Tropical Medicine and International Health doi:10.1111/j.1365-3156.2008.02095.x

VOLUME 13 NO 7 PP 943–952 JULY 2008

Predictive indicators for Ross River virus infection in the Darwin area of tropical northern Australia, using long-term mosquito trapping data

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Summary

OBJECTIVES To describe the epidemiology of Ross River virus (RRV) infection in the endemic Darwin region of tropical northern Australia and to develop a predictive model for RRV infections.
METHODS Analysis of laboratory confirmed cases of RRV infection between 01 January 1991 and 30 June 2006, together with climate, tidal and mosquito data collected weekly over the study period from 11 trap sites around Darwin. The epidemiology was described, correlations with various lag times were performed, followed by Poisson modelling to determine the best main effects model to predict RRV infection.
RESULTS Ross River virus infection was reported equally in males and females in 1256 people over the 15.5 years. Average annual incidence was 113/100 000 people. Infections peaked in the 30–34 age-group for both sexes. Correlations revealed strong associations between monthly RRV infections and climatic variables and also each of the four implicated mosquito species populations. Three models were created to identify the best predictors of RRV infections for the Darwin area. The climate-only model included total rainfall, average daily minimum temperature and maximum tide. This model explained 44.3% deviance. Using vector-only variables, the best fit was obtained with average monthly trap numbers of *Culex annulirostris, Aedes phaecasiatus*, *Aedes notoscriptus* and *Aedes vigilax*. This model explained 59.5% deviance. The best global model included rainfall, minimum temperature and three mosquito species. This model explained 63.5% deviance, and predicted disease accurately.
CONCLUSIONS We have produced a model that accurately predicts RRV infections throughout the year, in the Darwin region. Our model also indicates that predicted anthropogenic global climatic changes may result in an increase in RRV infections. Further research needs to target other high-risk areas elsewhere in tropical Australia to ascertain the best local climatic and vector predictive RRV infection models for each region. This methodology can also be tested for assessing utility of predictive models for other mosquito-borne diseases endemic to locations outside Australia.

keywords arbovirus, Ross River virus, epidemiology, tropical, mosquito-borne disease, climate change

Introduction

Ross River virus (RRV) infection is the most common and widespread arboviral disease in Australia, with an average of 4800 national notifications annually (Communicable Diseases Australia 2006). While not life threatening, the myalgia and fatigue of RRV infection are debilitating enough to be of national importance economically. Over 50% of cases take time off from their occupation, and a small portion of these continue with symptoms for greater than 6 months. Until the recent resurgence of dengue virus with outbreaks in north Queensland, RRV infection was the most important public health arbovirus in Australia (Russell 1994). RRV is endemic in Australia (including Tasmania) and in Papua New Guinea (Jacups *et al.* 2008). Epidemics occurred throughout the late 1970s to early 1980s on islands in the South Pacific, beginning in Fiji where an estimated 500 000 people were infected. But RRV appears to have disappeared from the region, presumably due to a lack of suitable animal host. Endemicity in countries outside Australia and Papua New Guinea has yet to be confirmed (Harley *et al.* 2001; Klapsing *et al.* 2005; Spratt 2005).

Ross River virus infection notifications fluctuate from year to year (Communicable Diseases Australia 2006). For example, early in 2006, New South Wales reported a doubling of monthly cases, prompting public health warnings to minimize mosquito exposure. While RRV and Barmah Forest virus infections are public health issues in northern Australia, the expansion of these arboviruses into previously non-epidemic areas has possible Australian and global implications. There is speculation that with the establishment of *Aedes notoscriptus* adjunct to a thriving Brushtail possum population, RRV could become endemic to New Zealand (Maguire 1994; Derraik & Calisher 2004; Spratt 2005). It is predicted that future climate change will result in longer periods of high mosquito activity in the tropical regions where these arboviruses are already common, such that endemic regions may expand and increase the frequency of epidemics (Russell 1998).

