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Biographies

Jeff Warner is an Associate Professor, Microbiology at James Cook university, Townsville. He has worked and conducted research in rural Papua New Guinea for almost 30 years and these experiences have helped shape his teaching and research interests. While he still has air in his lungs he will continue to prosecute the value of classical, descriptive microbiology because he believes these skills are still important in the rural laboratory workforce and provide valuable support to rural communities (he admits, maybe he is just old?). Jeff and Cathy Rush lead a research group of like-minded and keen students and researchers focusing infectious disease issues relevant to the tropics, including melioidosis and tuberculosis in PNG.

Cathy Rush is A/Professor of Immunology at James Cook University, Townsville. Cathy has worked in microbiology and immunology both here and overseas where she has been committed to unravelling the mysteries of the host immune response in terms of host-pathogen interactions, vaccinology and T-cell biology. Cathy has expertise in the immunobiology of tropical infectious diseases and is currently researching host susceptibility to tuberculosis and drug resistance development.

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Meningococcal surveillance in Southeast Asia and the Pacific

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Abstract. Meningococcal disease is an uncommon infection associated with high case fatality rates, especially in some low resource countries. The burden of meningococcal disease in the Asia Pacific region is relatively low although likely to be underreported. Carriage rates of the causative bacteria, *Neisseria meningitidis* are also lower than in many other countries, with those of Asian ethnicity having a lower carriage prevalence than other ethnicities. There is a large degree of variability in establishment of infectious disease surveillance and case definitions used across Southeast Asia and Pacific nations. Although disease surveillance is a critically important component of disease control, not all countries mandate reporting of meningococcal disease and many do not have molecular typing capability. Adequate surveillance must include serogroup distribution and disease burden estimation. Improving surveillance capability and transfer to a more active surveillance model with capacity for PCR and genome sequencing will be important for early detection of outbreaks in the future.

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Invasive meningococcal disease

Neisseria meningitidis is the cause of invasive meningococcal disease (IMD) and considered an opportunistic pathogen[1]. *N. meningitidis* colonises the pharyngeal mucosa with highest carriage prevalence in adolescents and young adults, likely due to higher rates of transmission through social and intimate interactions[2]. Rates of colonisation differ in different ethnic groups with

prevalence of carriage of *N. meningitidis* lowest in Asian people[2]. There are 12 different meningococcal serogroups (A, B, C, E, H, I, K, L, X, W, Y and Z) with possession of a capsule the key factor enabling survival of the bacteria within the blood stream resulting in the clinical manifestation of septicaemia and/or meningitis. Serogroups A, B, C, W, X and Y are the most common cause of IMD around the world. There are approximately 1.2 million cases of IMD annually worldwide[3] with case fatality rates (CFR) between 7–13% dependent on serogroup[4]. The highest age-specific incidence rates occur in young children and adolescents[5]. Up to 40% of survivors experience significant complications leading to life-long disability including loss of limbs due to ischaemia and gangrene, deafness, blindness and brain injury[6,7]. Real-time PCR to determine the genogroup is the basis of detection in high income countries whereas in low resource countries molecular diagnostic capability may be lacking with higher dependence confirmation by culture of the organism from a sterile site[8].

Surveillance of invasive meningococcal disease

To control IMD, adequate surveillance is of critical importance. Robust surveillance programs for outbreak detection must include accurate disease burden and incidence estimates and confirmation of causative organism including serogroup or genogroup determination by culture or polymerase chain reaction (PCR)[8]. Active surveillance is more likely to provide accurate estimates than passive reporting mechanisms with both mechanisms being used across the East-Asia Pacific region. Cost, resources, expertise and infrastructure are necessary considerations for all countries, in their ability to accurately describe the disease burden and potential for outbreaks in their communities. A large variation exists in surveillance methods applied across Southeast Asia and the Pacific making comparisons of incidence in IMD challenging. In some Southeast Asia countries such as Indonesia and Malaysia, surveillance is largely limited to those attending pilgrimage or mass gathering in another country (i.e. pilgrims travelling to the Kingdom of Saudi Arabia for the Hajj or Umrah)[9].

