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Breakpoint®
PO Box 8266, Angelo Street
South Perth, WA 6151
info@asainc.net.au

FROM THE EDITOR

From Small Beginings…

In this edition we highlight excellence in local scientific research. Notably, how small grants have helped researchers along the way. Although the drawcard for large funding bodies, such NHMRC funding, can predominate in the efforts for grant applications, the role of smaller grants, such as those offered by ASA and ASID, have a powerful role in promoting local research and providing early career emerging researchers vital building blocks toward larger funding opportunities.

In this issue we revisit the ASA Research Grant awardees over the last 10-years. The authors reflect on their research goals, what they have achieved, and how the seed funding from ASA has helped.

The ongoing support for local research in antimicrobials and infectious diseases is of critical importance to promote our national profile as a country that which produces high quality and impactful research, to attract philanthropic financial support, and cement our position of the international stage.

In addition to the special content, we include our standard items. This includes the photo quiz by **Dr Adrian Anderson**, and we shine the light on **Dr Brad Gardiner** and congratulate him on the completion of his PhD research program examining the complexities of CMV infection in immunocompromised patients.

Please contact me if you have comments or suggestions for future issues of the newsletter. Make sure you follow us on social media, and check out the updated ASA website. Also, a special call out for anyone who wants to contribute to the **front cover image** for future issues.

Dr Iain J. Abbott MBBS FRACP FRCPA PhD
The Alfred Hospital | Monash University | Melbourne
newsletter@asainc.net.au

Front Cover: Scanning electron microscopy image of a *Pseudomonas* biofilm on the internal aspect of a urinary catheter.

PHOTO QUIZ

A 49 year old male presents to the emergency department with complaints of progression of multiple ulcers on his left leg, some of which have been present for over a year. The patient is a seasonal worker, who has recently arrived in Tasmania from Vanuatu. He believed these ulcers were caused by friction from his work trousers. There is no history of trauma, animal or insect bite to the site and no known past medical history.

Examination findings revealed, multiple large ulcers on the left lower limb. They appear well defined and superficial with a punched out appearance. Two of the ulcers appeared to have a brown grey adherent membrane in the base.
An ultrasound of the area revealed multiple locules throughout the subcutaneous tissue with no oedema or invasion of deep tissues. The patient's ulcers were swabbed, cleaned and dressed and the patient was discharged home on oral antibiotics

The wound swab was sent for microscopy and culture. Wound swab microscopy revealed 3+ white blood cells and Gram stain revealed mixed organisms.

In view of wound characteristics and patient epidemiology a selective medium was used in addition to usual wound primary isolation media. Culture at 48h incubation on Horse Blood Agar (HBA) in 5% CO_2 at 35°C revealed mixed growth, which can be observed in Figure 2. Anaerobic cultures isolated additional mixed anaerobes. Culture of selective medium at 24h isolated our pathogen of interest.

Figure 3 is a Gram stain from the selective medium after 48h incubation in ambient air at 35°C.

Our causative pathogen was nitrate positive, urease negative, catalase positive, and pyrazinamidase negative on further biochemical testing.

What is the selective media used and what is the causative pathogen?

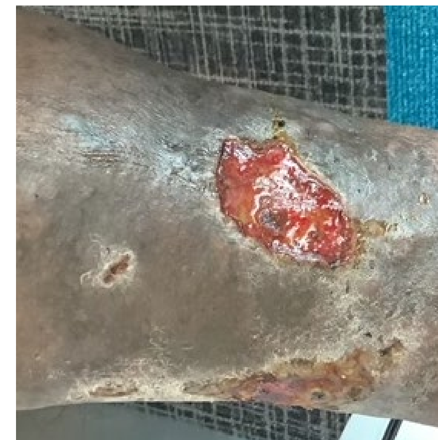


Figure 1
Patient leg wound

Figure 2
Culture at 48h incubation on HBA

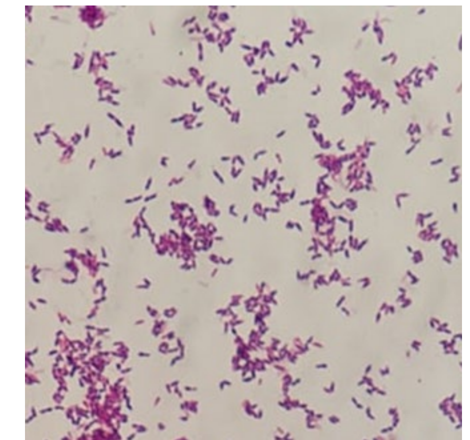


Figure 3
Gram stain from selective medium

IN THE SPOTLIGHT

UNRAVELLING THE COMPLEXITIES OF CMV INFECTIONS IN TRANSPLANT RECIPIENTS

Dr Brad Gardiner
B. App. Sc. MBBS FRACP MS PhD
Department of Infectious Disease
Alfred Health
Central Clinical School
Monash University
twitter | @BradGardiner6
bradgardiner@gmail.com

Cytomegalovirus (CMV) is a major contributor to morbidity and mortality in solid organ transplant recipients (SOTR). Preventative strategies are established but predicting who will develop CMV infection remains challenging. Promising new immune monitoring assays are now available, however studies informing their clinical use are limited. The overall aim of my PhD thesis is to improve prediction of CMV infection in SOTR. Specific aims are (1) explore absolute lymphocyte count (ALC) for prediction of recurrent CMV, (2) examine the relationship between recurrent CMV and long-term survival, (3) understand the predictive utility of Quantiferon®-CMV (QF-CMV) and (4) evaluate Quantiferon®-Monitor (QFM) as a biomarker of immunosuppression and predictor of infection.

We first examined the relationship between ALC and recurrent CMV infection in a retrospective cohort of 170 SOTR. Mean ALC in relapse-free patients was 1.08±0.69 versus 0.73±0.42 x10^3 cells/µL in those who relapsed, corresponding to an unadjusted hazard ratio of 1.11 (95% confidence interval 1.03-1.21, p=0.009) for every 100 cells/µL decrease in the ALC (Figure 1). After adjusting for potential confounders, the association between ALC and relapse remained significant (HR 1.11, 95% CI 1.03-1.20, p=0.01 for every 100 cells/µL decrease). We then assessed the effect of recurrent CMV on survival. Mortality amongst those who relapsed was 39% (19/49) versus 36% (43/121) in those who did not (adjusted HR 1.68, 95% CI 0.93-3.04, p=0.09).

Next, we retrospectively studied 263 lung transplant recipients (LTR) who

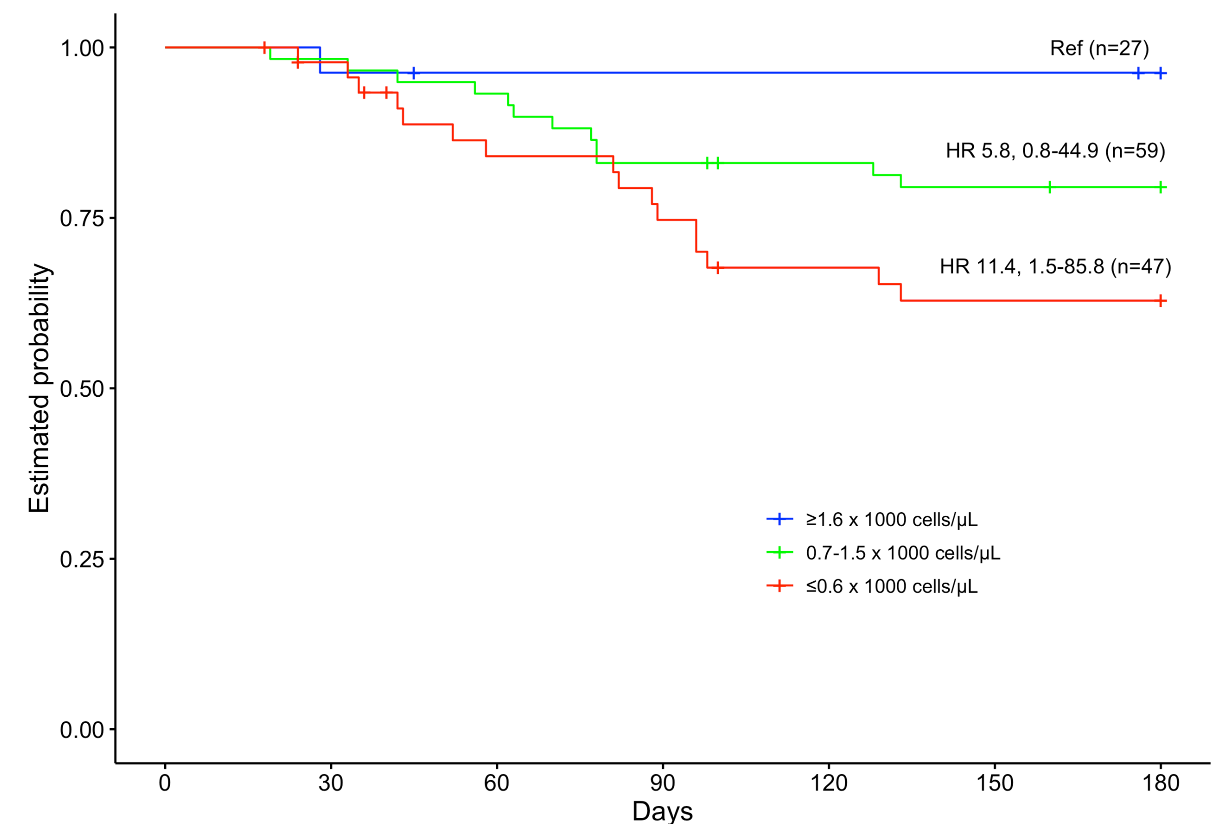


Figure 1: Unadjusted Kaplan-Meier estimates of relapse-free survival stratified by absolute lymphocyte count (x1000 cells/µL) at the time of treatment completion, n=133. Hazard ratios for relapse for each strata with 95% confidence intervals are displayed.