The purpose of this study is to describe the epidemiology of RRV infection in the Darwin region (latitude 12°S) of tropical northern Australia, where it is endemic (with cases reported in most months in most years), and to identify major climatic and vector determinants. We then develop a predictive model for RRV infection that can inform a public health response for the region.

Background

Darwin has coastal and flood plain swamp environs close to existing residential areas, particularly adjacent to the northern residential suburbs (Figure 1). Most swamp areas undergo routine drainage plus aerial insecticide larval control. The Holmes Jungle swamp is the most productive mosquito breeding area of the swamp systems and is a major source of seasonal vector mosquitoes in the northern suburbs. It is adjacent to a closed forest reserve which precludes tidal drainage, although aerial larval control is maintained. Another concern specific to the Darwin area is the increase in housing developments on reclaimed mangrove swamps close to mosquito breeding areas, posing difficulties for vector control.

Four mosquito species have been implicated as vectors of RRV in the Darwin area. *Culex annulirostris,* a freshwater breeder, appears to be a major vector in the mid to late wet season, while *Aedes vigilax* has been identified as a vector in the late dry season and early wet season (Tai 1992; Whelan & Weir 1993a; b; Whelan *et al.* 1997; Whelan 2006). These two are considered the principal vectors of RRV in the Darwin area. *Ae. notoscriptus*, a fresh water natural and artificial receptacle breeder, has also been

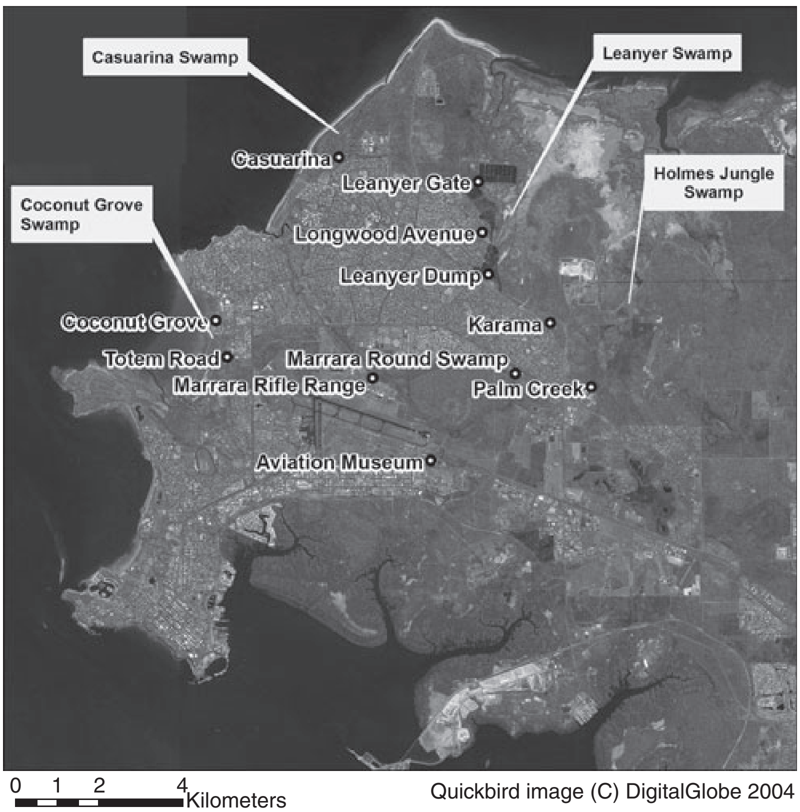

Figure 1 Aerial photograph of Darwin, showing swamps and the 11 mosquito trap sites.

implicated as a vector for RRV in the Darwin area. *Aedes phaecasiatus* is a possible vector implicated by virus isolation (Whelan & Weir 1993a; Whelan *et al.* 1997), but normal seasonal populations are very low compared with the other species.

The level of immunity in local animal host populations plays a key role in RRV transmission. An increase in the proportion of non-immune hosts (previously unexposed, i.e. juveniles) provides an opportunity for large numbers to become viraemic with RRV when mosquito abundance increases. This further intensifies the risk of RRV transmission to humans. The two implicated reservoir hosts of RRV in the 'Top End' of the Northern Territory are the Agile Wallaby (*Macropus agilis*) and the Dusky Rat (*Rattus colletti*) (Williams & Newsome 1991). Both are common to Darwin urban areas, particularly the northern suburbs.

