Risks for Ross River virus disease in tropical Australia

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Background There are no analytical studies of individual risks for Ross River virus (RRV) disease. Therefore, we set out to determine individual risk and protective factors for RRV disease in a high incidence area and to assess the utility of the case–control design applied for this purpose to an arbovirus disease.

Methods We used a prospective matched case–control study of new community cases of RRV disease in the local government areas of Cairns, Mareeba, Douglas, and Atherton, in tropical Queensland, from January 1 to May 31, 1998.

Results Protective measures against mosquitoes reduced the risk for disease. Mosquito coils, repellents, and citronella candles each decreased risk by at least 2-fold, with a dose–response for the number of protective measures used. Light-coloured clothing decreased risk 3-fold. Camping increased the risk 8-fold.

Conclusions These risks were substantial and statistically significant, and provide a basis for educational programs on individual protection against RRV disease in Australia. Our study demonstrates the utility of the case–control method for investigating arbovirus risks. Such a risk analysis has not been done before for RRV infection, and is infrequently reported for other arbovirus infections.

Keywords Communicable diseases, emerging, arboviruses, Togaviridae, Alphavirus, Ross River virus, epidemiology, case–control studies, risk, behaviour, mosquito, Diptera, insect repellents, camping, Queensland, Australia

Ross River virus (RRV) causes the most common arbovirus disease in Australia. Cases typically present with arthralgia or arthritis persisting weeks to months.1,2 The virus is transmitted from other vertebrates to humans by mosquitoes with an incubation period in humans from 3 to 21 days, typically 7–9 days.1 Kangaroos and wallabies are natural reservoir hosts for RRV but other species, such as birds, possums, flying-foxes, and horses, may play a role in urban settings.1 Each year in Australia an average of 5000 cases are notified and at least as many infections are not detected.1 The highest risk is in the north of Queensland, the state where the majority of cases occur.1,3,4 High temperature, rainfall, tides, and humidity are associated with increased transmission.5,6

No data exist to predict the risk of RRV disease at an individual or household level. To enable advice on personal prevention of RRV disease we studied these risks in tropical Queensland. Our results reveal the utility of the case–control design for studying behavioural and environmental risks for arbovirus diseases, a purpose for which this epidemiological method has rarely been used.7–10

Methods We performed a community-based prospective case–control study of RRV disease in Cairns and contiguous local government areas (Douglas, Mareeba, and Atherton) in North Queensland (Figure 1). Our surveillance system ascertained new cases of RRV infection as they were notified to Queensland Health by all private and public pathology laboratories in the study area. Although privacy legislation prevented us from obtaining complete identifying data for new cases, the laboratories

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provided the sex, date of birth, and treating doctor. We then asked general practitioners (GPs) to invite eligible RRV cases to join our study.

Eligible cases were defined as persons with locally acquired RRV disease occurring in the high-transmission wet season period from January 1 to May 31, 1998. Indirect ELISA using the only commercial RRV test kits then available (PanBio™, Brisbane, Australia) was used for serological diagnosis either as a single positive IgM test (40 cases) or IgG seroconversion (15 cases).1,11 All cases included had resided in the study area for ≥1 month before the onset of arthralgia or arthritis between January 1 and May 31, 1998. One of us (D.H.) then clinically examined all cases in their homes.

Concurrently a risk assessment questionnaire and household environmental proforma were completed. Using these instruments 108 exposures were measured. These included sporting and leisure activities (for example fishing, bushwalking, and golf), peri-domestic activities (for example gardening and smoking outside in the evening), exposure to reservoir hosts and vectors (for example seeing kangaroos or wallabies in the yard or being bitten by mosquitoes in the house), peri-domestic vegetation and other aspects of the peri-domestic environment (for example a bird bath, pond, ice-cream containers, or buckets), features of the dwelling (for example high or low set house and insect screening), work conditions (for example, air-conditioning of the work place and working outside), the use of protective measures (for example personal insect repellents), potential domestic reservoir hosts (for example dogs and cats), and other behaviours (such as the use of perfume or deodorant). Exposures were generally assessed during the incubation period, the year before symptom onset, or both. This is discussed further below.

