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Infectious diseases in Northern Australia

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Contents

Cover image: Staphylococcus argenteus *by Jayde Hopkins (owned by Menzies School of Health Research)* *– see page 129 for further details.*

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Vertical Transmission

Mark Schembri
President of ASM

I am honoured and excited to begin my term serving as your new ASM President. I have been involved with the ASM Executive since 2016, initially serving as a theme leader and then as President Elect over the past year. I am confident this experience has prepared me for the task ahead, and I am grateful to the current Executive Committee and the ASM Council for supporting my election to this important role. I especially thank Dena Lyras for the fantastic leadership she has given. Dena has led our Society as President for the past 4 years and will continue to support and guide me and the ASM over the coming year, a testament to her dedication and commitment to the ASM.

I am excited to see our process of renewal in all of our Vice President (VP) positions taking place. New members on our executive team are Martina Sanderson-Smith (VP Elect Corporate Affairs), Hayley Newton (VP Elect Scientific Affairs) and Sam Manna (VP Elect Communications). Each of these members will serve on the Executive Committee over the next year under the guidance of our current VP members (Anthony Baker, Kate Seib and Rebecca LeBard) and assume their full role after the 2023 AGM. This seems a long way ahead, but as we all know time flies and this induction period will allow a smooth transition with retention of corporate memory.

As we move into a new phase of the COVID-19 pandemic, the importance of the ASM continues to grow. In addition to our Annual Scientific Meeting, we support several specialist meetings that are also highly popular. Together, these meetings play an important role for our membership by enhancing networking opportunities, providing opportunities for our ECRs and students to showcase their research, enabling us to recognise outstanding achievements by our members through awards, and fostering engagement with industry. Looking forward, we are committed to finding ways to increase financial support for our members to attend these meetings and to showcase our extensive range of awards. We are also committed to promoting inclusion and diversity, and our 2022 meeting embraced these ideals. I am currently leading the development of a strategic review and plan for our Society and will keep you informed about the positive changes we are making. I also welcome your input and ideas on how we can provide what our members need from the Society, and will ensure there are opportunities for all of you to contribute to the review process.

Our recent Annual Scientific Meeting in Sydney was a great success, with 397 in-person registrations and 108 virtual registrations. We had an outstanding mix of international and national invited speakers, as well as fantastic talks from our ECR and student community. Our student and early career day was a highlight and showcased our Nancy Millis Student Award speakers. We also had fantastic and interactive poster sessions that inspired great discussion and networking. The Local Organising and Scientific Program Committees, chaired by Jai Tree and Martina Sanderson-Smith, respectively, did a fantastic job and deserve our thanks and congratulations for running a stimulating and engaging conference that displayed some of the best cutting-edge research being performed in Australian microbiology. Our next Annual Scientific Meeting will be in Perth next year during 3–6 July 2023. I hope to see you all there!

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Microbiology Australia

Infectious diseases in Northern Australia

Mark Mayo, Sean Taylor and Bart J. Currie

This issue of *Microbiology Australia* covers biomedical research and workforce training in Northern Australia and our northern neighbouring countries. The north of Australia is a tropical region and has a larger representation of Australian First Nations peoples than other States and Territories of Australia. In Australia, Aboriginal and Torres Strait Islander people represent 3.2% of the total Australian population. However, in the Northern Territory, the Australian census (2021) shows that approximately 26.3% of the total population identify as Aboriginal and Torres Strait Islander. This underpins the need for Northern Australia to have continued funding to enable health research, workforce training and health and community services that address the currently unmet and still growing needs of this population demographic.

In Australia the National Agreement on Closing the Gap for Aboriginal and/or Torres Strait Islander peoples has 17 national socioeconomic targets (https://www.closingthegap.gov.au/national-agreement/targets) across areas that have an impact on life outcomes for Aboriginal and Torres Strait Islander people. All the targets are important, but three targets are highly relevant to the work of clinicians and researchers writing in this issue: Target 1, Everyone enjoys long and healthy lives; Target 2, Children are born healthy and strong; and Target 7, Youth are engaged in employment or education.

In 2009, *Microbiology Australia* in its 50th year published an issue titled 'Indigenous Health' (Volume 30, Number 5, November 2009). It contained many articles that remain relevant to research and health challenges in Northern Australia. The first article in that issue was written by the then Chief Executive Officer of the CRC for Aboriginal Health Mick Gooda. Mick Gooda's paper laid out the framework for how successful research can be conducted with input from Aboriginal and Torres Strait Islander peoples: a framework that would lead to improving the flow of health information into primary healthcare delivery. The original CRCs were based in Darwin at the Menzies School of Health Research (1997–2009) and in 2010 transitioned to the Lowitja Institute in Melbourne, which continues today as Australia's National Institute for Aboriginal and Torres Strait Islander Health Research.

Research and training opportunities for local people in Northern Australia and neighbouring countries are vital to continuing the health and wellbeing of people in both urban and regional and remote locations. Strong, knowledgeable, and well developed programs are being run to attract future leaders in biomedical research and health workforce in hospitals, clinics, and Aboriginal and Torres Strait Islander Community Controlled Health Organisations. This is a necessity to ensure a long-term sustainable approach to combating the current and future health needs of the north. This issue covers some of the different training and education initiatives in north Australia presented in the articles, **Bridging the gap between science and indigenous cosmologies: Rheumatic Heart Disease Champions4Change** (Vicki Wade and Maida Stewart), **Building health workforce capacity in Northern Australia** (Michael Johnston, Heidi Smith-Vaughan, Sophie Bowman-Derrick, Jayde Hopkins, Kelly McCrory, Raelene Collins, Robyn Marsh, Kalinda Griffiths and Mark Mayo) and **What does microbiology have to do with the Hearing for Learning Initiative (HfLI)?** (Amanda J. Leach).

As elsewhere in Australia, in Northern Australia the COVID-19 pandemic caused serious concerns for First Nations communities. The health messaging about the COVID-19 infection and vaccination was sometimes not appropriate for the population. The article **Vaccine success and challenges in northern Australia** (Bianca F. Middleton, Jane Davies and Rosalind Webby) discusses some of the challenges faced by communities.

Evidence to be gathered from the study **A project to validate the GLU test for preterm birth prediction in First Nations women** (Kiarna Brown, Holger W. Unger, Margaret Peel, Dorota A. Doherty, Martin Lee, Agatha Kujawa, Sarah Holder, Gilda Tachedjian, Lindi Masson, Jane C. Thorn, John P. Newnham and Matthew S. Payne) will inform health service providers and address Closing the Gap strategy Target 2, whereby children are born healthy and strong.

Biomedical research in Northern Australia and neighbouring countries and other tropical regions of the world continues to develop and produce new knowledge. In these tropical regions the social determinates of health play a big role in health outcomes: from poverty, reduced health service delivery, remoteness, shorter life expectancy, social and emotional wellbeing, and economic growth. Infectious diseases represent many challenges including pathogen identification, optimum treatment and increasing antimicrobial resistance. Climate change is occurring on a global scale and with projected increases in temperature and severe weather events, the endemic regions for some infectious agents is predicted to expand into newer areas and affect a larger population of people. It is therefore important we try to fill knowledge gaps in our understanding of these diseases. Research on infections in this issue includes **Skin health in northern Australia** (Hannah M. M. Thomas, Stephanie Enkel, Tracy McRae,

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Victoria Cox, Heather-Lynn Kessaris, Abbey Ford, Rebecca Famlonga, Rebekah Newton, Ingrid Amgarth-Duff, Alexandra Whelan and Asha C. Bowen) and **Melioidosis in northern Australia** (Josh Hanson and Simon Smith). The increasingly established use of technologies such as whole genomic sequencing, is helping us better understand the epidemiology, virulence and evolution of the organisms that cause these diseases. This is reflected in the articles **Molecular epidemiology of tuberculosis in northern Australia** (Ella M. Meumann and Arnold Bainomugisa) and ***Staphylococcus aureus* and *Streptococcus pyogenes* in the north: distinctively different** (Deborah Holt and Philip Giffard).

Northern Australian researchers continue to strengthen ties with our collaborators in near-neighbouring countries in **Strong relationships between the Northern Territory of Australia and Timor-Leste** (Nevio Sarmento, Tessa Oakley, Endang Soares da Silva, Ari Tilman, Merita Monteiro, Lucsendar Alves, Ismael Barreto, Ian Marr, Anthony D. K. Draper, Gloria de Castro Hall, Jennifer Yan and Joshua R. Francis) to better understand and tackle the health challenges in our tropical region of the world.

This issue covers and discusses a broad range of health challenges faced in Northern Australia, with articles providing strong research plans, outcomes, generated knowledge and research translation from teams of dedicated researchers. The issue also outlines training and education pathways to mentor and deliver future leaders in the health and biomedical research workforce.

Biographies

Mark Mayo is of Aboriginal and Torres Strait Islander heritage whose great grandmother, Polly Warrumbul, was a Mudpurra woman from Wave Hill. Mark's Torres Strait Islander heritage comes from the descendants of the people of the islands of Mabuiag and Badu in the Torres Straits. Mark is a graduate of Charles Darwin University and is a research scientist with over 30 years' experience. Mark's interests in Australian First Nations people's health has led him to work on many research projects during his time at the Menzies School of Health Research from malaria, melioidosis, petrol sniffing and childhood ear diseases. Mark's primary research area has been melioidosis, a potentially fatal tropical disease found in Northern Australia. Mark's research into this disease covers many different aspects, from early detection of the disease in hospital and clinical settings, to understanding the environmental niche of the bacteria and the potential exposure risks to people and animals in an endemic region. Mark is adept at identifying the implications of range of developments on Aboriginal people and potential consequences for the land (especially soil). Mark is currently the manager of the Melioidosis Research Program and Associate Deputy Director of Indigenous Leadership and Engagement at the Menzies School of Health Research.

Dr Sean Taylor is descendent of the Dauareb Tribe, one of the eight tribes of Mer Island in the Eastern Torres Strait region. Sean has over 20 years of clinical experience in Aboriginal and Torres Strait Islander health, working at different levels across Australia in a range of academic and research interest, as well as clinical practice. He started his career as an Indigenous Health Worker in his home community of Mer (Murray) Island in the mid-1990s and later completed a Bachelor of Nursing Science, Graduate Certificate in Health: Diabetes Management and Education, Bachelor of Health Sciences (Honours) and later a Doctor of Public Health at James Cook University. Sean currently holds joint appointments as the Executive Director Aboriginal Health for NT Health, Top End, and Deputy Director Indigenous Leadership and Engagement, Menzies School of Health Research based in Darwin and is an Adjunct Associate Professor, Public Health and Tropical Medicine with James Cook University. Sean is a member of National Health and Medical Research Council Principal Committee Indigenous Caucus and Consumer and Community Advisory Working Group and also a member of the National Partnering with Consumers Committee. He is the current Chair of NT Health, Top End, Big River and East Arnhem Partnering with Consumers Committee, Communicating for Safety Committee, Aboriginal Health Committee, Aboriginal Health Partnership Committee, LGBTQIA+ Committee and Multicultural Committee and Chair of the Reconciliation Action Plan Committee with Menzies School of Health Research and NT Health, Top End, Big River and East Arnhem. Sean is a co-investigator on multiple successful nationally competitive grants.

Bart J. Currie is an infectious diseases and public health physician at Royal Darwin Hospital and Professor in Medicine at the Northern Territory Medical Program. He leads the Tropical and Emerging Infectious Diseases team at Menzies School of Health Research. He is a member of the Technical Reference Group for the Australian Government's Regional Health Security Initiative and chairs the APPRISE Expert Reference Panel. He was Director of the NHMRC-funded Tropical Disease Research Regional Collaboration Initiative (HOT NORTH), which finished in early 2022. He began both the Darwin Prospective Melioidosis Study and the Darwin Prospective Snakebite Study 33 years ago and both continue.

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Microbiology Australia

Bridging the gap between science and indigenous cosmologies: Rheumatic Heart Disease Champions4Change

Vicki Wade[A,*] and Maida Stewart[A]

For full list of author affiliations and declarations see end of paper

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ABSTRACT

Australia has articulated a commitment to eliminate rheumatic heart disease (RHD) by 2031. Business as usual will not achieve this goal. Diverse sectors need to work together in implementing complementary strategies towards this ambitious target. Rheumatic Heart Disease Australia's 'Champions4Change' program is one important element that provides a novel and vital approach. Champions4Change is a culturally safe program of people living with acute rheumatic fever (ARF) and rheumatic heart disease (RHD). The Champions support each other, advocate for ending RHD, design education and awareness programs and inform resource and program development through their lived experiences. New approaches that acknowledge the complex and challenging environments in which ARF/RHD exist are required to eliminate RHD and improve care for those living with ARF/RHD. Approaches taken by the program include local engagement, improved capacity and opportunities for Champions and their communities to make self-determined decisions based on culturally informed information. This paper highlights success stories using culture and locally appropriate approaches to improve community knowledge and awareness of RHD. We describe the rationale, development and purpose of Champions4Change, illustrating how this is far more than a peer-support group, and provides benefits for health services and researchers, as well as empowering community members.

Keywords: acute rheumatic fever, culturally appropriate care, indigenous health, peer support, rheumatic heart disease.

Introduction

Group A Streptococcus can result in post-infectious sequelae including acute rheumatic fever (ARF), and rheumatic heart disease (RHD). The link between streptococcal pharyngitis and impetigo, and the diverse manifestations of ARF – chorea, sore joints and damaged heart valves – can be very challenging to explain and understand. This is compounded in Australia's high-risk settings (remote areas, poor housing and infrastructure) where there might be language barriers and diverse cultural knowledges relating to illness causation and germ theory. Breaking down these complexities for communities is a critical part of disease prevention, empowerment and health literacy.

The Champions4Change program is an Australia-wide network of community members affected by acute rheumatic fever (ARF) or rheumatic heart disease (RHD), established in 2018 by Rheumatic Heart Disease Australia. Champions are people with ARF or RHD, or someone caring for them. Champions share personal stories and insights, and inspire others whose lives are affected by ARF/RHD. The name was chosen to describe who champions are and what they represent: 'Champions4Change – sharing, caring and inspiring'. Champions4Change is the first program of its kind in Australia. It aims to privilege and promote the voices of its Champions, acknowledge and respect Aboriginal cosmologies (world views), support Champions in their lives and work, and put culture, country and community at the centre of responses to RHD.

The value of peer support

Chronic disease peer support programs have demonstrated a wide range of benefits including high levels of satisfaction by participants, increased health knowledge, improved social support and social connectedness, emotional wellbeing and reductions

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in patient care time required by health professionals.[1–3] Within Australia, Aboriginal community and family support programs have been implemented across diverse care settings and health conditions including cancer, diabetes, asthma, child and maternal health and drug and alcohol and sexual health.[4–7]

Among Aboriginal people in the Northern Territory, where language diversity is amongst the highest in the world, there is a real need to provide accessible information and more support for ARF and RHD.[8,9] In Uganda, a RHD peer-support program showed improved health-related quality of life scores improving social connectedness.[10]

In Australia a small, pilot peer group of young Aboriginal people from the Darwin area brought participants closer, feeling supported by each other.[11]

The need for new approaches

Conventional health promotion messages sometimes assume that information is enough to modify behaviour. There is now considerable evidence demonstrating that health promotion in Aboriginal contexts is most effective when based on principles of self-determination including co-design and community-focused actions. Moving beyond standard principles of health promotion, Champions4Change draws on cultural cosmologies – that is, an appreciation of diverse Aboriginal world views and understanding of the functions of the universe – to provide a strengths-based approach. This supports and activates existing strengths, and develops abilities and critical thinking skills to facilitate action for change and a greater sense of control.[12]

Improving access to information, support and self-management capacity are important in improving the lived experience of ARF and RHD.[13] In a study promoting delivery of penicillin for secondary prevention of ARF, positive community engagement was recognised as a key required strategy to achieve success.[8]

Champions have the potential to play a critical role in closing the gap in health care for Aboriginal and Torres Strait Islander peoples with ARF or RHD. The Champions share and translate the meaning of health from an Aboriginal perspective into ways that allow service providers to understand what it is like to be living with ARF or RHD. This two-way learning drawing on 'lived experience' both empowers the community and benefits the health service, providing critical insights for healthcare providers into the everyday realities of ARF/RHD.

Embedding culture and connectedness into RHD care

Our approach with Champions4Change is to look beyond the biomedical model to the cultural, political and environmental factors that underpin these medical conditions.

The Champions developed a model, 'Keeping Our Campfires Burning' (Fig. 1), to describe the vision and implementation of the program. They wanted a clear message about staying strong in culture and feeling connected, to look after

Fig. 1. Keeping our Campfires Burning model.

themselves, their families and communities. The model has seven elements representing the whole, in keeping minds and bodies connected and strong. We are all connected to the fire like embers rising from the fire. These elements keep our fires alive and burning.

To work effectively with Aboriginal and Torres Strait Islander communities, acknowledgement and understanding of the unique cultures of First Nations peoples is needed. As some of the oldest living cultures on this planet, the richness, diversity and complexities of our cultures needs to be appreciated in a respectful and competent way. It is also necessary to acknowledge the impacts that colonisation has had, and continues to have, on the health and wellbeing of Aboriginal and Torres Strait Islander peoples.[14]

Champions4Change draw on their cultural knowledge to bring a richer understanding of what it truly means to be living with ARF and RHD. Champions, comprising culturally diverse Australian First Nations community members, draw strength from their own complex social structures which define roles and responsibilities to keep communities functioning safely. These roles include passing on and sharing knowledge, a process at the heart of traditional Aboriginal culture based on the kinship system.

Despite recent advances in the biomedical treatment of RHD, the associated health benefits at a population and community level have not been fully realised for Aboriginal and Torres Strait Islander peoples. Devastating health outcomes still occur in young people. Many of the barriers to better health sit outside the biomedical domain, driven by cultural, political and environmental factors. These challenges – the legacies of colonisation – require a shift in public health and research imperatives to generate healthy societies.[15]

Shaping health messages: the power of personal stories

There is significant power in the ability of personal stories to create understanding and change minds. For many years data showing high morbidity and mortality associated with ARF and RHD were presented in the medical literature

and at conferences. The figures roll off the tongue like a mantra. The Champions provide an opportunity to put a face to the statistics, telling first-hand the stories of being diagnosed with and living with ARF or RHD: stories about caring for a young child with the condition; the challenges of interacting with the healthcare system; critical insights that healthcare providers, policy makers and politicians need to hear. In a clinical environment, patients lack empowerment or opportunity to provide their story as they are rushed through a list of questions about signs and symptoms and whether they are adhering to treatment. Champions4Change provide an avenue to redress the balance. They are regularly invited to address health conferences at which moving experiences of the devastating impacts of these conditions are shared.

Success stories: champions in action

Chief among their efforts, Champions make sure that culture, language and understandings shape local health messaging. This is critical, for example, in places like Maningrida in the NT, one of the most linguistically diverse communities in the world, with 15 languages spoken and a high burden of RHD. Acknowledging the achievements of Champions in developing innovative multi-lingual education and awareness programs, Champions4Change was featured as an 'Aboriginal and Torres Strait Islander-led transformation' in the 2022 Close the Gap report.[16]

The Dillybag project

Champions4Change identified the need for culturally appropriate resources they can use within their communities. We developed, co-designed and attracted seed funding for a project currently underway called The Dillybag Project. The resources being developed, in English and selected Aboriginal languages, will help fill the gap in essential information about ARF and RHD. Content is fully designed for and by the communities living with, and at risk of ARF and RHD. Educational workshops will support the use of resources in communities for the Champions. The Dillybag project is designed to:

- Improve awareness and knowledge of what causes ARF and RHD and how to prevent ARF and RHD reflecting best practice care.
- Improve confidence and capability of individuals and communities to make informed decision about their care.
- Produce resources to improve community and health professional education and training.
- Be the foundation of a health promotion campaign.

Using hip hop and music

Champion Anne-Marie from Barunga worked with a leading national children's entertainer, Justine Clarke, and school children in her community, to create a music video called 'Boom Boom' (https://www.youtube.com/watch?v=X7HqzJafAr8). The video contains RHD prevention messages and was made in partnership with Skinnyfish music, END RHD, Menzies School of Health Research and Bupa Foundation. It has been shared widely on social and mainstream, receiving positive local feedback.[17]

Lúrra RHD project, Maningrida, East Arnhem land

The Lúrra RHD project arose during a medical research project in which community echocardiographic screening of children was being conducted in Maningrida and surrounding homelands.[18] Recognising the need for local language resources, a set of lessons on RHD for school students was developed by the school's Language and Culture Team, an experienced community health educator, and locally based Champions4Change, to create a curriculum of lessons on core RHD primary health messages in local languages. The units cover body systems such as the circulatory and immune systems, and germ theory of disease. Key primary and environmental health care messages are embedded throughout.

Future aspirations

In Australia, RHD is a First Nations health issue. Solutions must be informed by First Nations peoples. Champions4Change provides a unique mechanism to bridge the divide between community needs and knowledge, and Western medical approaches to ARF and RHD prevention and management. Two-way learning that informs health services and empowers community members is a crucial part of the journey towards RHD elimination. Programs such as Champions4Change have been shown, both internationally and nationally, to assist hard to reach communities with complex social and cultural needs. Achievements of Champions4Change to date highlight the unique role community members with lived experiences of RHD can play. Sustained funding to continue and expand our work is a priority.

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Biographies

Vicki Tooditj Wade is a Noongar woman from the Goreng, Minang, Bibelmen and Wadjari tribes in the south west of Western Australia. Vicki has worked for over 40 years in health and during that time has held many senior positions at state and national levels. Vicki has spent many of these years working in improving the heart health of her people. Vicki sits on the Close the Gap steering committee, as well as several research and health committees across Australia. For her efforts, Vicki has received two prestigious awards: first, the CSANZ achievement award for working with First Nations people in heart health; and second, the Sidney Sax medal for her outstanding contribution to the health system in Australia. Vicki is the Director for RHDAustralia and hopes one day her long-time efforts will have contributed to closing the gap for her grandchildren and their children.

Maida Stewart is a Wemba Wemba/Wergaia woman who has lived in the Northern Territory for over 29 years. For the past 18 years, Maida has been working as an Aboriginal Health Practitioner with the Danila Dilba Health Service in Darwin, Northern Territory, where she provided culturally appropriate and responsive health care to Aboriginal and Torres Strait Islander communities in the greater Darwin region. Maida has extensive experience in primary health care practice, and in health education and promotion. She's worked in the areas of women's health, child and maternal health, acute healthcare, mobile outreach and has been employed as a chronic disease coordinator. In 2018, Maida was awarded a Churchill Fellowship that focused on examining healthy housing in relation to primary prevention of ARF/RHD, which took her to Auckland on Aotearoa's (New Zealand) North Island in early 2020 to investigate the Healthy Homes Initiative. Starting with RHDAustralia in March 2021 as the Champions4Change Project Coordinator, Maida is the main point of contact for the Champions4Change program. She works closely with senior cultural advisor, Vicki Wade to develop, coordinate, and implement strategies and resources that provide training and education to Champions in the program. By establishing and building meaningful relationships and encouraging networking between individuals and communities, Maida will work with Champions to prioritise their social and emotional well-being, and support their capacity building, community education, and health promotion activities.

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Microbiology Australia

Building health workforce capacity in Northern Australia

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ABSTRACT

The Menzies Ramaciotti Regional and Remote Health Sciences Training Centre (Menzies-Ramaciotti Centre) is located within the Menzies School of Health Research (Menzies) in Darwin, Northern Territory (NT). The Menzies-Ramaciotti Centre is contributing to the development of a local health workforce in the NT, including a strong biomedical workforce. The Centre facilitates health workforce career progression for regional and remote youth, with a focus on career development for Aboriginal and Torres Strait Islander (First Nations) youth. The Centre works in collaboration with a range of industry and education partners, who also have strong workforce development goals and a commitment to serving a vital community need to build pathways into work and study with First Nations peoples. Part of the Centre's focus entails delivery of high-quality training in biomedical sciences, including theoretical and practical skill development in microbiology, laboratory techniques, immunology, public health, data science, allied health, and health research. The Centre uses a non-linear, strengths-based approach to training with a multiplicity of entry and exit points including high school work experience placements, traineeships, vocational placements, as well as undergraduate and postgraduate placements.

Keywords: Aboriginal and Torres Strait Islander health, biomedical, capacity building, First Nations, health sciences, northern Australia, regional, remote.

The need for a dedicated health sciences training centre

The widely dispersed First Nations students of the Northern Territory (NT) have a hunger for Science, Technology, Engineering, the Arts, and Mathematics (STEAM) but have the fewest opportunities. In the NT, almost half of the population live in areas classified as remote or very remote.[1,2] In remote and very remote areas of the NT, hurdles to education and training can be exacerbated by distance and significant socio-economic disparities. Approximately 57% of NT youth complete high school.[3] Low high school completion rates lead to limited numbers of young people entering health and biomedical science pathways, training, and employment opportunities.

