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## Do neglected Australian arboviruses pose a global epidemic threat?

Narayan Gyawali, <sup>1</sup> Richard S. Bradbury, <sup>1</sup> Andrew W. Taylor-Robinson <sup>1</sup>

1. School of Medical & Applied Sciences, Central Queensland University

Arboviruses (Arbo: ARthropod BOrne) remain a concern for public health in Australia. They are transmitted between their vertebrate nosts by arthropods (mosquitoes, ticks, sandflies and midges). Although more than 75 arboviruses have been identified in Australia, for most there is no information as to whether they infect or cause disease n people.1 Clinically, the most important Australian arboviruses are Ross River, Barmah Forest, Murray Valley encephalitis and West vile (Kunjin strain).2 However, several other irboviruses that are indigenous to Australia also infect humans, including notably (okobera, Stratford, Alfuy and Edge Hill virus.<sup>2</sup> symptoms of infection are similar to those produced by Zika virus, a mosquito-borne lavivirus discovered in East Africa in the 950s but which recently was proposed as he probable causative agent involved in housands of cases of microcephaly in Brazil ind associated with an ongoing epidemic n Latin American and Caribbean countries.3 This virus was hitherto seen as being of little :linical or public health importance, causing 'ery few, often asymptomatic, cases with mited fever, muscle pain, conjunctivitis, eye pain and sometimes maculopapular rash,3

he emergence of Zika in new regions of the vorld may have been enabled by climate onditions suitable to support the population prowth of its transmitting vectors4 - Aedes pecies mosquitoes - over an extended listribution, combined with an escalating nd rapid movement of people globally. he question that might obviously be raised ; do Kokobera, Stratford, Alfuy, Edge Hill r any of the other Australian arboviruses ose a potential threat similar to that of Zika irus for global transmission and epidemic utbreak? Can we foresee a scenario in hich one of these understudied Australian rboviruses could cause a public health event f international concern at either regional or 'anscontinental level?

The opinions expressed in this letter are those of the authors and do not necessarily reflect the policy of he institution for which they work.

Some Australian mosquito species have a range limited to within the immediate Australasian ecozone. Similarly, commonly attributed animal reservoir hosts for Australian arboviruses – kangaroos, wallabies and other macropods - are confined to Australia. Therefore, based on available knowledge of these arboviruses, their vectors and reservoirs, a superficial opinion may suggest that there is less potential for any of the neglected viruses to pose a global threat. However, expansion of the geographical range of mosquitoes is always possible through a combination of urbanisation, climate change and inadvertent human-assisted dispersal. Furthermore, there has been negligible research on vector competence most of these viruses and the true range of potential mosquito vector species may be wider than presumed. The involvement of migratory birds in the transmission cycle of some Australian arboviruses (Alfuy, Kunjin and Murray Valley encephalitis) allows the potential for spread beyond the region.5 Transmission by infected travellers may cause Australian arbovirus outbreaks outside the nation, as was experienced in the Ross River epidemic in the Pacific islands during the late 1970s.<sup>6,7</sup> This outbreak demonstrated that even in the absence of their established reservoir hosts, Australian arboviruses may be spread by nonendemic mosquitoes.

The competence of a widely distributed vector - Ae. aegypti - has been assessed for some lesser known Australian arboviruses (Edge Hill, Kunjin, Kokobera, Alfuv) and shown to be moderately capable of transmission of most of these viruses.8 The implication is disturbing since, should this capacity for transmission be sufficiently robust, the geographical range of these viruses could expand to match those of Zika and other globally established viruses (dengue, yellow fever, chikungunya). It is in this context that if a series of unforeseen climatic, anthropogenic or animal-related events were to lead to an outbreak of any of these overlooked native arboviruses within Australia or its near neighbours, there is no information as to the potential for side effects such as those now associated with Zika virus infection.

From a medical perspective, biomarkers for early diagnosis and identification of any possible associations with organ failure, organ tropism (e.g. central nervous system, cardiovascular, renal) or with congenital malformations are undetermined for most Australian arboviruses. Many remain

uncharacterised and are classified only on the basis of serology. For most, genome sequence information and clinical data are sparse. Not much is known of their transmission cycles and geographical distribution.

In order to evaluate the potential for emergence of these native Australian arboviruses, to address the public health impact of any disease outbreak and to prepare with confidence to limit rapidly its spread, the highlighted knowledge gaps should be addressed. Indeed, even the annual incidence of infection in this country is not known, let alone if there is any associated pathology such as that now highly suspected for Zika virus infection. We call for heightened interest in investigating these endemic arboviruses, underpinned by increased research funding. Australia should not be caught under-prepared to respond to a sudden increase in cases of infection caused by the emergence of one of its indigenous arboviruses.

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Correspondence to: Professor Andrew W. Taylor-Robinson, Infectious Diseases Research Group, School of Medical & Applied Sciences, Central Queensland University, Rockhampton, Queensland 4702; e-mail a.taylor-robinson@cqu.edu.au