limited by the ability to isolate pure pathogen nucleic acid, usually after solid medium culture. In addition a growing number of infectious agents are diagnosed using nucleic acid amplification techniques (NAAT), these specimens are not suitable for laboratory culture. Rebecca's current project aims to develop genomics capability directly from clinical specimens. This will enable public health laboratories to utilise NAAT specimens, to examine and monitor genomic markers of antibiotic resistance, transmission and vaccine escape.

CONTACT US

For more information on any articles or CIDM-PH & MBI events, or to join the e-lists and receive regular updates, please contact us at:

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Upcoming Events....

RESEARCH SYMPOSIUM HONOURING PROFESSOR LYN GILBERT **Advancing Control of Communicable Diseases through Innovation and Translational Research**

REGISTRATIONS ARE OPEN

The Centre for Infectious Diseases and Microbiology Laboratory Services, Pathology West (ICPMR), the Centre for Infectious Diseases and Microbiology - Public Health (CIDM-PH), the Marie Bashir Institute, University of Sydney (MBI), and the Centre for Research Excellence in Critical Infections, University of Sydney (CRE Critical Infections) are proud to co-host this wonderful event to celebrate a lifetime of Professor Lyn Gilbert's achievements with a research symposium **Advancing Control of Communicable Diseases through Innovation and Translational Research**.

Confirmed Invited Speakers

- Professor Chris Baggoley, Chief Medical Officer of Australia
- Professor Ian Gust, University of Melbourne
- A/Professor Jeremy McAnulty, NSW Ministry of Health
- Professor Dennis Clements, Global Health Institute, Duke University USA
- Professor Gail Cassell, Harvard Medical School, USA
- Professor Peter McIntyre, NCIRS, University of Sydney
- Professor Suzanne Garland, Royal Women's Hospital, Melbourne
- Professor Saul Tzipori, Tufts University, Boston USA
- Professor Paul Johnson, University of Melbourne and Austin Health
- Professor Ian Kerridge, University of Sydney

Date: Friday, 18th March 2016

Time: 8.30am - 5.00pm

Location: John Loewenthal Auditorium, Westmead Hospital, Sydney

Program: www.sydney.edu.au/mbi

Registrations: www.sydney.edu.au/mbi

RSVP: 1 March 2016



An evening dinner function will also be held to honour Prof Gilbert.

In conjunction with The Westmead Association, the Centre for Infectious Diseases and Microbiology - Public Health (CIDM-PH), Centre for Infectious Diseases and Microbiology Laboratory Services (CIDMLS ICPMR), Marie Bashir Institute for Infectious Diseases and Biosecurity University of Sydney (MBI), and CRE in Critical Infection University of Sydney, we would like to invite you to attend a celebration dinner honouring Professor Lyn Gilbert, on Friday 18th March 2016, at 'The Tearoom, Queen Victoria Building, Sydney'.

Date: Friday 18 March 2016

Time: 7.30pm

Cost: \$125pp

Where: The Tearoom, Queen Victoria Building Address: 455 George Street, Sydney

RSVP & Payment:

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