Mean rainfall for Darwin airport (12.4°S) between 1941 and 2007 was 1714 mm/annum. The mean 9 AM temperature is 26.4 °C and the mean 3 PM temperature is 30.7 °C (Australian Bureau of Meteorology 2006b) providing a warm environment throughout the year, but the prolonged dry season produces adverse conditions which pose a desiccation risk for the adults of many species of mosquitoes.

Methods

Case data

Laboratory confirmed cases of RRV infections notified to the Northern Territory Centre for Disease Control between 01 January 1991 and 30 June 2006 were included in this study. Laboratory definition is: (1) Isolation of RRV, (2) Detection of RRV by nucleic acid testing, (3) IgG seroconversion, or a significant increase in antibody level, or a fourfold or greater rise in titre to RRV and (4) Detection of RRV-specific IgM. Age, sex, date of diagnosis (blood test) and residential suburb, constituted the available information on cases. The date of diagnosis was used to calculate case-counts per calendar month.

Mosquito data

A mosquito monitoring program, using the same trap positions and trap locations, has been conducted around Darwin since 1990 by the Medical Entomology Branch of the Northern Territory Department of Health and Community Services. Once-weekly monitoring was conducted with battery-operated CO_2 baited light traps left overnight (Rohe & Fall 1979) in 11 locations around the Darwin suburbs (Figure 1). Mosquito collections were frozen and then identified using taxonomic keys. Mosquito monitoring serves the dual purpose of surveillance of exotic mosquitoes and monitoring mosquito numbers for arboviruses and human nuisance. Traps were positioned in shaded sites between residential areas and significant mosquito breeding areas (Russell & Whelan 1986; Whelan 1987): in tidal salt marshes, mangrove forests or freshwater swamps. The sites are not chosen to represent all residential areas, but rather act as indicators of adult mosquito abundance around Darwin.

During the wet season (16 November to 14 May, inclusive) mosquito numbers are often extremely high. For collections under 300, all specimens were identified and counted. For collections over 300, a subsample of 300 was weighed, identified and counted, and the remainder were estimated by weight. Monthly mosquito abundance was described as mean number of females captured per trap per night averaged over the calendar month. Mosquito control efforts were not included in this analysis.

Climate data

Daily rainfall at Darwin Airport, daily temperature (minimum, maximum, daily mean), humidity and tidal (sea level) data were all provided by the Australian Bureau of Meteorology for the study period inclusive (Australian Bureau of Meteorology 2006a, b).

Data analysis

Univariate analysis of RRV infection associations with mosquito vector and environmental factors were performed on monthly totals of human cases, monthly mosquito trap averages and monthly climate totals or averages for the 15.5-year period of the study. The Cochrane–Armitage test (Royston 2002) was used to test for trend and departure for annual RRV infections, for the years 1991–2005 (2006 data were omitted from these tests as an incomplete year). Chi-squared test was used to investigate proportions for wet *vs.* dry season (during 1991–2005). Modelling analysis was performed on monthly data counts. Using a generalized linear model, the Poisson distribution function was adopted with a log link to determine the best main effects model in relation to human RRV infection using all available data (15.5 years). Lag times were only included up to 3 months for vectors and 4 months for climatic variables, because beyond this time they were less significant and therefore no longer considered biologically plausible for association with infection. For each significant model, we calculated the percentage of deviance explained, as well as the relative contribution of each variable in the model. The relative contribution of each variable to structural fit was assessed by a process of removing each term, in turn, from the saturated model; then adding each term to the null model, and calculating the sum of each term's addition/deletion change in 'variable deviance explained' divided by the number of degrees of freedom; then normalizing the sum of these relative contributions to deviance so that they added to 1 (100%). The most parsimonious model was chosen as determined by Bayesian Information Criterion, and the Akaike Information Criterion (AIC) and change in AIC (ΔAIC) were used to compare the three final models. To validate the models, the last 3 years of data were omitted, the models re-run, predictions were then generated on the omitted 3 years of data. All statistical analyses were performed using Intercooled Stata 9.0 (Stata Corp., College Station, TX, USA) and the open source statistical package 'R-2.2.0' (http://www.r-project.org/).