> **"QF-CMV results were strongly correlated with serostatus, with D+/R- patients unlikely test positive while receiving prophylaxis... but after accounting for serostatus, the incremental predictive value of QF-CMV was limited."**

underwent Quantiferon®-CMV testing at 5 months post-transplant, many receiving extended prophylaxis to 11 months if negative. Patients receiving extended prophylaxis experienced less CMV infection if testing negative/ indeterminate (43% vs. 74%, p<0.01) or positive (15% vs. 52%, p<0.01). Only 5/59 (8%) D+/R- patients were QF-CMV positive compared to 155/204 (76%) R+ patients (adjusted OR 0.03, 0.01-0.07, p<0.001). After controlling for prophylaxis duration, only D+/R- serostatus remained independently associated with CMV infection (adjusted HR 4.76, 95% CI 2.62-8.74, p<0.0001).

Finally, we performed a prospective cohort study of 80 LTR to evaluate QFM, a global immune function assay. Median pre-transplant levels were 171 IU/mL (IQR 45-461), decreasing to 3 IU/mL (IQR 1-8) at 2 weeks post-transplant then recovering towards baseline over the following year. Prednisolone was strongly inversely associated with QFM level (0.1mg/kg dose increase correlating with 88 IU/ mL QFM decrease, 95% CI 61-114, p<0.001). Patients with QFM values <10 and <60 IU/mL were more likely to develop a serious opportunistic infection between 3-6 months (HR 6.38, 95% CI 1.37-29.66, p=0.02) and 6-12 months (HR 3.25, 95% CI 1.11-9.49, p=0.03) post-transplant respectively (Figure 2).

In summary, we explored several predictors for CMV infection in SOTR. Low ALC was an independent predictor for recurrent CMV disease. There was a possible increased mortality signal amongst patients with recurrent CMV. QF-CMV results were strongly correlated with serostatus, with D+/R- patients unlikely test positive while receiving prophylaxis. Extended prophylaxis was associated with delayed onset, reduced frequency and severity of CMV infection across all subgroups but after accounting for serostatus, the incremental predictive value of QF-CMV was limited. Low QFM levels were associated with infection beyond 3 months post-transplant, suggesting that QFM may be able to identify overly immunosuppressed patients. These strategies could improve our ability to predict CMV and other infections, improving outcomes in SOTR.

PhD supervisors
Professor Anton Peleg[1,2] | Professor Glen Westall[3] | Professor Orla Morrissey[1] | Dr David Snydman[4]
1Department of Infectious Disease, Alfred Health and Central Clinical School, Monash University, Melbourne, Victoria, Australia
2Infection and Immunity Program, Monash Biomedicine Discovery Institute, Department of Microbiology, Monash University, Clayton, Victoria, Australia
3Department of Respiratory Medicine & Lung Transplantation, Alfred Health and Central Clinical School, Monash University, Melbourne, Victoria, Australia
4Division of Geographic Medicine and Infectious Diseases, Tufts Medical Center and Tufts University School of Medicine, Boston, MA, USA

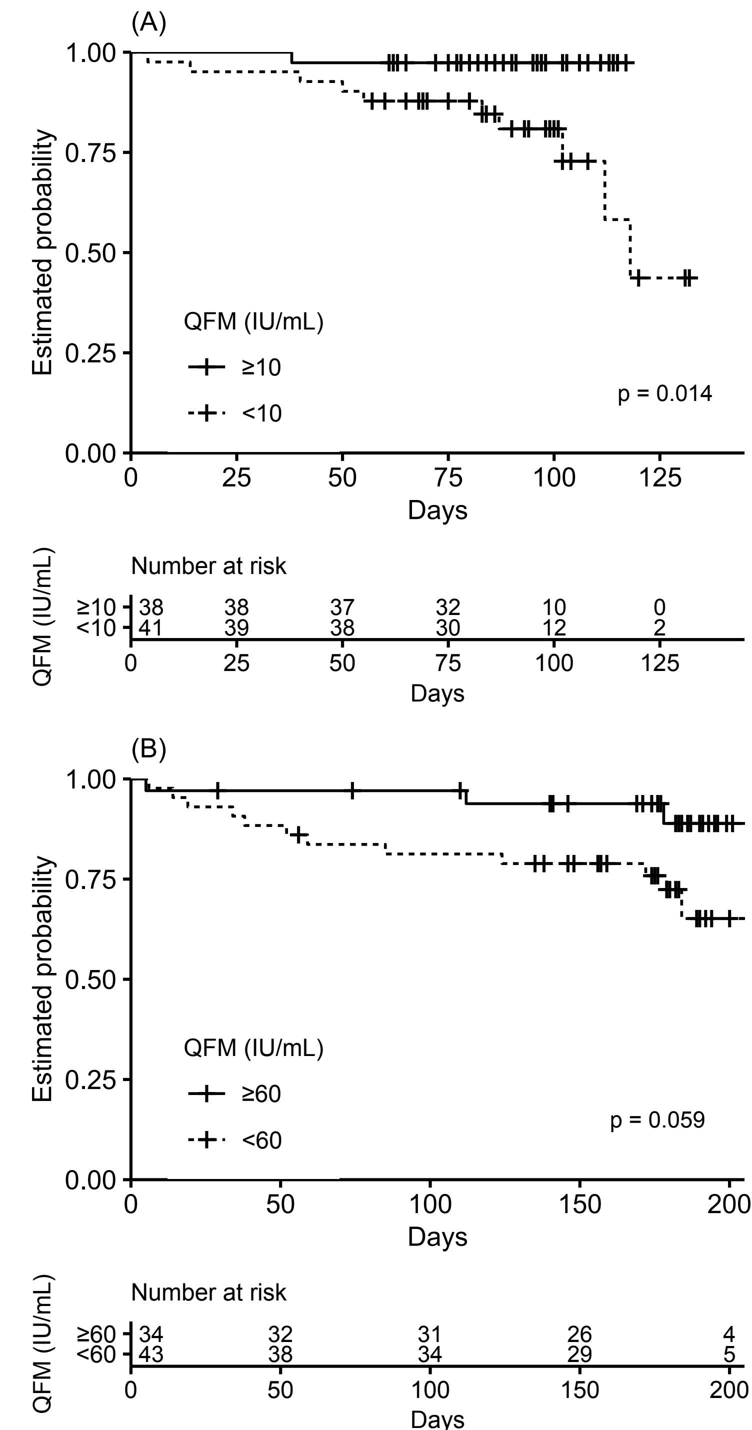


Figure 2: Unadjusted Kaplan-Meier estimates of freedom serious opportunistic infection 3 to 6 months (A) and 6 to 12 months (B) following transplantation, stratified by Quantiferon®-Monitor (QFM) results from the beginning of the period. P-values refer to log-rank test results.

Publications

Gardiner BJ, Nierenberg NE, Chow JK, Ruthazer R, Kent DM, Snydman DR. Absolute lymphocyte count: a predictor of recurrent cytomegalovirus disease in solid organ transplant recipients. Clin Infect Dis 2018; 67(9):1395-402
Gardiner BJ, Chow JK, Brilleman SL, Peleg AY, Snydman DR. The impact of recurrent cytomegalovirus infection on long-term survival in solid organ transplant recipients. Transpl Infect Dis 2019; 21(6): e13189
Gardiner BJ, Lee SJ, Robertson, AN, Cristiano Y, Snell GI, Morrissey CO, Peleg AY, Westall GP. Real-world experience of Quantiferon®-CMV directed prophylaxis in lung transplant recipients. *Submitted for publication.*
Gardiner BJ, Lee SJ, Cristiano Y, Levvey BJ, Sullivan LC, Snell GI, Peleg AY, Westall GP. Evaluation of Quantiferon®-Monitor as a biomarker of immunosuppression and predictor of infection in lung transplant recipients. Transpl Infect Dis 2021; 23(3): e13550

ASA Annual Research Grant

The 2023 Australian Society for Antimicrobials (ASA) Annual Research Grant of up to $25,000 to support original research is now available.

The following conditions apply:

- Funding is limited to ASA financial members.
- The Principal Investigator (PI) must have been an ASA member for at least twelve month
- Preference will be given to stand-alone projects
- Preference will be given to early career researchers
- The successful applicant will present their work at an ASA annual scientific meeting
- If applicable the PI will submit an article for the ASA newsletter and website
- ASA will be acknowledged on all resulting publications and presentations
- 12 and 24 month progress reports must be submitted to the ASA committee

The research funds are to be used for the project as per the budget application only. ASA does not support an institution's infrastructure or overhead costs.

The application must be performed on line via the ASA website Research Grant Application Form and must include:

- A copy of the PI's CV.
- Head of Department confirmation of the application and the Department has the resources required to undertake the project.

The grant application and CV will be assessed by a panel of at least six independent reviewers using a standardised scoring system. Applicants will be informed of the decision one week before the ASA annual scientific meeting "Antimicrobials 2023".

Applications will be accepted online up to **31 October 2022.**
Click here for the Research Grant Application Form.

For further enquiries, please contact the ASA secretary at info@asainc.net.au.