GPs whose practice included a case were asked to select controls from their practice list, matched on 10-year age group and sex. Controls had to be willing to provide a blood sample to demonstrate the absence of RRV IgG and IgM. Up to four controls were sought for each case, although most GPs provided one or two. Pragmatically, controls had to be selected by different methods: some GPs had computerized patient datasets and were able to generate lists of age and sex matched controls, while others had to rely on their own recall or that of their staff to identify potential controls. The GP or their staff contacted potential controls seeking their consent to be enrolled in the study. Data collection procedures for controls were identical to those for cases. A single investigator (D.H.) conducted all the interviews and inspections using a standard questionnaire and pro forma unblinded to the participant’s disease status.

Risk and protective factors were assessed in three ways: across the inferred incubation period; over the year before symptom onset; and without time reference. The incubation period (the ‘3-week exposure period’) included the 21 days ending four days before symptom onset, the period when infection would be most likely to occur (this period does not correspond precisely to the possible incubation period of between 3 and 21 days before symptom onset, but was used because we felt it would aid participant’s recall, being a 3-week period and including 3 weekends).1 We chose these three methods of assessing past exposure to avoid exclusive dependence on
potentially biased recall across the inferred incubation period. Time-related exposure data for controls related to the same periods as the cases to whom they were matched (for example, a case with symptom onset on March 2, 1998 would be presumed to have been exposed between February 5 and 26, and their matched control would be asked about activities during this period). Environmental risks relating to house design and garden features were assessed by direct inspection at the time of interview.

All analyses were performed using SPSS. All odds ratios (ORs) and confidence intervals (CIs) were calculated using Cox regression by a method equivalent to conditional logistic regression. These analyses were matched, and the use of this method allows for matching of a variable number of controls per case. We calculated ORs for all measured exposures, and present those that were statistically significant (95% CI excluding 1.0), suggestive of an epidemiological effect (OR < 0.7 or OR > 1.5) or biologically plausible. Having determined important exposures we assessed confounding and effect modification by stratification and multivariable analysis involving these factors.

The University of Queensland Medical Research and the Cairns Base Hospital ethics committees approved the study.

Results
Characteristics of cases and controls
The study included 55 cases and 85 controls, with one to four controls matched to each case.

The 55 cases accepted for our study represented nearly half the 129 RRV infections notified to the local surveillance system over the study period. The most common reason that notified cases were not included in our study was that doctors treating the cases did not consent to participation. A few did not qualify after assessment of their clinical or diagnostic profile. When notifications included were compared with those not in our study there was no difference in the proportion of females (χ^2 test, P = 0.84) or in the mean ages (t test, P = 0.14).

All 85 controls selected had negative RRV IgG and IgM ELISA tests. Nine further potential controls were excluded due to positive RRV IgG ELISA tests. Forty-eight controls had not seen their GP within one month before recruitment to the study. Of the remaining 37 controls, 16 presented for non-acute causes and 21 presented with various injuries, infections, or undifferentiated symptoms including lethargy and heart palpitations.

Cases and controls were similar for age (mean ages of 39 and 40 years, ranges of 17–63 and 16–69, respectively) and proportion female (cases 51%, controls 55%). Controls were more likely than cases to have had tertiary education (33% vs 24%) and to be professionals, managers or administrators (32% vs 22%), although these differences were not statistically significant (χ^2 tests, P > 0.20). Ninety-three percent of cases and 94% of controls lived in houses, the others in flats, caravan parks and so on. The frequency of alcohol consumption was similar for cases and controls; 20 and 24% did not drink at all or drank occasionally; 20 and 17% drank monthly or more often, but not every week; and 60% and 60% drank at least once per week to daily, respectively. Cases and controls were similar in terms of co-morbidities (Table 1). However, controls were interviewed a significantly longer time after the inferred exposure period for their matched case than were the cases (mean period between onset and interview 105 and 36 days, respectively).

Risk factor analysis
We first used crude (unadjusted but matched) ORs to assess exposures. Camping (ever vs never in the year before symptom onset) doubled RRV disease risk (Table 2). There was also a dose–response for the frequency of camping in the year before symptom onset. With never camping as the reference category, camping 1–3 times was associated with an OR of 1.87 (95% CI 0.76–4.60) and 4 or more times increased the risk 2.5-fold (OR 2.41, 95% CI 1.04–5.56; Wald chi-squared for linear trend 5.0, P = 0.08). None of the 15 other peri-domestic or sporting activities studied increased the crude risk significantly, although some had reasonably strong associations (data not shown).

