

# ASA

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**Breakpoint**

PO Box 6705  
East Perth, WA 6892  
[info@asainc.net.au](mailto:info@asainc.net.au)





FROM THE EDITOR

Treating infections in children can be complex due to several factors that influence the diagnosis, treatment, and management of infections in this population. Some of the complexities involved include:

- Varied Clinical Presentations
- Limited Communication
- Age-Related Differences
- Diagnostic Challenges
- Pharmacokinetics and Dosing
- Safety Considerations
- Compliance and Caregiver Involvement
- Ethical and Legal Considerations

Research in paediatric infectious diseases is crucial for protecting children’s health, developing tailored management approaches, advancing immunisation strategies, improving early detection and diagnosis, promoting antimicrobial stewardship, and addressing global health challenges. It significantly contributes to the well-being and future of our youngest and most vulnerable population.

In this themed edition of the newsletter, we present articles highlighting original research from Yara-Natalie Abo on Group A Streptococcus vaccine trials, Rachael Purcell on use of fosfomycin for UTI in children and Amanda Wilkins on individualised dosing of vancomycin in infants. Asha Bowen and colleagues provide an update on the Skin Health in Northern Australia, and the members of the ANZPID committee provide an insight into their current priorities.

In lieu of a Photo Quiz this month I thought we’d embrace the future and ask ChatGPT to write a short classic quiz on childhood infections in Australia. When asked to provide references for its answers, the response was “...as an AI language model, I don’t have direct access to the internet or the ability to browse websites, so I can’t provide live links.” So while AI may have a practical application for medicine in the future, currently its responses should be taken with a grain of salt.

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



CLASSIC QUIZ

1. What is the most common viral infection among children in Australia?
- a) Influenza  
b) Measles  
c) Chickenpox  
d) Rotavirus
2. Which of the following is NOT a common bacterial infection in children?
- a) Streptococcal throat infection  
b) Urinary tract infection  
c) Pertussis (whooping cough)  
d) Hand, foot, and mouth disease
3. What is the recommended age for children in Australia to receive the measles-mumps-rubella (MMR) vaccine?
- a) 2 months  
b) 6 months  
c) 12 months  
d) 18 months
4. Which infection is primarily transmitted through mosquito bites and can cause severe illness in children?
- a) Dengue fever  
b) Tuberculosis  
c) Lyme disease  
d) Meningitis
5. What is the most effective way to prevent the spread of gastrointestinal infections among children?
- a) Regular handwashing with soap and water  
b) Avoiding contact with sick individuals  
c) Getting a yearly flu shot  
d) Wearing face masks in public places



Answers:  
1. c) Chickenpox  
2. d) Hand, foot, and mouth disease  
3. c) 12 months  
4. a) Dengue fever  
5. a) Regular handwashing with soap and water

## ORIGINAL RESEARCH

# RISING TO THE HUMAN CHALLENGE of *Streptococcus pyogenes* vaccine development



Yara-Natalie Abo <sup>1, 2, 3, 4</sup>



Joshua Osowicki <sup>1, 2, 3</sup>



Andrew Steer <sup>1, 2, 3</sup>

**Strep A (*Streptococcus pyogenes*), a human-only pathogen, causes disease that directly affects more than 750 million people and kills more than 500,000 each year. Disease manifestations range from superficial infections (skin and throat) to life-threatening invasive infections and post-infectious complications including acute rheumatic fever, rheumatic heart disease and glomerulonephritis.<sup>1</sup> Rheumatic heart disease is the greatest cause of disparity in cardiovascular health between Indigenous and non-Indigenous Australians, making Strep A a national Indigenous health priority.<sup>2</sup> While Strep A has a disproportionately high burden among Indigenous Australians, throughout the Pacific region, and in settings of disadvantage worldwide, there is still a significant burden of Strep A disease distributed across all settings and all life stages. Incidence of invasive Strep A disease in high-income countries has surged considerably after the first two COVID-19 pandemic years,<sup>3,4</sup> on a background of rising global incidence**

**and a succession of epidemic invasive Strep A waves since the mid-1980s with emergence of hypervirulent Strep A clones.<sup>5</sup> The incidence of invasive disease is underestimated in low- and middle-income countries, where it is a significant cause of sepsis and death among children aged less than 5 years.**

Strep A has been listed by the World Health Organisation (WHO) as a priority pathogen for accelerated vaccine development.<sup>6</sup> Progress towards development of a Strep A vaccine has been complicated by scientific, commercial and regulatory barriers. There are multiple Strep A strains, defined by the M protein, a major surface virulence factor that has been the target of most vaccine candidates. Over 220 emm-genotypes encode the M-protein. M protein vaccines are designed to exclude auto-epitopes and contain either a mixture of hypervariable N-terminal fragments from clinically relevant M serotypes (e.g. University of Tennessee/Vaxent StreptAnova) or conserved epitopes from the protein's C-repeat

region (e.g. Griffith University p\*17/S2 Combivax, University of Sao Paulo StrepInCor). Other vaccine candidates are based on non-M-protein antigens that are protective against Strep A challenge in animal models (e.g. GSK Combo4, Vaxcyte VAX-A1, University of Queensland Combo5, University of Auckland Teevax).<sup>7</sup>

There are more than 25 modern vaccine candidates. While many pre-clinical trials have been undertaken, 4 vaccine candidates have completed early phase clinical trials and there are currently 8 candidates on a product development track (4 M-protein and 4 non-M protein based).<sup>8</sup> None has been evaluated for protective efficacy in humans, partly due to lack of investment. Another related barrier is that there are no known correlates of natural- or vaccine-induced protection against Strep A disease. ARF/RHD and invasive disease are the most important targets for a Strep A vaccine, however the low incidence and long latency, respectively, make these unrealistic endpoints in efficacy trials.