As more than one-quarter of the NT population comprises First Nations people,[4] strategies to address barriers to education and training must have a focus on enabling First Nations participation, engagement, and leadership. In regional, remote, and very remote parts of the NT, communities are reliant on a costly, fly-in fly-out (FIFO) health workforce model[5] that fails to develop essential capacities within the communities they serve. The Menzies-Ramaciotti Centre aims to simultaneously address this local workforce shortage, provide opportunities to those experiencing the greatest need, and tackle the underrepresentation of First Nations people in the health workforce.

The Menzies-Ramaciotti Centre

The Menzies-Ramaciotti Centre was established in 2020 and is based in Darwin, NT within the Menzies School of Health Research. The Centre logo (Fig. 1), titled 'Turtle on a Journey,' was created by two Australian First Nations people, a former Centre student and now graduate nurse, Zoe Fitzpatrick (Yanyuwa, Garrwa, Wambya and Wanyi woman) and Co-lead of the Centre, Mark Mayo (Mudburra and Mabuiag man). The turtle

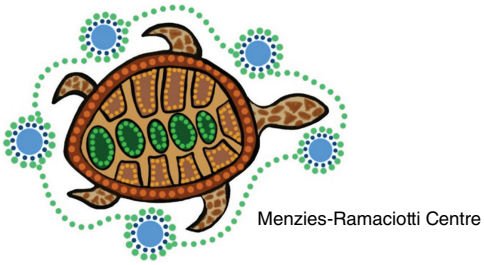
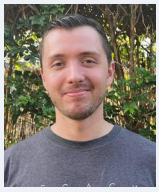


Fig. 1. Menzies-Ramaciotti Centre logo. Titled 'Turtle on a Journey', 2020, by Zoe Fitzpatrick and Mark Mayo.

is depicted on its journey through the sea, representing the journey we all take through life. The lines connecting the circles signify the connections between people, and the way they support and protect the individual on their journey. The Centre is guided by overarching values of equity, reciprocity, self-determination, mutual support, and trust; these values are represented as the shapes on the back of the turtle.

Student in focus



Brandon Turner
Brandon is an Aboriginal man from the Larrakia Nation in the NT with a Bachelor of Science, majoring in Biomedical Science at Charles Darwin University. He commenced with the Centre in 2021, completing a Hot North Vocational placement. He is currently undertaking the Doctor of Medicine at Flinders University while working part-time at Menzies.

The co-leadership model

The Menzies-Ramaciotti Centre has a shared leadership model with four Co-leads, Mark Mayo, Associate Professor Heidi Smith-Vaughan, Dr Robyn Marsh, and Dr Kalinda Griffiths who have worked together to build local health workforce capacity in the NT since the early 1990s. This shared leadership model enables innovative development of the Centre through the Co-leads combined research, teaching and supervisory experience. In this way, youth benefit from decades of mentorship and strategic development of pathways into careers in health that leverages access to networks across health research institutes, the higher education sector, and other partner organisations. Two of the Co-leads began their careers as First Nations laboratory trainees and are now nationally and internationally recognised leaders in their fields of research. This outcome was achieved because of the dedicated mentorship and training they received at Menzies (Fig. 2).

Mr Mark Mayo is a local Darwin man of Aboriginal and Torres Strait Islander (Mabuiag) heritage whose great grandmother Yrambul Nungarai, or Polly Warrumbul, was a Mudburra woman from Wave Hill, NT. Mr Mayo began his career at Menzies in 1992 as a First Nations biomedical laboratory trainee, completed his Bachelor of Science at CDU and now 30 years later is the Associate Deputy Director, Indigenous Leadership and Engagement at Menzies, as well as Senior Researcher and Program Manager for the Melioidosis Program (Fig. 3).

Fig. 2. Program Manager Michael Johnston, Trainee Royce Ramsamy, Laboratory Trainer Kelly McCrory, Co-lead Mark Mayo, Undergraduate Trainee Jayde Hopkins, Co-lead Dr Kalinda Griffiths, and Trainee Porsche Cahill at Menzies.

Fig. 3. Trainee Porsche Cahill and Co-lead Mark Mayo in the laboratory.

Associate Professor Heidi Smith-Vaughan is an Associate Director at Menzies where she has researched for 32 years. She is a microbiologist passionate about growing the next generation of biomedical scientists, and particularly building capability across the region among those with less opportunity.

Dr Robyn Marsh has a Bachelor of Applied Science (Medical Laboratory Science), Master of Science by Research and PhD in microbiology. Her research program supports foundational laboratory training opportunities for NT youth, with an additional focus on growing local bioinformatic capacity.

Dr Kalinda Griffiths commenced at Menzies in 1997 as a First Nations biomedical laboratory trainee and is now a post-doctoral epidemiologist at the Centre for Big Data Research in Health at the University of New South Wales, holding honorary positions at Menzies School of Health Research and the University of Melbourne. Dr Griffiths' work is focused on Indigenous data governance and the

Fig. 4. Laboratory Trainer Kelly McCrory and Co-lead Dr Kalinda Griffiths working in the laboratory.

measurement of population level health inequities, with a particular interest in cancer care and outcomes (Fig. 4).

Student in focus

Helena Warria
Helena, a Tiwi and Torres Strait Islander woman, is an Edwina Menzies and Ian Albrey training scholarship recipient at the Menzies-Ramaciotti Centre currently undertaking an Undergraduate Certificate in Biomedical Science. Helena moved to Darwin from the Tiwi Islands in January 2022. After developing an interest in medical science, she decided to apply for a position at Menzies to commence her career.

Who we work with

The Menzies-Ramaciotti Centre builds on existing training programs within the NT by partnering with significant stakeholders in health, including Royal Darwin Hospital (RDH), Charles Darwin University (CDU), Indigenous Allied Health Australia (IAHA), and NT schools. These collaborative partners provide the Centre opportunities to engage high school students in regional and remote areas to enable transitions into career pathways that lead to work and study in health and biomedical sciences.

The Menzies-Ramaciotti Centre works across Menzies School of Health Research divisions and programs such as the Biyamarr ma Traineeship Program and HealthLAB, a remote youth engagement and health promotion program led by Associate Professor Heidi Smith-Vaughan. HealthLAB travels throughout regional and remote NT to provide hands-on health education activities and information to school aged youth. Similarly, CDU and IAHA enable First Nations youth transitions from school into work or study in health sciences through targeted support and programs such as IAHA's National Aboriginal and Torres Strait Islander Health Academy and CDU's Bidjipidji School Camp program.

Student in focus

Nyasha Majoni
Nyasha is an 18-year-old Zimbabwean. In 2008 he and his family ventured to Darwin. After completing vocational training in laboratory sciences with the Menzies-Ramaciotti Centre, he commenced working on an ear disease project at Menzies. Nyasha has the long-term goal of studying medicine and working in health.

Training pathways

The Centre aims to provide opportunities to those who experience some of the greatest socio-economic disparities in Australia. It empowers and promotes the social and economic inclusion of those who experience exclusion from mainstream educational and employment opportunities. This includes those living in regional and remote areas, young parents, refugees, new migrants, people who are differently abled, those who are culturally and linguistically diverse, and those who may experience compounding factors at the intersection of race, class, responsibility, gender, sexual orientation, age, and ability. All these factors can impact opportunities.

We provide opportunities by offering entry into training that does not rely on the usual metrics (e.g. tertiary entrance scores) but rather on a hunger to learn, where vocational experiences are tailored to the individual needs of students. Our Centre also offers entry points that align with each individual's interests and prior experiences, so that training builds on existing strengths and enables youth to excel. Each First Nations student is given the opportunity to be paired with a mentor or supervisor who is First Nations themselves, to ensure that training can occur in a safe learning environment, where students' worldviews are reflected in the content and means by which they learn.

Student in focus

Porsche Cahill
Porsche is a First Nations woman who completed a Certificate III in Allied Health Assistance during her schooling through the IAHA NT Aboriginal Health Academy, which included a placement with the Menzies-Ramaciotti Centre. She is currently completing a Certificate III in Laboratory Skills through the Menzies-Ramaciotti Centre and the Biyamarr ma Traineeship Program. Porsche has grown to love working in the lab.

Laboratory training

Creating an industry-ready biomedical and health workforce relies on access to state-of-the-art laboratories. We are active in teaching laboratory skills to local, national, and international students. Our laboratory-based biomedical training

includes, but is not limited to, microbiology, immunology (including cell and tissue work), molecular biology, genomics, metagenomics, microbiomics, and bioinformatics. Students also undertake training in Good Clinical Laboratory Practice and clinical trials.

Our laboratory training program extends from introductory laboratory methods for high school students through to skills development in contemporary industry-relevant technologies including real-time PCR and matrix-assisted laser desorption/ionisation-time of flight (MALDI-TOF). All students participating in our laboratory training program learn fundamental skills that have high transferability across multiple industry contexts. We provide structured workplace learning for students prior to future study or those beginning their studies, enabling students to develop confidence in navigating the laboratory and higher education environments.

Student in focus

Shenea Tipungwuti-Edwards
Shenea is a proud Aboriginal woman from Tiwi and Burarra who grew up on Kunwinjku country in a community called Gunbalanya. She is currently working at Menzies through the Menzies-Ramaciotti Centre and Biyamarr ma Traineeship Program as a laboratory trainee. Throughout her traineeship she hopes to become exposed to different work areas within health research. Medicine has always been a passion for Shenea, and she would like to pursue a career within that path.

Student engagement and future directions

Since the establishment of the Menzies-Ramaciotti Centre in 2020, we have trained 20 work experience students, 27 certificate level trainees, 18 vocational placement students, and 15 undergraduate students have received ongoing support for up to 2.5 years to date. In addition, through our partnership with Menzies HealthLAB we have engaged 3479 regional and remote youth through health promotion activities and science outreach activities.

The next phase of this program is to refine the transferable and adaptive health sciences training model so that it can be implemented across jurisdictions within the nation, considering local needs and contexts. We are in the process of conducting an evaluation of the Centre's work to date and will identify barriers and enablers to youth completing and progressing through training pathways. The evaluation will develop a set of evidence-based recommendations and processes that can be used at the national level to implement training pathways for regional and remote youth so that our approach can be shared and replicated.

Regional and remote northern Australia suffers from a chronic health workforce shortage and rapid staff turnover. At the same time, the NT has rich, untapped potential in young people who are both underserved and culturally capable to meet the health needs of the region. We welcome potential collaborators and funders to join us on the next stage of our journey to share opportunities in health workforce pathways, which would be impossible to accomplish on our own.

Student in focus

Royce Ramsamy
Royce is an Aboriginal and Torres Strait Islander man from Cairns who applied for a position in the Biyamarr ma Traineeship Program shortly after finishing school in Darwin. He is now completing a Certificate III in Laboratory Skills with the Menzies-Ramaciotti Centre and Biyamarr ma team at Menzies School of Health Research.

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Conflicts of interest. The authors declare no conflicts of interest.

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Acknowledgements. The Menzies-Ramaciotti Centre acknowledges the Larrakia people, and their Elders, past, present, and future, upon whose lands our Centre is located. In addition, we acknowledge the Menzies-Ramaciotti Centre Steering Committee and Youth Advisory Group, for providing important input into our Centre's governance. We also acknowledge our peer trainers who have provided vital input into the development of the Centre's training pathways. Lastly, we acknowledge our collaborative partnerships that continue to grow. These include Menzies Biyamarr ma unit, Menzies Aboriginal and Torres Strait Islander capacity building unit, Charles Darwin University, Indigenous Allied Health Australia, Bridging the Gap Foundation, NT schools and many others.

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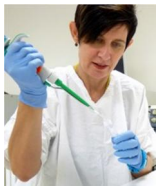
Biographies

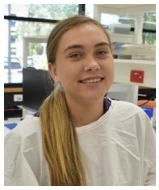
Michael Johnston is a senior research officer and program manager with the Ramaciotti Regional and Remote Health Sciences Training Centre (Menzies-Ramaciotti Centre), based at Menzies School of Health Research in Darwin, Northern Territory (NT). The Menzies-Ramaciotti Centre is developing a local and Aboriginal and Torres Strait Islander health sciences workforce in the NT. Following the completion of a combined Bachelor of Arts and Bachelor of Secondary Education and a Master of Human Rights in 2016 and 2019, Michael worked for the University of Sydney, the University of New South Wales, and the Tiwi Islands Regional Council in service of Aboriginal and Torres Strait Islander-led programs. Michael is a non-Indigenous person. Michael brings together his experience as a teacher, education designer, grants and policy officer, as well as a complex systems approach to address structural inequality in educational opportunities in Australia. In his current role, Michael takes an interdisciplinary approach to facilitating educational and career development opportunities with NT youth engaged in science, technology, engineering, the arts, and mathematics (STEAM).



Associate Professor Heidi Smith-Vaughan is Associate Director for Research (HDR and Ethics), Head of HealthLAB, and Co-lead of the Menzies-Ramaciotti Centre. She is an investigator on clinical trials of the efficacy of vaccines and antibiotics for carriage, otitis media and suppurative lung disease in Australia and countries in the region. She also leads government and philanthropy funded outreach and health education programs. Heidi has a strong record in training and mentoring. She supports scientists in Vietnam, Papua New Guinea and Timor Leste in a range of in-country projects, and has a growing program of training for scientists in disadvantaged regions. In 2014 she co-founded the Menzies HealthLAB with Associate Professor Sue Sayers (deceased). She continues to lead this immersive, interactive community health education initiative which travels around the Northern Territory delivering interactive health promotion with >13 000 participants to date.

Sophie Bowman-Derrick is a veterinarian. In 2019, she completed the Master of Philosophy (Applied Epidemiology) through the Australian National University, with her thesis focused on antimicrobial resistance. Sophie is currently completing the Doctor of Medicine through Flinders University's NT Medical Program and intends to train as a rural general practitioner. Alongside her studies, Sophie provides administrative and executive support for the Menzies-Ramaciotti Centre.

Jayde Hopkins is a proud Gurindji and Woolwonga woman from Darwin. She is currently completing her undergraduate degree in Biological Sciences at La Trobe University. She is fascinated by microbiology and genetics and hopes to become an infectious disease researcher. Jayde is currently working at the Menzies-Ramaciotti Centre as a project assistant, artist-in-residence, and peer trainer.



Kelly McCrory first started her journey at Menzies in late 2016 as a work experience student with the Melioidosis team. Her main role in the team is environmental work. The opportunity to get hands on experience in and outside of the lab sparked her interest in pursuing a career in environmental science. Kelly currently works as a Menzies-Ramaciotti Centre peer trainer, developing and delivering laboratory training. She commenced a Bachelor of Environmental Science degree in 2020 after completing a tertiary enabling program (an alternative pathway into university).

Raelene Collins is a Kuku Yalanji and Garawirrtja woman who grew up in Darwin. She is currently undertaking a Bachelor of Nursing degree at Charles Darwin University. Raelene completed a Certificate III in Laboratory Skills in 2019, currently works as a Menzies-Ramaciotti peer trainer, and develops health promotion resources.

Dr Robyn Marsh is a Senior Research Fellow in the Child Health Division of Menzies School of Health Research, Darwin, Australia where she leads the Paediatric Respiratory Microbiome Program. She is one of the Centre's Co-leads and is an Associate Investigator of the Centre for Research Excellence in Bronchiectasis in Children (https://www.crelungs.org.au/). She is a current Rebecca L Cooper Al and Val Rosenstrauss Fellow and a previous NHMRC Frank Fenner Fellow (2011). Her research focuses on microbiological drivers of chronic airway infections among children, with special interest in chronic suppurative lung diseases, upper airway health and middle ear infections among under-served paediatric populations.

Dr Kalinda Griffiths is a Scientia Senior Lecturer at the Centre for Big Data Research in Health, University of New South Wales. Kalinda's work addresses complex health disparities in populations by using existing administrative data. She holds honorary positions at the University of Melbourne and Menzies and is Deputy Editor of the *Health Promotion Journal of Australia*. Her research currently addresses issues of quality and the utilisation of Indigenous data with a focus on data governance, measurement and cancer care and outcomes. Kalinda is the recipient of a number of awards. Notably, she was awarded the Northern Territory Young Australian of the Year in 2011 and more recently, the 2019 Lowitja Institute Emerging Researcher Award. She was also a 2019–2021 Science and Technology Australia Superstar of STEM.

Mark Mayo is of Aboriginal and Torres Strait Islander heritage whose great grandmother, Polly Warrumbul, was a Mudpurra woman from Wave Hill. Mark's Torres Strait Islander heritage comes from the descendants of the people of the islands of Mabuiag and Badu in the Torres Strait. Mark is a graduate of Charles Darwin University and is a research scientist with over 30 years' experience. Mark's interests in Australian First Nations people's health has led him to work on many research projects during his time at the Menzies School of Health Research from malaria, melioidosis, petrol sniffing and childhood ear diseases. Mark's primary research area has been melioidosis, a potentially fatal tropical disease found in Northern Australia. Mark's research into this disease covers many different aspects, from early detection of the disease in hospital and clinical settings, to understanding the environmental niche of the bacteria and the potential exposure risks to people and animals in an endemic region. Mark is adept at identifying the implications of range of developments on Aboriginal people and potential consequences for the land (especially soil). Mark is currently the manager of the Melioidosis Research Program and Associate Deputy Director of Indigenous Leadership and Engagement at the Menzies School of Health Research.

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Skin health in northern Australia

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ABSTRACT

Achieving healthy skin requires the prevention of infectious diseases that affect the skin. Prevention activities range from environmental health improvements to address inequities in living situations, through to community-wide treatment programs to reduce transmission and improve skin health. In this paper we discuss the pathogens that cause and conditions that arise when skin is infected, the burden of disease in northern Australia, and some of the current research underway to address this high burden, which predominantly affects remote-living Aboriginal and Torres Strait Islander children and families.

Keywords: Aboriginal and Torres Strait Islander populations, environmental health, health promotion, impetigo, infectious diseases, northern Australia, scabies, skin health.

Introduction

The skin is the largest and only externally visible organ of the body, and healthy skin is crucial for holistic physical and social-emotional wellbeing. In remote northern Australia, a variety of skin infections are endemic, which can impact on wellbeing. These include pruritic infections such as scabies, tinea,[1] and headlice that can lead to skin disruption and subsequent impetigo.[2,3]

In remote northern Australia, up to 75% of all community members attend a clinic at least once each year for the treatment of a skin or soft tissue infection,[4] and there has been a long history of skin infection programs in individual communities to address this burden. In the Northern Territory (NT) these efforts include scabies mass drug administration (MDA) in Wadeye,[5] the East Arnhem Healthy Skin Program[6] and, more recently, a focus to prevent skin infections upstream of rheumatic heart disease (RHD) in Maningrida.[7] In the Kimberley region of Western Australia (WA), an outbreak of acute post-streptococcal glomerulonephritis (APSGN) from 2013 to 2017[8,9] has led to a strong focus on healthy skin, and the inclusion of prevention activities alongside diagnosis and treatment in the SToP (See, Treat, Prevent) Trial currently underway.[10] In northern Queensland (QLD), several older studies have documented the burden of skin infections,[3] with newer work emerging from the Torres Strait.[11]

Here we summarise the work to date in understanding the burden and control of skin infections in northern Australia and describe a potential road map for future action.

Burden

Impetigo

Impetigo, also known as skin sores, is a frequent diagnosis for children and adults living in remote northern Australia. Impetigo is a bacterial skin infection, and in northern Australia is driven by *Streptococcus pyogenes*[12,13] with *Staphylococcus aureus* also present independently or as a co-infection at high rates.[12] Impetigo begins as a blister that fills with pus, crusts and then eventually heals following re-epithelialisation of the skin surface.[14] At any one time, 45% of remote-living Aboriginal children in northern Australia are suffering from impetigo – this is by far the highest documented burden in the world.[2,3]

Skin infections, predominantly scabies with secondary infection with *S. pyogenes* and *S. aureus*, affect many infants in the first month of life, with the median timing of first

clinic presentation in the NT at 2 months of age[15] and 82% of children presenting to the clinic with an episode of impetigo before 12 months of age.[16] In WA skin infections, predominantly impetigo, are the chief reason for presentation to the clinic, with 72% of all children aged 0–5 years presenting at least once each year for skin infections.[17] This heavy, early burden of skin infections results in 15% of infants admitted to hospital in the first year of life[18] and this early *S. pyogenes* exposure increases the risk of subsequent acute rheumatic fever (ARF).[19] Despite their frequency, skin sores may be 'normalised' by clinicians in endemic regions, leading to under-recognition and under-treatment of impetigo in remote Australia.[20] Left untreated, bacterial skin infections can become complicated by *S. pyogenes* and *S. aureus* sepsis,[21] bone and joint infections,[22] and pneumonia,[23] as well as post-infectious sequelae including acute rheumatic fever (ARF) (and therefore RHD) and acute post streptococcal glomerulonephritis (APSGN)[24] (Fig. 1).

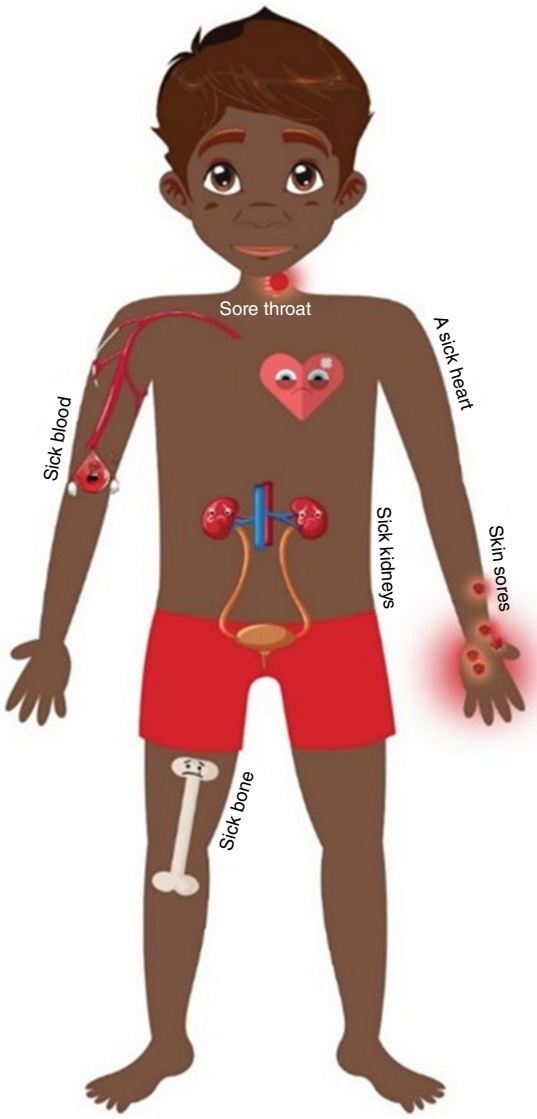

Fig. 1. The skin is a physical barrier that protects the body from disease. Breakages in the skin, often due to itchy infections, facilitate the development of impetigo. Left untreated, impetigo can progress to complex chronic diseases such as acute post streptococcal glomerulonephritis, acute rheumatic fever, and rheumatic heart disease.

Scabies

The scabies mite, *Sarcoptes scabiei*, is transmitted from human to human, and is endemic in remote northern Australia. Remote Australian children have some of the highest reported rates of scabies in the world,[25] with up to 35% of children affected at any time.[2] Scabies infestations can also be complicated by bacterial skin infectious, with common pathogens including *S. pyogenes* and *S. aureus*.

Attempts to control scabies through MDA of permethrin[5,26] and ivermectin[27] have been somewhat successful, but not sustained. Recently, community engagement in consideration of scabies treatment with an ivermectin mass drug administration approach has been important, and this has informed the recent change to make ivermectin available across Australia for first line treatment of scabies in Aboriginal or Torres Strait Islander people.[28] More recently, mathematical modelling has shown that up to seven rounds of MDA in a community might be required for sustained impact[29] – an approach that has not been trialled to date in Australia or globally.

In a hospital study in WA, no children with scabies were identified in a retrospective chart review, compared to 8% of children who were prospectively assessed for skin conditions when admitted to hospital.[20] This demonstrates that normalisation of scabies by health care providers may be a contributory factor to the ongoing burden, with education and training packages that can be accessed through the National Healthy Skin Guidelines[30] a key strategy to address this normalisation among healthcare workers. Similarly, the SToP Trial[10] has been designed to deliver the continuity of training required for healthcare workers in a heavy burden context. Empowering families as well as Aboriginal health workers to work alongside families and support access to culturally informed diagnosis, treatment and prevention activities will be key to successful change. With this in mind, further resources are available in the National Healthy Skin Guideline community care workers manual.