We did not demonstrate any statistically significant association between the presence of domestic and wild animals thought to be potential reservoirs for infection and risk for RRV disease. However, the ORs for having seen kangaroos or wallabies in the yard during the incubation period was suggestive of an association (Table 2). Because of missing data (four cases and eight controls could not recall their exposure status) and the importance of this association, we performed sensitivity analysis. If all cases and controls with missing exposure data were assumed exposed, the OR (95% CI) was 1.91 (95% CI 0.72–5.08); if they were assumed unexposed the OR (95% CI) was 3.50 (95% CI 0.87–14.1). However, if we assumed that a recall bias might operate where cases were more likely than controls to remember exposure, and that cases with missing data were unexposed and controls with missing data were exposed, then the association disappears (OR = 1.00, 95% CI 0.36–2.78). It is therefore possible that the association does not exist. There were no significant or suggestive associations between the observed presence of flying foxes, possums,

<table>
<thead>
<tr>
<th>Medical condition</th>
<th>Cases^a</th>
<th>Controls^a</th>
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</thead>
<tbody>
<tr>
<td><strong>Arthritides</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Osteoarthritis</td>
<td>4 (7)</td>
<td>3 (4)</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Gout</td>
<td>1 (2)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Ankylosing spondylitis</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Psoriatic arthritis</td>
<td>1 (2)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Other arthritides</td>
<td>2 (4)</td>
<td>2 (2)</td>
</tr>
<tr>
<td><strong>Other medical illnesses</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>1 (2)</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>3 (6)</td>
<td>8 (9)</td>
</tr>
<tr>
<td>Asthma</td>
<td>8 (15)</td>
<td>12 (14)</td>
</tr>
<tr>
<td>Epilepsy</td>
<td>0 (0)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Chronic fatigue syndrome</td>
<td>1 (2)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Fibromyalgia</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Other chronic illness</td>
<td>11 (20)</td>
<td>22 (26)</td>
</tr>
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^a For cases n = 55 and for controls n = 85, cells show n (%).
various species of bird, or mosquitoes in and around the house, and the RRV disease risk (data not shown). The presence of bromeliads or banana trees in domestic gardens had a possible association with RRV disease risk (Table 2).

A preference for light-coloured clothing decreased risk by nearly 3-fold, and use of personal protective measures against mosquitoes (particularly personal insect repellents, citronella candles, and mosquito coils) had similarly strong inverse associations with RRV disease risk (Table 2). A dose–response was noted with falling disease risk related to increasing use of multiple protective measures (repellents, aerosols, surface sprays, coils, citronella candles, or electrical pyrethroid dispensers) in the year before symptom onset (Figure 2). The OR when 5–6 measures were used was 0.28 (95% CI 0.09–0.89).

No consistent relationship between RRV disease and observed peri-domestic environments emerged. Thus, risk did not significantly increase with presence of a veranda, porch or patio, or a laundry under or outside the dwelling. Risk was not significantly affected by screening or air-conditioning of the dwelling or workplace, although the inverse association with domestic air-conditioning was suggestive for partial or complete vs no air-conditioning of the dwelling (Table 2).

ORs were then recalculated after stratifying by date of symptom onset (January 1–February 8 vs February 9–May 31; these periods were selected to reflect possible seasonally related vector shifts while aiming pragmatically to produce approximately equal strata), geographical area (coastal plain vs elevated inland zone ‘tablelands’), sex, and age group (15–39 years vs 40–69 years; these age groups were selected pragmatically to produce approximately equal strata). Only stratification by the first two suggested interactions of ecological or public health importance (Table 3). Use of insect repellents was protective in the early symptom onset period (January 1–February 8) but not the later period (February 9–May 31). The protective effect of wearing light-coloured clothing was also attenuated in the later period. Camping in the year before symptom onset was significantly associated with RRV disease risk in the coastal, but not the inland (tablelands) stratum. The presence of bromeliads (ornamental plants that hold water) in the garden was also significantly associated with risk in the coastal but not the tablelands stratum.

For important risk and protective factors simple models were constructed to test confounding of one variable by another.