Pharyngitis, and possibly impetigo, are the only realistic clinical trial endpoints, however, a phase 3 efficacy trial against pharyngitis has been considered too large, complex and speculative. The WHO and several private and public funders have supported a series of initiatives, including the Strep A Vaccine Global Consortium (SAVAC), to navigate these obstacles.<sup>9</sup> The WHO Group A Strep Vaccine Development Technology Roadmap, published in 2018, highlighted use of clinically relevant Strep A controlled human infection models as a key capacity to streamline the Strep A vaccine development pipeline.<sup>10</sup>

Human challenge studies model an encounter between human hosts and pathogens by deliberately exposing selected volunteers to a well-characterised pathogen under controlled conditions. Since 1980, more than 15,000 subjects have participated in human challenge studies in at least 30 pathogen models, including SARS-CoV-2. Modern human challenge research is characterised by high standards of research accountability,

<sup>1</sup> Tropical Diseases Research Group, Murdoch Children's Research Institute, Melbourne  
<sup>2</sup> Department of Paediatrics, The University of Melbourne  
<sup>3</sup> Infectious Diseases Unit, Department of General Medicine, Royal Children's Hospital Melbourne  
<sup>4</sup> Department of Microbiology, Infection Prevention and Control, Royal Children's Hospital Melbourne

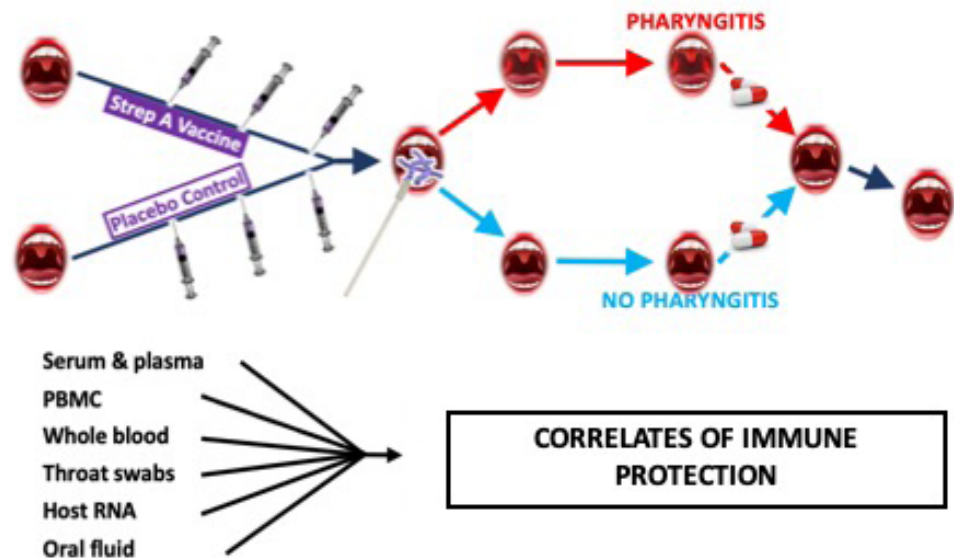


Figure. Strep A vaccine-challenge randomised controlled trial

ethical and regulatory scrutiny, and public engagement. A systematic review of 187 studies between 1980 and 2021 identified only 23 challenge-related Serious Adverse Events (e.g., hospitalisation) among more than 10,000 participants, with no deaths or permanent impairment.<sup>11</sup>

Controlled Human Infection for Vaccination Against Strep A (CHIVAS)-M75 is the world's only modern Strep A human challenge model.<sup>12</sup> In the CHIVAS-M75 trial, the emm75 Strep A strain at the confirmed dose level (~10<sup>5</sup> CFU single-dose vials) was swabbed onto the pharynx of 20 healthy adult volunteers and caused acute pharyngitis in 17 (85%), without serious adverse events. Culture and molecular methods illustrated the bacterial dynamics of experimental pharyngitis, and C-reactive protein levels, cytokine analysis, serology, and

immunophenotyping supported the clinical picture. The emm75 strain was carefully selected and possesses a wide array of vaccine candidate antigens and is a definite but uncommon contemporary cause of symptomatic pharyngitis.<sup>13</sup> Compared to typical animal models delivering 10<sup>7</sup> – 10<sup>8</sup> colony forming units (CFU), and 1970s Strep A human infection studies which used a similar swab transfer method from liquid media containing 10<sup>6</sup> CFU/mL, the dose applied in CHIVAS-M75 was smaller: the emm75 strain was applied by swab from a single dose vial containing 10<sup>5</sup> CFU/mL, with 10<sup>3</sup> – 10<sup>4</sup> CFU finally applied (1000 to 10,000 times less bacteria than in most animal models).

In the absence of overwhelming vaccine development momentum and funding to support very large, long, complicated, and expensive clinical trials (such as in a pandemic), controlled human

infection trials have multiple benefits for development of Strep A vaccines, including: 1) early proof-of-concept for efficacy as well as adding to Phase I safety findings; 2) far smaller, faster, and less expensive than Phase II or III field trials; 3) immunogenicity assessments; 4) inform studies to establish correlates of protection; and 5) build industry and regulator confidence to support large field trials. Strep A pharyngitis controlled human infection against purified M protein in the 1970s demonstrated efficacy of up to 89%, with no serious adverse events.<sup>14</sup> Controlled human infection trials cannot supplant large field trials for licensure of Strep A vaccines, at least until there are established immune correlates of protection and/or effective comparator vaccines.

CHIVAS-M75 will be used to test the safety, immunogenicity and protective efficacy of Strep A vaccine candidates

in randomised, double-blind, placebo controlled phase Ib/II trials (figure). Carefully screened healthy adult volunteers aged 18 to 40 years at low risk for complicated Strep A disease will be recruited and randomly assigned to receive the investigational vaccine (n = 30), or a control vaccine (n = 30). One month after the final vaccine dose, participants will be challenged by pharyngeal application of emm75 Strep A and closely monitored for development of pharyngitis as inpatients for up to 5 days at a clinical trials facility. All participants will be treated with antibiotics upon diagnosis of pharyngitis, or on Day 5 for those without pharyngitis, and monitored periodically as outpatients for 12 months. An extensive collection of blood, oral fluid and throat swab samples will be studied to interrogate the immune response to vaccination and infection.

The burden of Strep A disease remains an unmet public health challenge and a vaccine is urgently needed. No vaccine candidate has been tested for efficacy in humans for over 40 years. A Strep A vaccine-challenge trial using a controlled human infection model of pharyngitis will build confidence for industry, regulators, and funders and bridge the gap from preclinical and Phase I to late-phase field trials, to accelerate Strep A vaccine development.

