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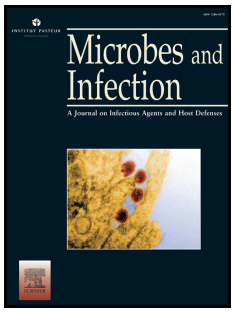

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Commissioned Review

Neglected Australian arboviruses: quam gravis?

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Abstract

At least 75 arboviruses have been identified from Australia. Most have a zoonotic transmission cycle, maintained in the environment by cycling between arthropod vectors and susceptible mammalian or avian hosts. The primary arboviruses that cause human disease in Australia are Ross River, Barmah Forest, Murray Valley encephalitis, Kunjin and dengue. Several other arboviruses are associated with human disease but little is known about their clinical course and diagnostic testing is not routinely available. Given the significant prevalence of undifferentiated febrile illness in Australia, investigation of the potential threat to public health presented by these viruses is required.

Keywords: Arbovirus; Australia; Vector; Transmission; Diagnosis; Undifferentiated febrile illness

Word Count: Abstract 97; Text 5,710

1. Introduction

*Ar*thropod-*bo*rne (arbo)viruses, viruses transmitted between vertebrate hosts by arthropods (mosquitoes, ticks, sandflies and midges), present a significant public health risk in Australia and worldwide. More than 75 arboviruses have been identified in Australia [1]. While only relatively few are known to cause disease in humans, there are limited or no data regarding the potential human pathogenicity of the majority of these viruses [2]. Ross River (RRV) and Barmah Forest (BFV) are major alphaviruses that are known to cause a debilitating and sometimes chronic polyarthritis [3]. Murray Valley encephalitis (MVEV) and West Nile Kunjin strain (KUNV) viruses are flaviviruses that cause encephalitis, while dengue (DENV) virus is commonly associated with febrile illness or sometimes haemorrhagic fever [4]. Most arboviruses have a zoonotic transmission cycle that alternates between arthropod vectors and susceptible vertebrate hosts, some of which act as reservoirs of infection in the environment [5,6].

Other Australian arboviruses, such as Sindbis (SINV) Alfuy (ALFV), Edge Hill (EHV), Kokobera (KOKV), Stratford (STRV) and GanGan (GGV), have been associated with human disease [4]. However, they appear to cause predominantly mild symptoms and no outbreak of any has yet been described. SINV is the most common isolate from mosquitoes [7], but its association with human infection is unclear. Similarly, there are many other arboviruses isolated from arthropods in Australia [6,7], and whose role in human infection is yet to be evaluated. These include the bunyaviruses Akabane (AKAV, Koongol (KOOV), Mapputta (MAPV) and Wongal (WONV), and the reoviruses Corriparta (CORV) and Eubenangee (EUBV).

It has been long since postulated that arboviruses may be responsible for causing some cases of undiagnosed febrile illness (UFI) observed in Australia [8]. Prior to the identification of the now commonly diagnosed RRV in 1959 [9] and BFV in 1974 [10], an aetiological agent could not be determined in patients presenting for medical attention with these infections. Even after

the identification of the viruses, it took almost 15 years before laboratory tests to diagnose infection with them became widely available. Today, more than half of undifferentiated fevers in Australia still go undiagnosed [11], in many cases because treating doctors may feel the cost of the testing is not warranted or the causative agent is novel, not known to cause human disease or there are no routine diagnostic tests available. In such cases, a possible association could be assumed regarding the role of these viruses to the UFI.

This review describes Australian arboviruses, their isolation and identification, distribution, relationship with hosts and vectors, and the infections/diseases that they are so far known to cause.

2. Arboviruses

Based on a combination of their antigenic or phylogenetic relatedness and their known transmission by arthropods the International Catalogue of Arboviruses lists 538 registered viruses that are absolutely or potentially infectious for humans or domestic animals [1]. Clinically significant arboviruses belong to the families and genera of *Togaviridae* (Alphavirus), *Flaviviridae* (Flavivirus), *Bunyaviridae* (Bunyavirus), and *Reoviridae* (Orbivirus) [12]. Some of the other arboviruses that are considered pathogenic to domestic and wild animals are classified as *Rhabdoviridae* (e.g. mosquito/sandfly-borne bovine ephemeral fever), *Orthomyxoviridae* (tick-borne Thogoto virus) and *Asfarviridae* (tick-borne African swine fever virus) [13].

More than 130 arboviruses cause mild to fulminant disease in humans [6]. Most are transmitted in zoonotic cycles, i.e. the principal vertebrate host is an animal other than a human. The distribution of arthropod-borne viruses is restricted by the areas inhabited by their reservoir and vector hosts [4,6]. Thus, many arboviruses have tightly defined ecological zones, while some are distributed globally.

3. Australian arboviruses

In the Arbovirus Catalogue maintained by the US Centers for Disease Control and Prevention (CDC) [1], around 75 viruses are described from Australia (Table 1). In terms of causing disease in humans, the most important are RRV, BFV, MVEV and KUNV [7]. Similarly, SINV, ALFV, EHV, KOKV, STRV and GGV are also recognised as being able to cause disease in humans [14].

3.1 Epidemiology and geographical distribution of Australian arboviruses

The Australian National Notifiable Diseases Surveillance System received notification of 43,811 cases of vector-borne diseases for the 5-year period between 2010-2014, the latest year for which data are available [15]. The alphaviruses BFV and RRV accounted for 10,043 (22.9%) and 24,620 (56.2%), respectively, of these. The number of overseas-acquired cases of DENV, almost 10 times higher than those acquired locally, has risen steadily from 219 reported in 2005 to 1,716 in 2014 [15]. Population forecasts for Australia predict that the number of people at risk of contracting DENV will grow in future, especially in northern Australia [16]. During the decade 2005-2014, cases of RRV were reported as increasing, in ascending order, from South Australia, Victoria and Western Australia whilst decreasing in Queensland and Northern Territory [15]. Clinical infections with RRV and BFV were detected most commonly in adults, with notification rates higher in the 35-54 year age groups [15]. Most flavivirus infections over this time were due to DENV but cases of MVEV and KUNV were also reported [15]. The overall trend for notifications nationally over the last two decades (1995-2014) is of DENV, BFV and RRV in ascending order (Fig. 1 a) [15].

The prevalence of anti-RRV and anti-BFV antibodies was found to increase with age and was marginally higher among males than females [17,18]. The anti-RRV sero-conversion rate in

Queensland has been calculated to be around 1.5% per year, with a significant linear association between age and antibody prevalence [19].

After a long pause, a notable increase in MVEV activity was observed in 2001, 2008 and 2011, in which years there were 6, 4 and 16 clinical cases, respectively (Fig. 1b) [15]. These outbreaks were the largest on record since the 1974 epidemic, a widespread outbreak on the Australian mainland in which 58 patients, the majority of whom lived in Victoria, developed MVEV infections [20]. In addition to these outbreaks MVEV has been identified sporadically in the last 16 years [15]. Unlike the epidemic of 1974, these sporadic cases have occurred not in Victoria but in other parts of Australia, especially in tropical and subtropical regions of Western Australia and Northern Territory. Similarly to MVEV, KUNV is a putative cause of a neurological disease syndrome, although the symptoms are milder than those linked to MVEV. In recent years, cases of KUNV infection have been recorded at a low but regular frequency (Fig. 1b) [15]. However, large numbers of patients infected with KUNV, 18 in 2003 and 12 in 2004, were recorded. In 2011 in south-eastern Australia there was an unprecedented outbreak of neurological disease that affected many horses; however, only a single human case was reported during that episode [21,22].

Almost all the Australian arboviruses known to cause human disease have been recovered from the Australian mainland, excluding Tasmania. MVEV, a clinically significant encephalogenic flavivirus, is enzootic in the northern parts of Western Australia and Northern Territory, cycling between waterbirds and *Culex annulirostris* mosquitoes. Spread of MVEV in other parts of Australia outside these foci is thought to be due to movement of infected birds consequent to heavy rainfall and flooding [23]. For instance, significant outbreaks have been reported after flooding of the Murray-Darling river basin and filling of Lake Eyre located in the

normally arid interior of south-eastern Australia, allowing migration of infected waterbirds from northern Australia as far south as north-western Victoria [23].

Another flavivirus, KUNV, which is classified in a clade of the West Nile virus group, is enzootic across much of northern Australia and occasionally epizootic in south-eastern Australia [24]. After extensive flooding in eastern Australia in 2011 an outbreak of equine encephalitis arose, primarily in New South Wales where the virulent strain of KUNV was isolated [21].

KOKV, which occasionally causes polyarthritis, has been found to infect humans in Queensland [25], and New South Wales [18]. Moreover, isolates of KOKV have been recovered from mosquitoes trapped in Queensland, New South Wales, Western Australia and Northern Territory [4]. Mosquito surveillance programs have also found EHV in Northern Territory, Queensland, Western Australia and New South Wales [26].

Dengue, one of the most important flaviviral diseases globally, was considered to be endemic in northern Australia until about 1920, after which improved sanitation started to restrict breeding sites for *Aedes* vector mosquitoes. In the intervening time, there have been repeated outbreaks following the introduction of DENV into regions where *Ae. aegypti* mosquitoes are abundant – specifically north-eastern coastal areas of Queensland [27].

RRV, an alphavirus causing polyarthritis, has been recovered in all states and territories of Australia. Outbreaks of human RRV infection (epidemic polyarthritis, EPA) occur in both urban and rural areas [3,4]. The virus exists across diverse environments, for example in areas of: uniform rainfall temperate inland, e.g. the Griffith region of New South Wales; wet winter/dry summer temperate, e.g. the Bunbury region, southwest Western Australia; wet summer/dry winter tropical, e.g. the Gove region, northeast Northern Territory and coastal areas from north to south in Queensland; and cold temperate region, e.g. the east coast and Tamar River valley

147 regions of Tasmania [2]. As with RRV, human infections with another alphavirus, BFV, are
148 recorded in all states and territories in Australia, although only thirteen cases have been reported
149 from Tasmania [15].

150 *3.3 Identification of Australian arboviruses and their role in human infection and disease*

151 Most of the CDC-registered arboviruses from Australia were first isolated during the second
152 half of the 20th century. Early reports of potential arbovirus activity on the continent include
153 patients experiencing dengue-like syndromes in Queensland, at Townsville in 1879 and
154 Rockhampton in 1885 [28]. Several epidemics (Darwin in Northern Territory in 1914, Western
155 Australia in 1909-10, South Australia in 1925-26) were described in the early part of the 1900s.
156 After a quarter of a century, dengue re-appeared in north Queensland in 1981-82 [29]. Unlike
157 previous epidemics in the same region, which were caused by the DENV-3 serotype, the 1981
158 outbreak was due to DENV-1 [30]. Since then, all four serotypes of DENV have circulated in
159 Queensland.