This study was approved by the Joint Human Research Ethics Committee of the Northern Territory Department of Health and Community Services and the Menzies School of Health Research, approval number 06/28.

Results

Ross River virus infection was reported in 1256 people during the study period (Table 1). Outbreaks of cases occurred in 1991, the first year RRV infections became notifiable, with subsequent peaks in 1994 and 1995. Chi-square indicates that RRV infection incidence has declined during the study period ($P < 0.0001$). This remained highly significant even when excluding 1991 cases from analysis. Total annual rainfall and annual cases were moderately correlated $r = 0.536$ ($P < 0.0001$) (Figure 2). The lowest rainfall year (2002) also had the lowest reported number of RRV infections, with only 12 cases reported.

Ross River virus infections peaked in February (27.1%) with January a close second (26.5%); over half of the cases occur in these 2 months (Figure 3). RRV infections occurred six times more often during the wet season than dry season with 1009 cases *vs*. 163 cases (Incidence Rate Ratio 6.1; 95%, CI 5.2–7.3, $P < 0.0001$).

Half (53.4%) the RRV infections occurred in males (Figure 4). Occurrence of RRV in both sexes peaked in the 30–34 age group. The median ages for infection was 37 years (range, 4–76 years), in males ($n = 669$) and 38 years (range, 5–90 years) in females ($n = 581$). Only 33 (2.6%) RRV infections occurred in children (under 15 years). The overall incidence of RRV infection during the study period was 113/100 000 with the highest age-specific rate being 234/100 000 in the 30–34 age group.

Univariate correlations revealed several strong associations between monthly RRV infection and mosquito populations (Table 2). All four species previously implicated as vectors for RRV had strong associations at various lag times. Monthly numbers of *Cx. annulirostris, Ae. notoscriptus* and *Ae. phaecasiatus* were most associated with RRV infection at zero lag, while average monthly *Ae. vigilax* was most strongly associated with RRV

Table 1 Annual Ross River virus (RRV) infections and incidence

Year	RRV infections- Darwin	Darwin urban population	RRV-incidence rate/100 000†	Total annual rainfall (mm)‡
1991	196	68188	286	1976
1992	88	68148	129	1407
1993	95	68589	136	1569
1994	160	69354	228	1581
1995	168	68210	246	2455
1996	39	68889	57	1803
1997	56	69415	81	2283
1998	37	69301	53	2777
1999	45	68463	64	1892
2000	22	68802	32	2141
2001	47	69051	70	1444
2002	12	68378	18	1214
2003	40	69775	60	1968
2004	84	69326	120	1779
2005	83	70055	118	1360
2006 (to June)§	84	72319		1511
Total	1256		113	

†Chi-square test proportions, significant $P < 0.0001$, downwards trend.
‡Correlation $P < 0.00001$.
§2006 incidence excluded as incomplete year.

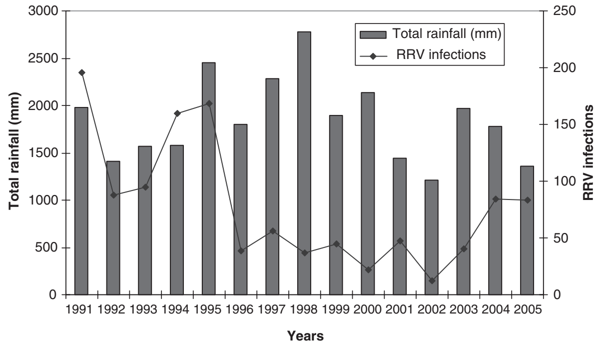

Figure 2 Ross River virus infections in Darwin, total rainfall (mm) 1991– 2005. 2006 data omitted as incomplete year.