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## ORIGINAL RESEARCH

# Oral fosfomycin a potential treatment option for URINARY TRACT INFECTIONS IN CHILDREN




Dr Rachael Purcell<sup>1,2,3,4</sup>

 @Rachael\_Purcell



A/Prof Amanda Gwee<sup>4,5,6</sup>

 @GweeAmanda

- <sup>1</sup> Centre for Health Analytics, Royal Children's Hospital, Melbourne
- <sup>2</sup> Public Health and Infection Prevention, Monash Health
- <sup>3</sup> Bioinformatics Group, Murdoch Children's Research Institute, Melbourne
- <sup>4</sup> Department of Paediatrics, The University of Melbourne, Melbourne
- <sup>5</sup> Department of General Medicine, Royal Children's Hospital, Melbourne
- <sup>6</sup> Infectious Diseases Group, Murdoch Children's Research Institute, Melbourne

Urinary tract infections (UTI) in children are a common reason for presentation to primary care providers and emergency departments. In infants aged less than 3 months, bacterial UTI accounts for 7.2% of hospital admissions.<sup>1</sup> Multi-drug resistant organisms (MDROs) are an increasingly common cause of UTI in children with the incidence of MDR Gram-negative UTIs ranging from 5-90% depending on the geographical region.<sup>2</sup> Whilst newer antibiotics for the treatment of MDR infections are available, many of these lack paediatric efficacy and safety data. This has led to an exploration of older, less commonly used antibiotics to treat these infections in children.

Fosfomycin is a phosphonic acid derivative antibiotic which has activity against Gram-positive and Gram-negative bacteria. Developed in 1969, it's mechanism of action disrupts bacterial cell wall synthesis. A key advantage of fosfomycin is that many MDR organisms remain susceptible to this drug. It is

“A key advantage of fosfomycin is that many MDR organisms remain susceptible to this drug.”

highly active against common urinary pathogens including *Escherichia coli*,<sup>3</sup> and has activity against extended-spectrum beta-lactamase (ESBL)-producing strains.<sup>4</sup> EUCAST have breakpoints for *E. coli* in uncomplicated UTI, and CLSI have urinary tract species-specific fosfomycin breakpoints for *Enterococcus faecalis* and *E. coli*.<sup>5,6</sup>

In Australia, fosfomycin is licensed for *E. faecalis* and *Enterobacterales* causing uncomplicated cystitis in females aged over 12 years.<sup>7</sup> It is registered for use in the treatment of acute uncomplicated UTI in females in several European countries, and in the UK for adolescents and adults. Registration in the USA is specific to cystitis caused by *E. faecalis* and *E. coli*.<sup>8</sup>

Our recently published multicentre study on the use of oral fosfomycin in children for Gram-negative UTI in Australia found that it was effective and well tolerated. Of note, positive treatment outcomes were observed for

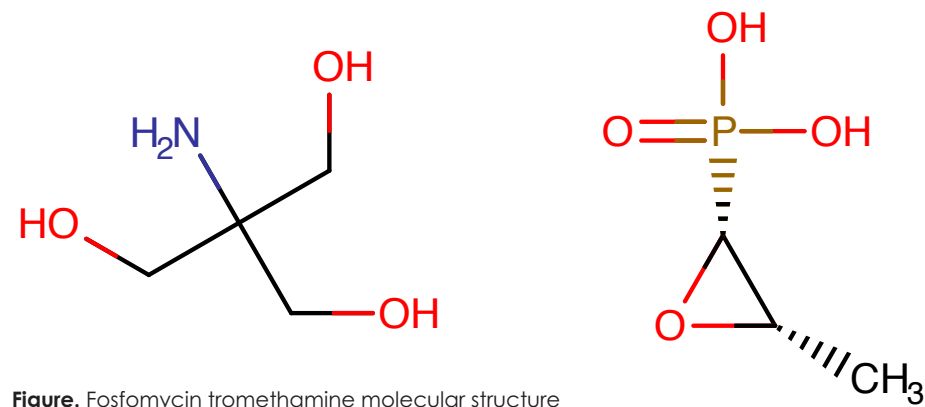


Figure. Fosfomycin tromethamine molecular structure

both uncomplicated and complicated UTI. This nationwide, retrospective audit of fosfomycin prescribing for UTI in tertiary paediatric hospitals included 91 children, of whom 63% (59/71) had a comorbidity, the most common being renal tract anomalies (24/91, 26%). Cure was achieved in 93% of children, including high rates of cure for febrile UTI (51/55, 93%) and pyelonephritis (13/14, 94%). A majority of children (80/91, 80%) had an ESBL-producing Gram-negative pathogen isolated, and treatment success occurred in 93% of children (84/90).<sup>9</sup> All 6 episodes of treatment failure occurred in children aged 1 year with complicated UTI and renal or urogenital comorbidities.

Although there are no consensus

guidelines for fosfomycin dosing in young children, the most common doses given were 1g, 2g and 3g for children aged <1 year, 1-12 years, and >12 years respectively for non-bacteremic UTI.<sup>9</sup> Single doses were commonly used (37%); alternatively, doses were commonly repeated at 48-72 hour dose intervals if clinically indicated (45%). This dosing strategy was similar to a literature review of older studies of fosfomycin use for paediatric UTI which found that doses of 1g were most commonly used in infants <1 years, and 2g for children aged 1-18 years.<sup>10</sup>

A number of prospective and retrospective studies have suggested that oral fosfomycin is well tolerated by children, with the most common

side-effect being gastrointestinal and experienced by small numbers of children.<sup>9,10</sup> Our study confirms these findings with only 2% of children experiencing side effects, all of which were mild gastrointestinal symptoms.<sup>9</sup>

A limitation of oral fosfomycin studies for paediatric UTI to date is their retrospective nature, or small sample sizes. There is an urgent need for more information regarding the best dosing strategy in children. Nonetheless, fosfomycin offers a possible alternative to intravenous antibiotics and hospital admission for children with MDR Gram-negative UTI.