Crusted scabies in all age groups may be a critical contributor to the heavy burden of classical scabies in young children due to stigma, 'shame', under-diagnosis, and frequent recurrences.[31] Crusted scabies is notifiable in the Northern Territory,[32] and considerable progress has been made in improving recognition, treatment, and facilitating a 'scabies-free environment' approach for those affected with crusted scabies to reduce recurrences.[33] Crusted scabies may be less common in other states of Australia, but there is limited data available to confirm this, as it is not a notifiable disease in WA or QLD.

Tinea

Tinea is a pruritic, scaly skin condition transmitted from human to human. Alternatively, it can also be acquired from the environment[1] or household pets,[34] and in northern Australia is caused by *Microsporum* spp. and *Trichophyton* spp. Estimates of the tinea burden in northern Australia are not well established;[1] however, tinea was recorded in 7% of children prospectively assessed for skin infections on admission to hospital in WA,[20] and 4.3% of participants had skin sores

associated with tinea in the Skin Sore Trial conducted across the NT.[13]

Kerion, onychomycosis, and other complications of tinea are well documented,[35] but may be misclassified as they are frequently under-recognised. Similar to bacterial skin infections, 'normalisation' of fungal infections by clinicians has also been noted in remote Australia.[20] As with other pruritic skin conditions, tinea predisposes to bacterial skin infections and the other sequelae previously mentioned, can be stigmatised, and is challenging to treat.

Head lice

The head louse is a hematophagous ectoparasite, *Pediculus humanus capitis*, readily transmitted by direct head-to-head contact. In Australia, head lice is the third most commonly reported outbreak in day-care centres and schools, with rates of up to 35% reported in school-aged children.[36] There are no published studies on the prevalence of head lice in remote Australia; however, the SToP Trial is measuring this burden in remote Kimberley communities of WA.[10] Breaks in the epidermis due to intense itching from head lice can be complicated by secondary bacterial infection[37] and have been known to cause severe impetigo of the scalp in remote-living Australian Aboriginal children.[38] In this way, ectoparasitic diseases like headlice and scabies can predispose to *S. pyogenes* infection and post-infectious complications, such as glomerulonephritis and rheumatic fever.[39]

Less common skin infections

Other skin infections occur with less frequency but remain present in northern Australia. Leprosy, a chronic granulomatous infection characterised by anaesthetic skin lesions and caused by *Mycobacterium leprae*, is diagnosed infrequently in Australia but remains at the highest burden in remote-living Aboriginal and Torres Strait Islander Australians.[40] Buruli ulcer is a neglected tropical skin disease which leads to skin and soft tissue destruction, predominantly on the lower limbs, after infection with slow-growing *Mycobacterium ulcerans*. This is endemic in coastal regions in south-east Victoria and in Far North Queensland but is uncommon in Western Australia and in the Northern Territory.[41]

The road to healthy skin

We offer guidance on treatment for skin infections in remote settings in the Australian National Healthy Skin Guidelines;[30] however, strengths-based, integrated, Aboriginal community-led and co-designed programs across the region will be required to comprehensively address the heavy burden of skin infections in northern Australia. In order to be successful, these programs must be informed by timely and consistent estimations of disease burden, give attention to the social and environmental determinants of health which underpin this burden, and employ holistic approaches to public health intervention which empower and support individuals and communities to improve health outcomes.

A contemporary understanding of prevalence to inform public health action

Studies of skin infection burden across northern Australia over the last few decades have been intermittent and community-based.[3] While this has informed community-based interventions,[5,27,42] broader regional skin disease control is needed. The prototype for this has been the East Arnhem Healthy Skin program[6] in the NT and, more recently, the SToP Trial in WA;[10] however, both are limited to small regions within their respective jurisdictions. Ongoing Aboriginal- and community-led skin burden studies across the entire northern region of Australia are crucial to inform skin disease control, improve quality of life and reduce the downstream consequences.

However, the barriers of remote distance and competing heavy burdens of chronic disease (further exacerbated by events such as the recent pandemic) make ongoing assessment of skin infection prevalence in remote regions of northern Australia challenging. The development and validation of accurate, sustainable, and community-led mechanisms to determine skin infection prevalence will be key to a contemporary understanding of the burden of these diseases, which is in turn crucial to advocate for and monitor the success of public health interventions. Empowering community-based health workers to facilitate skin assessments may be a way forward, such as described by Tsoi *et al.* in Fiji and the Solomon Islands,[43] and work is under way to explore the cultural security and accuracy of this approach in northern Australia. While prevalence studies can be informative to disease control, primordial prevention by addressing housing, environmental, and other determinants of health remains critical.

Environmental health

Environmental health occurs at the interface between humans and the broader environment in which we live.[44] It is a strong determinant of health, including skin health, existing within a socio-ecological model whereby external factors constrain and limit an individual's health behaviours. Colonisation and historical polices and determinants of health have impeded Aboriginal peoples' rights to access safe, effective, and culturally responsive healthcare and housing.[45] For populations in remote Australia, this has led to overcrowding, inadequate housing, and limited access to functional and regularly repaired health hardware (e.g. showers, washing machines) and software (e.g. soap, towels) in the home. To make real change, researchers and policy-makers must look beyond reducing overcrowding only through the provision of new housing stock, and instead invest in co-designed environmental health initiatives with significant community input to achieve the Healthy Living Practices.[46] Recent and ongoing work in WA and the NT suggests that the focus should be placed on functional hand and body washing facilities, functional washing machines, and regular maintenance cycles for housing as essential strategies to improve skin health, with additional benefits for other infectious diseases.[47]

Health promotion

As part of a holistic approach to addressing skin infections, health promotion and prevention programs must be developed

using a ground-up approach, to ensure they are meaningful to the environment in which they are implemented.[48] Approaching biomedical science from an Aboriginal cultural standpoint has the potential to transcend traditional Western prevention programs and create inclusive, empowering, and contemporary methods of promoting health and wellbeing.[49] Embedding of culture, language, and Aboriginal peoples' voices specific to the target communities within health messaging is likely to increase engagement and improve sustainability,[50] and this has been shown in previous work to improve the diagnosis, treatment, and prevention of a range of diseases in northern Australia including wet cough,[51] RHD[52] and skin infections.[53] In the Kimberley region of WA, work is underway in partnership with remote Aboriginal communities to co-design and implement culturally appropriate healthy skin resources.[10] At the request of community Elders, local language and culture are embedded within these resources with an aim to reduce the burden of skin infections. Moving forwards, initiatives to promote healthy skin across northern Australia will require this multifocal lens, with Aboriginal people's worldviews and ways of knowing, being, and doing central to the narratives and messaging of programs.

Conclusions

Skin infections remain a longstanding challenge across northern Australia, predominantly affecting Aboriginal children and families. While prevalence assessments followed by community-wide treatment is one approach to address this, more comprehensive co-designed and community-led programs with attention to the environments in which people live, achieving the healthy living practices, and culturally informed health promotion will be critical to achieve real change.

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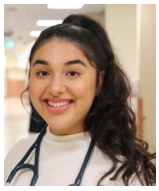

Dr Heather-Lynn Kessaris is an Alawa and Marra woman from the Northern Territory. She initially completed a Bachelor of Science at the University of Western Australia in 2014, majoring in Population Health and Aboriginal Health and Wellbeing, before going on to complete her Doctor of Medicine in 2018 in Perth, Western Australia. She is currently a resident medical officer based at the Royal Darwin Hospital and has a keen interest in dermatology.

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Associate Professor Asha C. Bowen is a clinician scientist working across the Perth Children's Hospital as a paediatric infectious disease specialist and the Telethon Kids Institute as Head of the Healthy Skin and ARF Prevention Team and the ENDRHD Program. Asha and her team launched the inaugural National Healthy Skin Guidelines to guide clinicians in the recognition and evidence-based treatment of skin infections, and are updating this resource in 2022. Asha has more than 10 years' experience leading infectious diseases research and investigator-initiated clinical trials focused on issues significant to Aboriginal child health.

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Staphylococcus aureus and *Streptococcus pyogenes* in the north: distinctively different

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ABSTRACT

Staphylococcus aureus and *Streptococcus pyogenes* are important contributors to disease in northern Australia. Both are opportunistic pathogens, frequently carried on the skin or in the respiratory tract in the absence of disease. A large proportion of the *S. aureus* strains causing infection in northern Australia possess the Panton Valentine (PVL) toxin, with ST93, ST5, and ST121 being significant. PVL + strains are associated with both community- and healthcare-associated infections, and a large proportion are methicillin-resistant *S. aureus* (MRSA). MRSA strains known to be healthcare associated (ST239 and ST22) are not prevalent. CC1 PVL− MRSA continue to cause infections. The diversity of *S. pyogenes emm* types in northern Australia is high with skin tropic and non-tropic *emm* types predominating. This contrasts with other parts of Australia where *emm* diversity is lower and rates of pharyngitis higher. The high diversity raises concerns for the likely efficacy of vaccines based on the variable region of the M protein, the nucleotide sequence of which underpins *emm* typing. It is likely that complex interactions occur between these two important bacterial pathogens, and other important skin pathogens in the region such as the scabies mite.

Keywords: *emm* typing, M protein, Panton Valentine leucocidin, PVL, pyoderma, rheumatic heart disease, skin infections, *Staphylococcus aureus*, *Streptococcus pyogenes*.

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Staphylococcus aureus and *Streptococcus pyogenes* are firmicutes, within the Bacillales and Lactobacillales respectively. Both are associated with asymptomatic colonisation but are also human pathogens of global significance, causing a range of infections from superficial to life-threatening invasive disease. They are important causes of skin infections in northern Australia[1] with distinct differences in epidemiology to that seen in other parts of the country.

S. aureus has long been one of the most notorious agents of nosocomial infections, but also causes disease in the general community. A dominant concept is the dichotomy between β-lactam resistant (known as methicillin resistant *S. aureus* (MRSA)) and sensitive (methicillin susceptible *S. aureus* (MSSA)) strains. The MRSA phenotype is homoplastic, due to mobility of the SCC*mec* genetic determinant of β-lactam resistance.[2] Also important is the dichotomy between community-associated MRSA (CA-MRSA), and healthcare-associated MRSA (HA-MRSA).[3] HA-MRSA strains are well adapted to the health care environment, are typically multiresistant, and in general do not cause community onset infections. CA-MRSA cause community onset infections, but also now predominate in healthcare facilities. CA-MRSA frequently carry a bacteriophage specifying the pore-forming toxin Panton-Valentine leukocidin (PVL). Phage mobility results in PVL+ CA-MRSA being within several evolutionary lineages, and PVL+ MRSA and MSSA are often closely related. The broad framework for understanding the core genome population structure *S. aureus* is based on 'clonal complexes' (CCs) consisting of closely related sequence types (STs) defined by the multi-locus sequence typing (MLST) scheme.[2]

Australia is similar to rest of the world in that the major HA-MRSA strain for many years was ST239. Recently, ST239 has become less prominent, with the most prevalent lineage now being ST22/CC22 'EMRSA-15'.[4–6] Northern Australia appears to have experienced the steep decline of ST239, but with only limited replacement with ST22.[7,8]

CA-MRSA strains in northern Australia are similar to Australia as a whole, but a contributor to this is expansion of strains originating in remote areas into urban Australia.[4,9,10] The most prominent is ST93. Essentially all ST93 are PVL+ and the strain is regarded as highly virulent. ST93 MRSA and MSSA co-exist. Genomic studies indicate that ST93 arose from a point source/genetic bottleneck in north-western Australia in the 1990s. ST93 is divergent from all other *S. aureus* evolutionary lineages, and the nature of the point source remains enigmatic.[10] Consequently, ST93 does not define an observed CC of a

substantial number of related STs. ST93 has disseminated throughout Australia and much of New Zealand[10] and is often isolated from health care facilities as well as the general community.[6] More recent is the emergence of a CC5 PVL+ CA-MRSA strain, also in north-western or northern Australia, and this appears to be in the expansion phase[11] perhaps repeating what was seen with ST93. Other PVL+ strains of current or recent significance in northern Australia include a ST30 MRSA that has long been associated with the Pacific region, and has reduced in prevalence in recent years,[8,12] and ST121 (CC121), which is a PVL+ strain mainly associated with south-east and east Asia, and almost always MSSA.[8,13,14] CA-MRSA strains are not always PVL+. In particular, PVL− CC1 MRSA, often designated as WA-1, has been causing community-acquired infections in north-western Australia for many years.[6,15]

We recently reported a multi-year longitudinal genomics-based study of *S. aureus* in Top End dialysis clinic clients, staff, and researcher.[8] The objective was identification of reservoirs underpinning infection. The genetic nature of the recovered isolates are largely consistent with other studies and provide 'in miniature' a picture of *S. aureus* epidemiology in the Top End (Fig. 1). The infections were nearly all 'skin and soft tissue', with a large proportion caused by the PVL+ MRSA (ST93 and ST5), PVL+ MSSA (ST121), and PVL− MRSA (ST762 (CC1)). Strikingly, asymptomatic carriage of the PVL+ strains was vanishingly rare. In contrast, the PVL− MRSA strains were associated with both carriage and infection, and putative transmission from carriage to infection was identified. ST762 is single locus variant of ST1. ST762 isolates are very rare in the MLST database but were prevalent in the STARRS isolates, and putatively transmitted from carriage to infection. These are potentially WA-1 or similar. The STARRs PVL− MSSA isolates largely reflect CCs found globally. They were stably carried, largely in the nasal cavity, are under-represented in the infection isolates, and the only putative transmission events identified were 'carriage to carriage'. HA-MRSA were rare, with ST239 represented by one carriage and one clinical isolate. No ST22 isolates were recovered.

It is of interest that the species *Staphylococcus argenteus* was first identified during a survey of *S. aureus* carriage and infections in a remote community in the Northern Territory. The species is now known to be globally distributed, with similar pathogenic properties and potential to acquire antimicrobial resistance as *S. aureus*.[16] It is one of five known species in the '*S. aureus* complex' with the others being *S. aureus*, *Staphylococcus schweitzeri, Staphylococcus singaporensis*, and *Staphylococcus roterodami.* In general, these newly defined species appear rare in humans, and in the case of *S. schweitzeri* are overwhelmingly associated with non-human animals. In the STARRs study a small minority of the carriage isolates and none of the clinical isolates were *S. argenteus*.[8] The current clinical impact of *S. argenteus* in northern Australia is unclear.

Streptococcus pyogenes (Group A streptococci (GAS)) are β-haemolytic, pyogenic organisms which cause a range

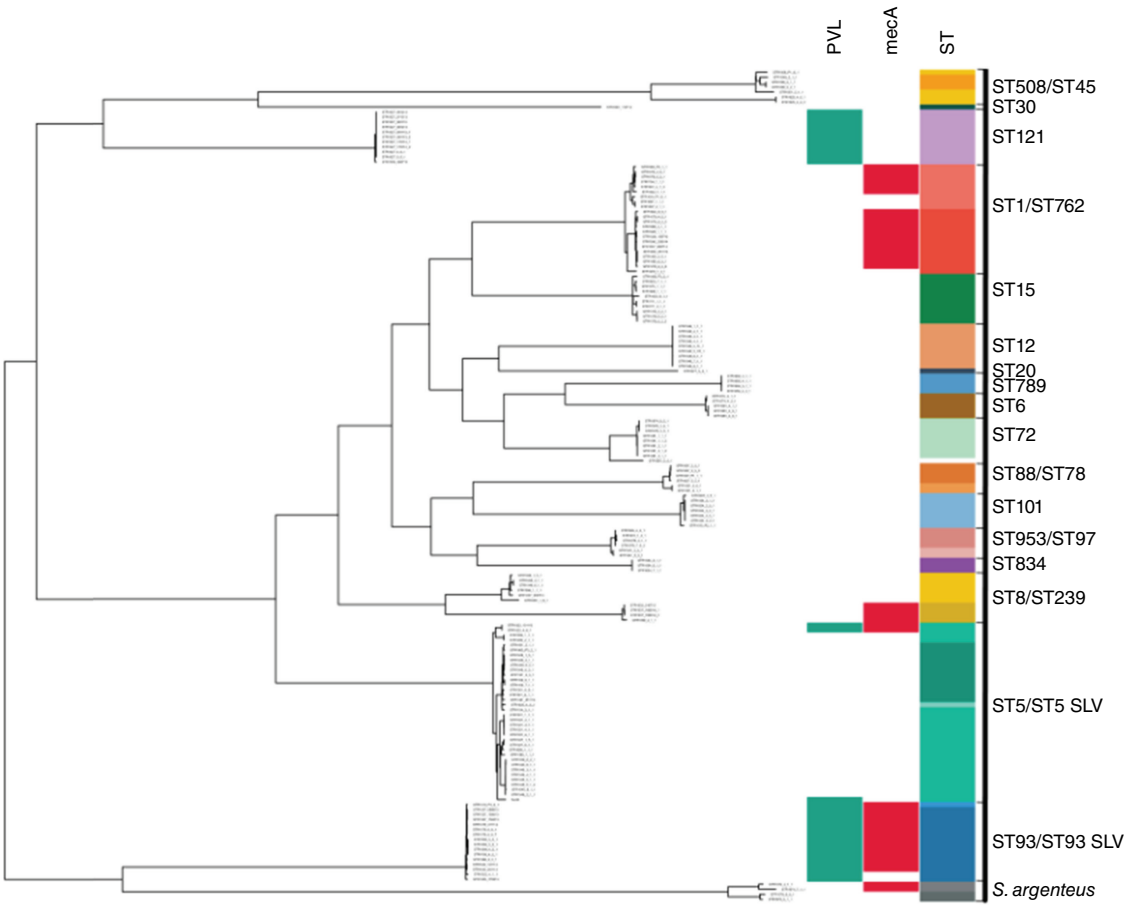

Fig. 1. *Staphylococcus aureus* sequence types (STs) recovered from carriage and infection in a study of transmission in dialysis clients in northern Australia. Maximum parsimony tree based on 20 651 orthologous SNPs generated from genome sequence alignment with *S. aureus* isolate Mu50. Reproduced from Holt *et al.*[8] (CC BY 4.0).

of infections from pyoderma and pharyngitis, to invasive diseases including necrotising fasciitis and toxic shock syndrome. Importantly, autoimmune responses post-infection can lead to significant sequelae including acute rheumatic fever (ARF), rheumatic heart disease (RHD), and acute post-streptococcal glomerulonephritis (ASPGN). It has long been recognised that the burden of ARF and RHD in northern Australia is among the highest reported in the world.[17]

The N-terminal region of the surface streptococcal M protein is highly variable and has been the basis of both serotyping and genetic typing methods. *emm* typing has classically been the main approach to genetic typing and involves sequence analysis of the region of the *emm* gene encoding the variable N-terminal region. Further analysis combining *emm* sequence type with other information including the arrangement of *emm* and *emm*-like genes, defines *emm* pattern types. Population based studies have indicated that *emm* patterns A–C show throat tropism, *emm* pattern D shows skin tropism, while *emm* pattern E does not appear to have a predilection for either site. Over 200 *emm* sequence types have been defined that correlate well with the *emm* patterns.[18]

In the temperate regions of Australia the molecular epidemiology of *S. pyogenes* is similar to that of other developed countries, where throat tropic *emm* types dominate and more restricted *emm* diversity is observed.[19] However, in northern Australia, the prevalence of *S. pyogenes* pyoderma is high, while pharyngitis is low compared with other areas of the country.[20] The *emm* types belonging to the skin tropic *emm* pattern D and non-tropic *emm* pattern E predominate.[21] Outbreaks of invasive disease related to a subset of *emm* types are seen on a background of high diversity and rapid turnover in the circulating *emm* types.[22–25] While novel *emm* sequence types have been found in remote communities in northern Australia, the overall diversity does not seem to be the result of local diversification but rather the circulating population represents a large subset of known global *S. pyogenes* diversity.[26,27] The pattern seen in northern Australia is consistent with what is seen in developing countries,[19] as well as in Indigenous populations in other developed countries such as New Zealand where the burden of ARF and RHD is similarly high.[17,28,29] In these regions, skin and throat tropic *emm* types co-exist, increasing the total diversity of circulating *emm* types.

The variable N-terminal region of the M protein is considered a useful vaccine target due to its immunogenic epitopes and low propensity to induce antibodies which cross react with human tissues. However, the high diversity of *emm* types in northern Australia and developing regions creates concerns for the likely efficacy of such vaccines in these areas.[21] An *emm* cluster system has been developed which is an elaboration of the *emm* typing scheme and is based on the surface exposed portion of the M protein and its binding capacity with six human serum proteins, and *emm* cluster can be inferred from the *emm* type.[30] This can serve as a resource for vaccine development as cross-opsonisation experiments have demonstrated cross-protection between some *emm* types.[30]

A 30mer M protein vaccine which has reached human trials is largely based on *emm* types prevalent in North America and Europe. It contains only a single *emm* pattern D sequence, which did not demonstrate a high proportion of cross protection for other pattern D *emm* types.[30] A study examining over 1700

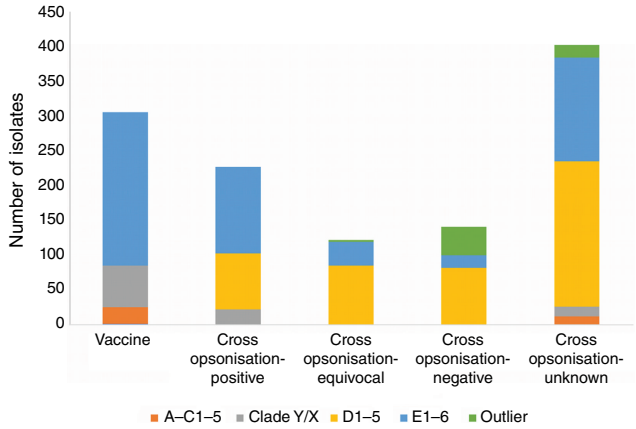

Fig. 2. *emm* clusters and vaccine coverage of skin and soft tissue isolates recovered from northern Australia from 1987 to 2008. Reproduced from Giffard *et al.*[21] (CC BY 4.0).

isolates from northern Australia collected over more than 20 years demonstrated that over 50% of the isolates were cluster D or outlier *emm* types. Based on the cross-opsonisation data,[30] the 30mer vaccine may not provide good protection against these isolates. In addition, poor coverage of the 30mer vaccine against APSGN associated strains such as *emm*55 is predicted[21] (Fig. 2). Broader protection may be elicited by the 26mer precursor of the 30mer vaccine, which contained two additional cluster D4 *emm* types that are prevalent in northern Australia, or by utilising a combination vaccine approach.[21] Alternatively, other vaccine strategies targeting more conserved regions of the M protein and non-M protein targets[29] may prove more effective in regions with high *emm* diversity.

S. aureus and *S. pyogenes* are significant pathogens causing substantial health impacts from acute infections and their serious sequelae. In northern Australia, rates of skin infections are high and there are likely complex interactions with other skin pathogens such as the scabies mite *Sarcoptes scabiei* and the dermatophyte *Trichophyton rubrum*.[1] *S. aureus* and *S. pyogenes* are commonly both recovered from impetigo lesions,[31,32] and *S. pyogenes* is more likely to be recovered from impetigo lesions if scabies infection is also present.[31,32] This dynamic creates particular challenges for public health programs targeting skin health in this region.[1]

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What does microbiology have to do with the Hearing for Learning Initiative (HfLI)?

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ABSTRACT

Where would we be without microbiology in tackling the high prevalence of otitis media (OM; middle ear infection) and disabling hearing loss that disadvantage Australian First Nations children living in remote communities? Understanding the microbiology of OM in this population has been critical in directing innovative clinical trials research and developing appropriate evidence-based practice guidelines. While these processes are critical to reducing disadvantage associated with OM and disabling hearing loss, a remaining seemingly insurmountable gap has remained, threatening progress in improving the lives of children with ear and hearing problems. That gap is created by the crisis in primary health care workforce in remote communities. Short stay health professionals and fly-in fly-out specialist services are under-resourced to manage the complex needs of the community, including prevention and treatment of otitis media and hearing loss rehabilitation. Hence the rationale for the Hearing for Learning Initiative – a workforce enhancement model to improve sustainability, cultural appropriateness, and effectiveness of evidence-based ear and hearing health care for young children in remote settings. This paper summarises the role of microbiology in the pathway to the Hearing for Learning Initiative.

Keywords: Aboriginal, antimicrobial resistance, child, clinical trial, guideline, hearing loss, non-typeable *Haemophilus influenzae*, otitis media, *Streptococcus pneumoniae*.