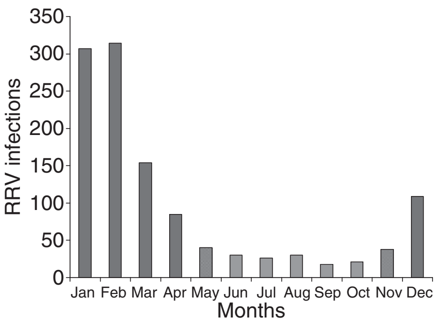

Figure 3 Total monthly RRV infections for each month, Darwin 1991–2005. 2006 data omitted as incomplete year.

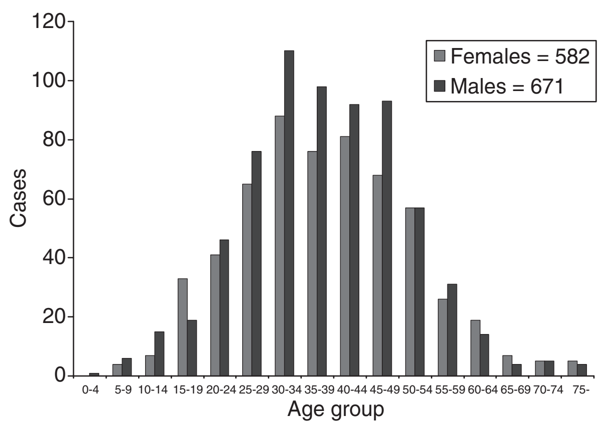

Figure 4 Age and gender distribution of RRV infections, Darwin 1991–June 2006 (three gender unknown excluded).

infection at a lag of 2 months. The climate variables, rainfall (total and mean) and minimum/maximum humidity were also strongly associated with RRV infections at zero lag. Average minimum temperature and maximum tide were associated with RRV at many lag times from 0 to 4 months. Maximum tide was most strongly associated with RRV infections with 0 or 1 month lag.

Multivariate modelling

Three multivariate Poisson models were developed to identify the best predictors of RRV infections for the Darwin area (Table 3). Using only climate variables in a multivariate Poisson model, the best fit occurred with the combination of total rainfall (1 month lag), average daily minimum temperature (3 months lag) and maximum tide (this current month). All coefficients were positive and significant ($P < 0.05$), except for tide ($P = 0.078$). Predictions based on this climate-only model were good when tested against 1991 to 2006 data, although some peaks were poorly predicted (Figure 5a). Using only vector variables, the best fit was obtained with average numbers of *Cx. annulirostris* and *Ae. phaecasiatus* without lag, plus average *Ae. vigilax* (1 month lag) and *Ae. notoscriptus* (2 months lag). All coefficients were positive and significant ($P < 0.01$), but the vector-only model failed to predict troughs in infections accurately and some peaks were poorly predicted (Figure 5b). The best global model (Table 3) incorporated climatic plus vector variables with different lag times employed. All coefficients were positive and significant. This global model explained 63.5% deviance, making it superior to the other models (AIC) and was demonstrated to predict disease accurately (Figure 5c).

Discussion

Darwin falls within the 'tropical savanna' region of Australia, with rain from November to May and a true 'dry' season where typically zero rainfall occurs for at least 3 months of the year between June and August. It is in a vegetation zone of tropical savanna with characteristic dense grasslands and scattered trees of open forest. This environment is unique within Australia and is vastly different from coastal Queensland and northern New South Wales where rainfall occurs sporadically throughout the year supporting lush vegetation, including rainforests. Furthermore, Darwin as a shipping port has an extensive mosquito trapping program which doubles as a surveillance system for exotic mosquito species potentially imported from the neighbouring malaria and dengue endemic East Timor and Indonesia.