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## DIGITAL HEALTH

# There's an App for that 👍

## Optimising vancomycin treatment in infants using a dosing app



**Dr Amanda Wilkins MBBS FRACP**

Amanda.wilkins@rch.org.au

General Paediatrician & Clinical Pharmacologist | Royal Children's Hospital Melbourne  
PhD candidate, Department of Paediatrics | The University of Melbourne  
Honorary fellow, Antimicrobials Group | Murdoch Children's Research Institute



**A/Prof Amanda Gwee, MBBS FRACP DTMH PhD**

Amanda.gwee@rch.org.au

Infectious Diseases Physician, Clinical Pharmacologist | Royal Children's Hospital Melbourne  
Clinical Lead of Research, Dept of General Medicine | Royal Children's Hospital Melbourne  
Leader of Antimicrobials Group | Murdoch Children's Research Institute  
Associate Professor, Department of Paediatrics | The University of Melbourne



“Model-based individualised dosing is increasingly used to improve dosing and ultimately, patient outcomes.”

A major cause of late-onset sepsis in infants is coagulase-negative staphylococci (CoNs) which can result in prolonged hospital stays in neonatal intensive care units and long-term neurodevelopmental sequelae.<sup>1,2</sup> Vancomycin is therefore often used as first-line treatment for late-onset sepsis however standard intermittent dosing regimens result in less than 50% of infants achieving target therapeutic concentrations at first steady-state level, which may result in delayed, suboptimal treatment of life-threatening infections<sup>3,4</sup>

Vancomycin can be administered via continuous infusion or intermittent dosing in infants. Intermittent dosing

regimens for infants vary worldwide and are based on one or more factors such as weight, postnatal age, postmenstrual age and creatinine and often include several dosing intervals (e.g. 6, 8, 12, 24 hourly). Vancomycin dosing is particularly challenging due to the narrow therapeutic range and wide inter-individual pharmacokinetic variability, necessitating routine therapeutic drug monitoring. The vancomycin pharmacodynamic target for *Staphylococcus aureus* is an  $AUC_{24} : MIC$  ratio of  $>400$ .<sup>5</sup> Although information on the therapeutic target for other staphylococci including CoNS are limited, a previous study found that a similar AUC target ( $AUC_{0-24} \geq 300$  mg/L.h and  $AUC_{24-48} \geq 424$  mg/L.h) correlated with increased bacteriological

cure.<sup>6</sup> Therefore, international guidelines now recommend AUC-guided rather than trough-guided dosing. However, AUC-guided dosing is particularly problematic in infants as the target trough concentration which correlates with the target  $AUC_{24}$  changes with different dosing intervals. Despite the recommendations to move to AUC-guided dosing, the lack of a reliable, user-friendly AUC calculator for infants has made this move challenging, and most neonatal and paediatric centres continue to use trough-guided dosing.

Model-based individualised dosing is increasingly used to improve dosing and, ultimately, patient outcomes.<sup>7</sup> Population pharmacokinetic (popPK) models can be

used to determine the key factors which influence the pharmacokinetic profile of a drug - for vancomycin in young infants, these factors are post-menstrual age (PMA), weight and serum creatinine.<sup>8</sup> Vancomycin popPK models can then be used to predict the dose required to achieve a target trough or AUC<sub>24</sub> based on these factors.

There are numerous published vancomycin popPK models and proposed individualised dosing approaches, however there are a lack of studies which have prospectively validated these in clinical practice. There have been two studies which have prospectively assessed the use of model-based individualised dosing for continuous infusions of vancomycin. Both of these studies evaluated the performance of the same excel-based calculator in neonates and found that 71% and 72% of infants achieved target vancomycin concentration between 15 to 25 mg/L at the first TDM sample.<sup>9,10</sup>

Our study, published in International Journal of Antimicrobial Agents, prospectively evaluated an individualised approach for intermittent vancomycin dosing.<sup>11</sup> This multicentre, prospective cohort trial recruited 40 infants aged 0 to 90 days with suspected Gram-positive infections, across four tertiary neonatal and intensive care units in Australia. The study used an online dosing calculator Vanc App (<https://vanc-app.mcri.edu.au/calculations/new>) which is based on

Vancomycin Intermittent Dosing Calculator for Young Infants

Calculated Dose

Post-menstrual age

52 week(s)0 day(s)

Weight (kg)

5.0 kg

Creatinine level (micromol/L)

50 micromol/L

Target trough level (mg/L)

15 mg/L

Edit

New Calculation

Vancomycin Area Under the Curve Calculator for Young Infants

✓

Your dosage is

79 mg 6 hourly

( 63 mg/kg/day )

The predicted AUC<sub>24-48</sub> is

543 mg/L.h

Copy results to clipboard

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Gwee A et al. Defining Target Vancomycin Trough Concentrations for Treating Staphylococcus aureus Infection in Infants Aged 0 to 90 Days. JAMA Pediatr. 2019 Jun 10.

a population pharmacokinetic model developed from prospectively collected data from young infants.<sup>12</sup> The patient's PMA, weight, creatinine and target trough concentration are entered into the calculator and the calculator recommends the dose predicted to achieve the target trough concentration and predicts the associated steady state AUC<sub>24</sub> for this dose. Using the dosing app, 75% of infants achieved a vancomycin trough concentration of 10-20 mg/L at the first steady state level (24-48 hours) and 83% achieved an AUC<sub>0-24</sub> of 400-650 mg/L.h. There were no infusion-related reactions or episodes of nephrotoxicity.

The use of model-based individualised dosing for antimicrobials such as vancomycin which have a narrow therapeutic index and wide inter-individual variability is a promising step in advancing antimicrobial use in infants. This approach is particularly useful in infants, given the rapid changes in organ function and body composition that occur in early life.

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## ESCMID Postgraduate Education Course

# Antimicrobial susceptibility testing with EUCAST criteria and methods

**Melbourne, Australia**  
28 - 31 October 2023



## ESCMID Postgraduate Education Course

### Organiser

European Committee on Antimicrobial Susceptibility Testing (EUCAST)  
Australian Society for Antimicrobials (ASA)  
Monash University Central Clinical School (CCS)

### Course Coordinators

**Iain Abbott**, Melbourne, Australia  
**Anton Peleg**, Melbourne, Australia  
**John Turnidge**, Adelaide, Australia

### Course Objective

To explain criteria and methods for determining breakpoints to antimicrobial agents (based on preclinical and clinical data) and the EUCAST methods by which these are implemented and controlled in microbiological laboratories. The course will also involve practical work on susceptibility testing and demonstrations of in vitro PK-PD models.