160 The aetiology of the EPAs that had been observed among Australian residents was unknown
161 for more than half a century. In Natimuk, Victoria, in 1886 an outbreak with symptoms of joint
162 pains and fever was reported at the time as typhoid or dengue fever. However, when reviewed
163 retrospectively, it is suspected that this was most probably EPA [31]. EPA that occurred in
164 Narrandera, New South Wales, in 1928 was reported contemporaneously as “a new unusual
165 disease” [32]. During and after the Second World War, many soldiers in Australia reported
166 symptoms of fever, pain and stiffness of joints, rash and headache [33]. Another outbreak of
167 EPA in the Murray Valley region, southern Australia, was recorded in 1956 [34]. In 1960 a viral
168 aetiology quite similar to chikungunya virus, an alphavirus, was reported as causing outbreaks of
169 polyarthritis in Africa since 1952 [35]. Symptoms of chikungunya were described as severe

arthritis and fever followed by rash. However, Australian outbreaks were characterised by the gradual onset of mild symptoms, with accompanying mild fever (< 38.3°C) rarely noted [35].

In 1959 RRV was isolated from *Ae.* (*Ochleratatus*) *vigilax* mosquitoes collected near Ross River in Townsville, north Queensland [9]. Since then, RRV has been isolated from at least 42 different mosquito species [36]. A serological survey in the mid 1960s found widespread infection with RRV among humans, horses, cattle, kangaroos and wallabies, as well as in goats, sheep, bandicoots and dogs [37]. Although attempts to isolate RRV from EPA patients in Australia using suckling mice or vertebrate cell cultures were unsuccessful, eventually it was isolated from a child without a history of arthritis but with undifferentiated fever [38]. There was a significant EPA outbreak in Australia during 1979 and 1980. This outbreak spread to several nearby Pacific islands, with RRV isolated from polyarthritis patients in Fiji, the Cook Islands and American Samoa [39-41]. During this time, the virus was isolated from two polyarthritis patients in Australia [42].

For almost a decade after the identification of RRV [9], very few patients were confirmed as having a clinical infection as diagnostic testing was limited to a research setting. Following the development of an enzyme-linked immunosorbent assay (ELISA) to detect anti-RRV immunoglobulin (Ig)M antibody, the number of patients diagnosed annually rose abruptly to 4,000-6,000 and epidemic EPA became a nationally notifiable disease in Australia [15]. The number of localities in which cases was observed to occur increased almost two-fold after 1985 when the anti-RRV ELISA became commercially available [43].

BFV, which was isolated for the first time in 1974 from *Cx. annulirostris* mosquitoes in the Barmah Forest of northern Victoria, causes a polyarthritis similar to that triggered by RRV [10]. The first human infection with this virus was diagnosed in 1986 in New South Wales [44], while the first successful culture isolation was from a patient from far north Queensland two years later

[45]. Following the first recorded outbreak of BFV in 1992, consisting of 16 confirmed cases in Northern Territory [45], successive outbreaks have been observed in other parts of the country; southwest Western Australia in 1993-94, New South Wales in 1995 and Victoria in 2002 [46]. The number of reported cases of clinical BFV infection has increased steadily to 1,000-4,000 per year following the routine use of a commercial ELISA kit to detect IgM against this virus [15]. The year 2013 has the largest number of notifications so far recorded, a total of 4,239 cases [15]. However, it is entirely possible that a sizeable proportion of these BFV notifications were due to false positive ELISA results. It may be that data were skewed by either the substandard quality of commercial assays used, the production of IgM regardless of a patient's clinical profile and/or antibody cross-reactivity to closely related arboviruses such as RRV [15].

MVEV and KUNV cause encephalitis in humans that can prove fatal. Early reports of encephalitic disease in south-eastern Australia, in 1917, 1918 and 1925, used the name "Australian X disease" [47]. It was suspected in hindsight that MVEV was responsible for these incidences when this agent was recovered from a fatal human case of encephalitis during an outbreak in the Murray Valley of Victoria in 1951 [48]. Subsequently, serological evidence of MVEV infection in humans and other animals was demonstrated in Queensland [49]. Sporadic cases of MVE occur almost annually, particularly in northern Australia, with less frequent larger outbreaks such as that of 1974 discussed previously [20]. Changes in environmental conditions have influenced MVEV activity and human infections caused by it. Heavy seasonal rainfall is the principal driver for virus activity in Western Australia and Northern Territory while its increased incidence in south-eastern Australia has followed extensive weather-related effects – for instance, significant outbreaks have been reported after flooding of the Murray-Darling river basin and filling of Lake Eyre located in the normally arid interior of south-eastern Australia,

prompting migration of infected waterbirds from northern Australia as far south as north-western Victoria [23].

Two of the recent outbreaks of MVEV, in 2000 and 2011, both appeared in areas where virus activity has previously only rarely been recorded. Prior to 2000, in Western Australia cases were limited to the Kimberley region in the far north of the state, but the two abovementioned outbreaks were focused predominantly in locations south of the Kimberley. This suggests a possible shift in epidemiology of the disease to an area where the resident population comprises a lower proportion of people having prior immunity to MVEV [50].

In 1960, KUNV, which shares a similar ecology with MVEV, to which it is related serologically, was isolated from *Cx. annulirostris* captured in northern Australia [51]. Subsequently, patients with encephalomyelitis, headache, mild fever, rash, photophobia, myalgia, arthralgia and lymphadenopathy were found to have been infected with KUNV [52].

ALFV, a member of the Japanese encephalitis virus (JEV) group, has been isolated from mosquitoes in northern Australia [53]. Serological surveys suggest that it infects humans, probably at a subclinical level [54].

Other alphaviruses like SINV, Bebaru (BEBV) and Getah (GETV), and flaviviruses including EHV and KOKV, were first isolated from mosquitoes trapped in north Queensland at Mitchell River Mission, now called Kowanyama, and Cairns and Normanton, during the early 1960s [9,37]. SINV is the arbovirus most commonly isolated from mosquitoes in Australia [55].

Australian strains of SINV are genetically distinct from those strains that are widely distributed in Eurasia and Africa, particularly those associated with infection outbreaks and clinical disease in parts of northern Europe and South Africa. Although Australian SINV is regarded as the minor human pathogen, sero-epidemiological studies have suggested that

frequent subclinical disease occurs in humans [17,56,57]. It has also been associated with human arthritic disease [17,58]. Additionally, a haemorrhagic manifestation following SINV infection has been described [59].

KOKV and EHV have also been linked to human infections. Sera were found to be reactive in a survey of antibodies to these arboviruses among humans in Queensland and Northern Territory [56]. KOKV had been shown to be associated with an acute polyarticular disease [18,25,54], while the possible clinical infection with EHV was also described [60].

STRV, which belongs to the Kokobera subgroup, was first isolated in 1961 from *Ae. vigilax* collected in Cairns, far north Queensland [51]. There is serological evidence of human infection by this virus [61].

Viruses that are classified in the family Bunyaviridae, namely KOOV, Kowanyama (KOWV), MAPV, Trubanaman (TRUV) and WONV, were also first in the early 1960s from Kowanyama, which is located on Cape York Peninsula in Queensland [9]. Although human disease has not been associated with infection with these viruses, antibodies to KOWV and TRUV were detected in local adult indigenous people [62]. Similarly, there are Orbiviruses like CORV and EUBV from the Reoviridae family that were isolated from mosquitoes in Queensland but which to date are not associated with human infection or disease [9].

Arboviruses are still being discovered in the Australia-Pacific region. Bamaga virus (BgV), which is suggested as a flavivirus by phylogenetic analysis of its nucleotide sequence, was isolated from *Cx. annulirostris* mosquitoes collected from northern Australia in the early 2000s [63].

Similarly, another new flavivirus in the yellow fever virus group has been detected in mosquitoes collected in northern Western Australia during the arbovirus surveillance activities of

2011 and 2012 [64]. The role of these novel viruses in human infection and/or disease is yet to be determined.

The catalogue of Australian arboviruses that are currently acknowledged to exist, each listed with its prototype number and source of initial isolation [1], are presented in Table 1.

4. Relationship between arboviruses and their vertebrate hosts

Reservoirs are the hosts that serve as a source of infection for insect vectors of virus transmission. In order to be an effective reservoir, the host should be present in large numbers, attractive to the vector and readily accessible to it. Furthermore, the viraemia should of sufficient titre and duration to be infective to susceptible blood-feeding arthropods. The focal host is often the reservoir host, while the secondary host is the species that may serve as a potential source of infection but that is less important in this role than the reservoir host. When a host does not develop a viraemia sufficient to infect a vector, it is termed a 'dead-end host' [6]. The number of urban-dwelling EPA patients in Australia and the rate of spread of RRV infection in the Pacific region epidemics of 1979-80 indicate that humans can be very efficient reservoir hosts for RRV [40,41]. However, birds and mammals other than humans may be the principal reservoirs for other Australian arboviruses.

4.1 Mammals other than humans

Mammals may be important hosts/reservoirs for Australian arboviruses [35]. Detection of antibodies specific to alphaviruses RRV, BFV, BEBV and GETV in mammals, especially marsupials and rodents, supported this concept [37]. The large macropod marsupials that are native to Australia, kangaroos and wallabies, are the natural reservoir of both RRV and BFV [65].

Marsupials, kangaroos and wallabies, exhibit the most intense known and longest RRV viraemias, matched by a correspondingly high prevalence of specific antibody, so these animals are considered to be the most likely hosts for RRV [35,66]. RRV has also been isolated from the agile wallaby, *Macropus agilis* [67], for which antibody prevalence surveys also suggest high rates of infection [68]. Moreover, a high viraemia of MVEV was detected in the western grey kangaroo, *Macropus fuliginosus* [69]. Neutralizing antibodies to both RRV and BFV have been identified in sera taken from the eastern grey kangaroo, *Macropus giganteus* [70]. Brushtail possums have also been found to carry high viral loads and antiviral antibody titres for RRV [71].

An ecologically significant association of macropods and marsupials, especially wallabies, with KOKV and EHV has been shown based on serological surveys [25,67]. However, serological data suggested dogs also are infected with EHV and horses also with KOKV [66].

RRV has been detected in domestic fowl and sheep following experimental infections. For each, viraemias were observed more consistently in juveniles than in adults [39,72]. Domestic pets, dogs and cats, remained aviraemic when challenged with RRV or BFV [73]. These observations suggest that these mammals may be less effective reservoirs than marsupials.

Horses and fruit bats with viraemias undetectable by cell culture were able to infect mosquitoes in experimental settings [74,75]. The presence of anti-RRV IgM in horses and the occasional clinical infection (horses are the only host apart from humans known to develop symptoms of disease following a natural infection) has prompted some researchers to propose that equines may act as amplifying hosts [37,76]. Viraemic horses and flying foxes are both suggested as possible means of transporting RRV from peri-urban to urban environments. In addition, sero-epidemiological studies in horses have detected antibodies to GETV, BEBV, SINV and MVEV [70,77].

4.2 Birds

Wild birds are considered to be a reservoir of MVEV [78]. This suggestion is supported by the detection of anti-MVEV antibodies in many ciconiiformes (storks, herons, ibis, bitterns and egrets) and pelecaniformes (pelicans, frigate birds, gannets, cormorants and shags) [57,79]. Prevalence rates of anti-MVEV antibody in ciconiiformes were 44% and 96% for juveniles and adult birds, respectively, after the MVE epidemic of 1974-1975, indicating a high infection rate during this outbreak [80]. Galahs, sulphur-crested cockatoos, corellas and black ducks have also demonstrated MVEV viraemias following infection in a laboratory setting [81].

Birds are considered to be the principal hosts for SINV and ALFV [58]. Strains of SINV and ALFV were isolated from wild birds collected in Kowanyama between 1963-1967 [9,37]. Moreover, RRV, CORV and KUNV were also isolated from birds during the same studies.