Submission Closing
Monday 31st October 2022

AUSTRALIAN SOCIETY FOR ANTIMICROBIALS

ASA RESEARCH GRANT RECIPIENTS

ASA Antimicrobials 2012 Research Grant Recipient
Sally Partridge
Westmead Hospital
Complete Sequencing of Selected, Informative Multi-Resistance Plasmids from Enterobacteriaceae Clinical isolates

ASA Antimicrobials 2013 Research Grant Recipient
David Paterson
University of Queensland
Randomised Controlled Trial of Meropenem versus Piperacillin-Tazobactam for Definitive Treatment of Bloodstream Infections due to Ceftriaone Non-Susceptible *Escherichia coli* and *Klebsiella* spp

ASA Antimicrobials 2014 Research Grant Recipient
Justine Gibson
University of Queensland
Promiscuous plasmids in avian pathogenic (APEC) and faecal Escherichia coli (AFEC): How to safeguard Australia

ASA Antimicrobials 2016 Research Grant Recipient
Norelle Sherry and Jason Kwong
University of Melbourne
Genomic Investigation of Carbapenem-resistant Enterobacteriacae in Victoria

ASA Antimicrobials 2017 Research Grant Recipient
Christopher Blyth
University of Western Australia
Invasive Staphylococcus aureus Infections and Hospitalisations (ISAIAH) in Australian Children: A Two-year Prospective, Multi-Centre Cohort Examining Contemporary Paediatric Clinical and Molecular Epidemiology of S. aureus

ASA Antimicrobials 2018 Research Grant Recipient
Shakeel Mowlaboccus
University of Western Australia
Molecular mechanism of reduced susceptibility to ceftriaxone and penicillin in Neisseria meningitidis

ASA Antimicrobials 2019 Research Grant Recipient
Kelly Wyres
Monash University
Understanding the Risks of Emergence of Last Line Drug Resistance in Distinct Strains of Klebsiella pneumoniae

ASA Antimicrobials 2020 Research Grant Recipients
Caitlin Keighley
ICPMR Westmead Hospital, NSW
Genomics of Antimicrobial resistance in Candida tropicalis

ASA Antimicrobials 2022 Research Grant Recipient
Iain Abbott
Monash University
Optimising antimicrobial therapy to treat problematic biofilms using a novel pharmacodynamic urinary catheter biofilm model

2014 RECIPIENT

Promiscuous plasmids in avian pathogenic & faecal E. coli.

I am a veterinarian, a veterinary microbiologist with an interest in antimicrobial resistance (AMR), stewardship, infection control and point of care diagnostics to improve animal and human health in Australia and Internationally. In 2014, I was an early career researcher and was awarded an ASA Research Grant for the research project titled: "Promiscuous plasmids in avian pathogenic (APEC) and faecal *Escherichia coli* (AFEC): How to safeguard Australia". In addition to identifying plasmid types in APEC and AFEC, this was an opportunity to work and develop a relationship with the Australian poultry industry.

The research identified high levels of antimicrobial susceptibility in APEC and AFEC for a range of antimicrobials though a small number (4%; 10/237) were resistant to extended spectrum cephalosporins (ECS) and/or fluoroquinolones (FQ). Isolates were diverse regarding their antimicrobial resistance, virulence genes, phylogenetic profile, and plasmid replicons. Plasmid replicons were detected in nearly all (92%; 219/237) isolates. This research was presented at ASA conference in 2016 (Awawdeh et al. 2016), and the research undertaken during this grant formed part of a PhD student's doctoral thesis and has recently been published in Avian Pathology (Awawdeh, Turni, et al. 2022).

The Australian meat chicken industry uses limited antimicrobials, with no history of ESC and FQ use, therefore, we hypothesised the source of resistant isolates was external to the shed. This has led to a second publication identifying risk factors associated with the carriage of APEC in meat chickens in Queensland (Awawdeh, Forrest, et al. 2022) and further research opportunities and identification of research priorities.

The Australian animal industries are tight-knit and having the opportunity to work with one of the major industries in Australia opened doors to other livestock industries. I have been able to work with Meat Livestock Australia (Schibrowski, Barnes, et al. 2018; Schibrowski, Gibson, et al. 2018; Wood et al. 2019), the Australian Pig Industry (Smith et al. 2016) and currently with the Australian Dairy Industry on a Corporate Research Centres Project "On-Farm Detection Platform; Mastitis-Causing Pathogens in Dairy Cattle". During this project, I am working with 30 dairy farmers in the subtropical dairy region to identify pathogens, risk factors, and outcomes associated with clinical mastitis. The development of on-farm point of care tests will also improve antimicrobial stewardship.

Working with the Australian livestock industries has led to international research opportunities with pigs in Vietnam (Smith et al. 2014), integrated poultry-fish farming in Myanmar (Gibson et al. 2020) and poultry in Bangladesh (Imam et al. 2020).

I am also part of a team of researchers from the Queensland Alliance for One Health Sciences, who are working with the poultry, dairy, and pig industries to collect environmental samples from farms and samples from farm workers. Samples will undergo metagenomic sequencing for antimicrobial resistance genes. This project will address the animal industries research priority of identifying biosecurity risks associated with human and other exogenous sources of antimicrobial resistant genes and bacteria on farms. Without the foundational relationships with the animal industries, this research would not be possible.

Since 2014, many things have changed. We no longer work with few farms and isolates, now we work with 'big data'. Phenotypic methods are now always used in conjunction with genotypic – to research AMR we rely on use of whole genome sequencing, microbiomics, and metagenomics. We are more likely to work in research teams with members representing industry, social science, veterinary science, human health, and the environment.

But you need to start somewhere, and small research grants lead to the development of research skills, students, publications, and relationships with industry partners that allows your research to grow.

Dr Justine Gibson
BVSc (Hons1) PhD SFHEA GCHed
Associate Professor in Veterinary Bacteriology and Mycology
School of Veterinary Science
The University of Queensland
Monash University
+61 409271896
gibson.j@uq.edu.au

Publications

Awawdeh, L., R. Forrest, C. Turni, R. N. Cobbold, J. Henning, and J. S. Gibson. 2022. 'Risk factors associated with the carriage of pathogenic Escherichia coli in healthy commercial meat chickens in Queensland, Australia', Poultry, 1: 94-110.
Awawdeh, L., C. Turni, J. L. Mollinger, J. Henning, R. N. Cobbold, Groves M., D. L. Wakeham, F. Shapter, and J. S. Gibson. 2016. "Low level presence of resistance to extended spectrum cephalosporins and fluoroquinolones in Escherichia coli in the highly regulated Australian poultry industry." In Australian Society of Antimicrobial. Melbourne Exhibition Centre, Melbourne.
Awawdeh, L., C. Turni, J. L. Mollinger, J. Henning, R. N. Cobbold, D. J. Trott, D. L. Wakeham, and J. S. Gibson. 2022. 'Antimicrobial susceptibility, plasmid replicon typing, phylogenetic grouping, and virulence potential of avian pathogenic and faecal Escherichia coli isolated from meat chickens in Australia', Avian Pathol: 1-12.
Gibson, Justine S., Honey Wai, Shwe Sin May Lwin Oo, Ei Moh Moh Hmwe, Soe Soe Wai, Lat Lat Htun, Hwee Ping Lim, Zin Min Latt, and Joerg Henning. 2020. 'Antimicrobials use and resistance on integrated poultry-fish farming systems in the Ayeyarwady Delta of Myanmar', Scientific Reports, 10: 16149.
Imam, Tasneem, Justine S. Gibson, Mohammad Foysal, Shetu Bhusan Das, Suman Das Gupta, Guillaume Fournié, Md. Ahasanul Hoque, and Joerg Henning. 2020. 'A Cross-Sectional Study of Antimicrobial Usage on Commercial Broiler and Layer Chicken Farms in Bangladesh', Frontiers in Veterinary Science, 7.
Schibrowski, M. L., T. S. Barnes, N. K. Wawegama, M. E. Vance, P. F. Markham, P. D. Mansell, M. S. Marenda, A. Kanci, J. Perez-Casal, G. F. Browning, J. S. Gibson, and T. J. Mahony. 2018. 'The performance of three immune assays to assess the serological status of cattle experimentally exposed to Mycoplasma bovis', Vet Sci, 5.
Schibrowski, M. L., J. S. Gibson, K. E. Hay, T. J. Mahony, and T. S. Barnes. 2018. 'Mycoplasma bovis and bovine respiratory disease: A risk factor study in Australian feeder cattle', Prev Vet Med, 157: 152-61.
Smith, M., T. N. Do, J. S. Gibson, D. Jordan, R. N. Cobbold, and D. J. Trott. 2014. 'Comparison of antimicrobial resistance phenotypes and genotypes in enterotoxigenic Escherichia coli isolated from Australian and Vietnamese pigs', J Glob Antimicrob Resist, 2: 162-67.
Smith, M. G., D. Jordan, J. S. Gibson, R. N. Cobbold, T. A. Chapman, S. Abraham, and D. J. Trott. 2016. 'Phenotypic and genotypic profiling of antimicrobial resistance in enteric Escherichia coli communities isolated from finisher pigs in Australia', Aust Vet J, 94: 371-6.
Wood, C., M. Muleme, T. Tan, K. Bosward, J. Gibson, J. Alawneh, M. McGowan, T. S. Barnes, J. Stenos, N. Perkins, S. M. Firestone, and S. Tozer. 2019. 'Validation of an indirect immunofluorescence assay (IFA) for the detection of IgG antibodies against Coxiella burnetii in bovine serum', Prev Vet Med, 169: 104698.

2016 RECIPIENT

GENOMICS FOR CARBAPENEMASE-PRODUCING ENTEROBACTERALES: FROM PILOT PROJECT TO PUBLIC HEALTH SURVEILLANCE

A/Prof Jason Kwong
Infectious Diseases Physician & Medical Director, Infection Prevention & Control, Austin Health
Honorary Early Career Research Fellow, Department of Microbiology & Immunology, University of Melbourne at the Doherty Institute
Clinical Associate Professor, Department of Medicine, University of Melbourne at Austin Health

Ms Courtney Lane
Epidemiology Section Lead, Microbiological Diagnostic Unit Public Health Laboratory at the Doherty Institute

Dr Norelle Sherry
Acting Deputy Director, Microbiological Diagnostic Unit Public Health Laboratory at the Doherty Institute
Infectious Diseases Physician, Austin Health

In February 2012, a patient was repatriated from Greece after spending 3 months in hospital and intensive care there, requiring repeated surgery for complex and extensive intra-abdominal infection.[1] The patient was transferred to a tertiary Melbourne hospital and admitted to a single room with an en-suite bathroom with intensive contact precautions applied for the duration of his hospital stay. Clinical samples from the patient cultured a KPC-producing Klebsiella pneumoniae isolate, and he required management in hospital for a further 3 months before being discharged home.