The strength of this study is in its immense mosquito surveillance dataset, with 15.5 years of weekly collections from 11 continuous traps in the Darwin area. This far exceeds continuous and intensive surveillance in other regions in Australia, such as northern New South Wales

Table 2 Correlations with monthly Ross River virus (RRV) infections, Darwin 1991–June 2006

Correlations: RRV infection	Lag (months)	R	*P*-value
Monthly vector variables			
Average *Culex annulirostris*	0	0.5510	0.0000
Average *Cx. annulirostris*	1	0.2790	0.0000
Average *Cx. annulirostris*	2	−0.0730	0.3230
Average *Cx. annulirostris*	3	−0.2690	0.0002
Average *Aedes vigilax*	0	0.1390	0.0570
Average *Ae. vigilax*	1	0.5470	0.0000
Average *Ae. vigilax*	2	0.6450	0.0000
Average *Ae. vigilax*	3	0.3820	0.0000
Average *Aedes notoscriptus*	0	0.6130	0.0000
Average *Ae. notoscriptus*	1	0.5780	0.0000
Average *Ae. notoscriptus*	2	0.2820	0.0000
Average *Ae. notoscriptus*	3	−0.0358	0.6300
Average *Aedes phaecasiatus*	0	0.5733	0.0000
Average *Ae. phaecasiatus*	1	0.4027	0.0000
Average *Ae. phaecasiatus*	2	0.0998	0.1755
Monthly climate variables			
Total rainfall (mm)	0	0.5360	0.0000
Total rainfall (mm)	1	0.5240	0.0000
Total rainfall (mm)	2	0.2530	0.0000
Total rainfall (mm)	3	−0.0100	0.8630
Mean rainfall (mm)	0	0.5420	0.0000
Mean rainfall (mm)	1	0.5140	0.0000
Mean rainfall (mm)	2	0.2540	0.0005
Average daily minimum humidity	0	0.4950	0.0000
Average daily minimum humidity	1	0.4477	0.6836
Average daily minimum humidity	2	0.2947	0.5352
Average daily humidity	0	0.4820	0.0000
Average daily maximum humidity	0	0.4110	0.0000
Average daily minimum temperature	0	0.2390	0.0010
Average daily minimum temperature	1	0.2552	0.0005
Average daily minimum temperature	2	0.2686	0.0002
Average daily minimum temperature	3	0.2954	0.0000
Average daily minimum temperature	4	0.1509	0.0421
Average daily maximum temperature	0	−0.0710	0.3380
Maximum monthly tide	0	0.2430	0.0000
Maximum monthly tide	1	0.1982	0.0067
Maximum monthly tide	2	0.1316	0.0734
Maximum monthly tide	3	0.0585	0.4312

which has 10 coastal traps north of Sydney to Tweed Heads, a distance of 710 km (NSW Arbovirus Surveillance & Vector Monitoring Program 2007).

The total incidence of RRV infections for the Darwin urban area was 113/100 000 per annum over the 15-year period (2006 data excluded as incomplete year), in comparison to the national rate for the same period of 19.7/100 000 per annum (1997). Infections have been reported in every month of the year, although wet season (summer) has rates six times higher than in the dry season. This distinct seasonal activity is similar to that reported in northern Western Australia and temperate southern Australia where RRV infection is usually associated with an increase in temperature and summer rains (Russell 1994). Coastal northern Queensland, which has little temperature variation throughout the year and has rainfall all year round, continues to report RRV infections throughout the year (Russell 1994, 1995). Although temperature variation is also minimal from 'dry season' to 'wet season' for the Darwin region, the absence of reliable rainfall in the 'dry' reduces mosquito breeding and survival, because adults desiccate quickly in the absence of moist micro environments (Russell 1998).