### Organisation

#### Registration fee

**On-site**  
EUR 450 ESCMID members/ YSM/ LMICs  
EUR 550 for all others

**Online**  
EUR 150 ESCMID members/ YSM/ LMICs  
EUR 200 for all others

The registration fee includes all lectures and workshops, coffee breaks, lunches, and dinner on Sunday night. Accommodation and travel are not included. A contingent of hotel rooms for participants is prereserved.

#### Registration Procedure

Register on the ESCMID website at [www.escmid.org/education](http://www.escmid.org/education) by 18 September 2023

## Contact

### Contact Person (Scientific Programme)

**Iain Abbott**  
Dept. Infectious Diseases and Microbiology Unit  
The Alfred Hospital and Monash University  
Commercial Road, Melbourne, Victoria, Australia

+61 4 1818 6581  
[iain.abbott@monash.edu](mailto:iain.abbott@monash.edu)

### Administrative Contact

**Brian Price**  
Dept. Infectious Diseases  
The Alfred Hospital and Monash University  
Commercial Road, Melbourne, Victoria, Australia

+61 3 9076 3981  
[B.Price@alfred.org.au](mailto:B.Price@alfred.org.au)

### Target Audience

Scientists, Clinical microbiologists, Infectious Diseases Specialists, Antimicrobial Pharmacists and trainees in Australia and New Zealand, the Western Pacific Region, and South East Asia.

### Faculty Members

**Anton Peleg**, Melbourne, Australia  
**Chris Coulter**, Brisbane, Australia  
**Christian Giske**, Stockholm Sweden  
**Cornelia Landersdorfer**, Melbourne, Australia  
**Erika Matuschek**, Växjö, Sweden  
**Gunnar Kahlmeter**, Växjö, Sweden  
**Iain Abbott**, Melbourne, Australia  
**Jackie Williams**, Melbourne, Australia  
**Jane Hawkey**, Melbourne, Australia  
**Jess Wisniewski**, Melbourne, Australia  
**Jian Li**, Melbourne Australia  
**John Turnidge**, Adelaide, Australia  
**Maryza Graham**, Melbourne, Australia  
**Rafael Cantón**, Madrid, Spain  
**Rick Streitberg**, Melbourne, Australia  
**Sonali Coulter**, Brisbane, Australia  
**Trisha Peel**, Melbourne, Australia  
**Xenia Kostoulis**, Melbourne Australia

### Course Venue

Level 5 Alfred Centre  
The Alfred Hospital and Central Clinical School  
Monash University  
55-99 Commercial Road, Melbourne, Victoria, Australia



Course Programme

Saturday, 28 October 2023

09:00 – 09:15	<b>Welcome</b> <i>Anton Peleg</i>
09:15 – 09:45	<b>The EUCAST system</b> <i>Christian Giske</i>
09:45 – 10:30	<b>Antimicrobial phenotypic susceptibility testing</b> <i>Erika Matuschek</i>
10:30 – 11:00	<b>Break</b>
11:00 – 11:30	<b>Definitions of S, I and R and the ATU</b> <i>Rafael Cantón</i>
11:30 – 12:00	<b>How clinical breakpoints are set</b> <i>John Turnidge</i>
12:00 – 12:30	<b>Navigating the EUCAST breakpoint tables</b> <i>Gunnar Kahlmeter</i>
12:30 – 13:00	<b>Panel discussion</b>
13:00 – 14:00	<b>Lunch break</b>
14:00 – 17:00	<b>Small group practical session</b> · Split into 3 groups · 10-15 per group  <b>1. Phenotypic AST:</b> BMD, disk diffusion, RAST, gradient strips, phenotypic mechanism of resistance <i>Erika Matuschek, Jackie Williams</i>  <b>2. Genotypic AST:</b> WGS and analysis <i>Jane Hawkey, Jess Wisniewski</i>  <b>3. PK/PD modelling:</b> TKA, HFIM, UTI dilution model, biofilm <i>Xenia Kostoulis, Iain Abbott</i>

Sunday, 29 October 2023

09:00 – 09:30	<b>MIC database, ECOFFs and how to use them</b> <i>John Turnidge</i>
09:30 – 10:00	<b>When and how to perform an MIC</b> <i>Gunnar Kahlmeter</i>
10:00 – 10:30	<b>Quality control and troubleshooting</b> <i>Rick Streitberg</i>
10:30 – 11:00	<b>Break</b>
11:00 – 11:30	<b>AST for anaerobes</b> <i>Christian Giske</i>
11:30 – 12:00	<b>AST for difficult bugs and difficult drugs</b> <i>Erika Matuschek</i>
12:00 – 12:30	<b>AST for mycobacteria</b> <i>Chris Coulter</i>
12:30 – 13:00	<b>Panel discussion</b>
13:00 – 14:00	<b>Lunch break</b>
14:00 – 17:00	<b>Small group practical session</b> · Split into 3 groups · 10-15 per group  <b>1. Phenotypic AST:</b> BMD, disk diffusion, RAST, gradient strips, phenotypic mechanism of resistance <i>Erika Matuschek, Jackie Williams</i>  <b>2. Genotypic AST:</b> WGS and analysis <i>Jane Hawkey, Jess Wisniewski</i>  <b>3. PK/PD modelling:</b> TKA, HFIM, UTI dilution model, biofilm <i>Xenia Kostoulis, Iain Abbott</i>
18:30	<b>Course Dinner</b>