A few months later, a second KPC-producing organism was identified in a urine sample from a patient in Victoria, followed by a third KPC-producing organism 3 weeks later from patients in different hospitals. In response, the Microbiological Diagnostic Unit (MDU) – the Victorian state public health laboratory – commenced surveillance testing for carbapenemases by PCR.[2]

These weren't the first KPC-producing organisms identified in Australia – this had been reported earlier again from a patient who had returned from Greece to Sydney in 2010.[3] The IMP-4 carbapenemase had also been identified in Gram-negative organisms as early as 2004, presumably following introduction from South-East Asia.[4] However, unlike the patients returning after overseas travel, the emergence of locally-acquired KPC-producing organisms without a clear epidemiological link raised some alarm bells.

Yet after a small outbreak in 2012 at one Melbourne hospital,[5] the number of new KPC cases fell away in 2013. Despite the additional information from the new cases, the initial cases remained unlinked. It wasn't until 2014 when things took off, with 31 new detections of KPC from samples submitted from 26 different hospitals and healthcare facilities, as well as community samples.

This was alarming. It was clear transmission was occurring locally. Where and how extensive this had happened was not clear. Director of MDU, Professor Ben Howden, urged the Victorian Department of Health to take control before it became too late. He offered the additional information from genomics, an emerging technology in the public health microbiology field at the time, to help understand the outbreak and focus control measures. This revealed the outbreak actually comprised four separate outbreaks, with a strong suggestion that transmission was occurring in healthcare facilities.[2] A concerted effort to look at both epidemiological and genomic data allowed genomic parameters to be established that helped predict what was likely to be transmission and what wasn't. In 2015, the Communicable Diseases Unit in the Department of Health drafted and implemented the first iteration of the Victorian guideline on carbapenemase-producing Enterobacteriaceae.[6] Notably, the guideline included the use of genomics to guide investigations – a concept that has been adopted and evolved into surveillance systems for other pathogens of public health significance including SARS-CoV-2.

> "...CPE remains a significant antimicrobial resistance threat, representing over 40% of the critical antimicrobial resistance..."

In 2016, we were awarded the ASA Research Grant for the research proposal 'Genomic investigation of carbapenem-resistant Enterobacteriaceae in Victoria'. This grant assisted us to examine all stored Victorian CPE isolates from

2012-2016 (beyond KPC), sequencing over 200 additional CPE isolates. This project identified the polyclonal nature of CPE in Victoria, with IMP-4, KPC-2, NDM and OXA carbapenemases each representing approximately one quarter of CPE isolates. These data were also used to define sample referral criteria for the state, noting the meropenem MIC distributions of CPE isolates were well below the 'susceptible' breakpoints. Additionally, the high sensitivity and specificity of carbapenem inactivation method (CIM) testing were established for local use.[7]

Has the genomics-guided "search and contain" approach to finding and isolating cases of CPE in Victoria been successful? Clearly, CPE remains a significant antimicrobial resistance threat, representing over 40% of the critical antimicrobial resistance organisms reported to CARAlert.[8] With the resumption of international travel, repeated incursions are likely to add to this burden. In Victoria, small healthcare-related outbreaks continue to punctuate surveillance numbers, with transmission often occurring prior to recognition of index cases. However, it's evident that early identification and implementation of control measures reduces the number of people exposed and, at least based on short term follow up, the subsequent number of new cases.[9] In this sense, the Victorian program has been successful in identifying a greater proportion of new cases early through screening processes, compared to cases identified when they present with clinical infections due to CPE.

Notable challenges and questions remain in our efforts to control CPE. How do we identify when carbapenemase-gene-containing plasmids are being transmitted between patients? How do we contain endemic populations of CPE permanently colonising healthcare environments? Can we and do we need to sustain transmission-based precautions for the growing burden of patients recognised to be colonised? How do we collaborate and assist with the global efforts to control CPE?

There is clearly plenty of work underway to address these and other questions. But the use of pathogen genomics has evolved into being a fundamental component of public health surveillance programs, involving interstate and international collaborations. The Communicable Diseases Genomics Network has continued to lead this in Australia, including the introduction of AusTrakka in 2020 – Australia's first real-time national pathogen genomics surveillance platform.[10] From investigating a local outbreak of KPC, pathogen genomics has grown into a significant tool for public health surveillance and control of CPE.

We are grateful to ASA for their support in the early stages of these CPE projects in Victoria.

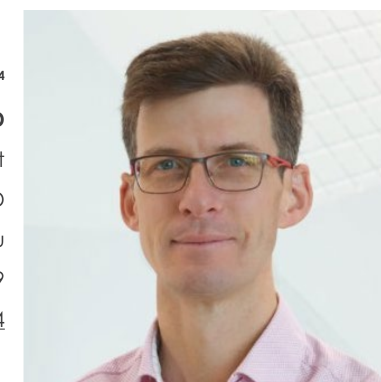
References

1. Chua KY, Grayson ML, Burgess AN, Lee JY, Howden BP. The growing burden of multidrug-resistant infections among returned Australian travellers. Med J Aust. 2014;200(2):116-8.
2. Kwong JC, Lane CR, Romanes F, Goncalves da Silva A, Easton M, Cronin K, et al. Translating genomics into practice for real-time surveillance and response to carbapenemase-producing Enterobacteriaceae: evidence from a complex multi-institutional KPC outbreak. PeerJ. 2018;6:e4210.
3. Coatsworth NR, Huntington PG, Hardiman RP, Hudson BJ, Fernandes CJ. A case of carbapenemase-producing Klebsiella pneumoniae in Australia. Pathology. 2012;44(1):42-4.
4. Peleg AY, Franklin C, Bell J, Spelman DW. Emergence of IMP-4 metallo-beta-lactamase in a clinical isolate from Australia. J Antimicrob Chemother. 2004;54(3):699-700.
5. Chang LW, Buising KL, Jeremiah CJ, Cronin K, Poy Lorenzo YS, Howden BP, et al. Managing a nosocomial outbreak of carbapenem-resistant Klebsiella pneumoniae: an early Australian hospital experience. Intern Med J. 2015;45(10):1037-43.
6. Department of Health. Victorian guideline on carbapenemase-producing Enterobacteriaceae for health services 2015 [Available from: https://www.health.vic.gov.au/infectious-diseases/victorian-guideline-on-cpe-for-health-services-version-21.
7. Sherry NL, Lane CR, Kwong JC, Schultz M, Sait M, Stevens K, et al. Genomics for Molecular Epidemiology and Detecting Transmission of Carbapenemase-Producing Enterobacterales in Victoria, Australia, 2012 to 2016. J Clin Microbiol. 2019;57(9).
8. Australian Commission on Safety and Quality in Health Care. CARAlert annual report: 2020. Sydney: ACSQHC; 2021.
9. Lane CR, Brett J, Schultz M, Gorrie CL, Stevens K, Cameron DRM, et al. Search and Contain: Impact of an Integrated Genomic and Epidemiological Surveillance and Response Program for Control of Carbapenemase-producing Enterobacterales. Clin Infect Dis. 2021;73(11):e3912-e20.
10. Hoang T, da Silva AG, Jennison AV, Williamson DA, Howden BP, Seemann T. AusTrakka: Fast-tracking nationalized genomics surveillance in response to the COVID-19 pandemic. Nat Commun. 2022;13(1):865.

2017 RECIPIENT

BIG THINGS ON THE HORIZON

Examining little people in national AMR



Professor Christopher C Blyth[1,2,3,4]
MBBS (Hons), DCH, FRACP, FRCPA, PhD
Paediatrician, ID Physician & Clinical Microbiologist
Perth Children's Hospital, Department of ID
christopher.blyth@uwa.edu.au
+614 1882 7009
twitter | @ChrisBlyth74

Dr Anita J Campbell[1,2,3]
MBBS, DCH, DipPID, FRACP, PhD
Paediatric ID Specialist
Perth Children's Hospital, Department of ID
anita.campbell2@health.wa.gov.au
+618 6456 2222
twitter | @Anita_JCampbell

A collaboration between the Australian Group on Antimicrobial Resistance (AGAR) and the Australian and New Zealand Paediatric Infectious Diseases Clinical Research Network (ANZPID-CRN) and supported by an ASA grant (2018) provided the opportunity to explore antimicrobial resistance (AMR), as well as the role Staphylococcus aureus AMR genes and toxins play in S. aureus bacteraemia (SAB) disease severity, management and outcome in children.

The Australian Society of Antimicrobials (ASA) grant facilitated additional whole genome sequencing (WGS) for paediatric methicillin-susceptible S. aureus (MSSA) bacteraemia isolates and NZ paediatric SAB isolates contributing to the data from already sequenced Australian MRSA isolates. This complete WGS SAB data was paired with clinical information from the ISAIAH cohort, a prospective multisite study of Australian and New Zealand children hospitalised with SAB over 24 months (2017-2018).