Ross River virus infections peaked in the 30–34 age group for both sexes, which is slightly younger than the nationally reported peak in the 35- to 49-year age group (Russell 2002). This reflects the lower age demographic in Darwin, with a median age of 31 *vs.* 37 for the rest of

Table 3 Predictors of Ross River virus (RRV) infections in the Darwin area during 1991–2006

	Coefficient	95% CI	Model deviance explained	Relative contribution of variable	AIC	AIC
Climate-only model			44.3%		1743	485
RRV infections-						
Rainfall (total) lag 1 month	0.002	0.00–0.00		51.2%		
Average minimum temperature lag 3 months	0.283	0.17–0.39		37.1%		
Maximum tide no lag	0.791	−0.09 to 1.67		11.7%		
Vector-only model			59.5%		1428	170
RRV infections-						
Average *Culex. annulirostris* no lag	0.003	0.00–0.00		27.7%		
Average *Aedes vigilax* lag 1 months	0.003	0.00–0.00		26.3%		
Average *Ae. notoscriptus* lag 2 months	0.059	0.04–0.08		23.2%		
Average *Ae. phaecasiatus* no lag	0.022	0.013–0.03		22.8%		
Global model			63.5%		1258	0
RRV infections-						
Rainfall (total) lag 1 month	0.002	0.00–0.00		28.5%		
Average minimum temperature lag 3 months	0.212	0.20–0.28		18.9%		
Average *Cx. annulirostris* lag 1 month	0.001	0.00–0.00		6.5%		
Average *Ae. vigilax* lag 1 month	0.003	0.00–0.00		27.8%		
Average *Ae. notoscriptus* lag 1 month	0.046	0.03–0.05		18.4%		

AIC, Akaike Information Criterion (see 'Methods').

Australia (Australian Bureau of Statistics 2007). RRV infections occurred almost equally in males and females as is the national trend (Muscatello & McAnulty 2000). Only 2.6% of cases occurred in children under 15 years, similar to that which is reported nationally, 'as clinically apparent infections are rare in children' (Mackenzie *et al.* 1998).

Ross River virus infections correlated with total and mean rainfall equally well. Although in multivariate models, total rainfall had stronger associations with RRV than mean rainfall. Rainfall has been almost universally included in models of RRV infections around Australia (Tai 1992; Tong & Hu 2001, 2002; Woodruff *et al.* 2002, 2006; Whelan *et al.* 2003; Tong *et al.* 2004, 2005). Correlations with temperature variables highlighted the benefit of minimum temperature over other temperature variables. In multivariate models, minimum temperature functioned as a surrogate for 'dry season' and was superior to calendar season. Other studies (Tong & Hu 2002; Tong *et al.* 2002, 2004; Woodruff *et al.* 2002) found maximum temperature a better predictor, but this failed to be sensitive (Table 2) in the Darwin environment where maximum temperature remains mostly within the optimal range for mosquito development and survival. Most humidity variables had strong positive correlations with RRV infections at various lag times. Although other researchers included humidity in multivariate models (Tong *et al.* 2001, 2002; Tong & Hu 2002; Woodruff *et al.* 2002), we found that it failed to improve the models once rainfall was included. In the Northern Territory, heavy rainfall increases the environmental humidity in both macro and micro environments, thereby prolonging the longevity of mosquitoes. Thus, rainfall was considered a better predictor of moisture in micro environments than humidity. The climate-only model explained 44.3% deviance. On testing against the 2003 to 2006 RRV infection notifications, the model was useful at predicting peak times and trough times, but it failed to predict the magnitude of some peaks.

Correlations between RRV infections and each of the four mosquito species indicate strong associations with *Ae. vigilax* at a lag time of 2 months. This is possibly related to tidal dependence for breeding. The vector-only model explained 59.5% deviance. When tested against the 2003 to 2006 RRV infection notifications, the model over-predicted infections in the dry season, possibly reflecting the low level, although constant presence of *Cx. annulirostris* and *Ae. vigilax* throughout the year.

Only recently have RRV models incorporated both climatic and vector data, with authors suggesting that climate variables alone are unreliable predictors of outbreaks or numbers of RRV infection (Tong *et al.* 2005; Woodruff *et al.* 2006). But Hu *et al.* (2006) compared the outcomes of climate-only models to climate-plus mosquito density models and found that climate-only models were adequate predictors of disease and 'sufficiently cheap and simple to apply to justify its usage'. The active surveillance