How does microbiology lead to a trial of an enhanced workforce model for ear and hearing services in remote community primary health care? This story follows a pathway from complex bacterial pathogen discovery, design of clinical trials that reveal the failure of standard therapies (based on trials in low-risk populations), and the need for innovative strategies to prevent or eradicate bacterial infections in high-risk populations. The story shows how understanding the underpinning microbiology has directed clinical trial design and evidence-based guidelines for management of otitis media (OM; middle ear infection) in high-risk Aboriginal children. These guidelines challenge national and international guidelines, and medical education. Yet in remote areas, services are largely delivered by practitioners trained in our major cities where the health profile is staggeringly different, leaving health practitioners who come to work in remote locations ill-prepared to diagnoses and manage major health problems of Aboriginal children. Local guidelines aim to assist management relevant to this unique context.[1,2]

The Hearing for Learning Initiative is evaluating a community-based workforce enhancement model designed to address ongoing high prevalence of persistent OM, disabling hearing loss and associated educational and social disadvantage.[3] Almost every infant and child in remote communities has early and persistent OM, which is largely asymptomatic despite apparently painful appearance of the tympanic membrane (marked bulging or perforation).[4] Failure to detect early acute OM (AOM) or middle ear effusions (OME) leads to chronic OM (all forms) which is the strongest predictor of developmental delay, high vulnerability on entering school, poor school attendance and performance.[5–8] Children with hearing loss are at increased risk of substantiated maltreatment.[9] OM must be prevented and appropriately managed to enable all children to develop their full potential.

Currently, for most children in Australia, OM is viral, acute, brief, and episodic. OM can be managed with pain relief and resolves spontaneously; judicious use of antibiotics can be applied, and watchful waiting is recommended.[2] However, a major shift in understanding OM in Australian Aboriginal children was made in the early 1990s, at a time when *Chlamydia trachomatis* was a key suspect pathogen.[10] Under leadership of

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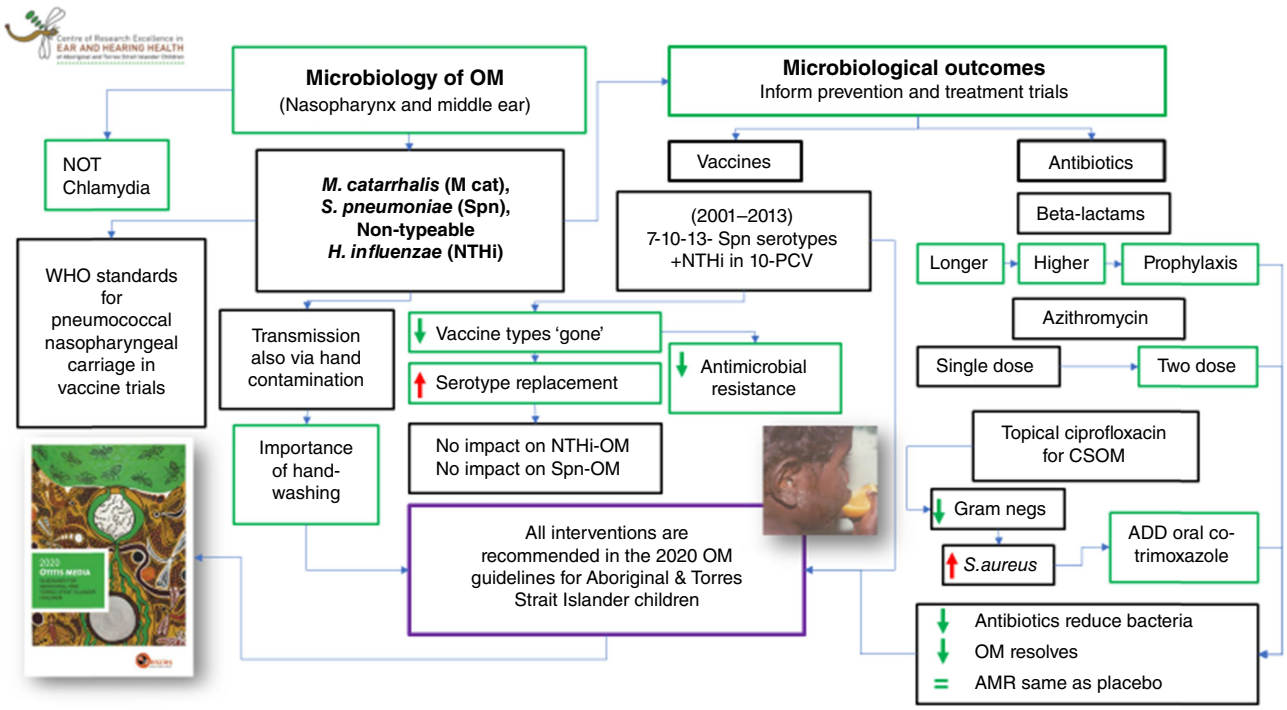

Fig. 1. Microbiology has under-pinned a critical clinical trials research pathway towards evidence-based guidelines targeted to address the ear and hearing problems of Australia's First Nations children.

Professor John Mathews, a birth cohort study established that major bacterial otopathogens were *Moraxella catarrhalis* (Mc), *Streptococcus pneumoniae* (Spn) and non-typeable *Haemophilus influenzae* (NTHi).[11,12] Respiratory viruses and *Chlamydia trachomatis* were very rarely recovered.[4] This study confirmed that OM in Aboriginal infants commenced soon after bacterial nasopharyngeal colonisation and within weeks of birth.[4] The multiple bacterial pathogens involved and the high diversity of strains and serotypes in the population drove recurrent and sometimes multiple concurrent pathogen infections throughout early childhood. This revelation shifted the focus of OM prevention and treatment research to early detection, trials of appropriate use of antibiotics[13–16] or watchful waiting,[17] and subsequently to pneumococcal conjugate vaccine trials (Fig. 1).[18,19]

A series of clinical trials has been completed over several decades (some trials take 6–7 years to complete) that confirm a benefit of antibiotics for high-risk Aboriginal children.[13–15] Importantly, the trials identified that longer courses and higher-dose antibiotics are needed compared with judicious use recommended from trials in low-risk populations.[20] Current trials are evaluating the generalisability for non-high-risk Aboriginal children living in Australian urban jurisdictions.[17,21]

For each randomised controlled trial (RCT) of antibiotics or pneumococcal conjugate vaccines the nasopharyngeal microbiology, and microbiology of ear discharge from spontaneously perforated ear drums (acute otitis media with perforation) has been critically important in understanding the impact of each intervention on the complex underpinning biology (Fig. 1).[4,12,22–24] Clinical outcomes alone tell us about clinical failure or success, but not why there is failure or success. Without microbiology we would be assuming clinical failure might be attributed to antimicrobial resistance (AMR), a higher virulence of strains in this population, viral interactions or high density bacterial load.[25] These assumptions could potentially lead to misleading recommendations, or misguided research.

Examples include the Chronic Otitis Media Intervention Trial 1 (COMIT1) RCT, which demonstrated clinical superiority of amoxycillin over placebo with no increased AMR in the active compared with placebo recipients.[14] The first trial of topical treatments for chronic suppurative otitis media (CSOM) found no difference in clinical outcomes; however, the microbiology identified superior eradication of Gram negatives in the ciprofloxacin arm, and persisting *S. aureus* in both arms.[13] This led to a further CSOM trial which added oral co-trimoxazole (to standard topical ciprofloxacin) to target the residual *S. aureus*.[16] The significant further clinical improvement (C. Wigger, pers. comm., 2019) has led to an OM Guideline recommendation for adjunct co-trimoxazole.[2] The first trial of azithromycin for acute OM (AAATAC) compared single dose azithromycin with 7 days of twice daily amoxycillin.[15] Clinical outcomes were not different; however, the microbiology and AMR prevalence confirmed the unexpected – that combined AMR was similar in both groups.[15] Importantly, this led to a recommendation for single dose azithromycin for Aboriginal children where compliance was known to be difficult, or where refrigeration (essential for amoxycillin) was not possible (often the case for families in remote communities).[2] The next RCT (azithromycin for asymptomatic acute OM (AAAOM)) went on to enrol children with asymptomatic AOM (almost all AOM is asymptomatic in this population) to receive either placebo or azithromycin. Fewer children in the azithromycin group had tympanic membrane perforations, and importantly again, the

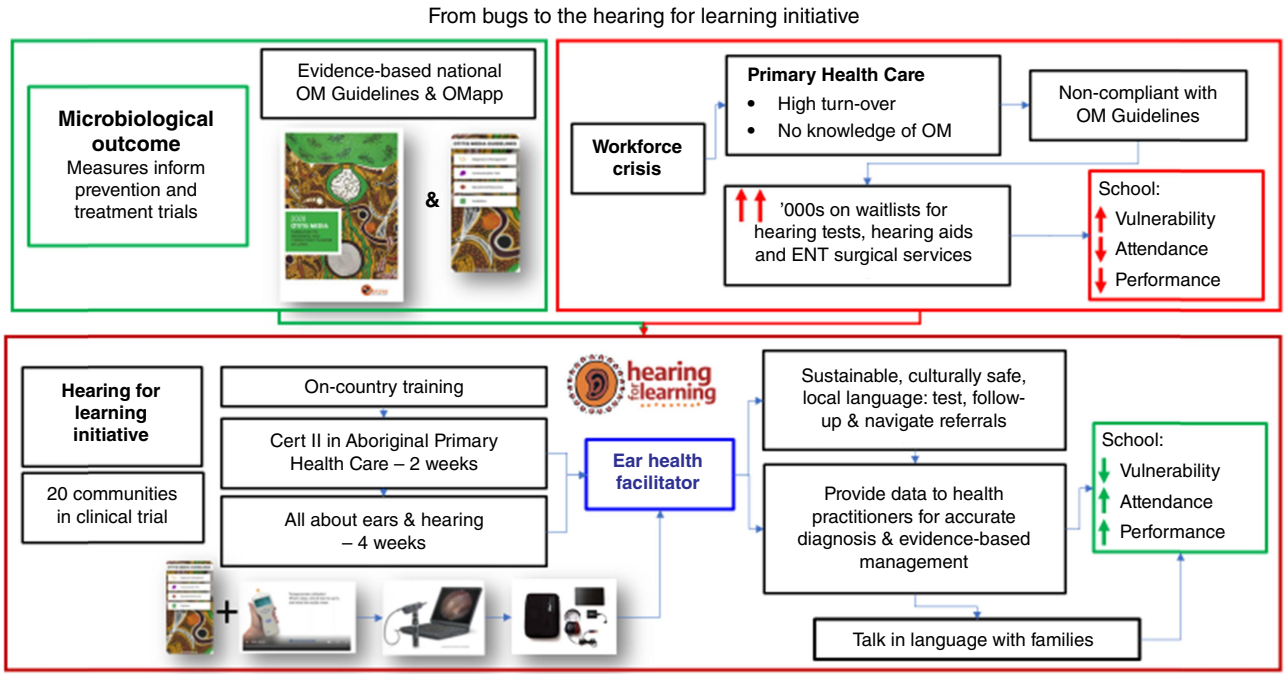

Fig. 2. The Hearing for Learning Initiative addresses hearing-related childhood vulnerability through local adult education and workforce enhancement, based on the 2020 Otitis Media Guidelines for Otitis Media in Aboriginal and Torres Strait Islander children.

microbiology showed the unexpected – that pneumococcal resistance to azithromycin was similar in azithromycin and placebo groups (P. S. Morris, pers. comm., 2015; Fig. 1).

Pneumococcal conjugate vaccines (PCVs) have been highly effective in reducing the burden of invasive pneumococcal disease (IPD) globally, and also in Australian First Nations' people.[26] The Northern Territory was the first jurisdiction to introduce PCV7 for Aboriginal infants in 2001, and was the only jurisdiction to introduce PCV10, 2 years prior to national transition to PCV13 in 2011. Throughout these three PCV eras we continued ongoing clinical and microbiological surveillance of OM and nasopharyngeal carriage of otopathogens across multiple Northern Territory communities.[27–29] One vaccine offered potential protection from NTHi-OM via inclusion of protein D of NTHi (HiD) as the conjugation protein.[30] Perhaps not surprisingly our surveillance identified a reduction in AOM,[31] reduced nasopharyngeal carriage of vaccine serotypes (but replacement by non-vaccine serotypes), and the microbiology of ear discharge confirmed reduced NTHi-OM[32] (Fig. 2). These surveillance data provided the strong rationale for higher quality studies (RCTs) of novel mixed PHiD-CV10 and PCV13 schedules to maximise coverage of otopathogens.[33] These RCTs found that: (1) early mixed PCVs are safe; (2) combined PCVs elicit strong immune responses to all vaccine targets; (3) responses to first dose of PHiD-CV10 given at age 1 or 2 months were superior to PCV13; (4) including at least one dose PCV13 is similar to three doses; (5) either vaccine can be the booster if priming included at least one dose PCV13; and (6) protein D immunity was not protective against NTHi infection in this population. These unique discoveries inform vaccine research and development, support flexibility of PCVs, allowing national programs to optimise sero-epidemiology and mitigate supply and cost risks, particularly for low- and middle-income countries. Unfortunately, in this population, the microbiology again revealed the challenge of preventing otitis media. Acquisition of nasopharyngeal NTHi and non-vaccine serotypes[22] was associated with OM onset within weeks of birth in all PCV schedule groups.[18,34] Follow up to 3 years of age showed that OM persists causing chronic disabling hearing loss throughout early years for an average of 80% children.[35]

This brings us back to the Hearing for Learning Initiative.[3] An additional and parallel crisis has been highlighted in remote primary health care where average length of stay of health care practitioners is 4 months, and many are infrequent brief but costly fly-in fly-out stays.[36,37] Lack of comprehensive primary ear health programs with scheduled surveillance and appropriate follow up is failing children and over-burdening specialist services (hearing and ENT surgical consultations), which have staggeringly long waitlists of several thousands of children.[38]

The Hearing for Learning Initiative is a 5-year stepped wedge cluster randomised controlled trial in 20 rural and remote communities in the Northern Territory. Each Community Reference Group selects community member trainees and supports the research team to deliver a 6-week course. Two Certificate II units of competency in Aboriginal Primary Health Care, and knowledge of ear and hearing and technical skills in otoscopy, tympanometry and hearScreen are learned and assessed. One or two successful graduates are then supported to join the health service workforce in new Ear Health Facilitator positions funded by the Hearing for Learning Initiative (Fig. 3). The Ear Health Facilitator residency, status in the community, cultural knowledge, local language, and communication skills are the foundation of a sustainable, culturally appropriate and skilled workforce to service the needs of children with undetected,

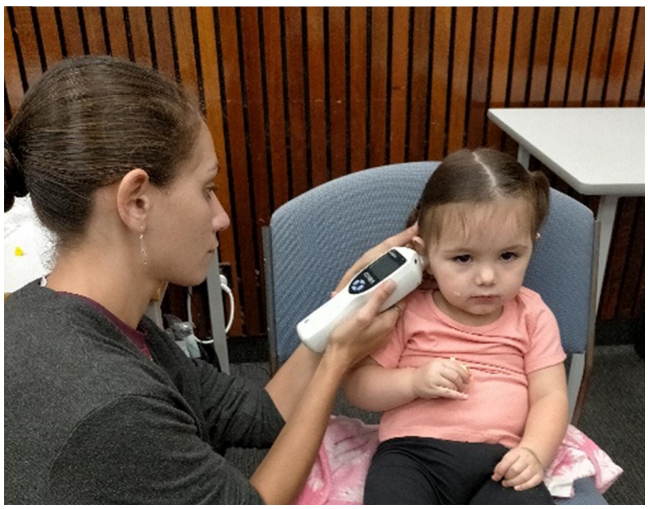

Fig. 3. Marlee Bryce is an Ear Health Facilitator employed by the Wurli Wurlinjang Health Service, Katherine, NT.

untreated chronic ear infections, hearing loss, and social isolation. Opportunities for on-country training and appropriate job creation can be successful in remote regions through co-design and local community leadership.

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Professor Amanda Leach, AM, is leader of the Ear Health Research Program, Child Health Division at the Menzies School of Health Research, in Darwin, NT, Australia. Professor Leach led the NHMRC Centre of Research Excellence in Otitis Media and Hearing Loss in Aboriginal and Torres Strait Islander children. She also led the 2020 revision of the OM Guidelines including an OM app, now endorsed as a Guideline by the Royal Australian College of General Practitioners. Professor Leach is Joint Chair with Professor Kelvin Kong, for the Hearing for Learning Initiative – a funding partnership between The Balnaves Foundation, the Northern Territory Government, and the Australian Government. In 2021, Amanda was awarded a Member of the Order of Australia for her research.

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Vaccine success and challenges in northern Australia

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ABSTRACT

Aboriginal and Torres Strait Islander people living in rural and remote Australia have lower vaccine coverage rates and experience higher rates of notification and hospitalisations for vaccine preventable diseases than non-Aboriginal people. This paper explores important public health and research activities being undertaken in the Northern Territory to reduce this disparity in vaccine program performance, with a particular focus on rotavirus, meningococcal, human papilloma virus and COVID-19 vaccines.

Keywords: Aboriginal and Torres Strait Islander, COVID-19, human papilloma virus, immunisation, meningococcal, Northern Territory, rotavirus, vaccine.

Introduction

Australian Aboriginal and Torres Strait Islander people living in remote locations have lower vaccine coverage rates and experience higher notification and hospitalisation rates for vaccine preventable diseases, than non-Aboriginal people living in major Australian cities.[1] This paper explores important public health and research activities in the Northern Territory over the past 10–15 years, which aim to reduce the disparity in vaccine coverage and vaccine program performance, highlighting success and ongoing challenges.

Rotavirus vaccines

Rotavirus remains a leading cause of childhood gastroenteritis.[2] Before the introduction of rotavirus vaccines into the Australian National Immunisation Program, it was estimated that rotavirus was responsible for 10 000 hospital admissions, 22 000 Emergency Department presentations, and 115 000 primary care presentations of Australian children aged <5 years every year.[3] The burden among Aboriginal and Torres Strait Islander children was greater, with a hospitalisation rate more than five times that of non-Aboriginal children aged <12 months.[4] In addition, the regular occurrence of large rotavirus outbreaks among children living in rural and remote communities placed enormous strain on families, remote health care clinics and aeromedical retrieval services.[5]

The introduction of rotavirus vaccines into the Northern Territory Childhood Vaccination Schedule in 2006 and the Australian National Immunisation Program in 2007, was associated with an immediate and sustained decrease in national rotavirus hospitalisations (>70%).[6] However, in the Northern Territory the decline in rotavirus hospitalisations was less substantial.[6] In 2010, Aboriginal and Torres Strait Islander children in the Northern Territory remained more than 20 times more likely to be hospitalised with rotavirus than non-Aboriginal children in other states and territories.[6] In addition, rotavirus vaccine effectiveness was reported to be as low as 19% and 21% during two rotavirus outbreaks in Central Australia in 2009 and 2017,[7,8] with 65 children admitted to Alice Springs Hospital with rotavirus gastroenteritis between March and June 2017.[8]

Strict upper age limits for rotavirus vaccine administration (dose 1 Rotarix recommended between 6 and <13 weeks and dose 2 Rotarix before 25 weeks old) contribute to poor rotavirus vaccine program impact, due to reduced vaccine coverage and limited opportunities for catch-up of missed immunisations in later infancy.[9] For the 2014 Northern Territory birth cohort, 83.2% of Aboriginal and Torres Strait Islander children compared with 90.6% of non-Aboriginal children, had received a complete two-dose course of rotavirus vaccine by age 12 months.[10] This underscores the importance of

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public health and primary health care activities to enhance vaccine timeliness in early childhood.

The ORVAC study – Optimising Rotavirus Vaccine in Aboriginal Children, is an adaptive clinical trial that relaxes the upper age limit of rotavirus vaccine administration and administers a third 'booster dose' of oral Rotarix rotavirus vaccine to Northern Territory Aboriginal children aged 6–11 months.[11] This clinical trial – a partnership between the Menzies School of Health Research, Darwin and Telethon Kids Institute, Perth – has demonstrated that administering a booster dose of oral rotavirus vaccine improves the proportion of children with evidence of vaccine seroresponse (85% post third dose of Rotarix vs 72% post-placebo; ORVAC Stage 1; 2018–2020),[12] and continues to enrol children to evaluate the clinical impact – decreased medical presentations with gastroenteritis in the first 3 years of life (ORVAC Stage 2; 2022–2027). An early generation rotavirus vaccine, Rotashield, was associated with an increased risk of intussusception among infants aged >3 months.[13] A systematic review of post-licensure studies suggests no increased risk of intussusception with Rotarix;[14] however, this continues to be monitored closely in the ORVAC study given the increased upper age limits of administration (age >6 months).

Meningococcal vaccines

Meningococcal disease is a rare but serious disease commonly causing septicaemia and meningitis, though atypical presentations including septic arthritis, pneumonia and epiglottitis can also occur.[15] There are several serogroups that cause invasive disease in Australia, A, B, C, W, X, and Y.[15]

Meningococcal infection is notifiable in the Northern Territory, and between 2012 and 2016 there were twelve cases of invasive meningococcal disease notified in the Northern Territory, with 11 cases caused by serotype B and 1 case caused by serotype C.[16] However, in 2017 there were 31 cases of invasive MenW disease and 3 cases of MenW conjunctivitis. All cases occurred among the Aboriginal and Torres Straits Islander population of the Alice Springs, Barkly and Katherine regions; and the majority (94%) of cases occurred among children and adolescents aged <15 years.[16] This outbreak prompted an intense public health response and targeted vaccination program, with more than 17 800 MenACWY vaccines administered to children aged 1–19 years in the Alice Springs, Barkly, Katherine, East Arnhem and Darwin Rural regions between February 2017 and March 2018.[17] It was estimated that 81% of eligible Aboriginal and Torres Strait Islander children and 49% of eligible non-Aboriginal children were vaccinated during this period.[17]

The MenACWY replaced the MenC vaccine on the Northern Territory Immunisation Schedule in December 2017 and was added to the National Immunisation Program from mid-2018.[18] By May 2019, it was estimated that 76% of Northern Territory Aboriginal and Torres Strait Islander children had been vaccinated with MenACWY, compared to 60% of non-Aboriginal children.[18] Since 2018, invasive meningococcal disease notifications have declined from 1.1 cases per 100 000 in 2018, to 0.8 cases per 100 000 in 2019 and 0.3 cases per 100 000 in 2020, although the reduction in 2020 may be partly attributable to the impact of public health measures implemented for the COVID-19 pandemic.[19]

Meningococcal B serotype remains an important cause of invasive meningococcal disease in Australia, causing 94% (24/25) cases among children aged <5 years and 80% (8/10) cases among adolescents aged 15–19 years, in 2020.[19] MenB vaccines were added to the National Immunisation Program for Aboriginal and Torres Strait Islander children aged <12 months in July 2020.[1] MenB vaccines are also currently being administered to adolescents through an observational study by the University of South Australia called 'B Part of it NT', which will evaluate the effect of 4CMenB vaccines on rates of meningococcal carriage, invasive meningococcal disease and gonorrhoea, among Northern Territory adolescents aged 14–19 years.[20]

HPV vaccines

Genital human papilloma virus (HPV) is a common infection transmitted through sexual contact.[21] In most cases, genital HPV infections are asymptomatic and self-resolve within 12–24 months.[21] However, a small proportion of HPV infections persist in the genital epithelium, and can cause cancer of the cervix, vagina, vulva, penis and anus.[22] Northern Territory Aboriginal and Torres Strait Islander women have a disproportionately high incidence of cervical and vulval cancer.[23]

In 2007, the Australian Government funded Gardasil – a three-dose vaccine protecting women against the four most common types of HPV known to cause cervical cancer and genital warts.[21] In the Northern Territory, a mass-vaccination program was delivered to all female secondary school students through a partnership between the Centre for Disease Control and Health Promoting School Nurses.[24] Catch-up vaccinations were also offered to women aged 18–26 years through remote community clinics and private GPs.[24] In addition, Women's Health Workshops were held in remote communities and HPV vaccine resources were translated into three Aboriginal languages for broadcast on Aboriginal radio stations in Central Australia and the Top End.[24] More than 32 500 doses of Gardasil HPV were administered between April 2007 and July 2008, including 14 600 first dose encounters, 11 700 second dose encounters and 6200 third and final dose encounters.[24] Reasons for the lower number of second and third dose HPV encounters during this time period more likely reflect problematic program delivery (unable to complete second or third visits to school/communities) or a delay in recording administered immunisations with the immunisation register, rather than a loss of confidence or intolerance of the HPV vaccine, as only 11 adverse events were reported to the Northern Territory Centre for Disease control during the same period, and all were reported to be mild.[24]

In 2013 the HPV vaccine program was extended to include boys aged 12–13 years, and in 2018 the new two-dose Gardasil-9 vaccine was funded under the National

Immunisation Program.[1] By 2020, 76.2% of Aboriginal and Torres Strait Islander girls and 63.7% of Aboriginal and Torres Strait Islander boys in the Northern Territory had received a complete course of HPV vaccine, slightly lower than the national average of 80.5% of all Australian girls and 77.6% of all Australian boys.[1]

Nationwide, HPV vaccination has resulted in a large demonstrable decrease in HPV-related disease.[25] However, there is a need to further increase HPV vaccine coverage, especially among Aboriginal and Torres Strait Islander women in the Northern Territory who continue to have higher rates of histologically confirmed high-grade cervical disease and lower participation in screening programs.[26]

COVID-19 vaccines

Australia's early response to the COVID-19 pandemic was among the most successful in the world.[27] From March 2020, individuals entering the Northern Territory from overseas and designated Australian 'hotspot' regions were required to undertake a 14-day period of quarantine.[28] As a result of this swift and successful public health strategy, there was no sustained SARS-CoV-2 community transmission or deaths in the Northern Territory until December 2021.[28]

The COVID-19 vaccination program began in the Northern Territory in February 2021 with priority for quarantine and border workers, frontline health care workers and vulnerable populations including the elderly. There were early concerns about limited vaccine supply, remote workforce shortages, and vaccine hesitancy within some sectors of the Northern Territory community.[29] Local vaccination programs were led by the Aboriginal Community Controlled Health Services sector, GPs and pharmacies and the Northern Territory Department of Health. The vaccination program was further supported by health promotion activities from NT land councils, Aboriginal controlled health organisations, and arts and language centres.[30] The Menzies School of Health Research partnered with Aboriginal leaders to produce short-videos about COVID-19 and COVID-19 vaccines in local languages, which were shared widely with government departments, clinicians, Aboriginal community-controlled health organisations, and on social medial platforms.[30] The Menzies School of Health Research also partnered with the Telethon Kids Institute to host a COVID-19 vaccine workshop – Sharing Success Stories & Smashing Myths – which provided an opportunity for health services in northern and central Australia to share success stories when promoting vaccine uptake. Despite these collaborative efforts, by June 2022, two-dose COVID-19 vaccination coverage remains as low as 60% in the Barkly region and in some Central Australian communities (vaccine eligible population aged >5 years).[31] Across all regions of the Northern Territory, two-dose COVID-19 vaccine coverage is lowest among children aged 5–11 years.[31]

Additional research work is being undertaken by Menzies School of Health Research in conjunction with the Doherty Institute in Melbourne, to examine the B- and T-cell response to natural COVID-19 infection and COVID-19 vaccination among Aboriginal and Torres Strait Islander people.