### Table 2 ORs and 95% CIs for RRV disease risk and protective exposures, tropical Queensland, 1998

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>OR</th>
<th>95% CI</th>
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<tbody>
<tr>
<td><strong>Risk exposures</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Camping&lt;sup&gt;a&lt;/sup&gt;</td>
<td>2.15</td>
<td>1.07–4.35</td>
</tr>
<tr>
<td>Camping&lt;sup&gt;b&lt;/sup&gt;</td>
<td>3.00</td>
<td>0.86–10.5</td>
</tr>
<tr>
<td>Bromeliads&lt;sup&gt;c&lt;/sup&gt;</td>
<td>1.80</td>
<td>0.83–3.92</td>
</tr>
<tr>
<td>Banana trees&lt;sup&gt;d&lt;/sup&gt;</td>
<td>2.50</td>
<td>0.83–7.53</td>
</tr>
<tr>
<td>Kangaroos or wallabies in garden&lt;sup&gt;e&lt;/sup&gt;</td>
<td>4.30</td>
<td>0.87–21.2</td>
</tr>
<tr>
<td>Working outside&lt;sup&gt;f&lt;/sup&gt;</td>
<td>1.95</td>
<td>0.88–4.34</td>
</tr>
<tr>
<td><strong>Protective exposures</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Personal repellents&lt;sup&gt;g&lt;/sup&gt;</td>
<td>0.44</td>
<td>0.20–1.00</td>
</tr>
<tr>
<td>Mosquito coils&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.42</td>
<td>0.19–0.90</td>
</tr>
<tr>
<td>Citronella candles&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.29</td>
<td>0.10–0.78</td>
</tr>
<tr>
<td>Preference for light-coloured clothing&lt;sup&gt;h&lt;/sup&gt;</td>
<td>0.37</td>
<td>0.15–0.89</td>
</tr>
<tr>
<td>Air-conditioning&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.52</td>
<td>0.26–1.04</td>
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</tbody>
</table>

<sup>a</sup> Year before onset, ever vs never.
<sup>b</sup> Three-week exposure period, ever vs never, data missing for 4 controls.
<sup>c</sup> Based on direct inspection, presence vs absence, data missing for 1 control.
<sup>d</sup> Based on direct inspection, data missing for 1 case and 1 control.
<sup>e</sup> Assessed by questionnaire for the 3-week exposure period, data missing for 4 cases and 8 controls.
<sup>f</sup> No specific time reference, none vs some time.
<sup>g</sup> Without time reference.
<sup>h</sup> Assessed by questionnaire at time of interview, any air-conditioning vs none.

**Figure 2** Odds ratios and 95% confidence intervals for number of protective measures used against mosquitoes in the year before symptom onset, with 0–2 as reference category.
Table 3 Influence of onset period and residential area on RRV risk estimates

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>OR</th>
<th>95% CI</th>
<th>OR</th>
<th>95% CI</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Onset Date</td>
<td></td>
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<tr>
<td>Insect repellentsa</td>
<td>0.16</td>
<td>0.05–0.58</td>
<td>0.96</td>
<td>0.38–2.42</td>
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<tr>
<td>Light-coloured</td>
<td>0.09</td>
<td>0.01–0.74</td>
<td>0.73</td>
<td>0.25–2.13</td>
</tr>
<tr>
<td>clothingb</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Campingda</td>
<td>2.42</td>
<td>1.10–5.29</td>
<td>1.27</td>
<td>0.24–6.62</td>
</tr>
<tr>
<td>Bromeliads in garden^c</td>
<td>3.59</td>
<td>1.33–9.71</td>
<td>0.35</td>
<td>0.07–1.77</td>
</tr>
</tbody>
</table>

Geographical Area

<table>
<thead>
<tr>
<th>Coastal</th>
<th>Tablelands</th>
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^a Year before symptom onset, ever vs never.
^b Without time reference.
^c Inspection of dwelling, presence vs absence.

Thus, camping and bromeliads were adjusted for each protective factor and the number of protective factors used in the year before symptom onset (see Figure 2). In all cases the adjustments had effects as expected, thus for camping in the year before symptom onset or in the 3-week exposure period, the protective factors boosted adjusted estimates from 1.9 to 2.6 and 3.1 to 5.8, respectively. For air-conditioning of the dwelling, bromeliads, and light-coloured clothing those protective factors did not significantly or consistently alter effect estimates, so we considered there was no interaction.