Overall, 353 SAB isolates were sequenced; 85% MSSA (301/353) and 15% MRSA, (52/353). There

1. Department of Infectious Diseases, Perth Children's Hospital, Nedlands. 2. Wesfarmers Centre of Vaccines and Infectious Diseases, Telethon Kids Institute, Perth, Australia. 3. School of Medicine, University of Western Australia, Perth, Australia. 4. Department of Microbiology, PathWest Laboratory Medicine, QEII Medical Centre, Perth, Western Australia.

were 92 sequence types (STs), most commonly ST5 (18%) and ST30 (8%), grouped into 23 clonal complexes (CCs), most frequently CC5 (21%) and CC30 (12%). MSSA comprised the majority of healthcare-associated SAB (87%, 109/125), with principal clones CC15 (48%, 11/21) and CC8 (33%, 7/21). Panton-Valentine leukocidin (PVL)-positive SAB occurred in 22% (76/353); predominantly MSSA (59%, 45/76), community-onset (92%, 70/76) infections. For community-onset SAB, the only microbiological independent predictor of poor outcomes in children was PVL positivity (aOR 2.6 [CI 1.0-6.2]). From this WGS paediatric SAB data, we demonstrated the previously limited-recognition MSSA has in harbouring genetic virulence (59% of MSSA isolates were PVL+) and causing healthcare-associated infections (CC15 and CC8 were identified as MSSA healthcare-associated clones). These findings highlight the importance of genomic sequencing of MSSA as well as MRSA and the need for further research to define the potential implications PVL-producing strains may have on approaches to S. aureus clinical management.

Additionally, we examined national AMR surveillance data from AGAR comparing children with adults, using consistent methodologies. Paediatric isolates from 2013– 2016 comprised 5% (2025/40,034) of all isolates submitted to the AGAR surveillance program. Significant differences were identified among AMR between children and adults, including a dramatic rise in community-onset MRSA among Australian Aboriginal and Torres Strait

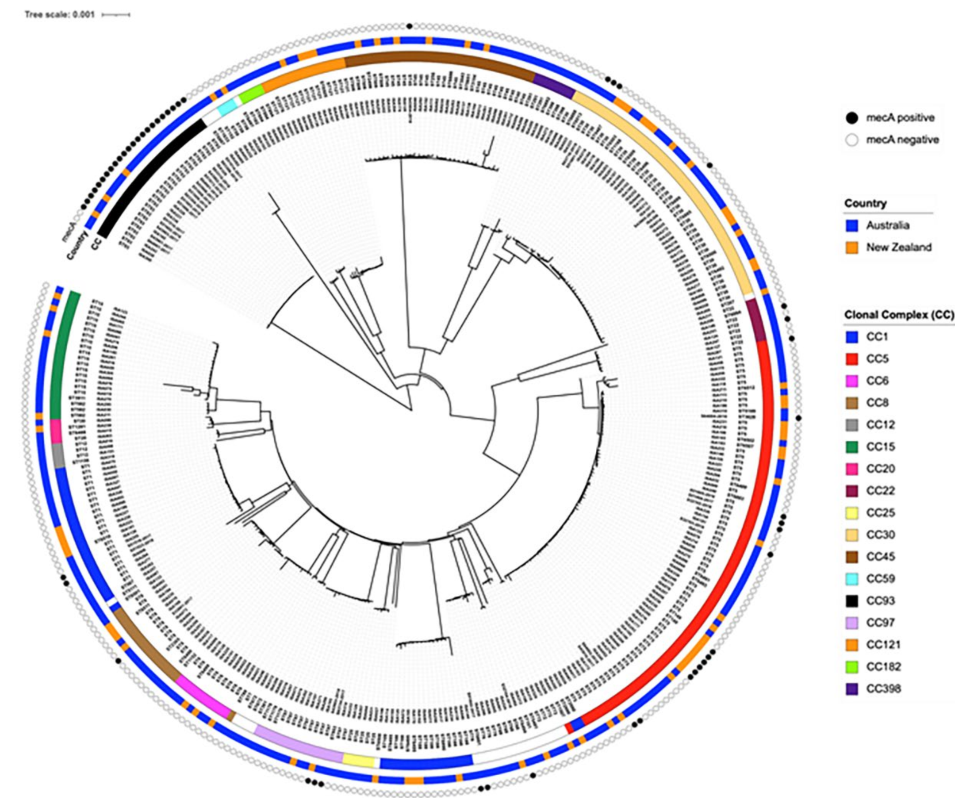


Figure 1 Phylogenetic tree for methicillin-resistant and methicillin-susceptible paediatric S. aureus bacteraemia isolates from Australia and New Zealand. CC, clonal complex. aMecA positive refers to the MecA genetic element found in MRSA strains. bMecA negative refers to the MecA genetic element not found in MSSA strains.

Islander children. PVL-positive MRSA bacteraemia was also more frequent in children compared with adults (61% vs 23%; p<0.0001). The burden of Gram-negative resistance was disproportionately experienced in young children, with higher odds of death with an extended spectrum beta-lactamase (ESBL) versus non-ESBL bacteraemia in comparison with adults (OR 2.7 [95% CI 1.0–7.1]; adults OR 1.2 [95% CI 1.0–1.5]). Whilst the resistance trends outlined, impacted children more than adults, overall children had lower rates of AMR and mortality for SAB and other significant bacteraemia's compared with adults.

These studies have facilitated an improved understanding of paediatric

AMR, as well as increased paediatric national representation (all major Australian paediatric hospitals are now included) in the AGAR surveillance program. This has culminated in formation of a paediatric focus within AGAR (AGAR-Kids). Key objectives of this stream of work will include ongoing reporting of neonates and children in the Australian national AMR surveillance program, along with examining emerging AMR trends over time. This experience provides an example of the importance of understanding infant and childhood AMR. These data also inform an array of wider applications including antimicrobial guidelines and stewardship, as well as national hospital and public health infection prevention policy. AGARKids will provide an ideal platform for ongoing collaborative projects including epidemiological studies, antimicrobial stewardship projects and as well AMR analysis for clinical trials such as the currently enrolling S. aureus network adaptive platform SNAP trial led by investigators Steve Tong and Josh Davis and SNAP-PY (the paediatric arm of the SNAP trial) led by Asha Bowen. This global, multicentre, open- label, novel platform trial will address multiple therapeutic questions to determine the best antibiotic treatments for adults and children with SAB. It also highlights the benefit of joining laboratory and surveillance networks, generating high-quality microbiology and genomic data with clinical research networks, ensuring the generation of new knowledge to inform our approach to Staphylococcus aureus treatment and other key pathogens in the future.

Acknowledgements:
We wish to acknowledge the AGAR laboratories for contributing the AGAR data and isolates used in this study, as well as all the participants who contributed data to this study and the Australian and New Zealand Paediatric Infectious Diseases (ANZPID) clinical research network (CRN).

Co-authors:
Shakeel Mowlaboccus
College of Science, Health, Engineering and Education, Murdoch University, Murdoch. Department of Microbiology, PathWest Laboratory Medicine WA, Fiona Stanley Hospital, Western. School of Biomedical Sciences, University of Western Australia, Nedlands.
Geoffrey W. Coombs
College of Science, Health, Engineering and Education, Murdoch University, Murdoch. Department of Microbiology, PathWest Laboratory Medicine WA, Fiona Stanley Hospital, Western Australia.
Denise A. Daley
Department of Microbiology, PathWest Laboratory Medicine WA, Fiona Stanley Hospital, Western Australia. The Australian Group on Antimicrobial Resistance.
Laila S. Al Yazidi
Child Health Department, Sultan Qaboos University Hospital, Muscat, Oman. Department of Immunology and Infectious Diseases, Sydney Children's Hospital, Randwick, Sydney. The Children's Department of Infectious Diseases and Microbiology, the Children's Hospital at Westmead, NSW.
Linny K. Phuong
Department of General Medicine, ID Unit, Royal Children's Hospital, Melbourne. Infection and Immunity Group, Murdoch Children's Research Institute, Melbourne.
Clare Leung
Department of Paediatrics, Wagga Wagga Base Hospital, New South Wales.
Emma J. Best
Department of Paediatrics; Child and Youth Health, The University of Auckland. The National Immunisation Advisory Centre, The University of Auckland. Department of Infectious Diseases, Starship Children's Hospital.
Rachel H. Webb
Department of Paediatrics; Child and Youth Health, The University of Auckland. Department of Infectious Diseases Starship Children's Hospital, Auckland. Department of Paediatrics, Kidz First Hospital, Auckland, New Zealand
Lesley Voss
Department of Paediatrics; Child and Youth Health, The University of Auckland. Department of Infectious Diseases, Starship Children's Hospital, Auckland.
Eugene Athan
Department of ID, Barwon Health, Geelong. School of Medicine, Deakin Uni, Geelong.
Philip N. Britton
Sydney Medical School and Marie Bashir Institute, University of Sydney, NSW. Department of Infectious Diseases and Microbiology, the Children's Hospital at Westmead, Sydney.
Penelope A. Bryant
IDs Unit, Department of General Medicine, The Royal Children's Hospital, Parkville, Victoria. Murdoch Children's Research Institute, The Royal Children's Hospital, Parkville, Victoria.
Coen T. Butters
Department of General Medicine, ID Unit, Royal Children's Hospital, Melbourne. Infection and Immunity Group, Murdoch Children's Research Institute, Melbourne.
Jonathan R. Carapetis
Department of Infectious Diseases, Perth Children's Hospital, Nedlands, Western Australia. Wesfarmers Centre of Vaccines and Infectious Diseases, Telethon Kids Institute, Perth, Western Australia. University of Western Australia. School of Medicine, Perth.
Natasha S. Ching
Infection and Immunity, Monash Children's Hospital, Monash Health, Clayton, Victoria. Department of General Paediatrics, Monash Children's Hospital, Monash Health, Victoria. Department of Paediatrics, Monash University, Clayton.
Joshua Francis
Global and Tropical Health Division, Menzies School of Health Research, Charles Darwin University, Darwin. Department of Paediatrics, Royal Darwin Hospital, Darwin.
Te-Yu Hung
Department of Paediatrics, Royal Darwin Hospital, Darwin.
Clare Nourse
Queensland Children's Hospital, Brisbane. Faculty of Medicine, University of Queensland.
Samar Ojaimi
Infection & Immunity, Monash Children's Hospital, Monash Health, Clayton, Victoria Department of Paediatrics, Monash University, Clayton. Monash Infectious Diseases, Monash Health, Clayton, Victoria.
Alex Tai
Department of Infectious Disease, Barwon Health, Geelong.
Nan Vasilunas
Infectious Diseases Department, Women's and Children's Hospital, Adelaide.
Brendan McMullan
Department of Immunology and Infectious Diseases, Sydney Children's Hospital, Randwick, Sydney. School of Women's and Children's Health, University of NSW. National Centre for Infections in Cancer, University of Melbourne.
Asha C. Bowen
Department of IDs, Perth Children's Hospital, Nedlands. Wesfarmers Centre of Vaccines and Infectious Diseases, Telethon Kids Institute. School of Medicine, University of Western Australia, Subiaco. Menzies School of Health Research, Charles Darwin Hospital, Darwin.
Jan M Bell
The University of Adelaide, Adelaide, South Australia.
Stanley Pang
Department of Microbiology, PathWest Laboratory Medicine, QEII Medical Centre, Royal Perth Hospital and Fiona Stanley Hospital, Western Australia. Antimicrobial Resistance and Infectious Diseases Research (AMRID) Laboratory, Murdoch University, Perth, WA.