5. Transmission cycles

Arboviruses are transmitted between hosts by their arthropod vectors. The transmission cycle starts when an arthropod feeds on viraemic blood. The virus must then replicate in the arthropod's mid-gut and disseminate to the insect's salivary glands so that when it feeds again on another host, transmission of virus to that mammal or bird may take place. Many species of arbovirus have more than one known vertebrate host [82]. Some but not all hosts develop viraemias that are sufficiently high to enable infection of susceptible vectors which feed on them. Failure to develop a viraemia adequate to infect a vector does not necessarily mean that the host will not develop clinical symptoms. Cycles of virus transmission may involve only humans and arthropods (e.g. epidemic cycle of DENV), only non-human vertebrates and vectors (e.g. AKAV), or transmission between human and non-human hosts (zoonoses, e.g. RRV) (Fig. 2) [83].

Most Australian arboviruses are zoonotic and maintain enzootic cycles involving mammals and birds as reservoir hosts [84]. In this cycle, the virus is maintained continuously in the environment and may or may not cause disease in the enzootic host. Infection of humans can arise from direct spillover of these enzootic and epizootic (exploiting domestic animals, e.g. JEV) cycles when virus amplification achieves a viraemia high enough for transmission (Fig. 2) [6].

RRV is maintained as an enzootic infection involving mammals, especially large marsupials, and mosquitoes such as *Ae. vigilax* and *Cx. annulirostris* and may be transmitted to humans during epizootic and epidemic periods [85]. However, the low sero-prevalence in non-human vertebrates, its rapid epidemic spread, and the demonstration of high titre viraemia in humans during the outbreak of 1979-1980 in Fiji, New Caledonia, Samoa and the Cook Islands has provided evidence of human-mosquito-human transmission without intermediate non-human hosts [39,40,86].

MVEV and KUNV both undergo enzootic transmission cycles involving avian hosts and mosquito vectors [87]. It was suggested as long ago as the 1950s that outbreaks of Murray Valley encephalitis may follow the introduction of MVEV into susceptible human populations by water birds migrating from enzootic areas of northern Australia [78]. The transmission cycle proposed for MVEV principally involves birds and *Cx. annulirostris*.

It has been proposed that KOKV and EHV is each maintained in a zoonotic cycle involving kangaroos, wallabies, other mammals and *Cx. annulirostris* [9]. AKAV and STRV are believed to be maintained in cycles involving cattle, horses and *Cx. brevitarsis* [88].

6. Relationship between arboviruses and arthropods

Different Australian arboviruses have been isolated from mosquitoes, ticks and biting midges. However, not all these arbovirus species have been shown to replicate in the insect from which they were recovered or to be able to be transmitted in their saliva [89].

6.1 Mosquitoes

Mosquitoes such as *An. annulipes, Cx. annulirostris* and *Cx. australicus* are ubiquitous across Australia [80]. Other species like *Ae. vigilax* (active in summer) and *Ae. camptorhynchus* (active in winter) breed in pools and saline marshes filled by tidal water [90]. *Cx. annulirostris*, a freshwater species found throughout the country, is the mosquito from which to date most indigenous arboviruses have been recovered [4,51,91,92]. A summary of the mosquitoes from which clinically important Australian arboviruses have been isolated, and their geographical distribution, is shown in Table 2.

RRV has also been isolated from *Aedes, Anopheles* and *Culex* mosquito species. *Ae. vigilax,* a northern saltmarsh mosquito from which the first strain of RRV was isolated [9], *Ae. camptorhynchus,* a southern salt marsh mosquito, and *Cx. annulirostris* are the mosquitoes from which RRV has been isolated most frequently [4,10,92]. Transmission of RRV to mice was demonstrated with each of *Ae. funereus, Ae. procax, Ae. vigilax, Cx. annulirostris, Cx. australicus* and *Mansonia uniformis* [93]. *Ae. notoscriptus,* a peri-domestic mosquito, is a competent vector for RRV and it is advised that this species be considered more seriously in the context of urban RRV transmission [94]. While no evidence of virus transmission by either *Ae. multiplex* or *Ae. notoscriptus* was found, these mosquitoes were susceptible to RRV infection [93]. Other species can transmit RRV, such as *Ae. clelandi* and *Ae. flavifrons,* which are distributed in the southern part of Australia including Tasmania [90].

BFV has been isolated from *Ae. bancroftianus, Ae. camptorhynchus, Ae. eidsvoldensis, Ae. normanensis, Ae. notoscriptus, Ae. procax, Ae. pseudonormanensis, Ae. vigilax, Cx. annulirostris,*

Cx. molestus, *Cx. quinquefasciatus*, *An. amictus*, *An annulipes* and *Ae. funereus* [4]. Vector competence for BFV of mosquitoes collected from Brisbane, Townsville and other regions [94-96] found the following mosquitoes to have potential based on susceptibility to infection and efficiency of virus transmission: *Ae. notoscriptus*, *Ae. procax* and *Ae. vigilax* [89]. Although BFV was isolated originally from *Cx. annulirostris* [10], this species was found to be an inefficient vector because of its low transmission rate, between 5-10% [95].

MVEV has been isolated from *Cx. annulirostris*, *Cx. australicus*, *Cx. bitaeniorhynchus*, *Cx. quinquefasciatus*, *Ae. normanensis* and *An. annulipes* [4,89]. In Western Australian isolates of MVEV were recovered from *Cx. palpalis*, *Ae. eidsvoldensis*, *Ae. pseudonormanensis* and *An. bancrofti* [4]. Studies have suggested *Cx. annulirostris* as the most competent vector for MVEV [91,97,98]. *Ae. sagax* is also competent to transmit MVEV [97]. *Ae. alboannulatus* [97], *Cx. pipiens*, *Cx. quinquefasciatus* [99] and *Ae. aegypti* [89] were determined to be poorly or not competent to transmit MVEV.

KUNV and KOKV were first isolated from *Cx. annulirostris* collected at Kowanyama in 1960 at the same time as when MVEV was isolated [51]. Subsequently, KUNV was recovered from *Cx. australicus*, *Cx. squamosus*, *Cx. quinquefasciatus* and *Ae. tremulus* [89]. KOKV was isolated from *Ae. normanensis* and *Ae. vigilax* [67,89]. *Cx. annulirostris* was found to be refractory to infection with KUNV and so is considered unlikely to be a significant vector [98].

After the first isolation of SINV in Australia from *Cx. annulirostris* collected at Kowanyama [51], it has been isolated from other mosquitoes including *An. annulipes*, *Ae. eidsvoldensis*, *Ae. lineatopennis*, *Ae. normanensis*, *Ae. theobaldi*, *Ae. vigilax*, *Ae. vittiger*, *Cx. edwardsi*, *Cx. pullus*, *Cx. quinquefasciatus*, *Cx. squamosus and Cx. starckeae* [66,91].

The principal vector of DENV, *Ae. aegypti*, which may have been introduced to Australia in the early or mid 19th century [27], is commonly found in urban environments throughout tropical north Queensland. Although *Ae. aegypti* was distributed widely across southeast Queensland until the 1950s, since that time a successful vector control program has meant that transmission has disappeared in this region and the activity of DENV-transmitting mosquitoes is now limited as far south as Wondai and Goomeri in the southeast and Charleville in the southwest of the state [100].

This vector is capable of transmitting RRV, MVEV, KUNV and Zika (ZIKV) in addition to DENV [101,102]. *Ae. albopictus*, which also is able to transmit DENV and ZIKV, is widespread in the Torres Strait Islands to the north of Queensland [103].

6.2 Ticks

Very little is known about tick-borne arboviruses in Australia. UPOV was isolated from the widely distributed soft-bodied tick of birds *Ornithodoros capensis* on Upolu Cay, a small atoll of the Great Barrier Reef, in 1966 [104]. Nugget (Orbivirus) and Taggert (Nairovirus) are Kemerovo and Sakhalin group viruses that have been isolated from a hard-bodied seabird tick, *Ixodes uriae*, on Macquarie Island [105], to the south of Tasmania. In addition, Saumarez Reef virus was isolated from both *O. capensis* and *I. eudyptidis* in Australia [106].

6.3 Biting midges

Most of the viruses of the Orbivirus serological group, Bluetongue (BTV), CORV, EUBV, Palyam (PALV), Wallal (WALV) and Warrego (WARV), were isolated from biting midges such as *C. brevitarsis* and *Culicoides marksi* [88,107]. There are reports of BFV replicating in, and being isolated from, *C. brevitarsis* and *C. marksi*. However, it is not known if this vector is

competent to transmit this alphavirus [108]. Thimiri virus (THIV), from the Simbu group, was isolated from *C. histrio* collected from northern Australia [109]. The previous isolations of THIV were from birds in India [110] but the vertebrate host in Australia is unknown and no neutralizing antibodies have been found in Australian hosts [111]. Another Simbu group virus, Facey's Paddock, was recovered from a pool of *Culicoides* collected near Charleville in south-western Queensland [112]. This virus was also isolated from *Culex* mosquitoes in the same vicinity [91].

7. Future Investigations

Over several decades, a large number of arboviruses have been identified in Australian mosquitoes, ticks and biting midges [1,2]. Little is known about the pathogenicity of these in humans, nor their potential to cause epidemics. Quite a few of these viruses are known to cause human disease but are not considered to be of public health significance. However, the salient example of massive increases in reported rates of infection caused by alphaviruses like RRV and BFV compared to historical records after the introduction of commercial testing may also apply to other, currently neglected, Australian arboviruses. Mosquitoes such as *An. annulipes, Cx. annulirostris* and *Cx. australicus* that are vectors for indigenous arboviruses are widely distributed throughout Australia [90]. In some cases, mosquitoes with much wider geographical ranges have been found to be competent vectors for neglected Australian arboviruses.

Kangaroos and wallabies are considered as potential reservoirs for RRV [37,65] and BFV [65,70], while birds such as herons and egrets are regarded as the host for MVEV, ALF and SINV [66,78]. There are many others viruses whose relationship with reservoirs and vectors, and their role in human infections or diseases, is yet to be defined clearly. It is important to elucidate their transmission by sylvatic, zoonotic and human-vector cycles. The complex transmission cycles of Australian arboviruses involving multiple hosts and multiple vectors make attempts to

control vectors and arboviral diseases extremely challenging. It is vitally important to understand the potential for arbovirus to be transmitted outside of a human-mosquito cycle. The realisation that wild mammals or birds living in close proximity to humans serve as unseen reservoirs for virus transmission has a great impact on our ability to control arboviruses in both rural and urban environments. Very little is known about the transmission cycles, clinical presentation or potential for sequelae of disease, such as birth defects or neurological disorders which might be associated with these neglected Australian arboviruses In consideration of these factors, and in light of the recent global pandemic of ZIKV, concerns have been raised that any one of these under-researched and under-diagnosed viruses may represent a potential public health threat in Australia, or even globally [113].