Finally, multivariable analyses were performed for each risk factor including in the model the three key negative confounders—use of repellents, citronella candles, and mosquito coils—identified in the initial analysis. This substantially increased the ORs for camping in the 3-week exposure period, to 7.90, and in the year before symptom onset, for working outdoors, and for banana trees around the dwelling (Table 4). It also reduced the magnitude of the effects of individual protective factors, with adjusted ORs (95% CIs) for personal repellents, citronella candles, and mosquito coils of 0.58 (0.25–1.38); 0.38 (0.13–1.06); and 0.55 (0.24–1.27); respectively, and for 5–6 relative to 0–2 protective measures 0.92 (0.18–4.61).

Discussion

Much research has focused on the vector associations of RRV and its possible emergence as an expanding climate-sensitive infection in Australasia.5,6,15,16 This study is the first to examine individual and household risks for RRV disease. The use of personal protective measures (mosquito coils, repellents, and citronella candles) each reduced risk at least 2-fold. Light-coloured clothing decreased risk by a factor of nearly three, while camping increased the risk 8-fold. There was significant effect measure modification operating between the risk associated with camping and personal protective factors (personal repellents, mosquito coils, citronella candles, and a preference for light-coloured clothing). These results provide evidence for safe, low cost prevention, and suggest that protection is particularly important when camping.

Our results cannot implicate specific vector or reservoir species, but were consistent with known associations. Seeing kangaroos and wallabies in the yard did increase risk, but the low prevalence of exposure (11 cases and nine controls) led to wide CIs and missing data may have biased the estimate. Nonetheless, the increased risk associated with camping suggests that entry of humans into bush areas, where sylvatic RRV transmission among kangaroos and wallabies occurs, is an important source of human infection. The protective effect of light-coloured clothing is consistent with RRV transmission by a mosquito that will feed during the day, because day-biting mosquitoes use visual cues and are attracted to dark colours.17

The most likely candidates are Oc. notoscriptus and Verrallina carmenti.1,18–20

The increased risk associated with bromeliad plants on the coast could reflect their role as breeding sites for Oc. notoscriptus and the potential vector Aedes aegypti.21–23 The significant waning in the protective effect of both repellents and light-coloured clothing later in the transmission season could result from a shift from early season transmission by species that feed during the day (probably Oc. notoscriptus and Oc. vigilax) to later transmission by crepuscular and nocturnal biters (such as Oc. annulirostris). There is some evidence for vector succession in RRV transmission.24

Overall then, these findings are biologically and ecologically coherent, which argues against their being simply a few chance findings among many observations. However, other challenges to a causal interpretation warrant consideration. With respect to measurement issues, misclassification of disease status is very unlikely. Clinical review, exclusion of other diagnoses, and the high specificity of the ELISA test for RRV IgM and IgG (96.5 and 97.6, respectively25 and Ming Qiao, personal communication) make misclassification of disease status unlikely among cases.

Controls had no clinical history or serologic evidence of RRV disease. Because of the sensitivity of the RRV IgG ELISA test, 84.6%25 and because IgG probably persists for life,26 it is unlikely that controls had past exposure to and were therefore protected from RRV infection. The RRV IgM ELISA test has high sensitivity of 98.5%.25 Controls had negative IgM tests, and had not consulted their GP within 1 month before recruitment, or presented with symptoms unlikely to be caused by RRV disease. Therefore, it is unlikely that controls were misclassified incident RRV disease cases.

Recall bias is a possible threat to the validity of our study. In particular, because there was a longer delay to control than case interview, controls might have been less likely to recall exposures in the inferred incubation period than cases. This might have been the reason for the association with camping in this period and our
sensitivity analysis suggests this could be so for the association of RRV disease with kangaroos and wallabies. However, the finding of an increased risk associated with camping was constant for both the year before symptom onset and the inferred incubation period and we believe the consistency and strength (an 8-fold increase in risk for the 3-week exposure period when confounders were adjusted for, see Table 4) of this finding, along with its biological plausibility make it unlikely to be an artefactual finding caused by recall bias. Similarly, use of personal protective factors was assessed in the year before symptom onset, lessening the possibility for this bias to operate. And preference for clothing colour was assessed without a temporal component, assuming this was a constant trait of the study subject this should not have been subject to recall bias.