2019 RECIPIENT

a personal story

Small research grants as stepping stones to academic independence

Dr Kelly Wyres DPhil
Senior Research Fellow
& NHMRC Emerging Leadership Fellow
Department of Infectious Diseases
Central Clinical School
Monash University

In 2018 I was working as a post-doctoral research fellow in the laboratory of Dr Kathryn Holt. I had held the role for three years after a two-and-a-half-year stint in industry, and was establishing a record of quality research contributions in the field of bacterial population genomics. My specific focus was, and continues to be, Klebsiella pneumoniae- a WHO priority antimicrobial resistant pathogen most well-known for causing healthcare-associated infections with growing rates of multi-drug resistance. I was embedded within arguably one of the leading bacterial genomics research teams globally, and I knew my craft. I loved the satisfaction of answering biological questions and solving analytical problems, and I wanted to keep doing research for as long as possible. But could I really ever make it to an independent research position? I'd had one small funding success- a University of Melbourne Early Career Researcher grant awarded two years prior; but a string of funding knockbacks- an NHMRC Early Career Fellowship, two ARC Discovery Early Career Researcher Awards and three NHMRC project grants as co-chief investigator- hardly a cause for optimism.

Fortunately, I had a fantastic mentor in Dr Holt, who encouraged and supported me to apply for the ASA Research Grant. This gave me the opportunity to design a small study leveraging my genomic analysis expertise and the laboratory skills I had once heralded as a PhD student, but which had remained unutilised in Dr Holt's largely computational microbiology group. It was also a key opportunity to practice the art of pitching a project proposal and designing a budget (a task which remains one of my least favourite academic endeavours). I submitted my application under the assumption it would be unsuccessful, but in early 2019 I was thrilled to discover that this was not the case. I had received my first external research funding award. It may be small by medical research standards ($25K AUD) but it was an important, confidence-boosting stepping stone and turning point on my academic journey.

> "The road to academic independence is paved with opportunities and, all too often, disappointments. Small funding wins can make a big impact, not only in terms of scientific knowledge and outcomes, but in terms of personal confidence, skills development and portfolio differentiation."

The funds from the ASA Research Grant have enabled me to complete a pilot project, combining experimental evolution experiments with whole genome sequence analysis, to explore the response of diverse K. pneumoniae to colistin exposure. Colistin is a last-line antimicrobial usually reserved for the treatment of carbapenem- and multi-drug- resistant K. pneumoniae strains. It is not used commonly in Australia at this time but its use is increasing elsewhere. K. pneumoniae colistin resistance usually evolves de novo in response to antimicrobial therapy, so understanding any strain-specific risks and mechanisms of resistance could help to inform personalised treatment decisions. The project has provided the resources and created space for designated time to optimise new laboratory work flows and data analysis approaches. The data support my hypothesis that diverse K. pneumoniae evolve in different ways in response to colistin exposure, although additional work is required to confidently quantify these differences and identify genomic risk markers that could be used for diagnostic purposes. Importantly, the project has provided the motivation and background knowledge that now supports ongoing work funded by an NHMRC Investigator Grant that I was awarded subsequent to the ASA grant in late 2019. Alongside an ARC Discovery Project grant awarded the same year, this has enabled me to step into an independent academic research role, recruit staff and students to my team, and secure additional funding that supports a diversified research portfolio unified by the goal of improving control strategies for K. pneumoniae.

@kelwyres

linkedin.com/in/kelly-wyres

holtlab.net/kelly-wyres

2022 RECIPIENT

CAUTI biofilm model

Optimising antimicrobial therapy to treat problematic biofilms using a novel pharmacodynamic urinary catheter *in-vitro* model

Dr Iain Abbott
MBBS PhD FRACP FRCPA
Infectious Diseases Physician & Clinical Microbiologist
The Alfred & Monash University
Department of Infectious Diseases
+61 418 186 581
iain.abbott@monash.edu

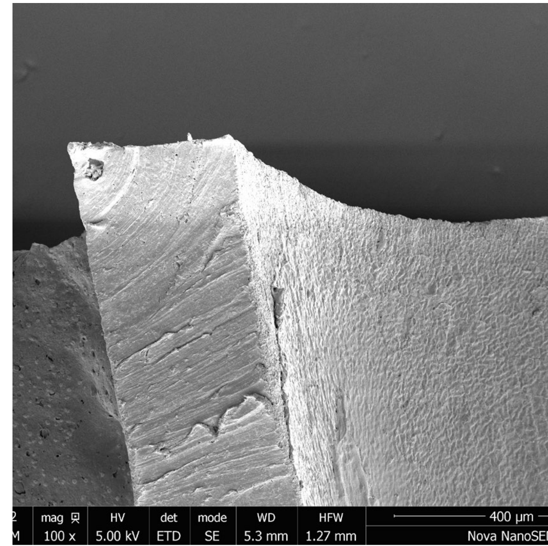
BACKGROUND

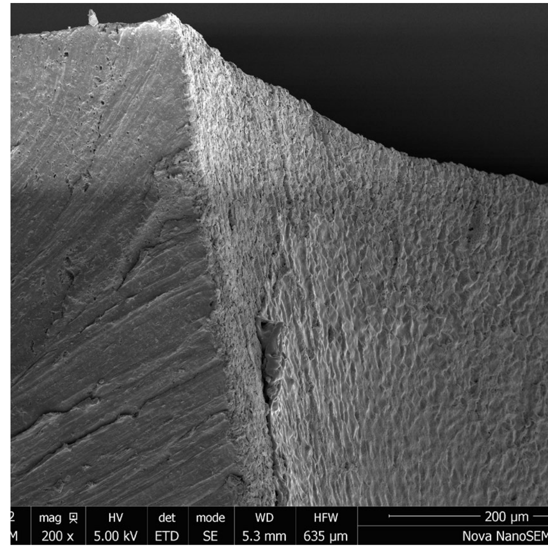
Urinary tract infections (UTIs), including catheter-associated infections (CAUTIs), are among the most common infections impacting the developed world and second most common cause of life-threatening sepsis. Urosepsis accounts for 25% of sepsis cases presenting to the emergency department, with a 6.2% in-hospital mortality and 8.6% ICU mortality (1). UTIs affect 150-million people worldwide every year, with massive medical, financial and societal implications (2). Vast amounts of antibiotics are used, representing a major driver of antimicrobial resistance (AMR). There has been an 8-fold increase in AMR among urinary pathogens over the past two decades (3). In Australia, CAUTIs account for 30% of healthcare-associated infections, leading to increased healthcare costs, increased antibiotic usage, prolonged hospital stays, and patient morbidity (4, 5).

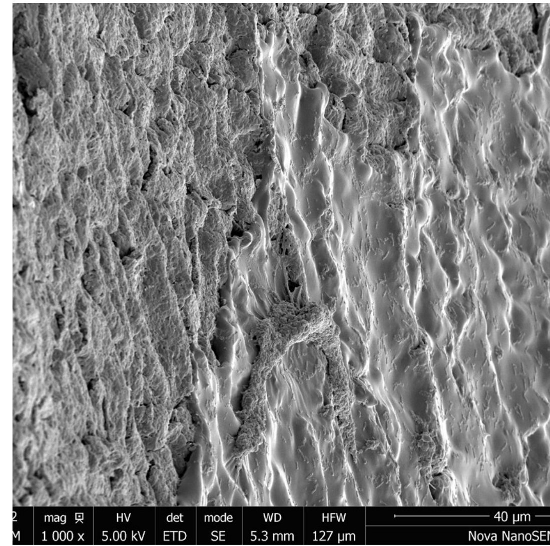
Robust data from pharmacokinetic/pharmacodynamic (PK/PD) models are now required for the licensing of new antibiotics. Yet, the study of antibiotic activity in CAUTIs and biofilms are in their infancy (6). Biofilms are complex microbial communities that represent heterogeneous environments with unique bacterial physiology (7). Biofilms enable microorganisms to colonise competitive niches and survive stressful environments, such as altered pH, osmolarity, nutrient scarcity, and mechanical and shear forces. Biofilms also block the access of antibiotics and the host's immune cells, and is a major cause of infection persistence, especially in nosocomial settings through indwelling devices. Given that standard antimicrobial treatments typically fail to eradicate biofilms, there is a pressing need to develop and evaluate effective therapies to counter challenging biofilm infections (8).