It may be speculated tentatively that native and domesticated animals are potential hosts of these viral diseases. In regard to the identification of possible reservoir hosts, a key focus should be to examine which species of animal are common hosts for mosquitoes in different regions of Australia. In this way, prospective investigations may shed light on which non-human hosts are involved in transmission of these arboviruses. Future research should aim to establish the role of common and uncommon Australian arboviruses in causing UFIs. Furthermore, it is worth determining if any of a range of Australian arboviruses that are currently not known to be aetiological agents of human disease cause clinical or sub-clinical infections in humans and if these might be associated with any hitherto unforeseen sequelae of disease. Most importantly, the true prevalence of neglected Australian arboviruses in human populations, as well as their clinical severity and potential to cause outbreaks must be determined.

8. Conclusion

In order to evaluate the potential for emergence of indigenous Australian arboviruses, to ascertain their potential public health impact, the likelihood of disease epidemics and to prepare

with assurance to quell the spread of any such outbreak, the knowledge gaps highlighted here must be addressed. For the majority of these neglected Australian arboviruses viruses even the annual incidence of infections is unknown, to say nothing of whether there is any associated pathology such as that now indicated for ZIKV infection in Latin America and elsewhere. Further investigation, including a detailed determination of transmission cycles, is merited in order to safeguard against Australia being underprepared to respond to a sudden outbreak of one or more of its native arboviruses.

Authorship contributions

NG conceived the paper and collated articles for review. RSB, JGA and AWTR supervised the paper writing and critically reviewed various versions of the manuscript. All authors contributed to preparation of the final version and provided consent for submission.

Conflict of interest

The authors state that there are no conflicts of interest to disclose.

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Disclaimer

RSB is co-authoring this manuscript in his personal capacity and in his role as an adjunct academic at Central Queensland University.

References

[1] Centers for Disease Control and Prevention. Arbovirus Catalog. CDC. Available at: https://wwwn.cdc.gov/arbocat/ [last accessed 15 May 2017].

[2] Russell RC. Mosquito-borne disease and climate change in Australia: time for a reality check. Aust J Entomol 2009; 48: 1-7.

[3] Tesh RB. Arthritides caused by mosquito-borne viruses. Annu Rev Med 1982; 33: 31-40.

[4] Russell RC. Arboviruses and their vectors in Australia: an update on the ecology and epidemiology of some mosquito-borne arboviruses. Rev Med Vet Entomol 1995; 83: 141-58.

[5] Pfeffer M, Dobler G. Emergence of zoonotic arboviruses by animal trade and migration. Parasit Vectors 2010; 3: 35.

[6] Weaver SC, Barrett AD. Transmission cycles, host range, evolution and emergence of arboviral disease. Nat Rev Microbiol 2004; 2: 789-801.

[7] Dunstan RA, Seed CR, Keller AJ. Emerging viral threats to the Australian blood supply. Aust NZ J Public Health 2008; 32: 354-60.

[8] Doherty RL. Arthropod-borne viruses in Australia and their relation to infection and disease. Prog Med Virol 1974; 17: 136-92.

[9] Doherty RL, Whitehead RH, Gorman BM, O'Gower AK. The isolation of a third group A arbovirus in Australia, with preliminary observations on its relationship to epidemic polyarthritis. Aust J Sci 1963; 26: 183-4.

[10] Marshall ID, Woodroofe GM, Hirsch S. Viruses recovered from mosquitoes and wildlife serum collected in the Murray Valley of south-eastern Australia, February 1974, during an epidemic of encephalitis. Aust J Exp Biol Med Sci 1982; 60: 457-70.

[11] Susilawati TN, McBride WJ. Undiagnosed undifferentiated fever in Far North Queensland, Australia: a retrospective study. Int J Infect Dis 2014; 27: 59-64.

[12] Fischer M, Hills SL. Arboviral diseases. In: Heymann DL, ed. Control of Communicable Diseases Manual. 20th edn. Washington DC: American Public Health Association, 2015; 26-46.

[13] Hubalek Z, Rudolf I, Nowotny N. Arboviruses pathogenic for domestic and wild animals. Adv Virus Res 2014; 89: 201-75.

[14] Smith DW, Speers DJ, Mackenzie JS. The viruses of Australia and the risk to tourists. Travel Med Infect Dis 2011; 9: 113-25.

[15] Australian Government, Department of Health. National notifiable diseases: Australia's notifiable diseases status. Annual reports of the National Notifiable Diseases Surveillance System, 1994-2014. Available at: http://www.health.gov.au/internet/main/publishing.nsf/Content/cda-pubs-annlrpt-nndssar.htm [last accessed 15 May 2017].

[16] Inglis TJ. Climate change and infectious diseases in Australia. Aust Prescr 2009; 32: 58-9.

[17] Boughton CR, Hawkes RA, Naim HM, Wild J, Chapman B. Arbovirus infections in humans in New South Wales. Seroepidemiology of the alphavirus group of togaviruses. Med J Aust 1984; 141: 700-4.

536 [18] Hawkes RA, Pamplin J, Boughton CR, Naim HM. Arbovirus infections of humans in
537 high-risk areas of south-eastern Australia: a continuing study. Med J Aust 1993; 159:
538 159-62.

539 [19] Aaskov JG, Chen J-Y, Hanh N, Dennington PM. Surveillance for Ross River virus
540 infection using blood donors. Am J Trop Med Hyg 1998; 58: 726-30.

541 [20] Bennett NM. Murray Valley encephalitis, 1974: clinical features. Med J Aust 1976; 2:
542 446-50.

543 [21] Frost MJ, Zhang J, Edmonds JH, Prow NA, Gu X, Davis R, et al. Characterization of
544 virulent West Nile virus Kunjin strain, Australia, 2011. Emerg Infect Dis 2012; 18: 792-
545 800.

546 [22] Roche SE, Wicks R, Garner MG, East IJ, Paskin R, Moloney BJ, et al. Descriptive
547 overview of the 2011 epidemic of arboviral disease in horses in Australia. Aust Vet J
548 2013; 91: 5-13.

549 [23] Spencer JD, Azoulas J, Broom AK, Buick TD, Currie B, Daniels PW, et al. Murray
550 Valley encephalitis virus surveillance and control initiatives in Australia. National
551 Arbovirus Advisory Committee of the Communicable Diseases Network Australia.
552 Commun Dis Intell Q Rep 2001; 25: 33-47.

553 [24] Flynn LM, Coelen RJ, Mackenzie JS. Kunjin virus isolates of Australia are genetically
554 homogeneous. J Gen Virol 1989; 70: 2819-24.

555 [25] Doherty RL, Carley JG, Gorman BM. Studies of arthropod-borne virus infections in
556 Queensland. IV. Further serological investigations of antibodies to Group B arboviruses
557 in man and animals. Aust J Exp Biol Med Sci 1964; 42: 149.

558 [26] Van den Hurk A, Nisbet D, Foley P, Ritchie S, Mackenzie J, Beebe N. Isolation of
559 arboviruses from mosquitoes (Diptera: Culicidae) collected from the Gulf Plains region
560 of northwest Queensland, Australia. J Med Entomol 2002; 39: 786-92.

561 [27] Mackenzie JS, La Brooy JT, Hueston L, Cunningham AL. Dengue in Australia. J Med
562 Microbiol 1996; 45: 159-61.

563 [28] Lumley GF, Taylor FH. Dengue: Part II. Medical. Sydney: Australasian Medical
564 Publishing Company, 1943.

565 [29] Guard RW, Stallman ND, Wiemers MA. Dengue in the northern region of Queensland,
566 1981-1982. Med J Aust 1984; 140: 765-9.

567 [30] Kay BH, Barker-Hudson P, Stallman ND, Wiemers MA, Marks EN, Holt PJ, et al.
568 Dengue fever. Reappearance in northern Queensland after 26 years. Med J Aust 1984;
569 140: 264-8.

570 [31] Kelly-Hope LA, Purdie DM, Kay BH. Ross River virus disease in Australia, 1886-1998,
571 with analysis of risk factors associated with outbreaks. J Med Entomol 2004; 41: 133-50.

572 [32] Nimmo JR. An unusual epidemic. Med J Aust 1928; 1: 549-50.

573 [33] Dowling PG. Epidemic polyarthritis. Med J Aust 1946; 1: 245-6.

574 [34] Anderson SG, French EL. An epidemic exanthem associated with polyarthritis in the
575 Murray valley, 1956. Med J Aust 1957; 44: 113-7.

576 [35] Shope RE, Anderson SG. The virus aetiology of epidemic exanthem and polyarthritis.
577 Med J Aust 1960; 47: 156-8.

578 [36] Russell RC. Ross River virus: ecology and distribution. Annu Rev Entomol 2002; 47: 1-
579 31.

[37] Doherty RL, Carley JG, Lee PE. Studies of arthropod-borne virus infections in Queensland. Aust J Exp Biol Med Sci 1966; 44: 365-78.

[38] Doherty RL, Carley JG, Best JC. Isolation of Ross River virus from man. Med J Aust 1972; 1: 1083.

[39] Aaskov JG, Mataika JU, Lawrence GW, Rabukawaqa V, Tucker MM, Miles JA, et al. An epidemic of Ross River virus infection in Fiji, 1979. Am J Trop Med Hyg 1981; 30: 1053-9.

[40] Rosen L, Gubler DJ, Bennett PH. Epidemic polyarthritis (Ross River) virus infection in the Cook Islands. Am J Trop Med Hyg 1981; 30: 1294-302.

[41] Tesh RB, McLean RG, Shroyer DA, Calisher CH, Rosen L. Ross River virus (Togaviridae: Alphavirus) infection (epidemic polyarthritis) in American Samoa. Trans R Soc Trop Med Hyg 1981; 75: 426-31.

[42] Aaskov JG. Isolation of Ross River virus from epidemic polyarthritis patients in Australia. Aust J Exp Biol Med Sci 1985; 63: 587-97.

[43] Tong S, Bi P, Hayes J, Donald K, Mackenzie J. Geographic variation of notified Ross River virus infections in Queensland, Australia, 1985-1996. Am J Trop Med Hyg 2001; 65: 171-6.

[44] Boughton CR, Hawkes RA, Naim HM. Illness caused by a Barmah Forest-like virus in New South Wales. Med J Aust 1988; 148: 146-7.

[45] Merianos A, Farland AM, Patel M, Currie B, Whelan P, Dentith H, et al. A concurrent outbreak of Barmah Forest and Ross River virus disease in Nhulunbuy, Northern Territory. Commun Dis Intell 1992; 16: 110-1.

602 [46] Jacups SP, Whelan PI, Currie BJ. Ross River virus and Barmah Forest virus infections: a
603 review of history, ecology, and predictive models, with implications for tropical northern
604 Australia. Vector-Borne Zoonotic Dis 2008; 8: 283-98.

605 [47] Perdrau J. The Australian epidemic of encephalomyelitis (X-disease). J Pathol Bacteriol
606 1936; 42: 59-65.

607 [48] Miles JA, Chir B, Fowler MC, Howes DW. Isolation of a virus from encephalitis in
608 South Australia: a preliminary report. Med J Aust 1951; 1: 799-800.

609 [49] Ludford CG, Cook I. Murray Valley encephalitis: a survey of human and animal sera in
610 Queensland. Med J Aust 1957; 44: 319.

611 [50] Selvey LA, Dailey L, Lindsay M, Armstrong P, Tobin S, Koehler AP, et al. The changing
612 epidemiology of Murray Valley encephalitis in Australia: the 2011 outbreak and a review
613 of the literature. PLoS Negl Trop Dis 2014; 8: e2656.