Conclusions

Ongoing monitoring of vaccine-preventable disease burden and vaccination coverage, is essential to address existing and emerging health disparities, particularly for Aboriginal and Torres Strait Islander populations in northern Australia.[10] Working in partnership with Aboriginal people to understand the drivers of vaccine hesitancy in each region and to deliver culturally appropriate education about vaccines and vaccine preventable diseases, is critical for the successful participation of Aboriginal and Torres Strait Islander communities in vaccination programs.[29]

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Microbiology Australia

Molecular epidemiology of tuberculosis in northern Australia

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ABSTRACT

Australia has one of the lowest rates of tuberculosis (TB) globally; however, the rates of TB in the Northern Territory (NT) Top End and in Far North Queensland are consistently higher than the national average. Genomic sequencing of *Mycobacterium tuberculosis* (MTB) is increasingly being implemented for transmission surveillance and antimicrobial resistance prediction. Genomic epidemiological studies in northern Australia have demonstrated the utility of sequencing for tracking TB transmission. In the NT Top End, this has demonstrated that most TB transmission is occurring in remote regions, with recent transmission and reactivation from latency contributing to incident TB. In Far North Queensland, genomics has been used to track transmission of a multidrug-resistant MTB clone across the Torres Strait. The next steps include implementation of MTB genomic sequencing in jurisdictional laboratories with real-time cross-jurisdictional analysis to inform public health management of TB.

Keywords: epidemiology, genomics, Mycobacterium, northern Australia, public health, sequencing, surveillance, tuberculosis.

Introduction

Prior to the COVID-19 pandemic, tuberculosis (TB) was the leading infectious cause of death globally.[1] The causative pathogen, *Mycobacterium tuberculosis* (MTB) is transmitted from person to person via droplet aerosols.[2] Humans are the major reservoir, and it is estimated that around a quarter of the world's population are infected.[3] Following infection, MTB can persist in a quiescent state, termed latent TB infection (LTBI).[4] People with LTBI have no symptoms and are considered non-infectious to others. Up to 15% develop active TB disease, with pulmonary disease being the most common manifestation.[5,6] Key components of TB control include timely diagnosis and effective treatment of active TB disease, screening of contacts and high risk groups, and LTBI diagnosis and treatment.[7] The World Health Organization's End TB Strategy 2016–2035 set the goals of 95% reduction in TB deaths and 90% reduction in TB incidence compared with 2015 levels by 2035.[7] The COVID-19 pandemic has had a devastating impact on global TB control, with decreased case ascertainment resulting in a reduction in notified cases from 7.1 million in 2019 to 5.8 million in 2020, and an increase in reported TB deaths.[1]

The rates of TB in Australia are amongst the lowest globally, with annual incidence approximately 5–6 per 100 000 since the 1980s.[8] 86–89% of TB notifications in Australia are in people born overseas.[8] Annual incidence in Australian-born non-Indigenous people is <1 per 100 000 population; however, the rates in Aboriginal and Torres Strait Islander peoples (First Nations Australians) are consistently approximately five-fold higher than this.[8] Much higher rates of TB are seen in countries to Australia's north, including Papua New Guinea, Indonesia, and Timor-Leste.[1] Multidrug-resistant (MDR) TB – defined as resistance to isoniazid and rifampicin – is an increasing challenge in the region.[9,10]

Tuberculosis epidemiology in northern Australia

The Northern Territory (NT) has had the highest overall and childhood TB rates in Australia,[8,11] but has low rates of MDR-TB.[12] Approximately one-third of the population are First Nations Australians, many of whom live in remote regions, and approximately 20% were born overseas.[13] The NT TB rate in First Nations Australians has dropped markedly over the past 30 years, from 114 per 100 000 in 1989 to 5–12 per 100 000 in 2015–2018.[8,14] The number of overseas-born cases has fluctuated: in 1999 there was an increase in cases when >1800 people were evacuated to the NT from Timor-Leste due to conflict associated with the transition to independence,[15] and increases in NT TB notifications have also occurred in association with on-shore detention of fishers from Indonesia and of asylum seekers and crew.[16,17]

To the east, Far North Queensland is in close proximity to Papua New Guinea (PNG). The Torres Strait is the body of water between Cape York, the northernmost tip of Australia, and the Western Province of Papua New Guinea; it is approximately 150 km at its narrowest length and comprises at least 274 islands. The Torres Strait Protected Zone was created after the 1978 treaty between PNG and Australia, allowing cross-border movement without passports or visas for traditional customs and economic activities in the Torres Strait. Rates of TB in Far North Queensland are higher than the national average, at 8.4–12.1 per 100 000 population per year in 2017–2019.[18] Although rates have fallen particularly in the Torres Strait (previously 35.5 per 100 000 in 2014), the rates of TB in First Nations peoples in Queensland remain 8–15 times higher than in the non-Indigenous Australian-born population.[18] The TB incidence in the Western Province of PNG is approximately 2900 per 100 000 with high rates of MDR-TB,[10,19] and approximately 80% of overseas-born cases in Far North Queensland are from PNG.[20]

Genomic sequencing of *Mycobacterium tuberculosis*

Genomic sequencing of MTB is increasingly being implemented as a tool for prediction of antimicrobial resistance, transmission surveillance, and global phylogeographic investigation, and provides much greater resolution than previous typing methods.[21,22] Commonly used sequencing methods include short-read Illumina technology, which has high throughput and high accuracy, and results in reads up to 300 bp in length. Long read sequencing by Oxford Nanopore Technologies results in much longer reads with data produced in real time, but is less accurate than Illumina sequencing.[23] The MTB genome comprises a single chromosome approximately 4.4 Mb in size, with estimated mutation rate 0.3–0.5 single nucleotide polymorphisms (SNPs) per genome per year, and no clear evidence of horizontal gene acquisition.[24,25] Antimicrobial resistance arises from chromosomal point mutations. In 2021 the World Health Organization published its first catalogue of mutations in MTB associated with antimicrobial resistance.[26] To aid phylogeographic analysis, a lineage nomenclature system based on lineage-defining SNPs has been described,[27] with each lineage having distinct geographic distribution linked to human migration history.[28] Transmission surveillance can be done by combining epidemiological data with pairwise SNP distances and phylogenetic analysis.[22,29,30] Core genome multilocus sequence typing can also be used to find possible transmission clusters for further investigation.[31] As genomic sequencing technology moves from research to public health, there is a need for validation and standardisation of wet and dry laboratory methodologies, and for development of processes and platforms for data sharing and analysis.[22]

Genomic epidemiology of tuberculosis in northern Australia

A 2021 study set in the NT Top End combined TB notification data for 741 culture-confirmed cases with genomic sequencing of 497 MTB isolates from 1989 to 2020.[32] There were 359/741 (48%) cases born overseas, and 329/741 (44%) cases were First Nations Australians. There were 235/359 (66%) overseas-born cases from Southeast Asia, with the largest numbers from Indonesia (87 cases) and Timor-Leste (61 cases). Of the 497 sequenced isolates, 52% were lineage 4 (Euro-American lineage), 31% were lineage 1 (Indo-Oceanic lineage), and the remainder belonged to lineages 2 and 3. Of 93 case-contact isolate pairs, 85 were separated by ≤ 12 SNPs (median 2 SNPs) providing support for using this threshold for defining transmission clusters. There were 28 genomic clusters involving 250 cases; 86% of clustered cases were First Nations Australians and 76% were from a remote region. There was little evidence of transmission arising from overseas-born cases, and no drug-resistant cases clustered together. Genomics was able to link six recent cases not previously identified as part of contact tracing to genomic clusters, and the study findings suggested that both reactivation from latency and recent transmission are contributing to incident TB in the NT Top End. Just seven cases had a second episode of culture-confirmed TB during the study; however, it was difficult to differentiate relapse from reinfection using genomics due to inadequate diversity in circulating MTB.

In the Torres Strait, a genomic epidemiological study included 100 isolates from notified culture-confirmed TB cases among PNG citizens in the Torres Strait Protected Zone between 2010 and 2015, and four isolates from Australian citizens with epidemiologic links to the region.[33] Eighty-three out of 104 isolates belonged to Beijing sublineage 2.2.1.1, of which 49 were closely related to isolates from the PNG Western Province.[9] Thirty-three out of 104 isolates were MDR and an additional two were also resistant to fluoroquinolones and injectable agents (XDR); all 35 MDR and XDR isolates belonged to Beijing sublineage 2.2.1.1. The four isolates from Australian citizens were linked to two separate genomic clusters, suggesting two cross-border MDR-TB transmission events. All 35 MDR or XDR isolates carried the *fabG1-inhA* C15T mutation. Twenty-eight out of 35 had high level isoniazid resistance; 27 had *ndh* (ΔG304) and *inhA* (Ile21Val) mutations, and one had a *katG* mutation (Trp191Arg). All rifampicin-resistant isolates carried *rpoB* (Ser450Leu).

Conclusion

The northern Australian studies described here demonstrate the utility of genomic sequencing for tracking and tracing TB in northern Australia. The Top End study provided evidence that TB transmission is continuing to occur in remote hotspot regions, with evidence that both reactivation from latency and recent transmission are contributing to incident TB. These findings support focus on timely diagnosis of active TB disease and effective treatment of LTBI in those areas, and further work is being undertaken to understand the factors contributing to late TB diagnoses and optimum LTBI treatment regimens. The Torres Strait study tracked the spread of a resistant MTB clone from neighbouring PNG, demonstrating the importance of collaboration with regional neighbours in TB surveillance and control. The next steps in public health implementation of MTB genomics in northern Australia include prospective MTB sequencing in jurisdictional public health laboratories with real-time cross-jurisdictional analysis to inform public health management.

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Melioidosis in northern Australia

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ABSTRACT

Burkholderia pseudomallei, the environmental bacterium that causes melioidosis, is endemic to northern Australia. Melioidosis is a strongly seasonal disease, occurring predominantly in individuals with specific comorbidities that include diabetes mellitus, chronic kidney disease, chronic lung disease, immunosuppresion, malignancy and hazardous alcohol use. Most patients are bacteraemic and the majority have pneumonia, however, the infection can involve almost any organ, with the skin, soft tissues, genitourinary system, bones, and joints frequently affected; multi-organ involvement is also common. Central nervous system involvement is less frequent but is more likely to cause death and long-term disability. The incidence of melioidosis is increasing in Australia, but improvements in management have resulted in the local case-fatality rate declining to approximately 10%. Further progress requires greater awareness of the disease and the development of technologies that might expedite diagnosis. A deeper understanding of the disease's pathophysiology – particularly the role of virulence factors – may also help define optimal management strategies, including the duration of antimicrobial therapy and the role of adjunctive treatments. Public health strategies that address the risk factors for this opportunistic infection – and the social inequity that drives them – would also reduce the morbidity and mortality of this life-threatening disease.

Keywords: bacterial infection, *Burkholderia pseudomallei*, clinical medicine, epidemiology, indigenous health, melioidosis, microbiology, public health, sepsis, tropical Australia.

Background

Melioidosis, caused by the environmental, saprophytic bacterium *Burkholderia pseudomallei*, is one of the most common causes of sepsis in tropical Australia.[1,2] Even with optimal supportive care, the case-fatality rate is approximately 10%, but outside endemic areas, it remains a neglected disease.[3] *B. pseudomallei* lives in the soil and surface water across the tropical north of Australia (above latitude 20°S), but outbreaks due to contaminated water have occurred further south (latitude 25.5°S) and focal areas of endemicity have even been described in temperate regions (latitude 31°S).[4] In humans, melioidosis can involve almost any organ, with the clinical presentation a result of the complex interplay between host, pathogen, and the environment.[5,6] *B. pseudomallei* can also infect animals, with pigs, goats, sheep, and camels among the most susceptible.[4]

Epidemiology

In tropical Australia melioidosis is strongly seasonal, with most human cases occurring during the summer wet season when moist soil provides optimal conditions for the growth and survival of *B. pseudomallei*. Heavy rainfall also disturbs the topsoil and clustering after severe weather events is documented.[7] The incidence of melioidosis is increasing in Australia and is highest in the Top End of the Northern Territory, where an annual rate of up to 50.2/100 000 population has been reported.[8,9] However, while anthropogenic climate change is anticipated to increase the future incidence of many seasonal infectious diseases, environmental disruption resulting from urban expansion appears to be having a greater impact on the incidence of melioidosis in Australia presently.[10,11]

The predominant mode of exposure is thought to be percutaneous, although inhalation and ingestion are also documented.[12] Very few of these exposures lead to clinical symptoms; however, patients with specific comorbidities – particularly diabetes mellitus, chronic lung disease, chronic kidney disease, immunosuppression, malignancy, and

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hazardous alcohol consumption – are more likely to develop disease.[8,13,14] Many of these comorbidities are more common among socioeconomically disadvantaged communities and this is one of the reasons why Aboriginal and Torres Strait Islander Australians bear a disproportionate burden of the disease.[8,12,15] As tropical Australia is a popular tourist destination, melioidosis should also be considered in patients who have travelled to the region and have predisposing comorbidities and a compatible clinical syndrome. Person-to-person transmission is extremely uncommon, and no special precautions are required for health workers caring for these patients.

Clinical presentation

Approximately 85% of melioidosis cases have an acute presentation although more subacute presentations – with symptoms present for longer than 2 months – are also seen; reactivation from latent infection occurs but it is less frequent than previously believed, representing approximately 3% of all cases.[8]

Melioidosis can involve almost any organ, but pneumonia is present in most cases[8,13,14] (Fig. 1). Lung involvement often resembles a typical community-acquired pneumonia with a short history of fever, rigors, cough, and dyspnoea. However, patients may also present with respiratory symptoms that have failed to respond to weeks of usual empirical outpatient therapies. This subacute presentation can bear some resemblance to tuberculosis, but in Northern Australia, pulmonary melioidosis is the more likely diagnosis.

Bacteraemia is present in 56–70% of Australian cases and up to a quarter present with septic shock.[16,17] Other typical presentations include skin and soft tissue infections, abscesses of the liver and spleen and infections of the bones and joints. Prostatic involvement, which occurs in ~20% of affected men, is a characteristic manifestation.[8] Multi-organ involvement is also common (Fig. 2). Central nervous system involvement occurs in only 4% of cases, but is one of the most feared manifestations and may present as encephalomyelitis, brain abscess, meningitis or as an extradural collection.[18] *B. pseudomallei* may also cause lymphadenopathy, nodules or masses that may be mistaken for neoplastic lesions, emphasising the importance of sending biopsies for culture in the appropriate clinical context (Fig. 2).

Less than 5% of cases occur in children, which is likely to be explained by a lower prevalence of predisposing comorbidities in this population. Affected children usually have

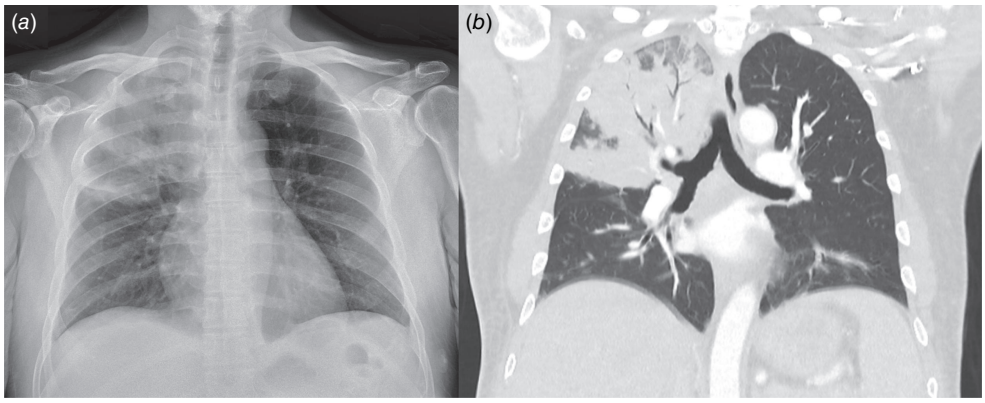

Fig. 1. A chest X-ray (*a*) and computed tomography scan (*b*) demonstrating right upper lobe pneumonia in a patient with diabetes who presented with 7 days of fever and cough.

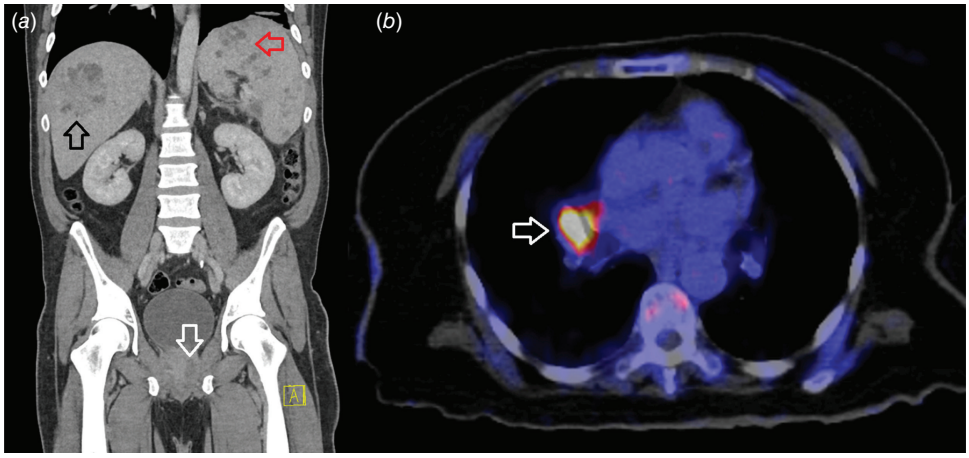

Fig. 2. Multi-organ involvement of liver (black arrow), spleen (red arrow) and prostate (white arrow) in a patient with disseminated melioidosis (*a*). Positron-emission tomography scan demonstrating mediastinal lymphadenopathy in another patient (*b*) who was believed to have a lung malignancy until *B. pseudomallei* was cultured from a biopsy.

milder disease, with localised skin infection the most common manifestation.[19] However, disseminated disease is also seen and fatalities have been reported in previously well children despite optimal supportive care.[20,21] Fatal paediatric cases may be due to the presence of virulence factors, which have been linked to clinical phenotype and prognosis in specific clinical situations, or the result of a larger inoculum.[18,22]

Microbiology

The diagnosis of melioidosis requires the culture of *B. pseudomallei* – a small, Gram-negative, oxidase-positive, motile, aerobic bacillus – from blood, sputum, urine, pus, or other clinical specimens.[23] Although the use of selective media can facilitate diagnosis, the organism also grows well on traditional media[24] (Fig. 3). True colonisation is extremely uncommon, therefore isolation of *B. pseudomallei* almost always warrants treatment. In high-volume centres, laboratory scientists are adept at identifying *B. pseudomallei*; however, laboratories unfamiliar with the organism may disregard it as an environmental contaminant.[5]

There is interest in the use of lateral flow immunoassay testing, PCR and MALDI-TOF to expedite the diagnosis of melioidosis, however PCR has not been sufficiently sensitive or specific for direct detection from clinical samples, and while the lateral flow immunoassay shows promise for the rapid diagnosis of melioidosis directly from pus and urine, it is not yet widely available, nor incorporated into validated diagnostic algorithms.[25–27] Serology has very limited utility in the diagnosis of the disease as it has poor sensitivity and may be positive in healthy individuals in endemic areas.[26]

Therapy

There are two phases of antimicrobial therapy for melioidosis: the initial intravenous intensive phase aims to prevent death, while the subsequent oral eradication therapy (beginning immediately after the initial intensive phase) aims to prevent disease relapse.

B. pseudomallei is intrinsically resistant to penicillin, ampicillin, first- and second-generation cephalosporins, gentamicin, tobramycin, and streptomycin, while *in vitro* testing of the organism against quinolones usually shows resistance or intermediate susceptibility. Therefore, during the initial intensive phase it is recommended that patients receive ceftazidime or meropenem; the duration of therapy varies with the clinical phenotype, although a minimum of 2 weeks is recommended and source control is essential.[28] Adjunctive trimethoprim-sulfamethoxazole (TMP-SMZ) is often added to patients with extrapulmonary infection due to its intracellular activity and ability to penetrate tissues, although the clinical benefit of this approach is uncertain.[28] Granulocyte colony-stimulating factor is used by some clinicians in the management of critically ill patients; however, there are no data from randomised controlled trials to support its routine use.[17]

Recrudescence and relapse – defined as return of clinical disease during and after the eradication phase respectively – can be fatal. Recrudescence occurs in approximately 5% of Australian patients while relapse occurs in up to 4%, and both are more common in patients who are unable to adhere to prescribed therapies.[8,29] However, adherence to currently recommended treatment regimens can be challenging: Australian treatment guidelines recommend a minimum of 3 months of high-dose TMP-SMZ during the eradication phase.[28] Even with the addition of daily folic acid, up to 30% of patients receiving high-dose TMP-SMZ have side effects that necessitate cessation, dose reduction or substitution of doxycycline or amoxycillin-clavulanate, agents that are less effective.[28,30] Accordingly, there has been a gradual evolution in clinical practice to prescribe longer courses of intravenous therapy and there is interest in high volume centres in abbreviating the duration of the oral eradication phase of therapy.[31]

Outcomes

The case-fatality rate of melioidosis has declined significantly in Australia over recent decades; this is likely to be explained, predominantly, by earlier recognition of the patient with sepsis and advances in critical care. Prompt administration of antibiotics with activity against *B. pseudomallei* has been facilitated by the electronic promulgation of national guidelines for melioidosis management, which also recommend empirical meropenem when melioidosis is a possible diagnosis.[28] However, even in Australia's well resourced

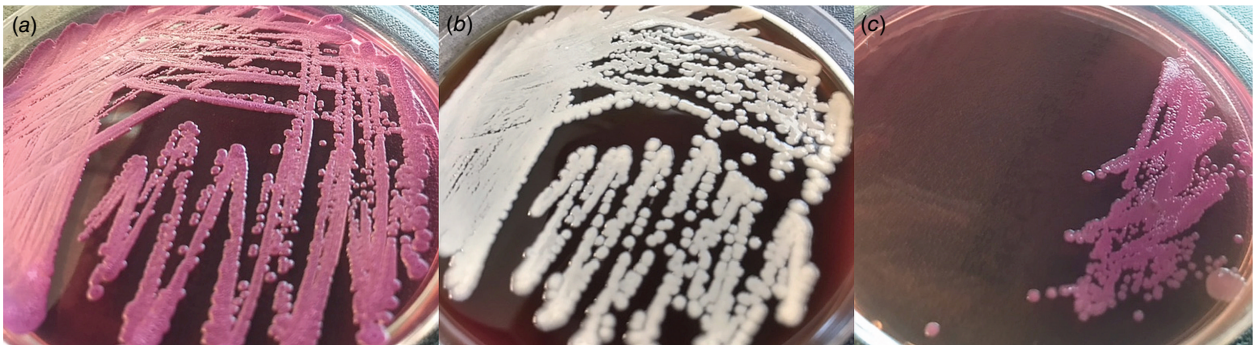

Fig. 3. Colonies of *Burkholderia pseudomallei* after 48 h of incubation on Ashdown's medium (*a*), horse blood agar (*b*) and MacConkey agar with crystal violet (*c*).

health system, the case-fatality rate remains approximately 10%. This is frequently linked to underlying comorbidities and the social determinants of health that drive them.[8,15] Furthermore, premature death in survivors is common, with approximately one-quarter of survivors dying within 5 years, frequently from the comorbidity that predisposed them to their melioidosis.[32] These deaths are often preventable; the episode of melioidosis is therefore also an opportunity for clinicians to optimise the management of these comorbidities to improve patients' overall long-term outcomes.