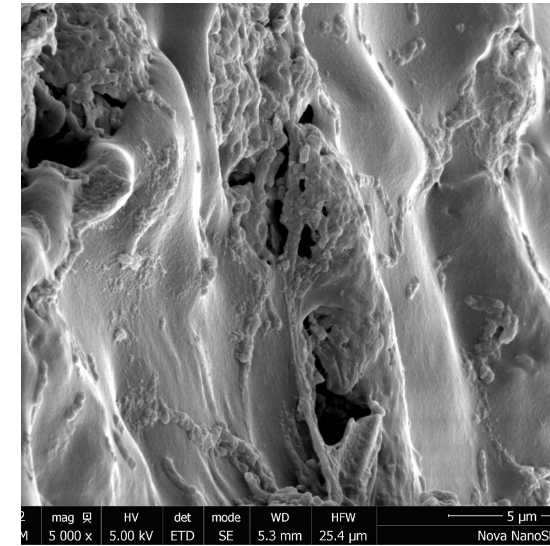
Figure 1 *in-vitro* model

1. Keijzers G. 2020. The Australasian Resuscitation In Sepsis Evaluation: Fluids or vasopressors in emergency department sepsis (ARISE FLUIDS), a multi-centre observational study describing current practice in Australia and New Zealand. Emerg Med Australas.
2. Flores-Mireles AL. 2015. Urinary tract infections: epidemiology, mechanisms of infection and treatment options. Nat Rev Microbiol.
3. Bezabih YM. 2021. The global prevalence and trend of human intestinal carriage of ESBL-producing Escherichia coli in the community. J Antimicrob Chemother.
4. Australian Commission on Safety and Quality in Health Care. Healthcare-associated infections. 2018. https://www.safetyandquality.gov.au/publications/hacs-informationkit-fact-sheet-healthcare-associated-infection/
5. Mitchell BG. 2017. The burden of healthcare-associated infection in Australian hospitals: A systematic review of the literature. Infect Dis Health.
6. Cortese YJ. 2018. Review of Catheter-Associated Urinary Tract Infections and In Vitro Urinary Tract Models. J Healthc Eng.
7. Rumbaugh KP. 2020. Biofilm dispersion. Nat Rev Microbiol.
8. Davies D. 2003. Understanding biofilm resistance to antibacterial agents. Nat Rev Drug Discov.









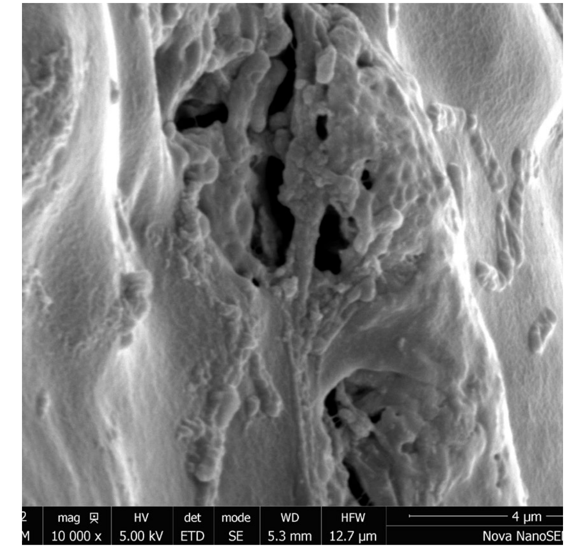


Figure 2 Scanning electron microscopy image of a Pseudomonas biofilm on the internal aspect of a urinary catheter.

RESEARCH PLAN

Hypothesis
Antibiotic therapies can be optimised for the treatment of CAUTIs, informed by the development of a novel dynamic urinary catheter biofilm infection model.

Study Design
Informed by a prospective collection of contemporary clinical urinary pathogens from a tertiary hospital setting, we will develop a novel pharmacokinetic/pharmacodynamic (PK/PD) model to simulate a urinary catheter biofilm infection to profile therapeutic options against our most problematic urinary pathogens.

Our infection model will be used to:
- Investigate the dynamics of bacterial biofilm formation within a urinary catheter, simulated under humanised urinary conditions.
- Quantify the impact of antibiotic administration on biofilm dispersion and elimination following dynamic simulation of antibiotic urinary exposures.
- Inform PK/PD modelling to optimise biofilm eradication and the suppression of the emergence of resistance. PK/PD modelling will enable the translation of observed in vitro findings over a wider range of clinical and pathogen parameters applicable to clinical translation.

To achieve this, we will:
- Adapt a published and validated bladder infection in vitro model (Abbott IJ et al. (2020) J Antimicrob Chemother) to simulate the infection of an indwelling urinary catheter.
- Assess biofilm formation under dynamic incubation conditions over drug-free dynamic incubation. Testing to be performed in standard laboratory media and compared with a customised synthetic human urine medium. Biofilm biomass to be quantified by a process of washing, sonication and plating to establish the CFU/cm2. The structure will be visualised by scanning electron microscopy.
- Selected oral and iv antibiotics (e.g., ciprofloxacin, fosfomycin, gentamicin) will be examined across a range of exposures that mimic humanised dosing regimens. The activity against the biofilm and emergence of resistance will be assessed.

EARLY FINDINGS

In vitro model design
A multi-compartment infection model, which applies a continuous flow of customised synthetic human urine, will enable the simulation of antibiotic absorption from the gastrointestinal tract, or distribution following intravenous administration, followed by renal elimination through simulated urine output to generate a dynamic urinary antibiotic exposure over time. By applying drug distribution PK equations, the variables of the antibiotic dose and dosing schedule, compartment volumes, and media flow rates will be modified to simulate a range of urinary antibiotic exposures to match that observed in different patients.

This dynamic experimental system will enable 16 individual bladder compartments to be run in parallel, each with a urinary catheter placed at the bladder outflow. Each bladder compartment will be inoculated with a bacterial isolate and incubated at 37°C with a continuous media inflow and outflow maintained at 25 mL/h. Biofilm formation within the urinary catheter will be quantified and visualised by scanning electron microscopy (see images above). Antibiotics will then be administered, simulating clinical dosing regimens, and targeting the known urinary exposures in humans. The impact on biofilm mass and structure will assessed over time. Whole-genome sequencing will complement culture-based susceptibility methods to determine bacterial changes following antibiotic exposure.

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All submissions must be made via the online Abstract Submission Portal.
You must follow the correct process (format, word length) for the submission of your abstract.
Incorrectly formatted abstracts and those over 350 words will be automatically rejected.

Accepted abstracts will be blind reviewed by an Abstract Review Panel.
The Antimicrobials Online Committee reserves the right to accept or refuse any abstract,
It is a requirement that all poster presenters are registered for the 2023 Conference and are a current Financial Members of ASA. Registration can be completed via the abstract submission portal and the deadline for registration is Friday 16th December 2022.

We look forward to receiving your submission for Antimicrobials 2023.

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ASA TRAVEL AWARD

ASA has made funds available for travel awards to assist Members wanting to attend Antimicrobials 2024. Awards are made to ASA financial members presenting a proffered paper (oral or poster) at the meeting. Applicants must have current ASA membership and must have been ASA members for at least the last 12 months. Recipients of an Award are required to write a report on the meeting for the ASA Newsletter.

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ASA members who wish to apply for this award are invited to submit their application to the ASA Secretary Denise Daley at info@asainc.net.au. The application should include a copy of the abstract and for abstracts with more than one author, a letter stating the relative contribution of the applicant towards the research.

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PHOTO QUIZ ANSWER

Selective tellurite medium, such as Hoyle's agar or Tinsdale agar to isolate *Corynebacterium diphtheriae*

There are currently 112 species and 11 subspecies in the genus *Corynebacterium*. Of these, around 55 species have been documented to cause infection in humans [1].

The potentially toxigenic corynebacteria comprise *C. diphtheriae*, *C. pseudotuberculosis* and *C. ulcerans*. Toxigenic strains harbour a lysogenic corynephage that carries the structural gene (*tox*) for diphtheria toxin, which inhibits protein synthesis, leading to cell death [6].

C. diphtheriae is commonly divided into four biotypes: gravis, mitis, belfanti, and intermedius. These biotypes can be distinguished based on colonial morphology on tellurite blood agar and biochemically.

Diphtheria causes a wide range of disease and while primarily an upper respiratory tract illness, can be manifest as cutaneous lesions.

Due to immunisation programs, the disease has nearly disappeared in countries with high socioeconomic standards, however it is still endemic in some subtropical and tropical countries [2-3].

Non-toxigenic *Corynebacterium diphtheriae* is increasingly common among migrant workers and within rural communities and is often mixed with other pathogens such as *Staphylococcus aureus,* Group A Streptococcus and mixed anaerobes as seen in our patient. While it can be associated with wound infections it may also be a frequent coloniser in these populations [3-4].

Corynebacterium species are Gram positive non-motile rods, often with clubbed ends, occurring singly or in pairs. They appear to group together to form a "V" shape or in palisades, which can be observed in Figure 2. They are aerobic or facultatively anaerobic and exhibit a fermentative metabolism under certain conditions [1].

Tellurite Blood Agar is a selective medium used for isolation of *Corynebacterium* species. Potassium tellurite acts as a selective agent and has inhibitory activity against most gram-positive and gram-negative bacteria except *Corynebacterium* species. Two formulations of tellurite media are commonly used for the primary isolation of *C. diphtheriae*. Tinsdale which contains tellurite and cystine and Hoyle's which contains tellurite without cystine. Colonies of *C. diphtheriae* appear greyish black through the reduction of potassium tellurite to tellurium and range in size and morphology based on biotypes as demonstrated in Figure 4. These colonies can usually be seen between 16-18 h with characteristic colonies appearing around 48 h in ambient air at 35-37°C [5].

Classically, the Elek method has been used for toxin detection, however PCR-based methods for the (*tox*) gene are also available and validated. The Elek test involves streaking test isolates and controls across an agar plate in straight lines and applying a strip of filter paper perpendicularly containing diphtheria antitoxin to the centre of the plate. Antitoxin diffuses away from the strip of filter paper, and toxin produced by toxigenic stains diffuses away from the line of growth. At the equivalence zone, a precipitin line is formed [2, 6].