614 [51] Doherty RL, Carley JG, Mackerras MJ, Marks EN. Studies of arthropod-borne virus
615 infections in Queensland. III. Isolation and characterization of virus strains from wild-
616 caught mosquitoes in North Queensland Aust J Exp Biol Med Sci 1963; 41: 17-39.

617 [52] Naim H, Wild J, Boughton CR, Hawkes RA. Arbovirus surveillance in the Murray-
618 Riverina region, New South Wales (1981-82). Commun Dis Intell Q Rep 1982; 82/22: 5-
619 6.

620 [53] Whitehead RH, Doherty RL, Domrow R, Standfast HA, Wetters EJ. Studies of the
621 epidemiology of arthropod-borne virus infections at Mitchell River Mission, Cape York
622 Peninsula, North Queensland. Trans R Soc Trop Med Hyg 1968; 62: 439-45.

[54] Hawkes RA, Boughton CR, Naim HM, Wild J, Chapman B. Arbovirus infections of humans in New South Wales. Seroepidemiology of the flavivirus group of togaviruses. Med J Aust 1985; 143: 555-61.

[55] Mackenzie JS, Lindsay MD, Coelen RJ, Broom AK, Hall RA, Smith DW. Arboviruses causing human disease in the Australasian zoogeographic region. Arch Virol 1994; 136: 447-67.

[56] Doherty RL. Surveys of haemagglutination-inhibiting antibody to arboviruses in aborigines and other population groups in northern and eastern Australia, 1966-1971. Trans R Soc Trop Med Hyg 1973; 67: 197-205.

[57] Liehne CG, Stanley NF, Alpers MP, Paul S, Liehne PF, Chan KH. Ord River arboviruses – serological epidemiology. Aust J Exp Biol Med Sci 1976; 54: 505-12.

[58] Doherty RL, Bodey AS, Carew JS. Sindbis virus infection in Australia. Med J Aust 1969; 2: 1016-7.

[59] Guard RW, McAuliffe MJ, Stallman ND, Bramston BA. Haemorrhagic manifestations with Sindbis infection. Case report. Pathology 1982; 14: 89-90.

[60] Aaskov JG, Phillips DA, Wiemers MA. Possible clinical infection with Edge Hill virus. Trans R Soc Trop Med Hyg 1993; 87: 452-3.

[61] Boughton CR, Hawkes RA, Naim HM. Illness caused by a Kokobera-like virus in south-eastern Australia. Med J Aust 1986; 145: 90-2.

[62] Doherty RL, Whitehead RH, Wetters EG, Gorman BM, Carley JG. A survey of antibody to 10 arboviruses (Koongol group, Mapputta group and ungrouped) isolated in Queensland. Trans R Soc Trop Med Hyg 1970; 64: 748-53.

645 [63] Colmant AM, Bielefeldt-Ohmann H, Hobson-Peters J, Suen WW, O'Brien CA, van den
646 Hurk AF, et al. A newly discovered flavivirus in the yellow fever virus group displays
647 restricted replication in vertebrates. J Gen Virol 2016; 97: 1087-93.

648 [64] Johansen C, Nicholson J, Power S, Wong S, Burley M, Wallace M, et al. The University
649 of Western Australia Arbovirus Surveillance and Research Laboratory Annual Report:
650 2012-2013. Available at: http://ww2.health.wa.gov.au/~/media/Files/Corporate/
651 general%20documents/Mosquitoes/PDF/Arbovirus-AnnRpt-2012-13.ashx [last accessed
652 15 May 2017].

653 [65] Inglis TJ, Bradbury RS, McInnes RL, Frances SP, Merritt AJ, Levy A, et al. Deployable
654 molecular detection of arboviruses in the Australian outback. Am J Trop Med Hyg 2016;
655 95: 633-8.

656 [66] Doherty RL. Arboviruses of Australia. Austr Vet J 1972; 48: 172-80.

657 [67] Doherty RL, Standfast HA, Domrow R, Wetters EJ, Whitehead HR, Carley JG. Studies
658 of the epidemiology of arthropod-borne virus infections at Mitchell River Mission, Cape
659 York Peninsula, North Queensland IV. Arbovirus infections of mosquitoes and
660 mammals, 1967-1969. Trans R Soc Trop Med Hyg 1971; 65: 504-13.

661 [68] Lindsay MDA, Breeze AL, Harrington SA, Johansen CA, Broom AK, Gordon CJ, et al.
662 Ross River and Barmah Forest viruses in Western Australia, 2000/01-2003/04:
663 contrasting patterns of disease activity. Arbovirus Res Aust 2005; 9: 194-201.

664 [69] Kay BH, Young PL, Hall RA, Fanning ID. Experimental infection with Murray Valley
665 encephalitis virus. Pigs, cattle, sheep, dogs, rabbits, macropods and chickens. Aust J Exp
666 Biol Med Sci 1985; 63: 109-26.

667 [70] Vale TG, Spratt DM, Cloonan MJ. Serological evidence of arbovirus infection in native
668 and domesticated mammals on the south coast of New South Wales. Aust J Zool 1991;
669 39: 1-7.

670 [71] Boyd AM, Hall RA, Gemmell RT, Kay BH. Experimental infection of Australian
671 brushtail possums, *Trichosurus vulpecula* (Phalangeridae: Marsupialia), with Ross River
672 and Barmah Forest viruses by use of a natural mosquito vector system. Am J Trop Med
673 Hyg 2001; 65: 777-82.

674 [72] Spradbrow PB. Experimental infection of sheep and pigs with Ross River virus. Aust Vet
675 J 1973; 49: 403-4.

676 [73] Boyd AM, Kay BH. Assessment of the potential of dogs and cats as urban reservoirs of
677 Ross River and Barmah Forest viruses. Aust Vet J 2002; 80: 83-6.

678 [74] Kay BH, Pollitt CC, Fanning ID, Hall RA. The experimental infection of horses with
679 Murray Valley encephalitis and Ross River viruses. Aust Vet J 1987; 64: 52-5.

680 [75] Ryan PA, Martin L, Mackenzie JS, Kay BH. Investigation of gray-headed flying foxes
681 (*Pteropus poliocephalus*) (Megachiroptera: Pteropodidae) and mosquitoes in the ecology
682 of Ross River virus in Australia. Am J Trop Med Hyg 1997; 57: 476-82.

683 [76] Pascoe RR, George TD, Cybinski DH. The isolation of a Ross River virus from a horse.
684 Aust Vet J 1978; 54: 600.

685 [77] Azuolas JK. Arboviral diseases of horses and possums. Arbovirus Res Aust 1997; 7: 5-7.

686 [78] Anderson SG. Murray Valley encephalitis and Australian X disease. J Hygiene 1954; 52:
687 447-68.

688 [79] Anderson SG. Murray Valley encephalitis: a survey of avian sera, 1951-1952. Med J
689 Aust 1953; 1: 573.

690

691 [80] Marshall ID, Brown BK, Keith K, Gard GP, Thibos E. Variation in arbovirus infection
692 rates in species of birds sampled in a serological survey during an encephalitis epidemic
693 in the Murray Valley of south-eastern Australia, February 1974. Aust J Exp Biol Med Sci
694 1982; 60: 471-8.

695 [81] Kay BH, Hall RA, Fanning ID, Young PL. Experimental infection with Murray Valley
696 encephalitis virus – galahs, sulphur-crested cockatoos, corellas, black ducks and wild
697 mice. Aust J Exp Biol Med Sci 1985; 63: 599-606.

698 [82] Kuno G, Chang GJ. Biological transmission of arboviruses: reexamination of and new
699 insights into components, mechanisms, and unique traits as well as their evolutionary
700 trends. Clin Microbiol Rev 2005; 18: 608-37.

701 [83] Jansen CC, Prow NA, Webb CE, Hall RA, Pyke AT, Harrower BJ, et al. Arboviruses
702 isolated from mosquitoes collected from urban and peri-urban areas of Eastern
703 Australia. J Am Mosq Control Assoc 2009; 25: 272-278.

704 [84] Go YY, Balasuriya UB, Lee C-K. Zoonotic encephalitides caused by arboviruses:
705 transmission and epidemiology of alphaviruses and flaviviruses. Clin Exp Vaccine 2014;
706 3: 58-77.

707 [85] Harley D, Sleigh A, Ritchie S. Ross River virus transmission, infection, and disease: a
708 cross-disciplinary review. Clin Microbiol Rev 2001; 14: 909-32.

[86] Fauran P, Donaldson M, Harper J, Oseni RA, Aaskov JG. Characterization of Ross River viruses isolated from patients with polyarthritis in New Caledonia and Wallis and Futuna Islands. Am J Trop Med Hyg 1984; 33: 1228-31.

[87] Broom AK, Lindsay MD, Wright AE, Smith DW, MacKenzie JS. Epizootic activity of Murray Valley encephalitis and Kunjin viruses in an aboriginal community in the southeast Kimberley region of Western Australia: results of mosquito fauna and virus isolation studies. Am J Trop Med Hyg 2003; 69: 277-83.

[88] Doherty RL, Carley JG, Filippich C, Kay BH, Gorman BM, Rajapaksa N. Isolation of Sindbis (alphavirus) and Leanyer viruses from mosquitoes collected in the Northern Territory of Australia, 1974. Aust J Exp Biol Med Sci 1977; 55: 485-9.

[89] Kay BH, Standfast HA. Ecology of arboviruses and their vectors in Australia. Curr Top Vector Res 1987; 3: 1-36.

[90] Russell RC. Mosquito-borne arboviruses in Australia: the current scene and implications of climate change for human health. Int J Parasitol 1998; 28: 955-69.

[91] Doherty RL, Carley JG, Kay BH, Filippich C, Marks EN, Frazier CL. Isolation of virus strains from mosquitoes collected in Queensland, 1972-1976. Aust J Exp Biol Med Sci 1979; 57: 509-20.

[92] Ritchie SA, Fanning ID, Phillips DA, Standfast HA, McGinn D, Kay BH. Ross River virus in mosquitoes (Diptera: Culicidae) during the 1994 epidemic around Brisbane, Australia. J Med Entomol 1997; 34: 156-9.

730 [93] Ryan PA, Do KA, Kay BH. Definition of Ross River virus vectors at Maroochy Shire,
731 Australia. J Med Entomol 2000; 37: 146-52.

732 [94] Watson TM, Kay BH. Vector competence of *Aedes notoscriptus* (Diptera: Culicidae) for
733 Barmah Forest virus and of *Aedes aegypti* (Diptera: Culicidae) for dengue 1-4 viruses in
734 Queensland, Australia. J Med Entomol 1999; 36: 508-14.

735 [95] Boyd AM, Kay BH. Vector competence of *Aedes aegypti*, *Culex sitiens*, *Culex*
736 *annulirostris*, and *Culex quinquefasciatus* (Diptera: Culicidae) for Barmah Forest virus. J
737 Med Entomol 2000; 37: 660-3.

738 [96] Ryan PA, Kay BH. Vector competence of mosquitoes (Diptera: Culicidae) from
739 Maroochy Shire, Australia, for Barmah Forest virus. J Med Entomol 1999; 36: 856-60.