Prevention

In endemic areas public health strategies to prevent melioidosis largely revolve around advising individuals with predisposing comorbidities to minimise exposure to soil and surface water during the wet season and to stay indoors during heavy rains. However, it is recognised that adherence to these recommendations is challenging. There are data to support chemoprophylaxis in selected populations, but the relatively low incidence in even high-risk populations and the potential life-threatening side-effects of TMP-SMZ means that this is likely to have a very limited role in combating the disease.[33,34] Vaccines are under development, although none have yet undergone human trials.[35] Public health strategies to reduce the incidence of predisposing risk factors – or at least optimise their management – might reduce the burden of melioidosis as well as other complications from these comorbidities.

Conclusions

Even with optimal supportive care approximately 10% of Australian patients with melioidosis will die. A greater understanding of the disease's pathophysiology will inform management strategies, including the optimal duration of antimicrobial therapy and the utility of adjunctive treatments. The development of effective public health strategies to prevent melioidosis would also be expected to reduce the significant burden of this life-threatening disease, which, despite a rising incidence, remains under-recognised outside of tropical Australia.

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Microbiology Australia

Strong relationships between the Northern Territory of Australia and Timor-Leste

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ABSTRACT

Strong, enduring partnerships exist between the Northern Territory and Timor-Leste, and in recent years collaborations have led to significant developments in health system capacity in Timor-Leste. Laboratory strengthening has been a key focus; improved diagnostic microbiology capability, especially in the National Health Laboratory, is having an impact on individual patient management and outcomes, epidemiological surveillance, and public health responses to communicable disease challenges including antimicrobial resistance.

Keywords: antimicrobial resistance, bacteriology, epidemiology, global health, health system strengthening, microbiology, Northern Australia, surveillance, Timor-Leste.

Introduction

The National Health Laboratory (*Laboratório Nacional de Saúde* (LNS)) in Timor-Leste provides a routine diagnostic microbiology service, using a combination of traditional bench methods and automated tests for organism identification and antimicrobial susceptibility testing (AST) (Fig. 1). It functions as a reference laboratory in Timor-Leste, while also providing an important clinical diagnostic service, especially for the National Hospital (*Hospital Nacional Guido Valadares* (HNGV)). Its capacity for diagnostic microbiological testing has increased substantially in recent years, with key partnerships into Northern Australia contributing to important laboratory strengthening initiatives.

Background

Timor-Leste is a small half-island nation situated between Indonesia and Australia, about 700 km from Darwin, Australia. Timor-Leste is a relatively new country, having achieved independence for the second time in its history in 2002. The health sector in Timor-Leste is heavily dependent on external funding, and currently has no internationally accredited medical diagnostic laboratories.[1] HNGV is the main referral hospital for the country, located in the capital city of Dili, adjacent to LNS. It has a 260-bed capacity and is the main hospital for the five neighbouring districts, accounting for 46% of Timor-Leste's total population.[2] HNGV has a diagnostic laboratory on site which includes haematology, biochemistry, and histopathology, but diagnostic microbiology services are provided by LNS, which is situated just outside its grounds.

The microbiology laboratory at LNS was established in 1980 during the Indonesian occupation and the service was limited to urine and stool microscopy and culture, pus/wound swab culture and tuberculosis (TB) slide microscopy. After the vote for independence in 1999, the microbiology laboratory was re-established with support from laboratory advisors who had previously worked at Royal Darwin Hospital (RDH) Pathology. However, maintaining continuity of service was challenging due to human resource constraints and limited availability of reagents and consumables, contributing to a lack of trust and use from clinicians at HNGV. Prior to 2015, the laboratory was primarily conducting research or program-based work, with minimal attention on expanding the range of tests available for clinical diagnostic samples, re-organisation of microbiology workflow, strengthening quality assurance or generation of antimicrobial resistance data.

In 2016, an initial working relationship between the Microbiology Department at LNS, the Menzies School of Health Research (Menzies) and the RDH microbiology service was initiated. This collaboration led to an increase in capacity of the diagnostic microbiology service, improvement of laboratory infrastructure and ongoing training of laboratory personnel. In this paper we highlight capacity building, research, and diagnostic microbiology aspects of the partnerships between LNS, Menzies, and the RDH laboratory.

Capacity building links

As part of the initial working relationship with Microbiology Laboratory at LNS, Menzies applied for and implemented small grant projects with a broad aim to increase diagnostic capacity (Fig. 2). In 2016, Menzies initially implemented a study titled 'Resistance in Urine and Skin isolates in Timor-Leste (RUSTLE)' – an analysis of bacterial isolates from urine and skin swabs and their antimicrobial resistance profile, with support from RDH for confirmation of organism identification and automated AST results.[3] The RUSTLE study marked the beginning of the long-term support between the Darwin and Dili institutions. Following RUSTLE, Menzies implemented a pilot study working on drug susceptibility and genotyping of *Mycobacterium tuberculosis* (MTB), assisting the National TB Program (NTP) to understand the burden of TB resistance and origin of MTB isolated in Timor-Leste.

Having experienced the limitations of the current diagnostic bacteriology service and identifying a need to support clinicians and surveillance, Menzies, with the support of the Australian Department of Foreign Affairs and Trade (DFAT), commenced a project titled 'Surveillance, Training, Research Opportunities and National Guidelines for Communicable Disease Control in Timor-Leste' (STRONG TL). The STRONG TL project was designed to support capacity-building across three key components of the health system, integral to responding to infectious diseases challenges: Clinical, Laboratory, and Surveillance.[4] The project included deployment of microbiology scientists from RDH Pathology in Darwin to mentor Timorese scientists at LNS, linked to similar activities in the surveillance department and in clinical settings including at HNGV, focused on improving awareness of the importance of laboratory diagnostics, infectious disease surveillance and antimicrobial stewardship. A key component of the STRONG TL project has been side-by-side mentoring by scientists and epidemiologists from Northern Australia who have provided guidance, support and encouragement to Timorese colleagues who observe similar communicable disease threats and encounter similar challenges of remoteness. This mentoring also extends back to the Australian staff who have developed their skills in working in cross-cultural and challenging environments. Three scientists travelled to Timor-Leste on a rotating basis between 2018 and 2019, for up to 2-month stints at a time. The STRONG TL project has supported development of empirical antibiotic guidelines and Integrated Disease Surveillance and Response (IDSR) guidelines, which have built a strong foundation for future capacity-building programs.[5]

Fig. 1. Microbiology scientists working in the National Health Laboratory of Timor-Leste.

In 2019, Menzies was awarded the Fleming Fund Country Grant to Timor-Leste, which has funded significant investment in capacity for antimicrobial resistance and antimicrobial use surveillance in human health and animal health in Timor-Leste. The Fleming Fund Country Grant has facilitated significant expansion and refurbishment of the LNS microbiology laboratory, as well as installation and use of advanced diagnostic microbiology equipment for automated organism identification and AST. A combination of side-by-side mentoring and remote training and support for LNS microbiology staff has resulted in a 7-day per week diagnostic microbiology service generating quality-assured microbiological results daily and high-quality antimicrobial resistance surveillance data. Now, up to 500 blood culture specimens are processed per month in the LNS microbiology laboratory (Table 1).

The coronavirus disease 2019 (COVID-19) pandemic signalled a need for rapid capacity-building in molecular diagnostics in Timor-Leste. With financial support from DFAT, Menzies assisted in the refurbishment of the molecular department at LNS and provided in-country technical support and training for scientists in diagnostic testing for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Confirmatory testing was conducted for the first 500 samples in the RDH laboratory, helping LNS to verify its assay and learn from the experience of RDH in establishing a new assay. Since then, Timor-Leste has experienced three distinct

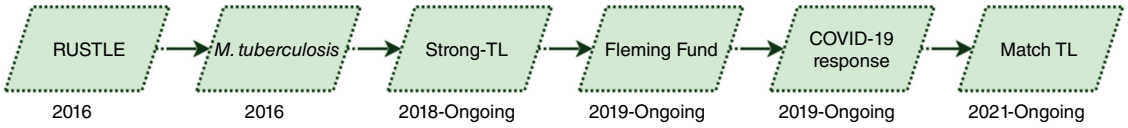

Fig. 2. Sequence of Menzies School of Health Research-led projects focused on capacity building and research in Timor-Leste.

Table 1. Diagnostic microbiology tests available in the National Health Laboratory of Timor-Leste.

Test	Purpose
Bruker MALDI-ToF	ID/AST
BD Phoenix M50	ID/AST
bioMérieux API 20E/20NE	ID
Biochemical tests (e.g. Indole, Catalase, Coagulase)	ID
Staph latex agglutination test	ID
Chromogenic media (e.g. ESBL, MRSA, SA, UTI)	ID
Disc diffusion	AST
bioMérieux Etest	AST
BioFire FilmArray Meningitis/Encephalitis Panel (ME)	ID
Cryptococcal antigen (CrAg LFA): IMMY	ID
GeneXpert CARBA-R	AST
GeneXpert CT/NG	ID

waves of community transmission of SARS-CoV-2 infection, and Menzies has supported the laboratory over times of high testing requirements, with capacity increased such that up to 1500 samples per day could be processed.

The capacity-building programs of STRONG TL and the Fleming Fund Country Grant provided the foundation for a strong laboratory response to COVID-19 in Timor-Leste, as part of ongoing effective collaboration between Menzies and the Ministry of Health across clinical, surveillance and laboratory areas.

Research links

The Northern Territory and Timor-Leste have collaborated on significant research projects, that have been deliberately linked to health system strengthening initiatives aimed at building capacity for diagnostic laboratory testing in Timor-Leste. Results from the RUSTLE study conducted in 2016 provided preliminary data on antimicrobial resistance in Timor-Leste. Over 200 isolates from urine and skin samples from inpatients at HNGV were cultured onto agar slopes and transported to the Microbiology Department at the Royal Darwin Hospital for bacterial identification and antimicrobial susceptibility testing. This study demonstrated high rates of bacterial resistance at HNGV, most notably a ceftriaxone resistance rate in species in the order: Enterobacterales of 35%.[3]

In 2018, the National Critical Care and Trauma Response (NCCTRC), based at RDH in Darwin, supported a Menzies, RDH and LNS collaboration that involved a trial of a deployable mobile laboratory for rapid diagnostic testing, using the multiplex RT-PCR BioFire® FilmArray® platform.[6] Through this research project, a blood culture service was established and LNS, and PCR screening of CSF and GI samples was introduced. Confirmation with concurrent standard culture methods allowed for rapid upskilling of scientists and verification of multiplex PCR results. One hundred and seventeen pathogens were identified including 25 organisms in blood culture and four separate CSF pathogens.[6]

There are ongoing research projects investigating the epidemiology of childhood meningitis, encephalitis, malnutrition, and pneumonia, with investigator teams including paediatric and infectious diseases clinician-researchers working across the Timor-Leste Ministry of Health, Menzies and the RDH contributing to provision of technical advice. The child mortality rate is high in Timor-Leste, and leading causes include malnutrition and pneumonia. Pulmaun Saudavel (PULSA, 'healthy lungs') study is a prospective cross-sectional surveillance study that aims to assess the prevalence of *S. pneumoniae* nasopharyngeal carriage in children aged 1–59 months admitted to HNGV with pneumonia and/or malnutrition between September 2019 and August 2020. The study, a collaboration between Menzies and Timorese researchers from LNS and HNGV, has provided preliminary data that has been used to inform Ministry of Health decisions regarding introduction of a pneumococcal conjugate vaccine in Timor-Leste. The Encephalitis and Meningitis Aetiology (EMA) study has identified cases of Japanese Encephalitis, and other causes of childhood meningoencephalitis. Data analysis and reporting is ongoing for these studies, but the public health impact is already apparent.

Menzies, LNS and researchers from the Ministry of Health, have collaborated with the Australian National Centre for Immunisation Research and Surveillance (NCIRS) to carry out seroprevalence studies involving healthcare workers,[7] residual serum samples from hospital laboratories, and a nationwide population-representative cohort of more than 5000 people. The research is aimed at improving understanding of the epidemiology and vaccine coverage for key vaccine-preventable diseases, including measles, rubella, COVID-19, dengue and hepatitis B. This research has enabled significant investment in serological testing capacity at LNS, and preliminary results are being used by the Ministry of Health to inform decision-making regarding vaccine policy and practice.

Menzies has also partnered with the Ministry of Health to deliver Structured Operational Research and Training IniTiative (SORT IT) training in Timor-Leste. Timorese participants in SORT IT training conduct a research project and learn research skills simultaneously. Practical skills learned in the program include development of study protocols, collection of high-quality data, publication in peer-reviewed journals and use of research in evidence-informed decision-making by public health authorities.

Microbiological links

As laboratory capacity has grown in Timor-Leste, improved understanding of the epidemiology and distribution of antimicrobial resistance provides important regional context and interesting comparisons with antimicrobial resistance rates in Northern Australia. Menzies has worked with LNS to generate antibiograms for clinically significant isolates from HNGV and surrounding Dili, modelled on the antibiogram used at RDH. Consistent with the findings of the RUSTLE study,[3] recent Timor-Leste antibiograms demonstrate high rates of Gram-negative resistance, especially Extended-Spectrum Beta-lactamase (ESBL) producing organisms. In 2021, 77%

of *Klebsiella pneumoniae* clinical isolates tested at LNS were phenotypic ESBL-producers. This is significantly higher than reported in the Northern Territory, where 5% phenotypic ESBL resistance was seen in *K. pneumoniae* in 2019.[8] Only 11% of *Staphylococcus aureus* isolates in the RUSTLE study were MRSA, however, analysis of recent clinical isolates from HNGV show much higher rates of MRSA (32% of 171 *S. aureus* isolates in 2020), comparable with MRSA rates reported in the Northern Territory (34% in 2020).[9]

In 2022, the LNS in Dili was able to culture and identify the first isolate of *Burkholderia pseudomallei* in Timor-Leste. A previous study on seroprevalence of *B. pseudomallei* antibodies was conducted on Timorese refugees evacuated to Darwin after the referendum for independence in 1999.[10] Leveraging extensive experience in the diagnosis and management of melioidosis,[11] the microbiology laboratory at RDH and the Melioidosis research group at Menzies have supported LNS by providing remote training as well as confirmatory PCR and AST testing of *B. pseudomallei* for Timor-Leste. Genomic sequencing is ongoing and will be informative in identifying possible epidemiological links between the two countries.

Conclusion

The close relationship between LNS, Menzies, and the RDH Microbiology Laboratory has enabled ongoing strengthening in diagnostic bacteriology and antimicrobial surveillance in Timor-Leste. Important work is continuing to establish greater capacity in municipalities outside of Dili, led by LNS but with ongoing support and collaboration from partners in Northern Australia.

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Menzies Art Gallery of Scientific Discovery

***Staphylococcus argenteus* by Jayde Hopkins (owned by Menzies School of Health Research)**

This painting represents the discovery of the new bacterium *Staphylococcus argenteus* by researchers at Menzies.

The middle of the image shows an agar plate growing the well known *Staphylococcus aureus* (Golden Staph) on the left with the newly discovered *Staphylococcus argenteus* (Silver Staph) on the right. The shapes around the agar plate signify the people of the scientific community involved in the new discovery with the three largest shapes representing the three scientists at Menzies: Steven Tong, Deborah Holt and Philip Giffard. The orange dots surrounding the people is the colour for Menzies. Spreading from either side of the agar plate is the knowledge passed on to the greater community. The background of the painting represents the clustered cocci Gram-positive stain as seen under the microscope.

About the artist

Jayde Hopkins is a Gurindji and Woolwonga woman from the Northern Territory. As an artist she specialises in vibrant colours, utilising dot painting and more contemporary techniques to paint the natural world. She is a lover of all things art and science and is completing her undergraduate degree in Biological Sciences.

This artwork is the property of Menzies School of Health.

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Microbiology Australia

A project to validate the GLU test for preterm birth prediction in First Nations women

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ABSTRACT

The protocol described in the present article aims to validate the GLU test, a test of mid-pregnancy vaginal microbiome, for PTB risk prediction in pregnant First Nations women. Preterm birth (PTB; birth before 37 completed weeks gestation) is associated with a higher risk of adverse neonatal outcomes. First Nations communities are affected by increasing PTB rates, highest in remote communities, reaching 23%. Being able to predict women at high risk of PTB is one of the greatest challenges of our time. No reliable clinical predictors of PTB risk currently exist, beyond a previous history. Spontaneous PTB (sPTB) is highly associated with microbial infection. Recently, a Western Australian research team developed an innovative mid-pregnancy vaginal microbial DNA test, the '*Gardnerella, Lactobacillus, Ureaplasma*' (GLU) test, capable of predicting up to 45% of sPTB cases. However, this test has only been validated in predominantly Caucasian pregnant women. The protocol described aims to validate the GLU test in pregnant First Nations women and where applicable, make modifications to this test to improve sensitivity and specificity within this population.

Keywords: Australian First Nations, diagnostic test, genotype, microbiome, pregnancy, preterm labour, preterm premature rupture of membranes, real-time polymerase chain reaction, vagina.

Introduction

Preterm birth (PTB; delivery before 37 gestational weeks) is the leading cause of death and disability in children under 5 years of age. Globally, approximately 10% of infants are born too early.[1] Australian First Nations (the Aboriginal and Torres Strait Islander people of Australia) women are at far greater risk of this major complication of pregnancy. Nationally, in 2019, 13% of babies born to First Nations mothers were preterm, compared with 8.3% of babies from non-First Nations mothers.[2] The PTB incidence is even greater for First Nations women in regional and remote parts of the Northern Territory (NT) and Western Australia (WA) with national data reporting rates up to 23%[3] (Fig. 1). The risk factors for PTB in First Nations women are multifactorial and not completely understood. Much of the discrepancy is likely the result of disparities in social determinants of health, fuelled by poverty, racism, and intergenerational trauma.[4] However, at least one-quarter of all PTBs, but especially those that occur due to spontaneous preterm labour (sPTB), are attributed to intrauterine bacterial infection, especially at earlier gestational ages (GA).[5]

Numerous bacterial taxa have been implicated, with the bulk of these represented by *Ureaplasma* spp. and anaerobic organisms associated with a dysbiotic vaginal state.[6] Conversely, dominance of certain *Lactobacillus* spp. in the vagina during pregnancy may offer some level of protection from sPTB.[7] However, the vaginal bacterial microbiome varies substantially between ethnic cohorts,[8] and little is known about its composition in First Nations women; the only study completed to date recruited 23 pregnant Australian First Nations women and reported a vaginal microbiome composition not dissimilar to that observed amongst African–American women, characterised by *Lactobacillus* spp.-depletion and presence of diverse anaerobic genera.[9]

Although infection may result in sPTB,[10] it is the mother's inflammatory response to infection that triggers preterm labour.[11] Whereas data exist on uterine inflammation during infectious and non-infectious scenarios,[12] very little is known about the pregnant

vaginal environment relative to the microbial profile.[13] Based on studies in non-pregnant women, McKinnon *et al.* have defined that a non-optimal vaginal microbiome elicits a pro-inflammatory milieu in the cervicovagina in contrast to an optimal vaginal microbiota that is non-inflammatory.[14] Hence, an understanding of the vaginal pro- and anti-inflammatory state in pregnancy, alongside its microbial composition and function, may identify additional host and microbial biomarkers for sPTB prediction, as well as furthering our knowledge of the mechanistic nature of infection-related sPTB, which remains poorly understood.

Payne *et al.* recently conducted the largest mid-pregnancy vaginal microbiology study to date, the Predict1000 study, which resulted in the development of a novel mid-gestation vaginal microbial DNA test for prediction of Australian women at high sPTB risk, the GLU test (Fig. 2).[15] In a cohort of 936 women, this test was able to detect women at risk of

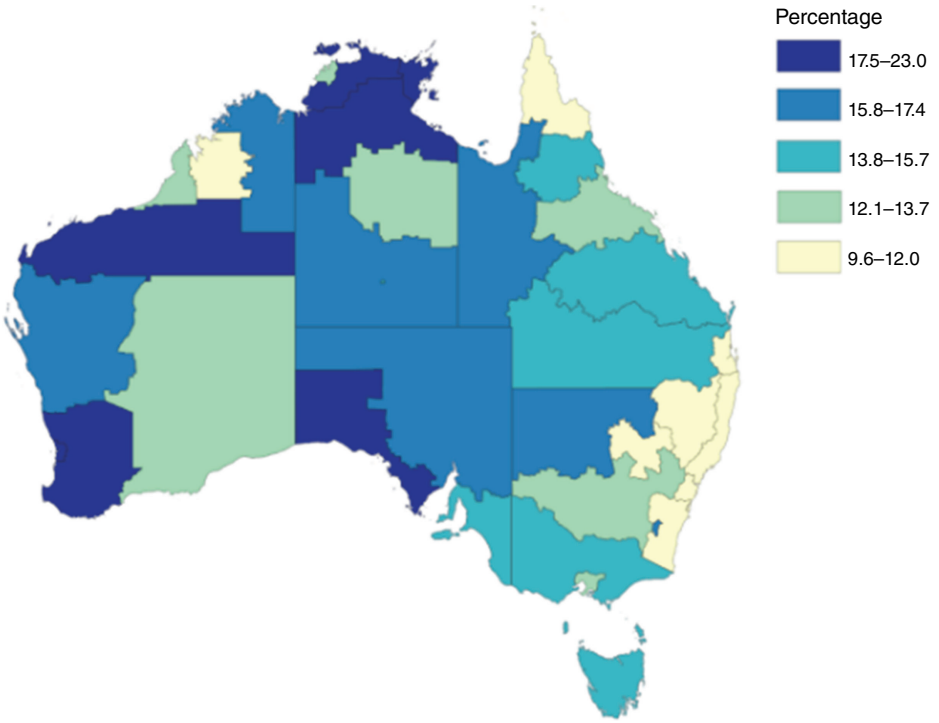

Fig. 1. Preterm births among babies born to First Nations mothers by region 2016–2017. Source: AIHW.[3]

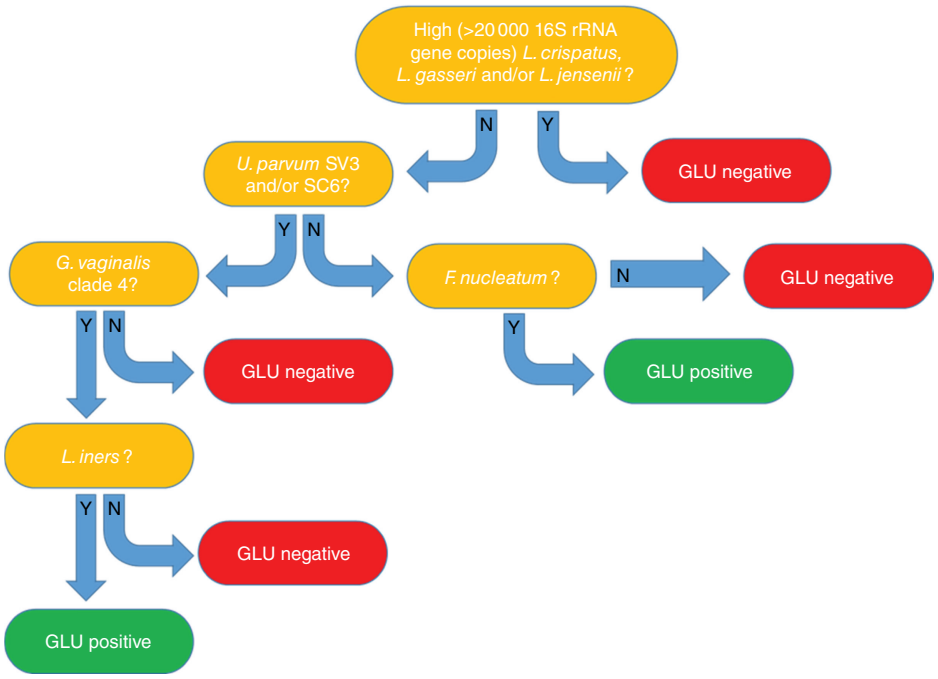

Fig. 2. The GLU algorithm.

sPTB <37 weeks' GA and ≤34 weeks' GA, with sensitivities of 37.9 and 44.4%, respectively. More importantly, women who had a prior history of sPTB, our current best clinical predictor of sPTB risk, were almost as likely to deliver via sPTB as women who were GLU-positive in mid-gestation (adjusted odds ratio 3.61 vs 3.28). This test now underpins a National Health and Medical Research Council-funded randomised controlled trial (RCT) (ACTRN12617001593325) to assess the efficacy of a novel antimicrobial and probiotic treatment regimen in GLU-positive women to reduce sPTB risk. However, data on performance of the GLU test came from a predominantly Australian Caucasian cohort; only 22 women recruited to the Predict1000 study identified as First Nation Australians (2.3%).