Monday, 30 October 2023

10:00 – 10:30	<b>In vitro models</b> <i>Iain Abbott</i>
10:30 – 11:00	<b>In vivo models</b> <i>Jian Li</i>
11:00 – 11:30	<b>PK/PD and Monte Carlo simulations</b> <i>Cornelia Landersdorfer</i>
11:30 – 12:00	<b>Break</b>
12:00 – 12:30	<b>Rapid AST from positive blood cultures</b> <i>Gunnar Kahlmeter</i>
12:30 – 13:00	<b>Novel phenotypic methods for AST and AMR detection resistance</b> <i>Rafael Cantón</i>
13:00 – 13:30	<b>Molecular methods for AST and AMR detection</b> <i>Anton Peleg</i>
13:30 – 14:00	<b>Panel discussion</b>
14:00 – 15:00	<b>Lunch break</b>
15:00 – 18:00	<b>Small group practical session</b> · Split into 3 groups · 10-15 per group  <b>1. Phenotypic AST:</b> BMD, disk diffusion, RAST, gradient strips, phenotypic mechanism of resistance <i>Erika Matuschek, Jackie Williams</i>  <b>2. Genotypic AST:</b> WGS and analysis <i>Jane Hawkey, Jess Wisniewski</i>  <b>3. PK/PD modelling:</b> TKA, HFIM, UTI dilution model, biofilm <i>Xenia Kostoulis, Iain Abbott</i>

Tuesday, 31 October 2023

09:00 – 09:30	<b>ESBL- and carbapenemase-producing Gram-negative bacilli: epidemiology in the Asia-Pacific</b> <i>Maryza Graham</i>
09:30 – 10:00	<b>Interpretive construction &amp; reading of antibiograms</b> <i>Sonali Coulter</i>
10:00 – 10:30	<b>Clinical application of AMR data into treatment guidelines and antimicrobial stewardship</b> <i>Trisha Peel</i>
10:30 – 11:00	<b>Break</b>
11:00 – 11:30	<b>The role and use of Guidance documents</b> <i>John Turnidge</i>
11:30 – 12:00	<b>Expert rules and Expected phenotypes</b> <i>Rafael Cantón</i>
12:00 – 12:30	<b>What to do when there are no breakpoints?</b> <i>Christian Giske</i>
12:30 – 13:00	<b>Panel discussion and course wrap-up</b>



The importance of

Community Voice

to improve skin health for remote living Australian Aboriginal kids



Hannah Thomas, Stephanie Enkel, Tracy McRae, Victoria Cox, Heather-Lynn Kessar, Abbey Ford, Rebecca Famlonga, Rebekah Newton, Ingrid Amgarth-Duff, Alexandra Whelan, Asha Bowen

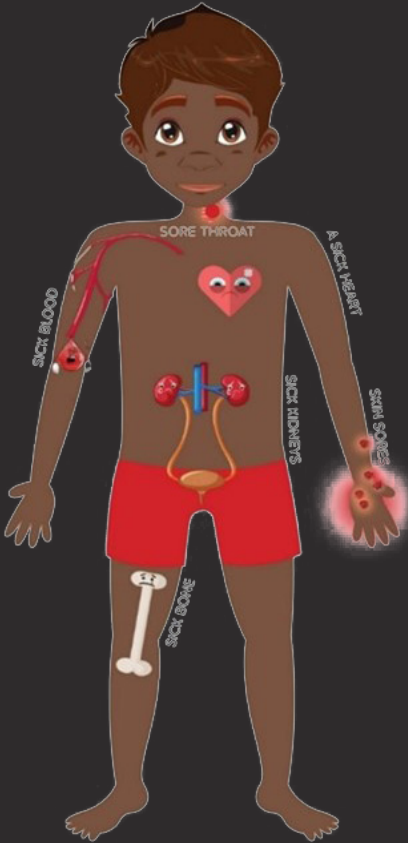
*We acknowledge the Nyoongar Wadjuk, Yawuru, Kariyarra and Kurna Elders, their people, and their land upon which the Telethon Kids Institute is located, as well as the traditional owners of the lands across Australia, lands that have never been ceded.*

*In this article Aboriginal refers to both Aboriginal and/or Torres Strait Islander peoples. We recognise and acknowledge the strong diversity between Aboriginal and Torres Strait Islander cultures, and we do not intend to diminish any identity.*

Skin health in Australia

Our skin is the largest organ of our bodies. It is crucial to protect our bodies, so strong and healthy skin is important to support holistic physical and social-emotional wellbeing. In many remote regions in the north of Australia, there is a high burden of itchy infections such as scabies, tinea and headlice that can cause scratching, leading to breaks in the skin and an entry point for bacteria such as *Streptococcus pyogenes* and *Staphylococcus aureus*. Left untreated, skin infections can become complicated by sepsis, bone and joint infections, and pneumonia, as well as acute rheumatic fever, leading to rheumatic heart disease or kidney disease (Picture 1).<sup>1</sup>

In remote northern Australia, three quarters of all Aboriginal community members require treatment at least once per year for a skin or soft tissue infection.<sup>2</sup> Four out of five children are presenting to clinics with their first skin



**Picture 1** Untreated skin infections can lead to sepsis, bone and joint infections, heart, and kidney disease.



infection before their first birthday,<sup>3</sup> and almost three quarters of children under the age of five years are diagnosed with at least one skin infection every year.<sup>4</sup> For many infants, this heavy, early burden of skin infections leads to a hospital admission in their first year of life.<sup>5</sup> Not only is this avoidable, but these early *S. pyogenes* exposures also increase the risk of acute rheumatic fever and rheumatic heart disease later in life.

Despite how many remote-living Aboriginal children have skin infections, studies indicate that they can be “normalised” by clinicians, especially in regions with the highest burden where children may also be presenting with other complex or chronic illnesses.<sup>6</sup>

When this happens, it leads to under-recognition and under-treatment of skin infections, and consequently an increased risk of complications. Additionally, it means that families are not provided with the information and support needed to achieve and maintain healthy skin.