Many countries do not have an active laboratory-based surveillance system in place making ascertainment of true IMD burden and comparisons across different countries difficult[3]. Although reporting of IMD tends to be lower in Southeast Asia compared to Australia and New Zealand there is likely to be a number of factors influencing this rather than a true low incidence. There is substantial heterogeneity with regard to case definitions for meningococcal disease amongst these nations[9]. The use of varying case definitions limits the comparability of the surveillance between different countries in the region. Under reporting is likely due to differences in and employment of narrow case definitions for reporting, inconsistent diagnostic testing practices and most importantly the passive reporting systems in place which are common across the Asia-Pacific region[7,8]. Although not readily available across the region, PCR is an important diagnostic tool in diagnosing suspected cases, especially when culture specimens are negative for viable *N. meningitidis.*

In Australia, New Zealand, the Philippines, Singapore and Vietnam IMD is nationally notifiable. In Australia, meningococcal disease surveillance is coordinated through the National Neisseria Network (NNN) with all laboratory cases reported to the National Notifiable Disease Surveillance System[10]. Positive samples detected by PCR or culture and when an isolate is available, are sent for whole genome sequencing (WGS), with this capacity for sequencing available now in most states. This enables nuanced contact tracing and ability to distinguish between cases and any cluster during outbreaks. Genomics can be used to better understand the changing epidemiology of meningococcal disease and was used to identify the causative serogroup in several unusual cases of IMD in Queensland, surprisingly due to serogroup E[11]. In New Zealand all cases are referred to the Meningococcal Reference Laboratory at the Institute of Environmental Science and Research (ESR) for routine grouping using slide agglutination or PCR[12]. In the Philippines and Singapore, probable and laboratory-confirmed cases of IMD are reported to Philippine Integrated Disease Surveillance Response (PIDSR) System and the Singapore Ministry of Health[13].

Epidemiology of meningococcal disease

The incidence of IMD is generally low and similar across the East-Asia Pacific region, ranging from around 0.02/100 000 (Philippines) to 1.5/100 000 (Australia) where data is available[9,14]. In Australia and New Zealand notification rates are higher than in other countries in the region. Serogroup B is the predominant serogroup causing disease across East-Asia and the Pacific, followed in frequency by serogroups W and Y. Serogroup W has most recently caused epidemics in Australia and New Zealand following epidemics in the UK and South America due to the hypervirulent cc-ST11[15]. Serogroup W was also identified in 16.7% of IMD cases in the Philippines in 2018[9]. CFR differ across the East-Asia and Pacific region, with high rates in young children in the Philippines with a CFR ≥50% and in Thailand at around 40%[9]. Countries with publicly available surveillance data are included below.

Australia

IMD epidemiology in Australia reflects the epidemiology in other high-income countries particularly Europe with serogroup B predominating. The overall CFR is around 5% in Australia[16,17]. IMD due to MenW:cc11 was associated with a higher CFR of 10.7% during the recent outbreak. During this outbreak notification rates peaked at 13/100,000 in Aboriginal and Torres Strait Islander

children with highest rates in Central Australia[18]. Due to the widespread MenW:cc11 outbreak in 2016-2018, Australia introduced a MenACWY conjugate vaccine program for infants and adolescents. Notification rates continue to be higher in Aboriginal and Torres Strait Islander children and are 6 times higher than for non-Indigenous children, for serogroup B. For this reason, Aboriginal and Torres Strait Islander infants up to 2 years of age receive meningococcal B vaccine through the National Immunisation Program. Social distancing and lockdown strategies have seen large reductions in the incidence of IMD across Australia, however serogroup B continues to be the predominant strain causing disease[19]. There is significant diversity in serogroups predominating across different states with serogroup W responsible for most recent cases in Western Australia and serogroup B predominating across most other states and territories. Even within serogroup B there is genetic diversity between states[20]. In South Australia, which over the past decade has had the highest notification rate of IMD amongst the mainland states, and highest proportion due to cc41/44, a state funded meningococcal B vaccine program was introduced for all infants from October 2018 and for adolescents from 2019[5]. Continuation of this program indefinitely, was recently announced due to its high effectiveness in significantly reducing IMD in these age groups and also showing vaccine effectiveness against gonococcal infections in adolescents, supporting findings from New Zealand[21,22].