Further research is needed to document the vaginal microbiome and associated inflammatory state in pregnant First Nations women. This includes an assessment of whether the GLU-test in its current form can identify First Nations women at increased risk of sPTB, and if not, ascertain if different host and microbial biomarkers can be identified that may be useful for this purpose.

Very few tools are currently available to identify women at high risk of sPTB during pregnancy. Identification of vaginal microbial biomarkers during mid-pregnancy has high potential for translation into clinically relevant tools that, importantly, can be acted on with suitable interventions to either prevent sPTB from occurring or delay the onset of preterm labour.

Methods

Aims and objectives

This research aims to develop approaches to identify pregnant First Nations women at risk of sPTB based on vaginal host and microbial biomarkers evaluated in early to mid-gestation. The specific research objectives are to:

(1) Assess performance of the GLU test for prediction of sPTB in First Nations women.
(2) Characterise the early to mid-gestation vaginal microbiome, inflammatory state, and host/microbial protein profile and document associations between these and maternal factors (such as smoking and diabetes).
(3) Identify microbial and host biomarkers that will enable modification of the existing GLU test to enhance sPTB prediction in First Nations women.

Study design

To address the aims and objectives we will conduct a prospective cohort study.

Study setting and population

In the Northern Territory, recruitment will occur from Royal Darwin Hospital (RDH), and Gove District Hospital (GDH). Both hospitals service towns and communities across the Top End. Approximately 600 First Nations mothers have babies across these two hospitals per annum.[16]

In Western Australia, recruitment will occur from the Geraldton Regional Aboriginal Medical Service (GRAMS), a community health service for First Nations peoples. GRAMS midwives provide antenatal care for over 100 pregnancies per year.

Pregnant First Nations women aged 16+ years attending antenatal clinics at ≤24 weeks' GA will be invited to participate. Exclusion criteria include multiple pregnancies, current symptomatic vaginal infections, current or recent (preceding 2 weeks) antibiotic/antimycotic use, cervical sutures, high dependence on medical care, illicit drug use, and lack of capacity to provide written informed consent.

Sample size

The anticipated recruitment number is 750 women, 500 at RDH/GDH and 250 at GRAMS. Assuming a baseline sPTB rate in Aboriginal women of ~7%, a cohort of 750 will attain ≥90% power to detect an increase in sPTB probability associated with a GLU (or modified version) positive test by an odds ratio ≥2.25 (increase from 7 to 14.5% sPTB risk), while simultaneously adjusting for other relevant microbial and clinical risk factors with partial $r^2 = 0.1$.

Sample collection

Participating women will first complete a medical/lifestyle questionnaire enquiring about key clinical and environmental factors that may impact the vaginal microbiome and pregnancy outcome. These include diabetes (type 1, type 2, or gestational), smoking and alcohol intake (assessed semi-quantitatively), and area of primary residence (urban vs rural). Women will then provide two self-collected vaginal swabs, one in liquid Amies media (COPAN e-Swab) for vaginal microbiome profiling and GLU analysis and one in QIAGEN Allprotect media for cytokine, chemokine, and host and microbial protein content analyses. A vaginal pH reading will also be obtained using a self-test kit (Canesten).

Laboratory methods

DNA will be extracted from swab 1 and GLU-status assessed via qPCR.[15] The vaginal microbiome will then be characterised using full-length *16S* rRNA gene sequencing on the PacBio Sequel II as per Goldenberg *et al.*[10] Sequences will be analysed using Mothur (v1.47).[17]

Swab 2 ($n = 180$) will undergo cytokine and chemokine quantification and metaproteomic analyses to define the host inflammatory state and microbial functional properties. Samples will be selected based on pregnancy outcome, with a 60:120 split between sPTB (all cases in the cohort) and term births. This subgroup will attain ≥80% power to detect medium effect sizes for binary descriptors and ≥95% power to detect a difference of 0.5 s.d. for continuous descriptors between groups. Cytokines and chemokines will be analysed using a multiplex Luminex assay; targets include IL-1α, IL-1β, IL-6, IL-8, TNF-α, IL-1RA, RANTES, CXCL10, MCP-1, MIP-1α, MIP-1β and MIP-3α. Metaproteomic analyses will involve shotgun liquid chromatography tandem mass

spectrometry using a Q-Exactive Quadrupole-Orbitrap mass spectrometer as per Alisoltani *et al.*[18]

End-points

The primary clinical end-point in this study is sPTB, defined as the spontaneous commencement of labour before 37 weeks' gestation. Secondary end-points include established PTB research Core Outcome Measures,[19] including sPTB ≤34- and 28-weeks GA. All end-points will be measured by obtaining delivery outcome data from NT and WA hospital pregnancy databases and patient medical records.

Statistical analysis

Evaluations of the effects of microorganisms, cytokines, host and microbial proteins, and maternal characteristics on the timing of birth will be conducted using linear, logistic and Cox proportional hazards regressions, as appropriate for gestational age at birth or sPTB. These regressions will be supplemented with recursive partitioning models, such as binary, regression and survival trees, designed to explore the non-linear relationships within the laboratory data alone and when combined with other obstetrics risk factors.

Ethics

Ethical approval to conduct this study was granted by the Human Research Ethics Committee of the Northern Territory Department of Health and Menzies School of Health Research (HREC-2020-3659), and the Western Australian Aboriginal Health Ethics Committee (HREC-937). The NT study was approved by the Menzies School of Health Research Child Health First Nations Reference Group.

Conclusion

PTB has devastating impacts on First Nations families and communities, with significant long- and short-term complications. There are substantial emotional, psychological, and financial costs to families and communities. The cost to health services remains high. The continued poor rates are unacceptable. Further understanding of the pathophysiology is required. The presence and abundance of some bacterial pathogens in the mid-trimester vaginal microbiome has been shown to increase the risk of PTB in Caucasian women but this information is yet to be validated in First Nations women. Data generated from this study will confirm whether the GLU test in its current form is suitable for prediction of First Nations women at increased sPTB risk. In the case that the test is unsuitable for this cohort, additional data from *16S* rRNA gene and inflammatory marker/protein profiling may allow cohort-specific microbial DNA and host and microbial protein signatures to be identified that predict First Nations women at high sPTB risk and who may benefit from mid-gestation treatment with specific antimicrobials/probiotics. Additionally, identifying protein biomarkers could be used to develop true point-of-care tests that are low cost and convenient to use in very remote settings where PTB rates are highest. This is likely to prolong pregnancy for many women and ultimately reduce mortality and morbidity for hundreds of infants each year.

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Data availability. Data sharing is not applicable as as no new data were generated or analysed during this study.

Conflicts of interest. The authors declare no conflicts of interest.

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Biographies

Dr Kiarna Brown is a First Nations Specialist Obstetrician and Gynaecologist and Clinical Research Fellow. Her research interests are in reducing preterm birth for First Nations women.

Dr Holger Unger is an Obstetrician and Gynaecologist at the Royal Darwin Hospital and a Senior Research Fellow at the Menzies School of Health Research. He conducts clinical research that focusses on the prevention of adverse birth outcomes in low-resource and remote populations.

Maggie Peel is an experienced midwife and the Practice Manager at the Geraldton Regional Aboriginal Medical Service. She prides herself on empowering Aboriginal women to be able to receive and access the best antenatal care possible to assist them in gaining better health outcomes during their antenatal, intrapartum, and post-partum periods.

Professor Dorota Doherty is Head of the Biostatistics and Research Design Unit at the Women and Infants Research Foundation at King Edward Memorial Hospital (KEMH), and an Adjunct Professor at the Division of Obstetrics and Gynaecology, the University of Western Australia (UWA). Her expertise in biostatistical techniques has been pivotal in translational research in clinical medicine with complex epidemiological models that explore associations between subject phenotypes and health outcomes.

Dr Martin Lee is the Lead Medical Coordinator of the Rural Clinical School of Western Australia in Geraldton, maintains clinical work at Headspace Youth Focus, provides anaesthesia at St John of God Hospital, conducts sessional work at WA Cardiology, and is the current Chair of the Western Australian Primary Health Alliance – Midwest Gascoyne region. He has a keen rural community focus, and is passionate about quality workforce development and retention.

Dr Agatha Kujawa is a Rural Generalist and GP-Obstetrician working in Nhulunbuy, East Arnhem Land. She is passionate about the provision of equitable healthcare for those living in rural and remote areas in Australia.

Sarah Holder is a senior midwife and former Maternity Unit Manager at the Gove District Hospital located in Nhulunbuy, Arnhem Land. She has many years of experience in working with and caring for First Nations pregnant women in the NT. Sarah currently coordinates care for women with complex medical and psychosocial needs with Darwin's Midwifery Group Practice.

Professor Gilda Tachedjian is Head of Life Sciences at The Burnet Institute. She is a microbiologist with >25 years of experience in identifying and developing HIV antiviral strategies, and is recognised as an expert on HIV prevention in women and the role of the vaginal microbiome and their metabolites in HIV acquisition. She has a growing interest in its role in adverse reproductive health outcomes.

Dr Lindi Masson is a Senior Research Fellow at the Burnet Institute, Honorary Research Associate at the University of Cape Town (UCT), Associate Member of the Institute of Infectious Disease and Molecular Medicine at UCT, Honorary Research Associate of the Centre for the AIDS Programme of Research in South Africa, and Adjunct Senior Lecturer at Monash University. She has been involved in genital microbiome and immunology research for >14 years.

Dr Jane Thorn is a Senior Obstetrician and Gynaecologist, and current Head of the Department of Obstetrics and Gynaecology at the Royal Darwin Hospital. She has provided antenatal and obstetric care for First Nations women in remote and urban communities at the Top End for over a decade.

Professor John Newnham is a Professor of Obstetrics at The University of Western Australia, and a sub-specialist in Maternal Fetal Medicine at KEMH. His enduring research interest has been to discover strategies to safely reduce the rate of preterm birth. He has published widely on this subject and is recognised as one of the world's leading authorities.

Dr Matt Payne is a Senior Research Fellow at UWA with expertise in perinatal molecular microbiology. His major research interest is the role of the perinatal microbiome in preterm birth. Dr Payne is the lead investigator on the current study and designed the GLU test.

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ASM2022 Sydney conference review

Jai Tree, Karl Hassan, Tom Jefferies and Martina Sanderson-Smith

From 11 to 14 July the Australian Microbiology community gathered for ASM2022 on Darling Harbour in Sydney. The event marked a return to our annual in-person conference after a 2-year hiatus due to COVID-19. The excitement at seeing colleagues old and new was palpable as delegates caught up over coffee, drinks, and the dance floor (at the Rubbo celebration).

ASM2022 had originally been scheduled for 2021, but with border restrictions in place for much of 2020/2021, and ASM2020 postponed, Sydney was rescheduled for 2022 and we were fortunate enough to welcome an intrepid group of international and interstate colleagues to the conference. With many colleagues still unable to travel, or concerned about the risks associated with travel, the prudent course was taken and ASM2022 was offered in hybrid format. This also allowed speakers the option of presenting online at short notice – which ultimately saw a few of our colleagues presenting from their hotel rooms. We were joined in-person by 385 delegates and online by an additional 122 attendees.

The event kicked-off with our Public Lecture, hosted at the picturesque Australian National Maritime Museum. It was a packed house as Professor Justin Seymour and Associate Professor Diane McDougald gave us some big picture cautionary tales on the influence of pollution and climate change on the occurrence and behaviour of aquatic pathogens such as cholera, coliforms and *Vibrio parahaemolyticus* to name just a few. This set the scene well for the importance of the research presented later at the conference.

Our plenary speakers this year represented a broad cross-section of microbiology – from clinical to molecular and environmental, bacterial to fungal and viral, and combinations thereof. Our inaugural ASM Distinguished Orator Award started proceedings and was presented to Professor Elizabeth Hartland (Hudson Institute, Vic.). Professor Hartland gave an overview of her work on the functions of bacterial effectors in host-pathogens interactions. Many pathogens inject a cocktail of proteins into host cells and teasing apart the molecular biology of these effectors has revealed a sophisticated level of manipulation of host cell processes. The day closed with drinks at the trade show and poster presentations that afforded an opportunity to chat with students, many that were attending an in-person conference and meeting their interstate peers for the first time. The quality of research from our PhD students and ECRs is always impressive and this year was no exception, with outstanding poster presentations both in person and online.

Tuesday was awards day and an opportunity for the Society to recognise the work of our students and colleagues. Our Nancy Millis prize winners are awarded by each State branch and present their PhD research at the national conference. This year they were Adrianna Turner (Vic.), Miljar Stupar (Qld), Clare Moran (WA), Joanna Rothwell (NSW-ACT), and Clare Hayward (SA-NT). Distinguished Service Awards were presented to Ulrike Kappler, Sarah Foster, Lisa Shepherd, and Renato Morona for their service to the society. Ulrike Kappler was also awarded the David White Award for Excellence in Teaching for her contributions to education. Finally, our Jim Pittard Early Career Awards went to Rachael Lappan and Daniel Enosi Tuipulotu, and our Frank Fenner Awardees were Amy Cain, Jai Tree and Karl Hassan. Congratulations to all.

Our Tuesday plenary session featured talks from Professor Ana Traven (Monash, Vic.) and Dr Craig Spencer (Columbia, USA). Professor Traven discussed her work on *Candida albicans* and the often underappreciated role of host and fungal metabolism during infection. Dr Spencer joined us virtually from New York where he works as an emergency medicine doctor. Craig reflected on his experiences in Guinea working with Doctors without Borders to contain Ebola, contracting Ebola himself, and lessons learnt that may be applicable to the COVID-19 pandemic.

Our Wednesday program was always going to be a highlight with our Rubbo Oration, Rubbo Celebration, and NSW Chief Health Officer speaking. Our plenary speakers were Associate Professor Rebecca Vega-Thurber and Professor Jeff Errington and both delivered memorable and enlightening talks. Rebecca presented virtually from Oregon State University, USA and spoke about her work on coral microbiomes. Jeff had recently arrived in Sydney to take up an ARC Laureate Fellowship and spoke about his work on cell wall-less, antibiotic resistant L-form bacteria.

We were fortunate to be joined by the NSW Chief Health Officer, Dr Kerry Chant in the Wednesday lunch session. Dr Chant advised the NSW Government through the pandemic and presented some of the major challenges that faced the state in the future. Her talk was warmly received and afforded an opportunity to discuss public health challenges at length including efficient data sharing and the role of microbiologists as trusted sources of information during the pandemic.

Thanks to the hard work and advocacy of Associate Professor Maurizio Labbate and Dr Heema Vyas, ASM2022 hosted a LGBTQIA+ Networking Session on Wednesday.

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A follow up to the inaugural LGBTQIA+ Network event hosted by the NSW-ACT Branch, this lunchtime session generated discussion around a support network for LGBTQIA+ microbiologists and their allies, and was a great opportunity to meet with like-minded people, learn more and appreciate some quality memes.

Our Rubbo Orator this year was Professor Jillian Banfield FRS FAA and joined us from the University of California, Berkley, USA. Professor Banfield is a Geomicrobiologist that has advanced our understanding of the function of microbial communities in the soil. Professor Banfield presented an impressive breadth of work spanning terrestrial metagenomics, re-coding of structural genes in phage, and work on the genetics of soil microbiomes. The session adjourned to the Rubbo Celebration where The Zinc Fingers got the crowd moving, including many of our plenary and invited speakers.

Thursday was the final day of the conference with proceedings finishing at lunchtime. Despite some foggy heads following the Rubbo Celebration, Thursday morning was jam packed with outstanding symposia. This year the organising committee wanted to highlight the important contributions of microbiologists to the rapidly expanding field of Synthetic Biology. A Thursday morning symposium session on this topic was followed by our final plenary speaker, Professor Ian Paulsen FAA FRSN FASM, Director of the ARC Centre of Excellence in Synthetic Biology (ARC CoESB). Professor Paulsen is a long-time advocate for microbiology in Australia and spoke about the cutting-edge microbiology research projects being conducted in the ARC CoESB.

A common comment as the conference closed was how valuable informal meetings and chance discussions were after 2 years of online meetings. Our hope is that new and old collaborations were established and renewed at ASM2022. We left the conference excited about seeing colleagues again in Perth at ASM2023.

ASM2022 Local Organising Committee: (Top L-R) Karl Hassan, Jai Tree, Martina Sanderson-Smith and Megan Lenardon, and (Bottom L-R) Amy Cain, Slade Jensen and Tim Newsome (Members not pictured: Thomas Jefferies, Willa Huston and Dennise Leyton).

Congratulations to South Australian ASM members: Andrew Lawrence, OAM, and Steph Lamont-Friedrich

Andrew Lawrence was admitted to the Order of Australia (OAM) for his services to microbiology.

Andrew has done so much for the discipline of microbiology over a sustained period of time – professionally, within his role in SA Pathology/IMVS/Women's and Children's Hospital and also personally through almost 40 years of committee service to the Australian Society for Microbiology (ASM) in SA and NT, including many roles, National conference chair, inaugural Tri-State, Branch officer, to name but a few. His involvement most recently was as a key player within the 'B Part of it' Men B vaccine study, a globally significant work.

Well done, Andrew; so very well deserved to receive recognition on the public stage.

Stephanie Lamont-Friedrich was announced as one of South Australia's 40 Under 40, and awarded the Game Changer Award for 'recognition of a person who has re-written the rules of business to challenge, inspire and spark significant change for her work in supporting girls and Women in STEMM and bridging the gap between Academia and Corporate. She is proud to represent KPMG Australia and the University of South who continue to support her work.

Steph has been an active member of the ASM SA-NT Branch committee for many years, including differing roles over time: student representative; social media content representative; and especially, as the coordinator of the Science Alive! exhibition for the past 4–5 years inclusive.

Science Alive! is the largest interface of its kind in the country between the ASM and the general public; see report by Dena Lyras in the 2018 issue of *Microbiology Australia*: https://www.publish.csiro.au/MA/pdf/MA18057. This event has been successfully run each year from 2018 onwards under the coordination of Stephanie. See https://womeninscienceaust.org/portfolio/stemm-profile-steph-lamont-friedrich/.

(2022) *Microbiology Australia* **43**(3), 136.
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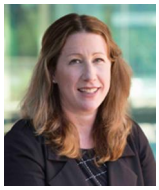
ASM Summer Student Research Awards: 2022



Priscilla Johanesen

Chair, ASM Standing Committee for Professional Development

The Australian Society for Microbiology is committed to supporting the future generations of Microbiology researchers. One of the ways in which ASM is able to support our early career-stage microbiologists is through the ASM Summer Student Research Awards, which provide opportunities for students to work on short research projects across the summer period. This year the society awarded 12 ASM Summer Student Research Awards across Australia. The successful awardees were: Valentin Slesarenko and Kellynn Tan from Queensland; Maia Perry from South Australia; Nicholas Slamen from Tasmania; Isni Buthgamuwa, Rylee Deehan, Nhu Quynh Doan and Desirel Ng from Victoria; Emma Catchpole, Dávid Szabó, Vanessa Tenaglia and Crystal Young from Western Australia. The ASM would like to offer our warmest congratulations to all of our 2022 Summer Student Research Awardees, and we look forward to supporting them in other ways as their careers in Microbiology progress.

Queensland

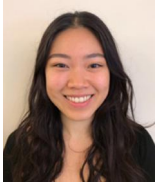
Pneumococcal strain characterisation in children

Valentin Slesarenko, Taha, Jessica Brown and Kate L. Seib

Institute for Glycomics, Griffith University, Queensland, Queensland, Australia

Abstract: *Streptococcus pneumoniae* is one of the most common bacterial pathogens responsible for acute respiratory tract infections. This research project aimed to determine the sequence types (STs) within a subset of pneumococcal-positive nasal swabs taken from children at weekly intervals, using multilocus sequence typing (MLST). We discovered that pneumococcal STs tend to be persistent over time, whereas a shift between STs is possible but rare. These findings improve our current understanding of the pneumococcal strains involved in colonisation and disease. This may aid the future development of antibiotics and vaccines to reduce the global burden of pneumococcal disease.

Counteracting antibody-mediated serum resistance



Kellynn K. Y. Tan and Timothy J. Wells

Diamantina Institute, The University of Queensland, Brisbane, Queensland, Australia

Abstract: *Pseudomonas aeruginosa* is an important nosocomial pathogen which causes acute infections that commonly lead to bloodstream infections (BSI) and sepsis. Clinical management is problematic due to intrinsic and acquired resistance to many antibiotics. Complement-mediated killing (serum killing) is one of the major ways the immune system combats Gram-negative infections. Antibodies usually promote serum-killing; however, a sub-set of patients with *P. aeruginosa* infection produce specific antibodies that protect bacteria from serum-killing. These 'cloaking antibodies' (cAb) belong to the IgG2 or IgA subclass and target lipopolysaccharide on the bacterial surface. Importantly, the presence of cAbs correlates with worse outcomes in bronchiectasis and lung transplants and was identified in 14% of patients with *P. aeruginosa* BSI. Methods to counteract this antibody-mediated protection would allow the immune system to quickly kill these pathogens regardless of multi-drug resistance. The LPS-binding antibiotic Polymyxin-B (PmB) and its derivative nonapeptide (PMBN), can sensitise innately serum-resistant bacteria to serum-killing. However, it is unknown whether these molecules could counteract serum resistance by cAb. We tested whether PmB or PMBN treatment of *P. aeruginosa* clinical isolates will counteract cAb serum-protection. We found that although these molecules do sensitise bacteria to healthy serum killing, it does not affect serum resistance mediated by cAbs.

South Australia

The transfer of antimicrobial resistance plasmids between bovine respiratory disease pathogens via liquid conjugation and electroporation

Maia Perry, Abiodun David Ogunniyi and Darren Trott

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Abstract: Bovine respiratory disease (BRD) is the leading cause of death in feedlot cattle, resulting in economic losses of an estimated A$40 million annually. This significant loss makes BRD a substantial concern for the cattle industry. Due to the use of antibiotics for prophylaxis and metaphylaxis against BRD, antimicrobial resistance and the transfer of resistance genes needs to be carefully observed. Two *Pasteurella multocida* isolates, exhibiting resistance to macrolides or β-lactams, and four *Mannheimia haemolytica* isolates, resistant to macrolides or sensitive, were subject to liquid mating and electroporation experiments. Neither liquid mating nor electroporation experiments were successful. Although growth was observed on SBA plates, no colonies of the desired species were observed on antibiotic selective plates. It is unknown why the macrolide resistance plasmid could not be transferred into either *P. multocida* or *M. haemolytica* via either method used, however previous research has been successful in using *P. multocida* in both experiments. Liquid mating was only attempted using a *M. haemolytica* donor, and it would be beneficial to conduct it again, using a *P. multocida* donor. Knowledge gained from future research could be vital in understanding the spread of resistance among BRD pathogens.

Tasmania

Characterising the DinB (DNA polymerase IV)-dependent mutation generation pathway in *Pseudomonas aeruginosa*

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Abstract: *Pseudomonas aeruginosa* is an important human opportunistic bacterial pathogen whose infections are difficult to eradicate because of its intrinsic resistance to various classes of commonly available antibiotics, as well as its ability to generate resistance mutations during relevant treatment regimens. Here, the role of the damage-inducible SOS-controlled error-prone DNA polymerase IV (DinB) in generating ciprofloxacin-resistance mutations in stationary phase bacterial cells was investigated. The overall numbers of ciprofloxacin resistant (Cip^R) mutants able to be recovered under conditions of selection were greatly reduced when the bacterial cells concerned carried a defective *dinB* gene. Importantly, the yields of Cip^R mutations recovered in *dinB*-defective cells could be elevated to levels approaching wild-type when they were supplied with the *dinB* gene on a low-medium copy number plasmid, but not when they were made to overexpress either of the SOS-response *recA* or *imuC* (DNA polymerase ImuC) genes; in turn, suggesting that DNA polymerase IV is one of the main SOS regulated error-prone polymerases responsible for generating ciprofloxacin-resistance mutations in stationary phase *P. aeruginosa* cells. In addition, the full operation of the DNA polymerase IV-dependent mutation generation pathway in part at least required sufficient cellular levels of the bacterial general stress response sigma factor σ^s, RpoS. Collectively, these data improve our understanding of the cellular processes likely controlling the expression of the DNA polymerase IV (DinB)-dependent mutation generation pathway operating in stationary phase *P. aeruginosa* cells and highlight possible cellular targets for therapeutic intervention.