**Working together with communities for healthy skin**

Many studies documenting the burden and impact of skin infections for Australian Aboriginal children have also trialled skin infection programs with individual communities to address this burden. Examples of such programs include mass drug administration of topical permethrin to address scabies in

Wadeye, NT,<sup>7</sup> the East Arnhem Healthy Skin Program, NT,<sup>8</sup> ivermectin mass drug administration in Galiwinku, NT,<sup>9</sup> and our work on the SToP (See, Treat, and Prevent Skin Sores and Scabies) Trial in the Kimberley, WA (Picture 2).<sup>10</sup>

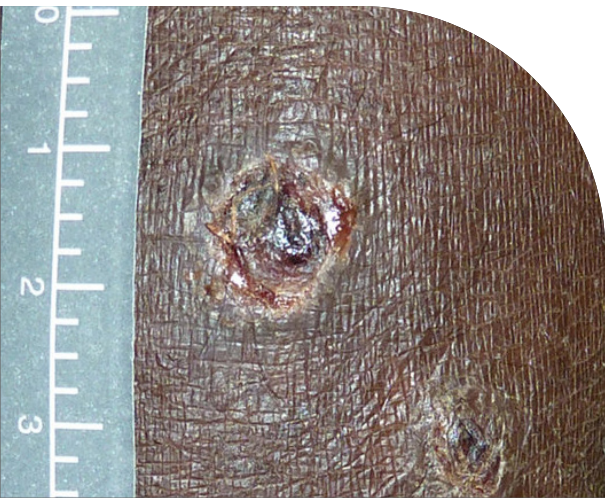
Over the years, researchers and clinicians are increasingly recognising the importance of working in partnership with communities to guide prevention activities alongside diagnosis and treatment. Comprehensive co-designed and community-led prevention programs elevate and hear community voice and have the potential to effect real change. Key to this is acknowledgement of how the environments in which people live influence their opportunities for healthy



Picture 2. ‘SToP’ Trial skin surveillance in the Kimberley, WA.

**Skin sores**

A bacterial skin infection, driven in northern Australia by *S. pyogenes* with high rates of *S. aureus* co-infection. Skin sores begin as a blister that fills with pus, crusts over, and then eventually heals following re-epithelialisation of the skin surface. At any time, almost half of remote-living Aboriginal children in northern Australia are living with skin sores. This is by far the highest documented burden in the world.<sup>12</sup> The SToP Trial aims to reduce this burden by 50% with results expected in late 2023. Skin sores are treated with a short course (3 days) of oral cotrimoxazole or an injection of intramuscular benzathine penicillin G.<sup>13</sup>



**Scabies**

Caused by the scabies mite, *Sarcoptes scabiei*, scabies is itchy and can be transmitted from human to human. Remote-living Australian Aboriginal children have some of the highest reported rates of scabies in the world, with approximately a third of children affected at any time.<sup>12</sup> Scabies infestations can also be complicated by bacterial skin infections, most commonly *S. pyogenes* and *S. aureus*. Recently oral ivermectin has been approved as first line treatment of scabies for Aboriginal Australians. Alternatively, topical permethrin can be used including for children < 5 years and pregnant or breastfeeding persons.

**Head lice**

Caused by an ectoparasite, *Pediculus humanus capitis*, head lice can be easily transmitted by direct head-to-head contact. In Australia, head lice is the third most reported outbreak in day-care centres and schools. The burden of head lice in remote Australia has not yet been established, however this information is currently being collated in the Kimberley through the SToP Trial. Treatment for head lice with topical therapies is important to control symptoms and prevent transmission.



**Tinea**

An itchy, scaly fungal condition, which can be transmitted from human to human or acquired from the environment or household pets. In Northern Australia, tinea is caused by *Microsporum spp.* and *Trichophyton spp.* Estimates of the tinea burden in northern Australia are not well-established, however tinea was recorded in 7% of children prospectively assessed for skin infections upon admission to hospital in WA<sup>6</sup> and associated with skin sores in 4.3% of participants in a study in the NT.<sup>13</sup> The SToP trial will also report on tinea burden in the Kimberley. Treatment for tinea is either topical antifungal therapy for small skin lesions or oral antifungal for scalp, extensive skin, or nail lesions.





Picture 3. Learning from Elders during healthy skin resource co-design.



Picture 4. Portable Orange Sky washing machines. The laundromat of the future.

living practices. As such, programs should include prevention strategies, such as the co-development of culturally informed health promotion projects in partnership with communities.

In the Kimberley region of WA, our team is working side-by-side with remote Aboriginal communities to co-design and create culturally appropriate healthy skin resources. This has required deliberate and meaningful engagement over many years, with respect for the existing decision-making structures and processes already established in participating communities. Throughout the development of eight unique community-led and community-specific health promotion resources focussed on keeping skin strong and healthy, some recurring themes have emerged. Community Elders across the region have unanimously recommended the inclusion of local language, artwork, story, music, and culture; and have

generously shared this knowledge, including that of traditional activities for healthy skin in our collaborative effort to reduce the burden of skin infections (Picture 3). Community co-researchers have also highlighted the importance of healthy environments, and recognition of the barriers to sustaining these due to colonisation, historical and current policies and wider systems that have and continue to impede Aboriginal peoples’ rights to access safe, effective, and culturally responsive healthcare and housing.<sup>11</sup> As such, health promotion initiatives must not be implemented alone, they must be accompanied by tangible strategies to improve peoples’ environments to support healthy habits, such as the Orange Sky initiative which provides mobile laundry facilities in remote communities (Picture 4).

Achieving healthy skin for all Australians will require consistent adoption of this

multifocal lens. Only when Aboriginal people’s ways of knowing, being, and doing become central to the narratives and messaging of programs will we see real change. This is a clear example of how Aboriginal leadership and voice is influencing clinical care and research activities in a meaningful way to effect sustained change for Aboriginal children and their families.



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SPECIAL INTEREST GROUP

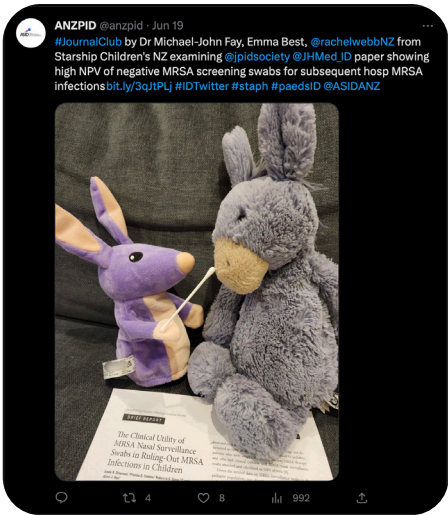
A big group passionate about little people

At the end of last year, paediatricians and clinicians welcomed the release of the 3rd edition of the ASID-ANZPID Management of Perinatal Infections guideline. Frequently used in the care of children, it provides useful algorithms for the maternal and neonatal management of perinatal infections.

