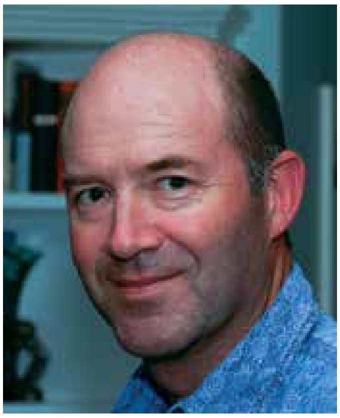
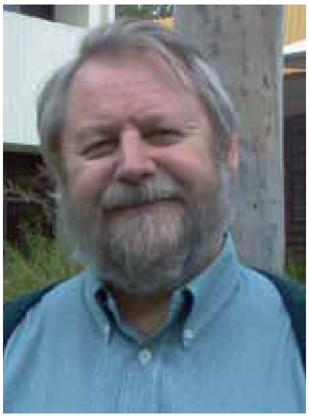
Ross River virus – at the interface between humans, animals and the environment

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Ross River virus (RRV) is the most common cause of mosquito-borne illness in Western Australians. The virus is maintained in nature principally via transmission between competent mosquito vectors and native (marsupial) vertebrate hosts, although humans are suspected of being amplifiers of RRV in some situations. The influence of prevailing environmental conditions on the ecology of RRV has been extensively documented. Indeed, monitoring of environmental variables, together with vector mosquito populations and infection rates with RRV, now provides effective early warning of elevated levels of RRV activity in several different regions of Australia. Serosurveys provide convincing evidence that western grey kangaroos (WGK; *Macropus fuliginosus*) are commonly infected with the virus in south-west coastal regions of Western Australia. There is also evidence of seroconversions in WGKs coinciding with outbreaks of human disease. Such outbreaks have been preceded by favourable environmental conditions for breeding of WGKs, presumably leading to an increase in numbers of non-immune individuals in the environment. More recently, GIS analyses of clusters of human cases of RRV has shown a relationship between proximity of residence to mosquito and WGK habitat and risk of RRV disease. These findings indicate that monitoring of seroprevalence to RRV in vertebrate hosts of RRV, such as the WGK, may assist in predicting outbreaks of RRV disease and for determining whether strategies to manage natural host populations in close proximity to human habitation may be worth further consideration.

Ross River virus (RRV) causes fever, rash, arthalgia, and myalgia in clinically infected people[1,2], with an average of over 4000 cases reported across Australia each year[2]. The most common mosquito species capable of transmitting RRV include the principal rural pest species *Culex annulirostris*, *Aedes vigilax* and *Aedes camptorhynchus*. In urban environments, the container-breeding *Aedes notoscriptus* is also important[2,3].

The extent and timing of RRV transmission varies dramatically between regions due to inter-seasonal and inter-annual variation in environmental conditions. Studies have demonstrated correlation between disease incidence and the Southern Oscillation Index, La Niña and the Quasi-Biennial Oscillation[4-6]. In the south-west of Western Australia (WA), some outbreaks of

RRV have been linked to short-term rises in sea level associated with a strengthening of the Leeuwin Current, leading to tidal inundation of saltmarsh mosquito habitat throughout late spring and summer[7]. Other major outbreaks associated with well above average late spring and early summer rainfall[8], have underlined the importance of both rainfall and temperature in the ecology of RRV[9,10]. The adaptability of RRV to the extremes of the Australian climate is perhaps best illustrated by evidence of its persistence during periods of drought in arid regions of north-west WA in desiccation-resistant eggs of *Aedes* mosquitoes[11].

Regular surveillance of mosquito populations, infection rates in mosquitoes and environmental conditions (rainfall, tides and temperature) have been shown to provide effective early warning of the potential for outbreaks of human disease[1,7,9,10]. The close and complex inter-relationships between RRV, its mosquito vectors, vertebrate hosts and the environment have also led to considerable deliberation about the potential impacts of climate change on the incidence and distribution of RRV and the challenges for managing RRV disease in the future[7,12-14]. The contemporary view is that activity of RRV may increase in some areas, but may decrease in others. The complex ecology will mean that changes in risk will be difficult to predict and will require detailed, locality-specific surveillance of vector, host, environmental and human influences on RRV ecology[14].

Major outbreaks in south-west WA only occur every two to four years[7-10,15]. Such outbreaks are often associated with above average mosquito populations and apparently predisposing climatic and environmental factors. However, outbreaks have also occurred in the absence of these key drivers[8,10,15], suggesting that vertebrate host abundance and immunity may have a significant role in determining the potential for RRV activity in the region.

Despite this, the role of vertebrate hosts in the epidemiology of RRV remains poorly understood. Marsupials are recognised as more efficient amplifiers of RRV than eutherian mammals, which in turn are more efficient than birds. The most frequently implicated marsupials are macropods (kangaroos, euros and wallabies), while horses are amongst the most commonly implicated Eutherian mammals[2,3,16-18].