Antimicrobial susceptibility of coryneform should be performed with clinically significant isolates. EUCAST breakpoints were developed for *Corynebacterium* species other than *C. diptheriae*, for which there are currently no specific breakpoints [2]. Preliminary study results indicate that the current *Corynebacterium* spp. breakpoints for benzylpenicillin and rifampicin are not useful for *C. diptheriae*.

Susceptibility testing methodology includes MH-F broth/agar incubated at 35±1°C in air for 18 ±2 h. Where there is insufficient growth, plates should be re-incubated and read after a total of 40-44h incubation.

In combination with wound care, the patient was treated with Augmentin Duo Forte and Ciprofloxacin for 7 days with near complete resolution of symptoms.

References
1. Rods, G.P., 2014. UK standards for microbiology investigations. Public Health England.
2. Jorgensen, J.H. and Pfaller, M.A., 2015. Introduction to the 11th Edition of the Manual of Clinical Microbiology. Manual of Clinical Microbiology, pp.1-4.
3. May, M.L., McDougall, R.J. and Robson, J.M., 2014. Corynebacterium diphtheriae and the returned tropical traveller. Journal of travel medicine, 21(1), pp.39-44.
4. Lowe, C.F., Bernard, K.A. and Romney, M.G., 2011. Cutaneous diphtheria in the urban poor population of Vancouver, British Columbia, Canada: a 10-year review. Journal of clinical microbiology, 49(7), pp.2664-2666.
5. Department of Health | Diphtheria lLaboratory Case Definition (LCD)
6. JCM Brief Case – Nontoxigenic Corynbacterium

Dr Adrian Alexander
Infectious Diseases Registrar
Royal Hobart Hospital | Tasmania
Alfred Health | Melbourne
ad.alexander@alfred.org.au
twitter | @aalexa129

Supervisor
Dr Louise Cooley
Royal Hobart Hospital | Tasmania
louise.cooley@ths.tas.gov.au

Editor's Note

In the photo quiz, Dr Alexander states that EUCAST breakpoints do not exist for Corynebacterium diphtheriae. I am pleased to now provide an update from EUCAST.

EUCAST have recently released a consultation document, open for feedback up until 11 September 2022, on the new breakpoints and susceptibility testing of C. diptheriae and C. ulcerans. This is after fantastic work performed by The EUCAST Development Laboratory, The Pasteur Institute and The Bavarian Food and Health Authority.

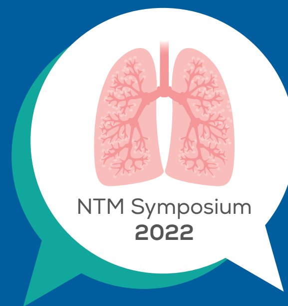
The new breakpoints will accompany the breakpoints already available on the "Corynebacterium species" tab in the current version of the EUCAST breakpoint table. In some instances, C. diptheriae and C. ulcerans can share breakpoints with other members of the genus. In other instances, they will have their own breakpoints listed.

To view the consultation document please go to: https://www.eucast.org/fileadmin/src/media/PDFs/EUCAST_files/Consultation/2022/C._diphtheriae_and_C._ulcerans_-_consultation_July_2022.pdf

Iain J. Abbott
ASA Newsletter Scientific Editor

NTM Australian Research Network

2022 NTM Symposium



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2. Disseminate the latest translational research from around the world
3. Provide a forum for researchers to present and discuss their work
4. Facilitate collaborations across Australia to enhance research quality and outcomes
5. Deliver patient-focused presentations on managing and living with NTM.

Event Details

Date: Thursday 3 – Saturday 5 November 2022

Time: 9am – 5pm (3pm finish time on Saturday)

Location: Mayne Medical School at UQ Herston Campus | 288 Herston Road, Herston Brisbane, Queensland

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MEDICAL RESEARCH FOUNDATION

32nd International Congress of Antimicrobial Chemotherapy (ICC)

Welcome to 32nd ICC2022

On behalf of the Organising Committee of the 32nd International Congress of Antimicrobial Chemotherapy (ICC), we are delighted to invite you to participate in the Congress, which will take place at the Perth Convention and Exhibition Centre, Perth, Australia on 27 – 30 November, 2022.

The ICC is the biennial congress of the International Society of Antimicrobial Chemotherapy (ISAC). This year, it is co-hosted by ISAC Member Society, the Australian Society for Antimicrobials.

TITLE

32nd International Congress of Antimicrobial Chemotherapy (ICC)

DATE

27th - 30th November 2022

VENUE

Perth Convention and Exhibition Centre, Perth, Australia.

ORGANISED BY

Co-Hosted by
AUSTRALIAN SOCIETY FOR ANTIMICROBIALS

PERTH
WWW.32ICC.ORG

PLENARY SPEAKERS

Dr. Robin Patel | Dr. James Musser | Prof. Jonathan Iredell | Prof. Sharon Lewin | Dr. Ramanan Laxminrayan

Important Dates

Accommodation Bookings OPEN
9th March 2022

Registration OPENS
9th March 2022

Abstract Notification
9th August 2022

Early-Bird Registration CLOSES
27th September 2022

Accommodation Bookings CLOSE
1st November 2022

REGISTRATION RATE

Registration rates are decided by each country's development status per the United Nations Human Development Report. If your country has a rating of 0.80 of higher, you are considered a developed country. If your country has a rating below 0.80, you are considered a developing country.
To view your countries status, please refer to page 28 of the Human Development Report 2020.

	Early Bird	Standard
Developed Countries Attendee	$865.00*	$1,085.00
Developing Countries Attendee	$645.00*	$865.00
Day Attendee	$435.00*	$545.00

All registration fees are in AUD.
*Early Bird Discount expires **Tuesday 27 September, 2022.**

WEBSITE is NOW AVAILABLE: www.32icc.org

HOST CITY: PERTH, WESTERN AUSTRALIA

Western Australia is where you can expect the unexpected in a place filled with extraordinary natural wonders, global industries and some of the world's best minds. It is Australia's largest State, located in the same time zone (GMT +8) as 60 per cent of the world's population, including Singapore, China and Hong Kong, making it an attractive destination for international business delegates.
Our capital city, Perth, is home to two million people and is consistently ranked in the world's top most liveable cities, following billions of dollars of investment that has transformed the city.
Perth has a range of high-quality conference and meeting options including an abundance of outdoor meeting space that capitalises on its sunny climate.

Register Now!

Early-Bird Registration CLOSES
27th September 2022

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PERTH
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32nd International Congress of Antimicrobial Chemotherapy

PERTH, WESTERN AUSTRALIA
27th – 30th November 2022

Co-Hosted by
AUSTRALIAN SOCIETY FOR ANTIMICROBIALS

Workshops

Sunday | 27th November 2022

WS1 - Early Career Scientist Workshop
- Scientific Presentations by Early Career Researchers

Chair: Dr. Jinxin (Jason) Zhao

WS2.1 - Anti-Infective Pharmacology Working Group and the International Society of Anti-Infective Pharmacology (ISAP) Part 1
- Introduction to Key Pharmacokinetic Parameters and Their Significance

Speakers: A/Prof. Cornelia Landersdorfer
- Pharmacodynamics: Introduction to Important Concepts in Antimicrobial Pharmacodynamics

Speakers: Prof. Lena Friberg
- TDM: Translation of Antimicrobial PK/PD Knowledge for the Effective Treatment of Infections

Speakers: Prof. Sebastian Wicha

WS2.2 - Anti-Infective Pharmacology Working Group and the International Society of Anti-Infective Pharmacology (ISAP) Part 2
- Setting and Applying Clinical Breakpoints using PK/PD

Speakers: Prof. John Turnidge AO and Prof. Jian Li
- Use of In *Vitro** and Animal Models to Elucidate the PK/PD Driver of Antimicrobial Activity

Speakers: Prof. Jian Li

WS3 - EUCAST
- The Why, Who and What of EUCAST

Chair: Prof. John Turnidge AO

WS4 - Getting Your Paper Published: What You Need to Know as an Author
- Overview of the Publishing Ecosystem
- What Editors Look For: Insights from the Editors-in-Chief | **Speakers: Jean-Marc Rolain and Stefania Stefani**
- How to Respond to Peer Review Comments

Organised by Elsevier

WS5 - Infection Control
Chair: Prof. Andreas Voss

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ACIPC INTERNATIONAL CONFERENCE
SYDNEY, AUS & ONLINE
13-16 NOV 22
ACIPC Australasian College for Infection Prevention and Control
LEADING THROUGH THE EXPANDING HORIZONS OF IPC

APCCMI 2023
The 19th Asia Pacific Congress of Clinical Microbiology and Infection
July 6 (Thu) - 8 (Sat), 2023 COEX, Seoul, Korea
1st Newsletter
APSCMI
KSCM The Korean Society of Clinical Microbiology
SEOUL

SUBSCRIPTION

For ASA Subscriptions please fill the online form at:
https://www.asainc.net.au/registration

ASA has three levels of membership:

1. ASA Member $99.00
2. ASA Associate Member $55.00
3. ASA Retired Membership $55.00

Postal:
Australian Society for Antimicrobials
PO Box 8266, Angelo Street,
South Perth, Western Australia 6151

Email:
info@asainc.net.au

ANTIMICROBIALS 2023
23rd - 25th February
22nd Annual Scientific Meeting
Brisbane Convention and Exhibition Centre \\Brisbane
#ANTIMICROBIALS2023
www.antimicrobials2023.com

19th International Symposium on Staphylococci and Staphylococcal Infections
ISSSI 2024
18 - 24 August 2024
Perth, Western Australia
Hosted by Australian Society for Antimicrobials
#isssi2024

AUSTRALIAN SOCIETY FOR ANTIMICROBIALS
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NEXT ISSUE
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Editor
Iain J. Abbott
newsletter@asainc.net.au

Publisher
Jacson Chung
jacson@asainc.net.au

PO Box 8266
Angelo Street
South Perth WA 6151