An update on the burden of group A streptococcal diseases in Australia and vaccine development

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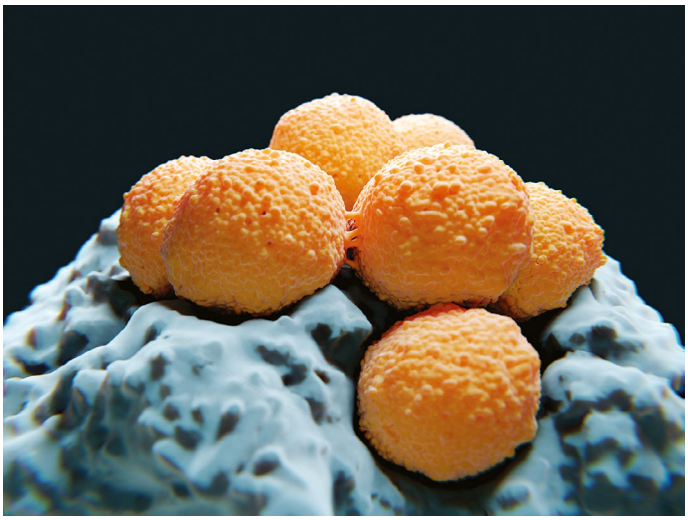
National surveillance would facilitate strategies for preventing or managing conditions that predispose people to severe streptococcal disease

Surveillance of severe diseases caused by group A *Streptococcus* (GAS) is needed in Australia.[1] Data reported in this issue of the *MJA* by Wright and colleagues[2] — the first from Western Australia — are timely, as the Australian government is considering recommendations to include invasive group A streptococcal diseases (iGAS) on the National Notifiable Diseases List. iGAS is a subset of the broad range of diseases caused by GAS, from superficial disorders (pharyngitis, impetigo) to invasive (sepsis, necrotising fasciitis, cellulitis, toxic shock syndrome) and autoimmune conditions (acute rheumatic fever, rheumatic heart disease, acute post-streptococcal glomerulonephritis). In Australia, GAS caused more than 750 000 health care episodes per year during 2005–2015, or 3.4 episodes/100 person-years for all GAS diseases, including 4.1 episodes/100 000 person-years caused by iGAS.[3] The estimated health care-related cost of GAS diseases was $185 million per year, making vaccination an economically viable prevention strategy.[3]

Wright and his colleagues offer new and important insights into the iGAS burden.[2] They found that its incidence increased between 2000 and 2018 among both Indigenous and non-Indigenous Australians, with an annual mean increase of 9% and peaking at 9.1 cases/100 000 person-years in 2017. The authors noted that incidence was greatest in the very young (first year of life) and among the old (over 74 years of age). An increase in iGAS incidence, as well as higher rates among the very young and very old, were also recently reported for Victoria.[4] However, the Victorian analyses were based on voluntarily submitted data, and the level of case ascertainment changed over time. The WA study, in contrast, was based on data from the state-owned pathology provider, together with data on all public and private hospitalisations for GAS-specific invasive disease, resulting in more accurate and consistent case ascertainment across the study period.

Wright and colleagues also found that the burden was greater among Indigenous than non-Indigenous people and, in a possibly related finding, that the incidence was higher in tropical than temperate regions.[2] Despite their analysis including



temperate regions of WA, with lower incidence rates, their reported peak incidence for Indigenous people of 79.9 per 100 000 person-years in 2017 is similar to rates found by other studies in northern Australia.[5,6] Major disparities in burden have also been reported for other GAS diseases; for example, the incidence rate of rheumatic heart disease among Indigenous people under 45 years of age during 2015–2017 was 45.5 cases per 100 000 person-years, almost 50 times higher than for non-Indigenous people.[7] Including iGAS (but not taking acute rheumatic fever and acute post-streptococcal glomerulonephritis into account), the rate of severe GAS disease among middle-aged Indigenous Australians (25–44 years of age) exceeds 100 cases per 100 000 person-years.

Skin infections, particularly impetigo and cellulitis, are key drivers of iGAS. The burden of impetigo for Indigenous children living in remote regions (median prevalence, 45%)[8] is higher than for anywhere else in the world, and in one recent study 75% of all Indigenous people in a remote community presented at least once a year for management of skin infections.[9] Cellulitis rates are also increasing in WA — more rapidly among younger than older adults[10] — and are higher for Indigenous than non-Indigenous people.[10,11] Strategies for reducing the incidence of iGAS must include a renewed focus on healthy skin, in keeping with the National Healthy Skin Guidelines,[12] prophylaxis for household and close contacts,[13] timely diagnosis of GAS pharyngitis by scaling up molecular point-of-care tests[14] (similar to coronavirus disease 2019 testing[15]), and the development of GAS vaccines.

Building on the Trans-Tasman Coalition to Advance New Vaccines for group A Streptococcus (CANVAS) initiative,[16] the Australian government funded the Australian Strep A Vaccine Initiative (ASAVI) in 2019, with the aim of facilitating progress by 2024 to an efficacy trial of a GAS vaccine for preventing pharyngitis.[17,18] Three of the vaccine candidates closest to efficacy

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testing (MJ8CombiVax, P*17, Combo5) are being developed in Australia.[19-21] Overseas, the Wellcome Trust funded the Strep A Vaccine Global Consortium (SAVAC) in 2019 to undertake non-laboratory elements of vaccine research and development, examine the global epidemiology of GAS diseases (including iGAS), develop safety protocols for vaccine trials, investigate factors associated with protection, and prepare investment cases from commercial, public health sector, and societal perspectives.[22]

The increasing burden of iGAS reinforces the need for a vaccine, and the situation can be contrasted with another vaccine-preventable disease that causes sepsis. During 2006–2015, the rate of invasive meningococcal group B disease among Indigenous Australians was 2.8 cases per 100 000 person-years and 0.7 cases per 100 000 person-years among non-Indigenous Australians; the rate of invasive meningococcal disease (all serotypes) peaked at 3.5 cases per 100 000 person-years in 2001, just before routine meningococcal group C vaccination commenced.[23] At its peak, the iGAS burden reported by Wright and his colleagues was more than double that of the much feared invasive meningococcal disease, with similar mortality.[2]

Wright and colleagues provide the analyses needed to better understand the burden of GAS diseases and to develop investment cases for prospective vaccines.[2] iGAS surveillance across Australia is needed, and including acute rheumatic fever/rheumatic heart disease and acute post-streptococcal glomerulonephritis as nationally notifiable diseases would also be appropriate for obtaining a complete picture of GAS burden.[1] Monitoring trends in severe GAS diseases will allow us to investigate, evaluate, and optimise strategies that prevent or manage conditions that predispose people to severe GAS diseases.

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