This is just one of the landmark guidelines developed by a group of Australian and New Zealand paediatricians, paediatric and adult infectious diseases physicians, microbiologists and trainees who are passionate about all things child health.

The Australian and New Zealand Paediatric Infectious Diseases (ANZPID) Special Interest Group of the Australasian Society for Infectious Diseases (ASID) is a relatively young group, formed fourteen years ago in 2009. Since then, it has increased in size (249 members) and capacity and is a thriving community.

A cornerstone of ANZPID's work is education in infection prevention and management of infections in children.



May 2023 ANZPID Journal club submission: The Clinical Utility of MRSA Nasal Surveillance Swabs in Ruling-Out MRSA Infections in Children Submitted by: Michael-John Fay, Emma Best, Rachel Webb.

The educational activities include an annual clinical meeting where there is exchange of great learning cases, teaching on the run and with dinners shared with colleagues and friends. The ANZPID symposia at the ASID Annual Scientific Meeting has grown considerably over the past decade with many elements of the meeting inclusive of paediatric infectious diseases topics and speakers.

The online monthly ANZPID Journal club<sup>1</sup> started in 2011 and was one of the first online journal clubs of its time. The committee provides oversight to the journal club which now incorporates quiz questions and collaborative submissions with international paediatric infectious diseases societies including the European Society of Paediatric Infectious Diseases (ESPID) and the American Paediatric Infectious Diseases Society (PIDS). Other features of ANZPID's educational initiatives include speakers on a variety of paediatric topics in the ASID Intrepid series.

ANZPID has made significant collaborative contributions to the ASID Clinical Research Network to promote the need for paediatric multi-centre, high quality research. The group have led multiple publications on a variety of priority topics including HIV exposure in infants, bone and joint infections and invasive Staphylococcus aureus infections in children. There are currently 7 multi-centre studies underway, including some which are shared with our colleagues working in adult infectious diseases. As a community,



ANZPID Committee Members: Brendan McMullan (Chair), Anita Campbell (Deputy Chair), Phoebe Williams (WSPID member), Linny Phuong (WSPID member), Nan Vasilunas, Archana Koirala, Rachel Webb, Michelle Mahony (Trainee representative), Ameneh Khatami (ASID clinical research network member)

ANZPID members are highly active in clinical research, embracing novel methodologies (platform trial on Staph aureus blood stream infections: SNAP) and interventions (phage therapy to treat problematic infections: STAMP); as well as challenging dogma with evidence (treating bone and joint infections in children with oral antibiotics only: BEST).

ANZPID has harnessed its collective voice to advocate on key issues in child health and infectious diseases including vaccinations in children and congenital syphilis. The group also ensures a paediatric lens is provided on national policies, guidelines and funding opportunities and provides representation

on numerous national and international professional committees. As well as the ASID-ANZPID Management of Perinatal Infections guideline (see Publications on the ASID website) the group published a systematic review and guidelines on antibiotic duration and timing of IV to oral switch for 36 bacterial infections in children in the Lancet infectious diseases with a useful summary guideline table.

ASID-ANZPID invites anyone with an interest in paediatric infectious diseases and those providing care to children to join us. Together we are a united force committed to improving infection management and prevention for children in Australia, New Zealand and abroad.

<https://asid.net.au/special-interest-groups>  
anita.campbell2@health.wa.gov.au  
b.mcmullan@unsw.edu.au  
@ANZPID @ASIDANZ

<sup>1</sup>Bowen AC, Connell TG, Bryant PA. Evaluating a web-based paediatric infectious diseases journal club: more than just critical appraisal? BMC Med Educ 2014; 14: 242.





PRESIDENT’S REPORT

Dear ASA members

After two COVID-related postponements, ASA will be hosting the 19th International Symposium on Staphylococci and Staphylococcal Infections (ISSSI) in Perth from 18th to 21st August 2024.

**ISSSI 2024** will cover many interdisciplinary subjects regarding staphylococci and staphylococcal infections. Sessions will be presented by the world’s leading experts in each of the research fields. Oral and poster sessions will be an integral part of the program as well, and all delegates are invited to submit abstracts. To promote discussion and interaction between delegates and the invited speakers, the meeting’s registration includes the welcome and farewell receptions, the conference dinner, lunches and morning and afternoon teas.

Over the four days, five plenary sessions, nine symposia and two poster sessions are scheduled.

You can find further details on the program and the meeting’s registration, on the ISSSI 2024 conference website: [www.issisi2024.org](http://www.issisi2024.org)

Important Dates

Registration Opens:	Monday 3 July 2023
Abstract Submission Deadline:	Friday 31 May 2024
Early Bird Registration Deadline:	Friday 12 July 2024

On behalf of the organising and scientific committees, I look forward to welcoming you to ISSSI2024 and the beautiful city of Perth.



**Professor Geoffrey Coombs**  
PhD, BSc (MedSc), PGrad Dip Biomed Sc, FFSc (RCPA), FASM, FISAC  
President | Australian Society for Antimicrobials  
Chair | Australian Group on Antimicrobial Resistance  
President | International Society of Antimicrobial Chemotherapy



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# ANTIMICROBIALS 2024

23rd Annual Scientific Meeting  
15<sup>TH</sup> - 17<sup>TH</sup> FEBRUARY 2024  
SYDNEY ICC / SYDNEY, NEW SOUTH WALES

## 19th International Symposium on Staphylococci and Staphylococcal Infections

18 - 21 August 2024  
Perth, Western Australia

Hosted by Australian Society for Antimicrobials

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- |                           |         |
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Postal:  
Australian Society for Antimicrobials  
PO Box 6705  
East Perth, Western Australia 6892

Email:  
[info@asainc.net.au](mailto:info@asainc.net.au)



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Editor  
Dr. Iain J. Abbott  
[newsletter@asainc.net.au](mailto:newsletter@asainc.net.au)

Publisher  
Jacson Chung  
[jacson@asainc.net.au](mailto:jacson@asainc.net.au)