Victoria

The stability of the short-beaked echidna's microbiome through gestation

Isni Buthgamuwa, Ashley Dungan and Linda Blackall

The School of BioSciences, University of Melbourne, Melbourne, Victoria, Australia

Abstract: The short-beaked echidna, *Tachyglossus aculeatus*, is a cherished and iconic native Australian animal and is one of five currently existing monotremes. Having diverged from Eutherian/placental mammals roughly 184 million years ago, monotremes have evolved unique reproductive strategies, specifically egg laying. The composition of the gut microbiota of female mammals is quite important, as it provides an opportunity for vertical transmission of microbes to offspring as well as maintaining foetus health. Very little is known about the composition and role of the echidna microbiome, hence, this study aims to characterise the gut microbiome of female short-beaked echidnas and gain better understanding of the changes that may occur in their microbiome as they go through pregnancy. Faecal samples from four female and five male echidnas were obtained from the Currumbin Wildlife Sanctuary and underwent DNA extraction, with the V4-V5 region of the bacterial *16S* rRNA gene amplified for metabarcoding. While some bacteria were unique to sections of the gestation cycle, overall, the bacterial community composition was not significantly different between reproductive stages. Furthermore, the study is the first to describe the microbiome composition of both female and male echidnas.

Harnessing experimental evolution for bacteriophage therapy of *Enterobacter cloacae* complex infections

Rylee A. Deehan and Jeremy J. Barr

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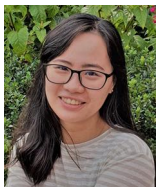
Abstract: Antibiotic resistance is arguably the greatest public health challenge of the 21st century. Immediate action is required to overcome this challenge. Bacteriophages (phages) are viruses that kill bacteria. The therapeutic use of phages, known as bacteriophage therapy, could be crucial in combatting antibiotic-resistant bacterial pathogens. However, a major issue is phages are often poorly adapted to clinical

bacterial isolates. Fortunately, experimental evolution can improve therapeutic phages. Here, I experimentally evolved two ancestral phages against eight clinical antibiotic-resistant *Enterobacter cloacae* complex strains to produce novel evolved phages with enhanced killing efficiencies. Bacterial growth curves and derived phage scores, which range from 0 (no reduction in bacterial growth) to 1 (full reduction in bacterial growth), were completed to assess the phage's killing efficiencies. Six of the 16 evolved phages had between 1.3 and 4.3-fold increase in their killing efficiency on their evolution host when compared with the ancestral phage. Additionally, one of the evolved phages gained the ability to effectively kill its evolution host, with a phage score of 0.76 compared with 0 for the ancestral phage. Going forward, enhancing the killing efficiency of therapeutic phages via harnessing experimental evolution may be key to the enduring success of bacteriophage therapy.

Investigating the mechanisms of H_2 production and consumption in the human gastrointestinal tract



Nhu Doan, Caitlin Welsh, Rachael Lappan and Chris Greening

Department of Microbiology, Monash Biomedicine Discovery Institute, Monash University, Melbourne, Victoria, Australia

Abstract: Hydrogen gas in the human gastrointestinal tract (GIT) is exclusively produced by the gut microbiota. Given that H_2 gas is linked with a variety of human disorders, our current understanding of H_2 cycling is limited. Therefore, this study aims to investigate the hydrogenogenic activity of human GIT bacteria that contain the Group B [FeFe]-hydrogenase. Recent research, based on sequence and phylogeny similarities to the Group A1 [FeFe]-hydrogenase, has predicted that the Group B [FeFe]-hydrogenase may play a hydrogenogenic role in the GIT; however, there is currently no experimental evidence to confirm this prediction. Seven *Bacteroides* species were tested for their H_2 production capability, in which all species produced large amounts of H_2, providing support that the Group B [FeFe]-hydrogenase is responsible. Additionally, *Bacteroides caccae* and *Bacteroides faecis* showed significant declines in H_2 concentration from day 2 of growth. This finding suggests that the Group B [FeFe]-hydrogenase may operate in a reversible manner, depending on the availability of organic sources.

Inhibiting *Clostridioides difficile* PBPx mediated resistance to sporulation inhibition

Desirel Ng, Yogitha N. Srikhanta and Dena Lyras

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Abstract: *Clostridioides difficile* infection (CDI) is the leading cause of nosocomial diarrhoea worldwide and is perpetuated by *C. difficile* spores; however, no cost-effective treatments target spores. Our previous work showed that the β-lactam cephalosporin, cefotetan, can reduce *C. difficile* sporulation by inhibiting the spore penicillin-binding protein (spore-PBP), *Cd*SpoVD, which is essential for spore peptidoglycan synthesis. However, some *C. difficile* animal isolates have acquired an accessory spore-PBP, PBPx, which maintains sporulation in the presence of cefotetan, highlighting the need for strategies that can also target PBPx+ strains. Here, we determined if the PBP inhibitor, DN1, could block the activity of PBPx and reduce sporulation in the PBPx+ animal isolate, *Cd*As, by performing sporulation assays and identifying its PBP targets using PBP profiles. DN1 was found to reduce spore numbers completely on day 1 and by 2150-fold on day 2 by targeting cefotetan-induced PBPx. These results suggest that DN1 may be a viable route to expanding our anti-sporulation strategy to *C. difficile* PBPx+ strains and potentially improve CDI treatment by reducing spores.

Western Australia

An investigation into the prevalence of commensal *Neisseria* spp. and the co-carriage of commensal *Neisseria* spp. with *N. meningitidis* and *N. gonorrhoeae*

Emma Catchpole, August Mikucki and Charlene Kahler

The Marshal Center for Infectious Disease Research and Training, School of Biomedical Science, University of Western Australia, Perth, Western Australia, Australia

Abstract: The *Neisseria* genus is comprised of 10 species capable of inhabiting human mucosal surfaces. Two of these species are pathogenic: *N. meningitidis*, which causes invasive meningococcal disease in susceptible patients, and *N. gonorrhoea*, which causes the sexually transmitted disease gonorrhoea. The remaining eight species are considered commensal. In recent years, studies have suggested commensal *Neisseria* species may have an inhibitory effect on the pathogenic species. This study used qPCR to investigate the carriage of commensal and pathogenic *Neisseria* species in oropharyngeal samples collected in a previous study in the Pilbara, Western Australia. The results indicate co-carriage of both *N. meningitidis* and *N. gonorrhoea* with commensal *N. mucosa* and *N. subflava*. Validation of the primers used, and the early design of a *N. lactamica*-specific primer was also carried out, which highlighted the challenges of creating commensal species-specific qPCR primers. This study provides exciting early insight into the prevalence of commensal *Neisseria* species and also the relationship between commensal and pathogenic *Neisseria* species.

Does the stringent response prime mobile genetic elements for horizontal gene transfer?

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Abstract: Integrative and conjugative elements (ICEs) are a type of mobile genetic element that allow the transfer of nitrogen-fixation capability from *Mezorhizobium* sp. to non-symbiotic soil bacteria. In *M. japonicum* strain R7A, ICE*Ml*Sym^{R7A} normally has a low rate of horizontal transfer. However, ICE*Ml*Sym^{R7A} can stimulate epigenetic differentiation of R7A cells into a subpopulation termed R7A*, which exhibits enhanced ICE conjugation and is activated for quorum sensing and production of N-acyl homoserine lactones (AHLs). Details concerning the induction and maintenance of this state remain unclear, though RNA sequencing of R7A* cells has revealed downregulation of numerous ribosomal subunit genes, potentially implicating the amino acid starvation-triggered 'stringent response'. In this study, we investigated a potential role of the stringent response in R7A* differentiation by constructing mutations in the (p)ppGpp synthetase/hydrolase gene *spoT*. Deletion of *spoT* could not be achieved, suggesting the gene may be essential in *M. japonicum*. However, an insertion mutation in a *spoT* regulatory domain exhibited decreased AHL synthesis, suggesting the stringent response is at least indirectly involved in maintenance of the R7A* state. We also established that R7A* differentiation could not be stimulated by paraquat-induced oxidative stress or by the ribosome-inhibiting antibiotic kasugamycin.

Adapting nasopharyngeal bacteria to synthetic nasal medium

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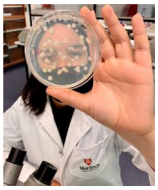
Marshall Centre for Infectious Diseases Research and Training at The University of Western Australia, Perth, Western Australia, Australia

Abstract: The nasopharyngeal environment supports a diverse community of microorganisms. Maturation of the bacterial microbiome of the nasopharynx over the first year of life is characterised by succession of different bacterial taxa, and aberrant maturation has shown to negatively affect respiratory health in children. The objective of this study was to use synthetic nasal medium (SNM) to mimic the nasopharyngeal environment and to grow nasopharyngeal bacteria in this medium. Bacterial strains cultured from nasopharyngeal swabs of infants were successfully adapted to and propagated in SNM. Colony forming unit (CFU) fold changes after growth in SNM were nearly 500-fold for *Staphylococcus epidermidis* and over 7000-fold for *Staphylococcus aureus* after 40 h. Growth of *Moraxella catarrhalis, Moraxella osloensis, Moraxella lincolnii, Corynebacterium propinquum* and *Haemophilus influenzae* in SNM was substantially slower. This study highlights that SNM, which was originally developed to mimic the metabolic environment of the anterior nares, is well-suited to support growth of Staphylococci but may need further adaptation to better simulate the nasopharyngeal environment and support optimal growth of other members of the nasopharyngeal flora.

Production of the keto-carotenoid astaxanthin in *Dunaliella salina* via heterologous expression of codon-optimised β-carotene hydroxylase and ketolase



Crystal Young[A], Navid Moheimani[B], Damian Laird[B] and Wayne Reeve[A]

[A]Bioplastic Innovation Hub, Food Futures Institute, Murdoch University, Perth, Western Australia, Australia
[B]Centre for Water Energy and Waste, Harry Butler Institute, Perth, Western Australia, Australia

Abstract: Astaxanthin, a highly valuable keto-carotenoid antioxidant, is currently produced in *Haematococcus lacustris,* but production is limited by β-carotene precursor availability. In contrast, *Dunaliella salina* produces the highest amount of β-carotene but cannot naturally produce astaxanthin. Here, we report the development of a chloroplast integration vector to express *H. lacustris* β-carotene ketolase (Brt) and hydroxylase (CrtZ) astaxanthin biosynthetic enzymes in *D. salina*. *D. salina* (MUR08) was isolated from Rottnest Island, Western Australia and used as a photosynthetic chassis for vector integration. MUR08 was unable grow on the surface of solid laboratory media but this was rectified using Ramaraj Media containing 15% glycerol overlaid with seeded agar overlays or by spreading cells over cellulose nitrate filter papers overlays. The growth of MUR08 enabled the *brt-crtZ* genes to be integrated into the chloroplast using microparticle bombardment. The work described provides an important foundation to deliver novel heterologous genes into a defined locus in the chloroplast genome of *D. salina* without disrupting cell growth.

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EduCon 2022 report

Thiru Vanniasinkam

EduCon 2022 was held in Sydney at the NSW Teachers Federation Conference Centre on 15 July, and was organised by a team comprising Thiru Vanniasinkam (Convenor), Megan Lloyd (Past Convenor), Meredith Hughes, Priscilla Johanesen, İpek Kurtböke, Rebecca LeBard, Megan Lenardon, Senaka Ranadheera and Gal Winter. The conference was attended by a small group of enthusiastic and committed educators.

Meredith Hughes as the 2021 David White Teaching Award winner gave a presentation on designing authentic assessments in microbiology, providing useful examples that attendees could use to develop assessments in courses they teach. The keynote presentation was on Promise and Practice of the inclusive given by a leading researcher in this area, Dr Bryan Dewsbury (Florida International University, USA). The talk was highly relevant to all participants as the presenter shared his experiences teaching a culturally diverse classroom with a large of number of students from low socioeconomic backgrounds.

There were two workshops. One was a 'back to basics' workshop run by a team from Charles Sturt University (Wouter Kalle, Thiru Vanniasinkam and Kerry Hicks) looking at learning outcomes in the context of a novel model of course delivery to a diverse student cohort. The other workshop delivered by Nick Andronicus from UNE looked at animation in teaching. Participants used Adobe Captivate to build a lesson in the workshop, with Nick's expert advice.

Four oral presentations were included in the program. Lara Grollo from The University of Melbourne shared her experiences on using COVID-19 as a 'teaching moment', while Daniel Clark (The University of Melbourne) gave an interesting presentation on innovation in the parasitology class. Graça Carvalho and Nelson Lima (from the University of Minho, Portugal) shared their perspective on transposition of science knowledge to school teaching. Petra Czarniak (Curtin University) talked about the importance of simulation-based education in the context of treating infectious diseases.

There were six posters presented on a range of interesting topics, many of these stemming from experiences teaching during the COVID-19 pandemic. Poster topics (and presenters) included infection and immunity using craft materials (Charmaine Lloyd, Swinburne Institute of Technology), microbiology capstone projects (Senaka Ranadheera, The University of Melbourne), authentic student-led research projects (Brianna Steed, The University of Melbourne), strategies for online student engagement (Lana Ly, University of New South Wales), authentic scenarios in microbiology education at home (Gal Winter, University of New England) and self-regulated learning (Nathan Higgins, Monash University).

The final session was a roundtable discussion led by İpek Kurtböke from the University of the Sunshine Coast on teaching microbiology for achieving sustainable development goals. This session gave participants the opportunity to share their ideas on microbiology education and was a great way to end the conference.

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Microbiology AUSTRALIA

Gurindji termite project

Gregory Crocetti and Briony Barr

Scale Free Network: art-science collective

Readers of *Microbiology Australia* might be aware of the Small Friends Books series, created by Scale Free Network with support from the Australian Society for Microbiology and published by CSIRO Publishing. The series was sparked by a series of conversations with Professor Linda Blackall in 2013, where we developed the idea to counteract common negative perceptions about microbes by creating stories that describe mutualistic partnerships between microbes and larger life forms. Together with Linda, writer Ailsa Wild and illustrator Aviva Reed, we created our first book, *The Squid, the Vibrio & the Moon*, about the symbiotic partnership between bobtail squid and bioluminescent *Aliivibrio fischeri* bacteria. This was followed by stories describing: microbial interactions within coral polyps (and what happens when coral bleaches); how some soil nematodes partner with bacteria to infect and kill insects; and how plants work together with networks of mycorrhizal fungi and bacteria to create a healthy soil environment around their roots. In each case, we collaborated with scientific experts to ensure scientific accuracy, as well as create an engaging story with beautiful artwork.

After releasing the fourth and final title in the Small Friends Books series in mid-2020, we turned our creative attention to symbiotic microbes living in the termite hindgut. Our interest in termite gut symbionts started where you might expect, with the protozoan *Mixotricha paradoxa* (first described by 1933 University of Melbourne researcher Jean L. Sutherland), and later beautifully depicted by Lynn Margulis and Dorion Sagan:

> Scrutinizing any organism at the microscopic level is like moving ever closer to a pointillist painting by Georges Seurat: The seemingly solid figures of humans, dogs, and trees, on close inspection, turn out to be made up of innumerable tiny dots and dashes, each with its own attributes of colour, density, and form.

However, the exquisite *Mixotricha* (together with their endo- and ecto-symbionts) and their host *Mastotermes darwiniensis* were not to feature in our termite picture book. Because unlike our previous books – where we chose the symbiotic partnership and then collaborated closely with relevant (Western) scientific experts – with this project, we wanted to find different ways of working and collaborate with First Nations experts (particularly elders, rangers and artists), in the hope of drawing on and sharing their own ecological knowledge about termites, developed over millennia.

The first challenge was to find where this knowledge was still active. Over a period of several years, we kept a keen eye out for mention of termites in children's books, contemporary literature or scientific articles and in early 2020 found the book, *Karu: Growing up Gurindji* (by Violet Wadrill, Biddy Wavehill Yamawurr, Topsy Dodd Ngarnjal and Felicity Meakins; Spinifex Press, 2019). The book describes the child-rearing practices of Gurindji women, which includes using termite mound (*tamarra*, roughly pronounced *DAH-mar-ra*) for a range of medicinal (bush medicine) reasons: ingested in a mix to treat diarrhoea; rubbed over mammary glands to promote lactation; or smothered over babies to help strengthen their blood, bones and spirit (particularly to help close the fontanelle; Fig. 1).

For some context: the Gurindji people are based in remote central-western Northern Territory, on the Northern edge of the Tanami desert. Gurindji elders led the Wave Hill Walk-Off in 1966 (protesting against mistreatment by the station managers), which helped to start Australia's Land Rights movement. Kev Carmody and Paul Kelly captured elements of this story in their iconic song, *From Little Things, Big Things Grow*.

Through conversations with Professor Felicity Meakins (linguist with the School of Languages & Culture, UQ) and Penny Smith (manager of Karungkarni [Gurindji] Art & Culture Centre), we developed a broad approach to meet, listen and learn from local Gurindji elders, cultural custodians, rangers, artists and of course… termites. Through further conversations with Gurindji elders, Penny and Felicity refined the proposal and gained the necessary consent and permissions for our project to go ahead and we started planning the 5000 km drive up from Melbourne.

Upon arriving in Gurindji Country, we had a lot of questions: *Which termites were most important? What was special about them? How would we work with Gurindji and other First Nations artists and knowledge keepers to create a collaborative methodology? What languages would the story be told in? Where would the story artwork come from?*

Over the subsequent 4 months we delivered workshops across all year levels at the local school (in English and Gurindji Kriol; Fig. 2); went on several trips out onto Country with Gurindji elders and rangers; and collaborated

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(*a*) (*b*)

Fig. 1. (*a*) A Gurindji baby is treated with termite mound. (*b*) Karu Kamparnup (treating baby with termite mound) by Lucy Tanami.

Fig. 2. Cecelia Edwards and Gregory Crocetti introducing termites to students at Kalkaringi School.

with local artists to develop termite-inspired artwork. During our visits on Country with elders, we encountered a lot of spinifex (*Triodia*) grasses around the termite mounds preferred for use in Gurindji bush medicine. Close-up microscopy of these termites (with help from Professor Theo Evans, UWA) revealed them to be the Spinifex termite (*Nasutitermes triodiae*). Identifying this species of termite then led us into conversation with Professor Phil Hugenholtz, who had previously explored their gut microbiome at the Australian Centre for Ecogenomics (UQ), and helped us simplify the main digestive processes for the purposes of our picturebook.

Across this period, we were incredibly privileged to work closely with a large group of (mostly Gurindji) First Nation collaborators, including: artists and cultural custodians Violet Wadrill, Topsy Dodd and Leah Leaman; artists Lucy Tanami, Rosemary Johnson and Cecelia Edwards; and language worker Cassandra Algy. We were also fortunate to receive a grant from the Australia Council for the Arts to financially support our project, which also allows us to direct all of the future royalties from this book back to our Gurindji collaborators through the art centre.

The manuscript that emerged was written in a combination of Gurindji, Gurindji Kriol and English. The story was inspired by the web of ecological and cultural relationships

Fig. 3. Microbes breaking down spinifex grass fragments in the termite hindgut by Briony Barr, Joanne Stevens, Margaret Winbye and year 2/3/4 students.

around termites and termite mounds; from their symbiotic partnerships with gut bacteria and spinifex grasses (Fig. 3) to their connections to Gurindji people as a source of food and an important bush medicine. We are happy to report that our manuscript has just been accepted for publication by Hardie Grant, and is scheduled for release in July 2023.

Before our adventure, we understood the importance of openness and reciprocity in working with First Nations collaborators. However, through this journey, we learned a lot about putting these values into practice and about how incredibly important it is to first listen to and learn from people's needs and wants…before trying to impose our ideas or agendas. These and other principles are explained in the recently published *True Tracks: Respecting Indigenous knowledge and culture* (UNSW Press), written by Meriam/Wuthathi lawyer Terri Janke – a fantastic resource to consult if you have the opportunity to work with First Nation people – with specific chapters covering scientific and research collaborations.

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Microbiology AUSTRALIA

Vale Professor Ruth Frances Bishop AC 1933–2022

Celeste M. Donato, Graeme Barnes and Julie E. Bines[#]

Professor Ruth Bishop is known nationally and globally as one of the co-discovers of rotavirus – an immeasurable contribution to global child health and microbiology.

Ruth graduated with a Bachelor of Science (1954), followed by a Master of Science (1958), PhD (1961), and a Doctor of Science (1978); all from the University of Melbourne. She was also awarded a prestigious Honorary Fellowship from the Royal Australasian College of Physicians (2008) and an Honorary Doctorate of Medical Science (2010) from the University of Melbourne. Ruth had a longstanding involvement with the Australian Society for Microbiology, becoming a member in 1978, a Fellow (1989), and was awarded an Honorary Life Membership (2008).

In the early 1970s, Dr Rudge Townley, Director of Gastroenterology at the Royal Children's Hospital (RCH), persuaded Ruth to focus on acute diarrhoea. At the time paediatric gastroenteritis was a significant cause of mortality globally and the aetiological agent was often unknown. For 2 years Ruth meticulously analysed intestinal specimens taken from infants with gastroenteritis at the RCH. No conclusive bacterial cause could be determined but severe damage was found in the duodenum. Ruth began to suspect a virus may be involved and in 1973 intestinal biopsies were sent to the University of Melbourne to be examined by electron microscopy. Virus particles were observed in the first sample examined.

The discovery of rotavirus by Ruth and her colleagues Geoffrey Davidson, Ian Holmes, and Brian Ruck changed global child health. Rotavirus was ultimately found to be the leading cause of acute gastroenteritis in children worldwide, with almost every child experiencing an infection in the first years of life. In children aged <5 years, rotavirus caused 114 million episodes of diarrhoea annually worldwide, resulting in an estimated 453 000 deaths. There are several licensed rotavirus vaccines that are included in national immunisation programs in over 112 countries worldwide and the burden of rotavirus disease has greatly diminished. However, challenges remain in providing vaccines to the most vulnerable children in low- and middle-income countries. Ruth also made a substantial contribution in addressing these challenges when her studies revealed newborns in Melbourne obstetric hospitals were asymptomatically excreting a unique rotavirus strain. The RV3 vaccine program emerged from follow-up studies that revealed these children were protected against subsequent community outbreaks of rotavirus. Decades of work by Ruth and a global team of colleagues has led to successful clinical trials of the RV3-BB vaccine in New Zealand, Indonesia, and Malawi.

Ruth had extensive involvement with the WHO, including roles as Chair of the Steering Committee on Viral Diarrhoeal Diseases, Director of the WHO Regional Collaborating Rotavirus Laboratory and Special Adviser to the WHO Vaccine Development Program. As leader of a dynamic research team at the Murdoch Children's Research Institute (MCRI) for many years, Ruth set an enduring tone of global collaboration and a supportive environment.

Following her retirement in 2009, Ruth continued to play an active role in rotavirus research at MCRI, joining the weekly lab meetings until her health declined in 2015. She was immensely proud of all the students she supervised and mentored over her career, many of whom have gone on to become leaders in their respective fields. Her passion for the education of women and advocacy for women in STEMM was enduring and she actively encouraged many of her female staff to pursue higher education in the form of MD and PhD degrees.

An extensive array of national and international honours were bestowed on Ruth during her career, including the University of Melbourne Selwyn-Smith Prize for Clinical Research (1978), the Clunies Ross National Science and Technology Award (1998) and the Children's Vaccine Initiative Award (WHO Geneva 1998). Ruth was awarded the Prince Mahidol Award in the Field of Public Health presented by the Thai Royal Family (2011) and became the first woman to be awarded the Florey Medal (2013). In 1996, she was made an Officer of the Order of Australia and in 2019 was promoted to the highest national honour, Companion of the Order of Australia (AC), in recognition of her service to global child health and to medical research. Of particular note, Bill and Melinda Gates cited Ruth as a major influence in their establishment of their global health foundation.

Ruth leaves behind an incredible legacy, not only for her scientific discoveries and achievements, but in the numerous scientists and clinicians around the world whom she taught, mentored, and inspired.

[#]This tribute was written on behalf of former friends, staff and colleagues who generously shared many wonderful memories of their time with Ruth.

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ASM Ambassadors:
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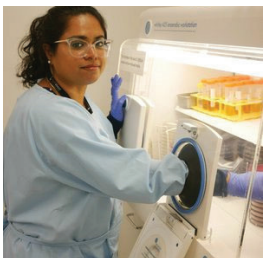

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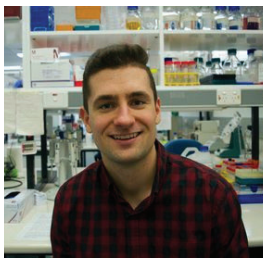

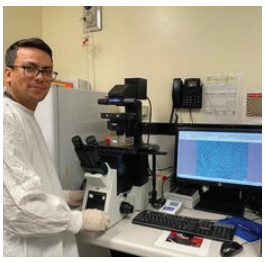

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Australian Microbial Ecology Conference

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