Experimental infection of macropods with RRV has shown that the eastern grey kangaroo (*Macropus giganteus*) and agile wallaby (*Macropus agilis*) are capable of developing a viraemia persisting for approximately 3.4 and 6.0 days, respectively, following infection[17]. It is expected that a similar response would occur in the western grey kangaroo (WGK) because these species are closely related.

Serosurveys provide overwhelming evidence that WGKs are commonly infected with RRV. In two unpublished surveys from WA, the seroprevalence of neutralising antibodies to RRV was found to be 35%[15] and 43.9%[19]. The seroprevalence among WGK samples collected in the south-west WA during an outbreak of human disease was 87.5%[15]. Bloodmeal analyses undertaken in WA also demonstrate that putative RRV mosquito vectors commonly feed on marsupials[20]. It is, therefore, hoped that surveillance of potential vertebrate host populations may provide an additional dataset to assist in the prediction of human outbreaks of RRV disease.

A low seroprevalence of RRV neutralising antibodies noted in WGK populations near the south-west town of Capel (C. Gordon, unpublished results) was a likely predisposing factor for high levels of RRV activity in 2003–2004[9,10]. In a separate study, the seroprevalence in local WGK populations at two locations dropped significantly by 10% over an interepidemic period of 12 months[19]. This latter finding was the likely result of naïve juveniles being born and older, immune animals dying. In the years immediately following an epidemic, it seems likely that elevated immunity within vertebrate host populations suppresses viral activity.

A statistically significant cluster of human cases of RRV occurred around a densely vegetated wetland and nature reserve in Perth's southern suburbs during the summer of 2011–12. However, similar wetlands in the same locality but without the surrounding nature reserve were not linked to an increase in RRV disease. The WGK population in the nature reserve was culled to below 100 animals in 2006, but this has subsequently increased to an estimated several hundred animals. This circumstantial evidence suggests that a combination of favourable environmental conditions (a strong La Niña event) for mosquitoes in 2011–12 and several seasons of breeding of WGKs may have provided suitable conditions for an epizootic of RRV, once the virus was introduced into the locality during a large south-west WA outbreak in spring-summer 2011–12.

Current surveillance programs take into account vector abundance and infection rates but do not factor in the influence of vertebrate host factors on RRV ecology. However, surveillance of seroprevalence of RRV in WGKs needs to continue over a number of RRV cycles to determine whether a significant drop in seroprevalence is a prerequisite for a major outbreak.

Additionally, serosurveys in kangaroos may provide an indicator of the level of background risk of RRV for any given location. Unpublished data indicates that differences in the average seroprevalence of RRV neutralising antibodies within local kangaroo populations between regions reflects variation in the number of cases of RRV disease reported in people[19]. Both the reported number of cases of RRV disease in people and the seroprevalence among local kangaroo populations is high at Capel, a known focus of RRV activity[19]. Conversely, seroprevalence among kangaroos is very low at two localities north of Perth (Badgingarra and Eneabba), where RRV disease incidence is extremely low[19].

With the increasing awareness of the role of wildlife species in infectious disease maintenance and transmission, the kangaroo harvesting industry is a potentially valuable resource that can be used for surveillance purposes. Nationwide, more than 3,000,000 kangaroos are harvested annually[21]. It had been hoped that continued surveillance in kangaroo populations in the south-coastal regions of WA would provide a unique approach to predicting the potential for spillover of RRV activity to the human population. Unfortunately, selection bias associated with the commercial harvesting industry means that predominantly older, male animals are targeted. Adult kangaroos are more likely to be seropositive than sub-adults (Potter, unpublished). Assays to detect RRV IgM antibodies (recent RRV infection) in a range of wildlife species are not widely available. Therefore, regular monitoring of adult populations does not currently provide a sensitive means of determining sudden changes in the level of viral activity. Development of a marsupial RRV IgM assay would provide a practical means of determining the proportion of animals with recent RRV infection, which may assist in predicting impending RRV outbreaks. Further consideration also needs to be given to the role of other potential vertebrate hosts of RRV. For example, within urban environments, possums, horses and domestic animals may play a role in viral transmission.

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Biographies

Abbey Potter is currently a lecturer in Veterinary & Biomedical Physiology at Murdoch University. After completing a degree in Veterinary Science and working in small animal practice, she undertook a PhD in disease surveillance in kangaroos. The focus of her research was on the potential role that kangaroos play in the maintenance of transmission of Ross River virus in the southwest of Western Australia.

Dr Michael Lindsay is Managing Scientist of Environmental Health Hazards with the Western Australian Department of Health and an adjunct senior lecturer at The University of Western Australia. Michael has been involved in research and management of vector-borne diseases for over 20 years, initially with The University of WA and, since late 1999, with the Department of Health. He has published over 70 papers and book chapters on the ecology, epidemiology and molecular biology of mosquito-borne diseases of public health importance, including early papers on the influence of climate on the ecology of arboviruses.

John Mackenzie's biography is found on page 4.