New Zealand

The incidence of meningococcal disease in New Zealand was 2.8/100 000 overall and 52/100 000 in <1 year olds in 2019[22]. Serogroup B has been the predominating serogroup in New Zealand over the past decades. In response to a cc41/44 epidemic which occurred from 2000–2007, a meningococcal B strain-specific OMV vaccine was developed and implemented nationally from 2004-2008[23]. Rates of IMD fell from 17.4/100 000 to 1.2/100 000 and the program was ceased. Although IMD incidence has been increasing since 2014, no meningococcal vaccine has been included in the national immunisation program although meningococcal vaccines are recommended for high-risk groups[22].

Singapore

IMD incidence is 0.2/100 000 overall and 1.6/100 000 in young infants (0–4 years). Serogroup B has been the predominant serogroup among IMD cases[9].

The Philippines

IMD incidence in the Philippines is 0.02–0.1/100 000 with a very high CFR in children of ≥50%. Serogroup B predominates, causing 68% of cases between 2017–1018[9].

Thailand

IMD incidence is 0.04/100 000 with serogroup B the most common cause of cases with a CFR of 37.5% in 2012[24].

Vietnam

Serogroup C has historically been the main cause of outbreaks with serogroup B the predominant serogroup since 2012[9].

There are no national data on IMD notifications in Brunei, Cambodia, East Timor, Fiji, Kiribati, Laos, Marshall Islands, Micronesia, Nauru, Niue, Palau, Papua New Guinea, Samoa, Solomon Islands, Tonga, Tuvalu, or Vanuatu. There are no national meningococcal vaccines programs in any countries in South-East Asia and variability in the types of meningococcal vaccinations available. Several countries recommend meningococcal vaccines only for high-risk groups, mainly due to low incidence of disease.

Future of meningococcal surveillance

The risk and disease burden across East-Asia and the Pacific is relatively low with the current surveillance systems in place. Monitoring practices vary considerably with some countries not including active reporting of meningococcal disease through national notifiable surveillance programs. An evaluation of current surveillance strategies would be of benefit in guiding future surveillance in the region. Not only is monitoring of *N. meningitidis* cases important, but also the ability to confirm the genogroup/serogroup causing disease. Some but not all countries across East-Asia and the Pacific now have the infrastructure in place for serotyping/genotyping analysis for case confirmation and therefore the ability to identify cluster or emergence of hypervirulent strains.

Of future importance is the opportunity for whole genome sequencing to be incorporated into surveillance systems with the ability to track epidemic strains over time. The potential for expansion of hypervirulent clonal complexes remains a concern, not only for their potential to rapidly cause outbreaks, but also due to the potential of antimicrobial resistance, an ever-present and escalating problem[15]. For smaller and low resource countries this may not be possible but agreements between countries to enable use of WGS facilities could provide a better understanding of the molecular epidemiology in our region and better predict epidemics through detection of hypervirulent strains. Improving surveillance capability and transfer to a more active surveillance model with standardised case definitions improved laboratory capability and matching of epidemiological and laboratory data will be important for early detection of future outbreaks.

Conflicts of interest

HM is an investigator on meningococcal vaccine studies. Her institution has received funding for investigator-led studies sponsored by GSK, Sanofi-Pasteur and Pfizer.

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Biography

Professor Helen Marshall, MBBS DCH MPH MD, is a clinician researcher and National Health and Medical Research Council Practitioner Fellow with specialist training in child health, public health and vaccinology having completed a Bachelor of Medicine and Surgery, Doctorate of Medicine, Master of Public Health and Diploma in Child Health and the Advanced Vaccinology Course at the Pasteur Merieux Institute, France. She holds the position Professor in Vaccinology in the Adelaide Medical School and is the Deputy Director of the Robinson Research Institute at The University of Adelaide, Senior Medical Practitioner and Director of the Vaccinology and Immunology Research Trials Unit, VIRTU, at the Women's and Children's Hospital, South Australia. She is an international leader in vaccines and vaccine preventable diseases particularly meningococcal disease with translation of her research to policy and practice locally, nationally and internationally. In recognition of research excellence she was awarded the National Health and Medical Research Council's '10 of the Best' research projects nationally and the South Australia Science Award for Excellence in Research for the Public Good and South Australia Science Award for Excellence in Research Collaboration. In 2020 she received the Inspiring South Australian Women Award, Australia Day Council, South Australia, and is the 2022 SA Australian of the Year.