740 [97] Kay BH, Edman JD, Fanning ID, Mottram P. Larval diet and the vector competence of
741 *Culex annulirostris* (Diptera: Culicidae) for Murray Valley encephalitis virus. J Med
742 Entomol 1989; 26: 487-8.

743 [98] Kay BH, Fanning ID, Carley JG. The vector competence of Australian *Culex*
744 *annulirostris* with Murray Valley encephalitis and Kunjin viruses. Aust J Exp Biol Med
745 Sci 1984; 62: 641-50.

746 [99] Kay BH, Fanning ID, Carley JG. Vector competence of *Culex pipiens quinquefasciatus*
747 for Murray Valley encephalitis, Kunjin, and Ross River viruses from Australia. Am J
748 Trop Med Hyg 1982; 31: 844-8.

749 [100] State of Queensland (Queensland Health), 2015. Queensland Dengue Management Plan
750 2015-2020. Available at: https://www.health.qld.gov.au/__data/assets/pdf_file/0022/
751 444433/dengue-mgt-plan.pdf [last accessed 15 May 2017].

752 [101] Kay BH, Carley JG, Fanning ID, Filippich C. Quantitative studies of the vector
753 competence of *Aedes aegypti*, *Culex annulirostris* and other mosquitoes (Diptera:
754 Culicidae) with Murray Valley encephalitis and other Queensland arboviruses. J Med
755 Entomol 1979; 16: 59-66.

756 [102] Gyawali N, Bradbury RS, Taylor-Robinson AW. The global spread of Zika virus: is
757 public and media concern justified in regions currently unaffected? Infect Dis Poverty
758 2016; 5: 37.

759 [103] Ritchie SA, Moore P, Carruthers M, Williams C, Montgomery B, Foley P, et al.
760 Discovery of a widespread infestation of *Aedes albopictus* in the Torres Strait, Australia.
761 J Am Mosq Control Assoc 2006; 22: 358-65.

762 [104] Doherty RL, Whitehead RH, Wetters EG, Johnson HN. Isolation of viruses from
763 *Ornithodoros capensis* Neumann from a tern colony on the Great Barrier Reef, North
764 Queensland. Aust J Sci 1968; 31: 363-4.

765 [105] Doherty RL, Carley JG, Murray MD, Main AJ Jr, Kay BH, Domrow R. Isolation of
766 arboviruses (Kemerovo group, Sakhalin group) from *Ixodes uriae* collected at Macquarie
767 Island, Southern ocean. Am J Trop Med Hyg 1975; 24: 521-6.

768 [106] St George TD, Standfast HA, Doherty RL, Carley JG, Fillipich C, Brandsma J. The
769 isolation of Saumarez Reef virus, a new flavivirus, from bird ticks *Ornithodoros capensis*
770 and *Ixodes eudyptidis* in Australia. Aust J Exp Biol Med Sci 1977; 55: 493-9.

771 [107] Standfast HA, Dyce AL, St George TD, Muller MJ, Doherty RL, Carley JG, et al.
772 Isolation of arboviruses from insects collected at Beatrice Hill, Northern Territory of
773 Australia, 1974-1976. Aust J Biol Sci 1984; 37: 351-66.

774 [108] Standfast HA, Dyce AL. Attacks on cattle by mosquitoes and biting midges. Aust Vet J
775 1968; 44: 585-6.

776 [109] Standfast HA, Dyce AL. Isolation of Thimiri virus from *Culicoides histrio* (Diptera:
777 Ceratopogonidae) collected in northern Australia. J Med Entomol 1982; 19: 212.

778 [110] Carey DE, Reuben R, George S, Shope RE, Myers RM. Kammavanpettai,
779 Kannamangalam, Sembalam and Thimiri viruses: four unrelated new agents isolated
780 from birds in India. Indian J Med Res 1971; 59: 1708-11.

781 [111] St George TD, Cybinski DH, Filippich C, Carley JG. The isolation of three Simbu group
782 viruses new to Australia. Aust J Exp Biol Med Sci 1979; 6: 581-2.

783 [112] Blacksell SD, Lunt RA, White JR. Rapid identification of Australian bunyavirus isolates
784 belonging to the Simbu serogroup using indirect ELISA formats. J Virol Methods 1997;
785 66: 123-33.

786 [113] Gyawali N, Bradbury RS, Taylor-Robinson AW. Do neglected Australian arboviruses
787 pose a global epidemic threat? Aust NZ J Public Health 2016; 40: 596.

Table 1. Australian arboviruses with their prototype number and source of initial isolation

Virus Name	Strain number	Family/Genus	Sero-reactive vertebrates	Relation to infection/ disease	Source of initial isolation	
					Year/Place	Species
Adelaide River	DPP61	*Rhabdoviridae*	Bovine		1981/Adelaide river, NT	Sentinel steer
Alfuy	MRM3929	*Flaviviridae/ Flavivirus*	Wild birds and domestic fowl		1966/Kowanyama, QLD	Bird *(Centropus phasianinus)*
Aino	JaNAr 28	*Bunyaviridae/ Bunyavirus*	Cattle	Domed skull, sunken eyes in cattle	1968/Samford, QLD	*Culicoides brevirarsis*
Almpiwar	MRM4059	*Rhabdoviridae*	Reptiles		1966/Southern Australia, NSW	Skink (*Ablepharus boutoniivirgatus*)
Akabane	R7949	*Bunyavirus*	Cattle, horses and sheep	Congenital abnormalities of the central nervous systems in cattle, goats, sheep	1968/Rockhampton, QLD	*Culicoides brevirarsis*
Buffalo Creek	DPP186	*Bunyaviridae*	Cattle, pig, human		1982/ Darwin, NT	*Anopheles meraukensis*
Bunyip Creek	CSIRO 58	*Reoviridae/ Orbivirus*	Cattle		1976/NSW	Cow *(Bos taurus)*
Bovine Ephemeral Fever	BB7721	*Rhabdoviridae*	Cattle	Fever in cattle	1968/Charters Towers, QLD	Cattle

Belmont	R8659	*Bunyaviridae/ Bunyavirus*	Wallabies, kangaroos, cattle		1968/Rockhampton, QLD	*Culex annulirostris*
Barmah Forest Virus	BH2193	*Togaviridae/ Alphavirus*	Wallabies, kangaroos	Polyarthralgia fever, rash	1974/Barmah Forest, Northern Victoria, NSW	*Culex annulirostris*
Berrimah	DPP63	*Rhabdoviridae*	Bovine sentinel		1981	Cattle
Charleville	Ch9824	*Rhabdoviridae*	No host detected		1969	Sandfly (*Phlebotomus* spp.)
Corriparta	MRM1	*Reoviridae/ Orbivirus*	Man, cattle, horses, kangaroos, wallabies, domestic fowl, wild birds		1960/Kowanyama, QLD	*Culex annulirostris*, Bird (*Charadrius melanops*)
Coastal Plains	DPP53	*Rhabdoviridae*	Cattle, wallabies, pigs		1981/Coastal plain	Steer
CSIRO Village	CSIRO 11	*Orbivirus*	Cattle, sheep, deer		1974/Beatrice Hill, NT	*Culicoides* spp.
D'aguilar	B8112	*Reoviridae/ Orbivirus*	Cattle, sheep		1968/South-east QLD	*Culicoides brevitarsis*
Douglas	CSIRO 150	*Bunyaviridae/ Bunyavirus*			Not specified	Mosquitoes
Edge Hill	C281	*Flaviviridae/ Flavivirus*	Wallabies, bandicoots, ?domestic fowl and cattle		1961/Cairns, QLD	*Aedes vigilax, Culex annulirostris*

Eubenangee	IN1074 (4)	*Reoviridae/ Orbivirus*	Kangaroos, wallabies, cattle		1963/Innisfail, QLD	Many mosquito spp.
Facey's Paddock	Ch 16129	*Bunyaviridae/ orthobunyavirus*				*Culicoides* spp.
GanGan	NB6057	*Bunyaviridae/ Bunyavirus*	Kangaroos, wallabies, rats, cows, horse	Polyarthralgia fever	1970/NSW	*Aedes vigilax*
Gadgets Gully	CSIRO 122	*Flaviviridae/ Flavivirus*	Birds, penguin		1976/ Macquarie Island	*Ixodes uriae*
Getah	MM2021	*Togaviridae/ Alphavirus*	Cattle, horses and man (doubtful)		1961/Normanton, QLD	*Anopheles amictus*, *Culex bitaeneorhynchus*
Holmes Jungle	DPP1163	*Rhabdoviridae*	Cattle, buffalo, humans		1987/Darwin, NT	*Culex annulirostris*
Harrison Dam	CSIRO75	*Rhabdoviridae*			1975/ Beatrice Hill, NT	*Culex annulirostris*
Kimberley	CSIRO 368	*Rhabdoviridae*	Cattle		1973/ Ord River Valley, WA	*Culex annulirostris*
Kununurra	OR194	*Rhabdoviridae*			1973/Kununurra, WA	*Aedes myiacatastica*
Kokobera	MRM 32	*Flaviviridae/ Flavivirus*	Wallabies, kangaroos, man, horses and cattle		1960/Kowanyama, QLD	*Culex annulirostris*
Koongal	MRM31	*Bunyaviridae/ Bunyavirus*	Cattle, bandicoots, wallabies, wild birds, domestic fowl		1960/Kowanyama, QLD	*Culex annulirostris*

Kowanyama	MRM1178	*Bunyaviridae*	Wallabies, kangaroos, man, cattle, sheep, horses pigs, rats, bandicoots, wild birds		1963/Kowanyama, QLD	*Anopheles annulipes*
					1966/Kowanyama, QLD	Skink (*Ablepharus boutoniivirgatus)*
Kunjin	MRM16	*Flaviviridae/ Flavivirus*	Man, domestic fowl and cattle		1960/Kowanyama, QLD	*Culex annulirostris*
					1963/Brisbane, QLD	Human
Lake Clarendon	CSIRO 704	*Reoviridae*	Cattle egret (*Bubulcus ibis*)		1981/Gatton, QLD	Tick (*Argas robertsi*)
Mapputta	MRM186	*Bunyaviridae*/ Bunyavirus-like	Kangaroos, wallabies, man, cattle, horses, pig		1960/Kowanyama, QLD	*Anopheles meraukensis*
					1969/Charleville, QLD	Mosquito species
Marrakai	CSIRO 82	Orbivirus	Cattle		1975/Beatrice Hill, NT	*Culicoides schultzei*
Maprik	MK7532	*Bunyaviridae*/ *Bunyavirus*-like			1966	*Aedes funereus*
Mitchell River	MRM10434	*Reoviridae*/ Orbivirus	Wallabies and cattle		1970/ Kowanyama, QLD	*Culicoides* spp.
Murray Valley Encephalitis	MVE/1/1951	*Flaviviridae/ Flavivirus*	Man, domestic fowls, cattle and horses	Encephalitis	1951/Southern Australia	Human
					1960/Kowanyama, QLD	*Culex annulirostris*