Because the interviewer could not be blinded to the disease status of a participant he was interviewing, it is possible observer bias could have resulted were he to have formulated aetiological hypotheses regarding disease risk. However, we believe both the complex ecology of the virus (meaning that the investigator was unlikely to form simple a priori hypotheses, as might be the case in a study investigating, say, an association between radiation and fetal malformations) and the forced objectivity of data collection (resulting from the uniform use of the same instruments for data collection from cases and controls) limited the scope for such misclassification of exposure status.

GPs selected controls from age and sex matched patients attending their practice. With regard to the potential for selection bias influencing estimates, the controls clearly met the desirable practical criterion of being likely to appear in the case series if they developed RRV disease.27 The age and sex matching worked well, and cases and controls were also similar for arthritides, other illnesses, housing and alcohol consumption, but the differences in social markers (controls were more highly educated and more likely to hold professional and managerial positions) probably reflect some self-selection, and perhaps vagaries of the GP selection too. These differences were modest; nonetheless, it remains possible that an association of these characteristics with risk or protective factors could have conflated the results, as might, of course, unmeasured factors.

Because of the small size of the study and the large number of exposures assessed, only limited control of confounding was possible during analysis. Use of protective measures did confound other associations and we could adjust for that. The matching of cases and controls for age, sex, exposure period, and geographical area prevented confounding by matched factors, and by ecological determinants such as temperature and rainfall.5

Despite the large numbers of mosquito species from which RRV has been isolated, at present there is good evidence for a virus–vector association only with a small number of species. Ochlerotatus vigilax and Oc. campytorhynchus are important vectors in the northern and southern parts of Australia, respectively, and Culex annulirostris plays a major role in transmission throughout Australia.1,20 Some other species, such as the peri-domestic container breeder, Oc. notoscriptus may also play a more minor role.22 Because being bitten by an infected vector mosquito represents the primary proximal determinant for RRV infection we believe that our findings on the protective effects of repellents, coils and citronella candles, and light-coloured clothing can be generalized to at least the rest of the Australian continent, and perhaps to other arboviruses occurring in South East Asia, such as the Japanese encephalitis virus.

Thus on the basis of the study we can recommend personal protective measures, particularly repellents, citronella candles and mosquito coils, and the wearing of light-coloured clothing. These methods lowered risk for disease in this study and have minimal costs. The use of multiple measures had a greater effect than a single measure, and we particularly recommend that they be used while camping. While there is evidence for the efficacy of these methods in repelling and preventing mosquito bites we are not aware of any evidence, before our study, for protection against RRV disease. However, a recent study of an outbreak of Plasmodium vivax malaria amongst campers in North Queensland pointed to failure to use mosquito protection as a risk factor.32 Our findings should be promulgated in Australia as public health messages to reduce the incidence of RRV disease.

As we have noted previously, it seems unlikely that enzootic transmission cycles in kangaroos and wallabies could fuel large suburban outbreaks of RRV disease.1 However, the results presented above are consistent with transmission to humans from kangaroos and wallabies while camping in endemic regions with a seasonal transmission pattern, such as tropical North Queensland. Recall bias and missing data may weaken our finding of an association between kangaroos and wallabies, and RRV disease risk. But there is evidence from serological surveys and virus isolation that kangaroos and wallabies are reservoir hosts for RRV.1 Therefore, we postulate that the virus can be maintained in enzootic sylvatic cycles, and that in large outbreaks human-to-human transmission, as may have occurred in the Pacific epidemic of the late 1970s1 and in Australian outbreaks,33 perhaps with transmission among other non-human vertebrates,1 maintains epidemic transmission until numbers of non-immune hosts have dropped to too low a number to maintain transmission.

Finally, our study has demonstrated that the case–control method of studying arbovirus disease risks is feasible, efficient, and useful for prevention-oriented field research. Indeed, case–control studies are probably the only feasible method for assessing individual risks for RRV disease. Case–control design has only rarely been used for the study of arbovirus risks,7–10 but we recommend this design for this purpose, and for studies of RRV and other arboviruses in other ecological zones of Australia and internationally.

Acknowledgements

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KEY MESSAGES

• Protective behaviours, principally the use of personal insect repellents, citronella candles, and mosquito coils, and wearing of light-coloured clothes, protect against Ross River virus disease in tropical Australia.

• Camping increases the risk for Ross River virus disease in tropical Australia.

• The case–control design is a viable methodology for studying risks for Ross River virus and other mosquito-borne diseases.

References


Ochlerotatus notoscriptus

Culex annulirostris

Ochlerotatus vigilax