Ngaingan	MRM14556	*Rhabdovirus*	Wallabies, kangaroos, cattle	1970/ Kowanyama, QLD	*Culicoides* spp.
Nugget	MI14847	*Reoviridae/ Orbivirus*	Man, domestic fowl, horses, cattle	1972/Macquarie Island	*Ixodes uriae*
Peaton	CSIRO 110	*Bunyaviridae/ Bunyavirus*	Cattle, sheep, horses, goats	1976/Peachester, QLD	*Culicoides brevitarsis*
Picola	PK886	? *Orbivirus*		Picola, VIC	*Culex annulirostris*
Precarious Point	MI19334	*Bunyaviridae/ Uukuvirus*		1975/ Southern Ocean, Australia	*Ixodes* (*Ceratixodes*) *uriae*
Paroo River	GG668	*Reoviridae/ Orbivirus*		1973/Paroo River, NSW	*Culex annulirostris*
Ross River	T48	*Togaviridae/ Alphavirus*	Man, kangaroos, wallabies, cattle, horses and dogs Polyarthralgia	1959/Townsville, QLD	*Aedes vigilax*
				1965/Kowanyama	Birds *(Grallina cyanoleuca, Microeca fascinans)*
				1968/Kowanyama, QLD	*Wallabia agilis*
				1971/Edward River, QLD	Human
Sindbis	Ar 339	*Togaviridae/ Alphavirus*	Human, cattle, dogs, domestic fowl, wild birds and wallabies	1960/ Kowanyama, QLD	*Culex annulirostris*

Saumarez Reef	CSIRO 04	*Flaviviridae/ Flavivirus*		1974/Saumarez Reefs	*Ornithodoros capensis*
Samford	B7974		Cattle, horses	1968/South-East Queensland	*Culicoides brevitarsis*
Stratford	C338	*Flavivirividae/ Flavivirus*	Cattle (doubtful)	1961/Cairns, QLD	*Aedes vigilax*
Taggert	M14850	*Bunyaviridae/ Nairovirus*		1976/Red River	*Ixodes* (*Ceratixodes*) *uriae*
Termeil	BP8090	*Bunyavirus*		1972/ Termeil State Forest, NSW	*Aedes camptorhynchus*
Tibrogargan	CSIRO132	*Rhabdoviridae*	Cattle	1976/Peachester, QLD	*Culicoides brevitarsis*
Tilligerry	NB7080	*Reoviridae/ Orbivirus*		1971/Nelson bay, NSW	*Anopheles annulipes*
Tinaroo	CSIRO 153	*Bunyaviridae/ Bunyavirus*	Cattle		*Culicoides brevitarsis*
Trubanaman	MRM3630	Bunyaviridae/ Bunyavirus-like	Man, cattle, sheep, wallabies	1965/Kowanyama, QLD	*Anopheles annulipes*
Upolu	C5581	*Bunyaviridae/ Bunyavirus*-like	No host detected	1966/Upolu Cay, QLD	Tick *(Ornithodoros capensis)*
Wallal	CH12048	*Reoviridae/ Orbivirus*	Wallabies, kangaroos	1970/Charleville, QLD	*Culicoides dycei, Culicoides marksi*
	MRM13443 MRM14SS6			1970/Kowanyama, QLD	*Culicoides brevitarsis*
Warrego	CH9935	*Reoviridae/ Orbivirus*	Wallabies, kangaroos, cattle	1969/Charleville, QLD	*Culicoides* spp., *Culicoides dycei, Culicoides marksi*

Wongorr	MRM13443	*Unclassified/ Orbivirus*	Cattle and macropods	1970/ Kowanyama	
Wongal	MRM168	*Bunyaviridae/ Bunyavirus*-like		1960/Kowanyama, QLD	*Culex annulirostris*
Yacaaba	NB6028			1970/Nelson Bay, NSW	*Aedes vigilax*

NSW = New South Wales; NT = Northern Territory; QLD = Queensland; SA = South Australia; VIC = Victoria; WA = Western Australia

Table 2. Arbovirus vectors (mosquitoes) and their distribution in Australia

Mosquito species	Distribution	Associated arboviruses
Anopheles amictus	NSW, QLD, WA	RRV, BFV, SINV, EHV
Anopheles annulipes	All States/ Territories	BFV, RRV, MVEV, SINV, TRUV
Anopheles bancroftii	NT, QLD, WA	MVEV, SINV
Anopheles hilli	WA	SINV
Anopheles meraukensis	WA	SINV
Aedes aegypti	QLD	DEN
Aedes alternans	NSW, QLD, NT, SA, VIC, WA	RRV, SINV
Aedes bancroftianus	NSW, QLD, NT, SA, VIC, WA	BFV, RRV, GGV, EHV
Aedes camptorhynchus	NSW, SA, TAS, VIC, WA	BFV, RRV, SINV, KOKV
Aedes clelandi	SA, TAS, VIC, WA	RRV
Aedes flavifrons	NSW, SA, TAS, VIC	RRV
Aedes eidsvoldensis	QLD, WA	BFV, SINV, GGV, MVEV
Aedes procax	NSW, QLD, VIC	BFV, RRV
Aedes normanensis	NSW, NT, QLD, WA	BFV, MVEV, RRV, SINV, GGV, EHV, Facey's Paddock
Aedes pseudonormanensis	WA	BFV, SINV, MVEV
Aedes theobaldi	NSW, QLD, SA, VIC,WA	RRV, SINV, GGV
Aedes tremulus	WA	RRV, SINV, KUNV, MVEV
Aedes sagax	NSW, QLD, SA, VIC, WA	RRV
Aedes vigilax	All States/Territories	RRV, BFV, SINV, GGV, EHV, KOKV, STRV

Aedes notoscriptus	NT, NSW, QLD	RRV, BFV
Coquillettidia linealis	NSW, QLD, SA, VIC	BFV, RRV, GGV, TRUV, EHV
Culex annulirostris	All States/Territories	RRV, BFV, KUNV, MVEV, KOKV, ALFV, EHV, GGV, TRUV, SINV, KOOV, WONV, CORV, KOWV, EUBV, Facey's Paddock
Culex australicus	All States/Territories	RRV, SINV, KUNV, MVEV
Culex quinquefasciatus	All States/Territories	BFV, KUNV, MVEV, RRV, SINV, KUNV
Culex palpalis	WA	RRV, MVE
Culex sitiens	WA, QLD, NSW	RRV, BFV, SINV
Mansonia uniformis	NSW, NT, QLD, VIC, WA	BFV, MVEV, RRV

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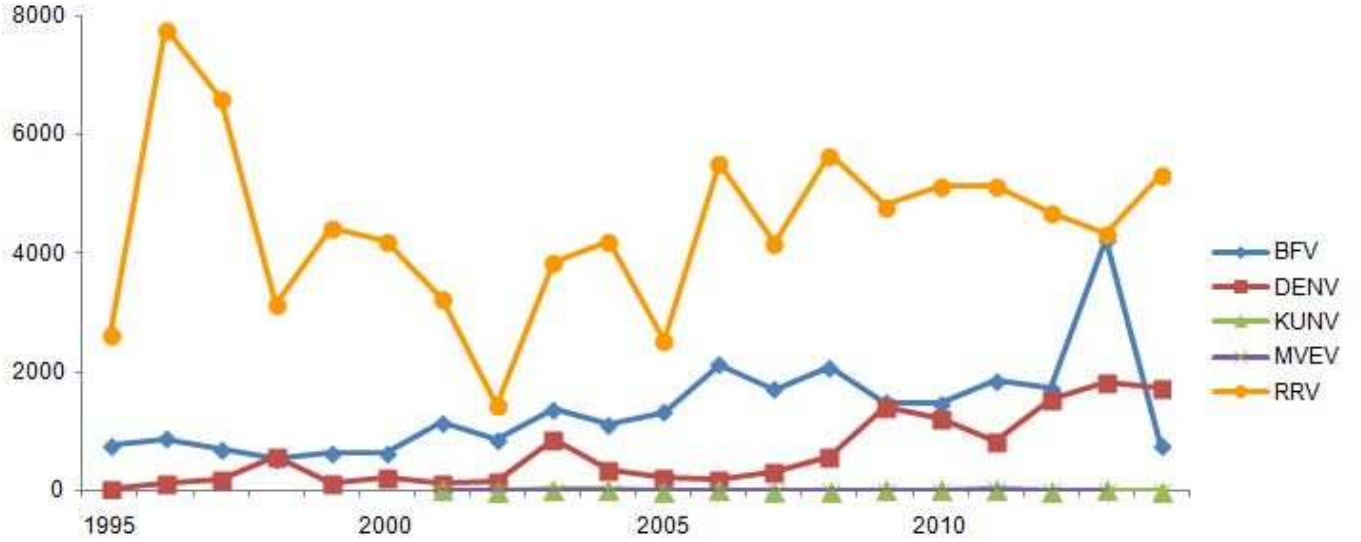
FIGURE LEGENDS

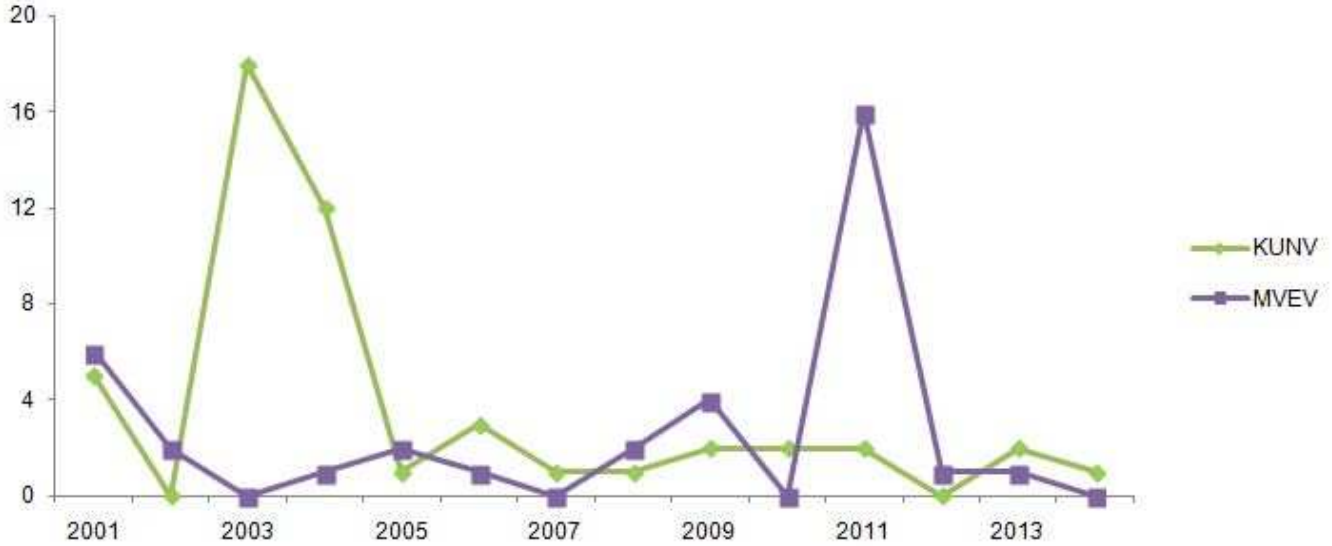
Figure 1. Notified cases of arbovirus infections in Australia over the 20 year period 1995-2014. (a) notifications of arboviruses Barmah Forrest (BFV), dengue (DENV), West Nile Kunjin strain (KUNV), Murray Valley encephalitis (MVEV) and Ross River (RRV); (b) notifications of KUNV and MVEV in magnified scale. Data source: Australian Government, Department of Health. National notifiable diseases: Australia's notifiable diseases status. Annual reports of the National Notifiable Diseases Surveillance System, 1995-2014. Available at: http://www.health.gov.au/internet/main/publishing.nsf/ Content/cda-pubs-annlrpt-nndssar.htm

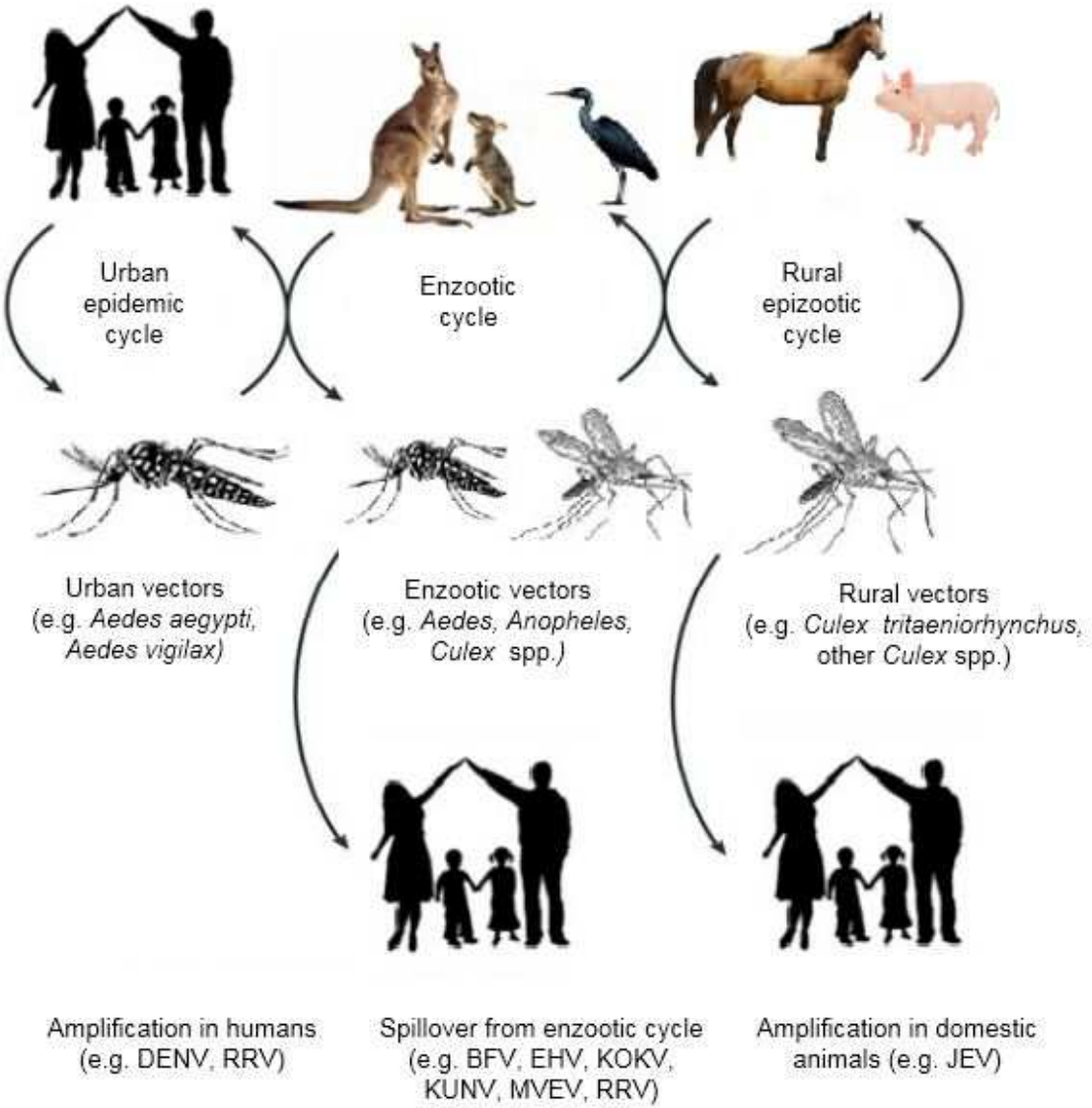
Figure 2. Transmission cycle of Australian arboviruses.

(a)



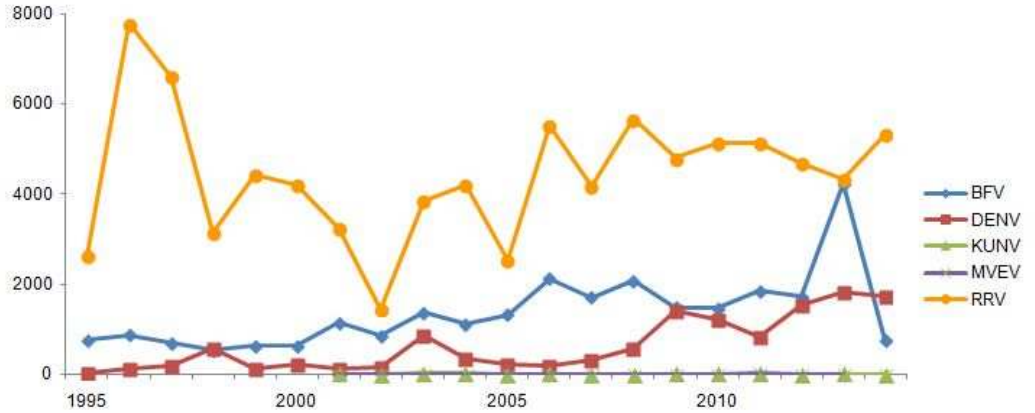
(b)



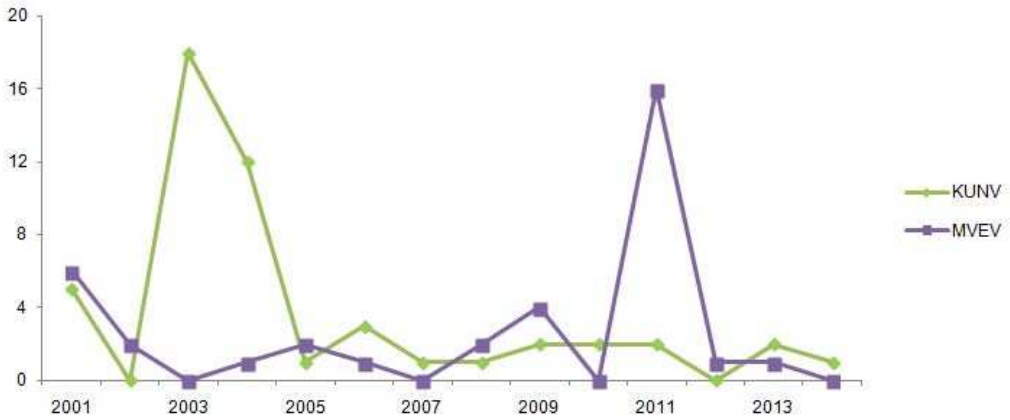


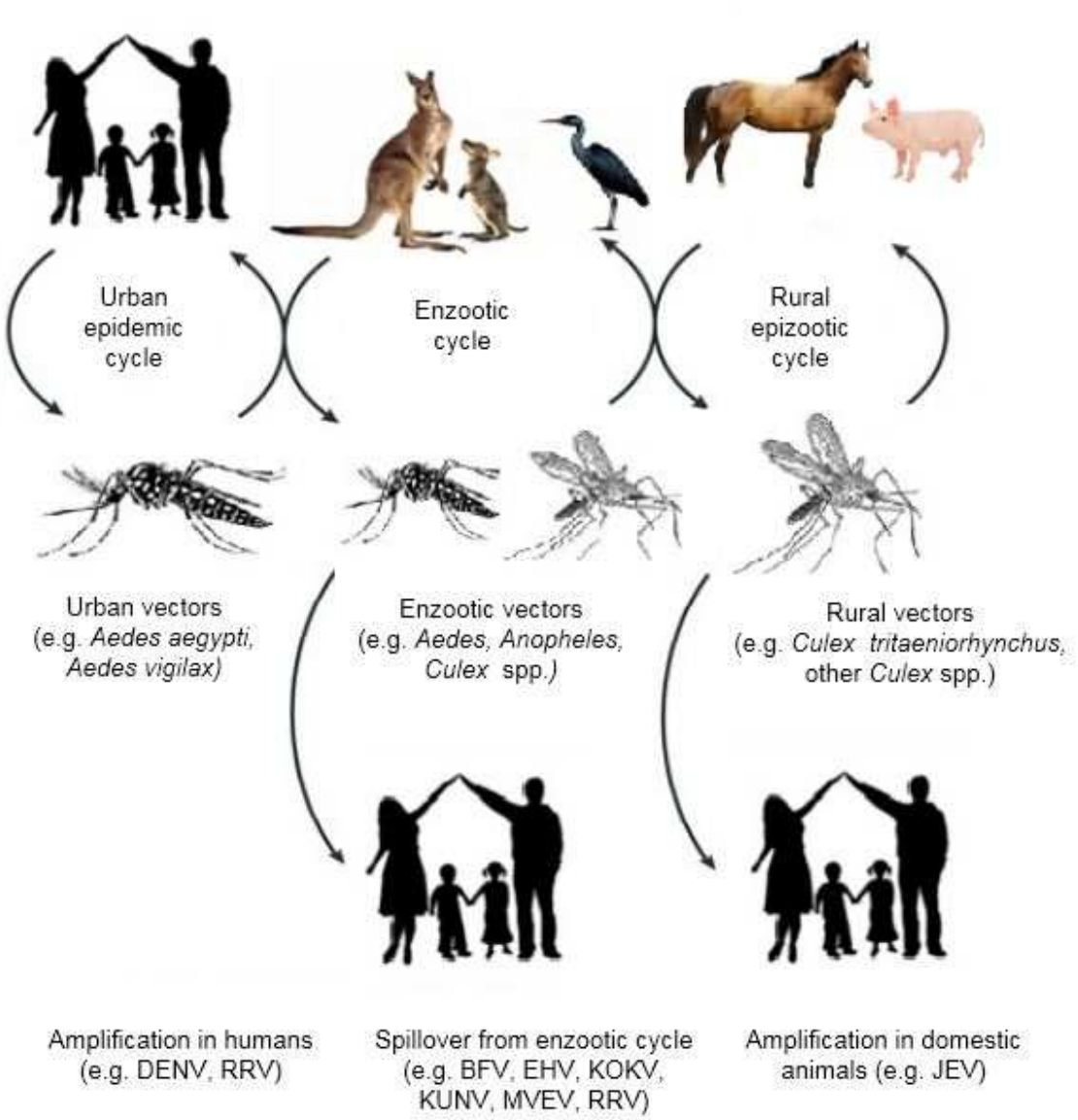
Arboviruses – BFV: Barmah Forest; DENV: Dengue; EHV: Edge Hill; JEV; Japanese encephalitis; KOKV: Kokobera; KUNV: Kunjin; MVEV: Murray Valley encephalitis; RRV: Ross River

(a)



(b)





Arboviruses – BFV: Barmah Forest; DENV: Dengue; EHV: Edge Hill; JEV; Japanese encephalitis; KOKV: Kokobera; KUNV: Kunjin; MVEV: Murray Valley encephalitis; RRV: Ross River