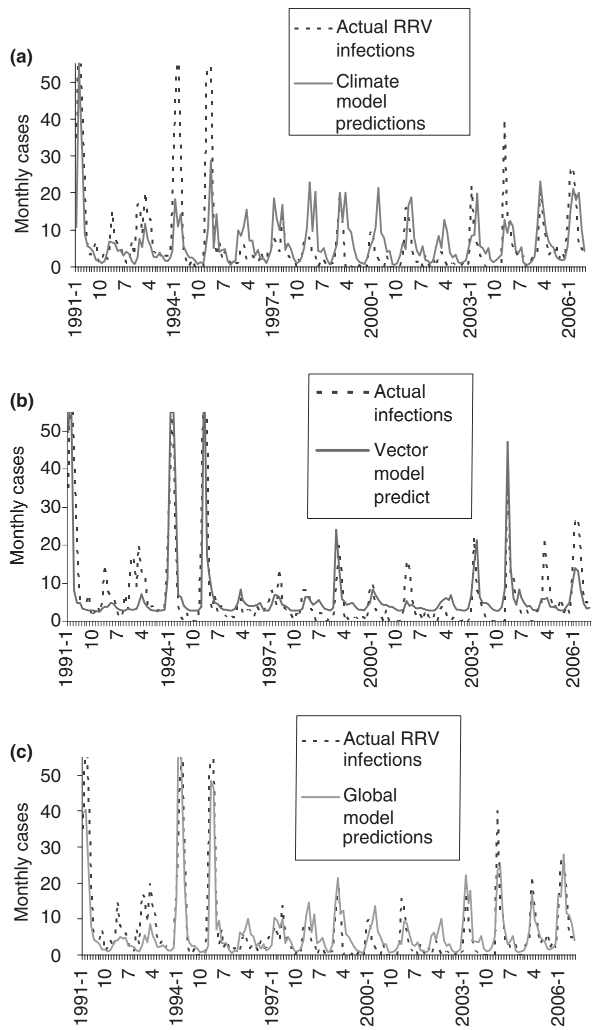

Figure 5 (a) Predicted RRV infections for 2003–2006 based on climate-only multivariate Poisson model. (b) Predicted RRV infections for 2003–2006 based on vector-only multivariate Poisson model. (c) Predicted RRV infections for 2003–2006 based on global multivariate Poisson model.

of mosquitoes undertaken here is labour intensive and expensive (Woodruff *et al.* 2006). Nevertheless, our final, global model (which includes rainfall, average minimal temperature and three mosquito vectors at a lag of 1 month) is a superior predictor of RRV infections than climate-only or vector-only models, with 63.5% deviance explained and both peaks and troughs closely projected, when tested against the 2003 to 2006 RRV infection notifications. The vector variables in our study reflect both natural variations from climate events such as heavy rainfall and unnatural variations in response to vector control efforts such as insecticidal spraying.

Mosquito progression through life stages is mostly determined by temperature, with warmer temperatures resulting in shorter times between egg development, larval instars, pupal development, blood meals, quicker extrinsic incubation times for viruses and a shorter life expectancy for adults (Russell 1998; Harley *et al.* 2001). Temperature therefore affects the capacity for individual mosquitoes to survive, and virus incubation and transmission to a host (Weinstein 1997; Epstein 2002), but temperature increase without rainfall compensation can lead to desiccation of adult mosquitoes that require humid micro environments for resting (Russell 1998). RRV activity is usually highest in areas of moderate rainfall, because too frequent precipitous rainfall can reduce RRV activity by flushing away eggs and larvae, or by allowing predatory fish infiltration (Ritchie 1984). Therefore the dynamics of each arbovirus-climate-vector-human host interaction is specific to any geographical location.

It is argued that mosquito-borne infections are the most likely to be impacted by global climate change (Patz & Kovats 2002). If global climate change predictions become a reality, mosquito numbers would increase as larval development times are reduced and mosquitoes complete their lifecycle before larval habitats dry after inundation by tides or rain. Furthermore, warmer and wetter conditions could further extend larval vector habitat (Russell 1998; b, 2002). A change in balance of rainfall and tides may result in a shift in the dominance of different vector mosquito species. Based on our global model, rainfall and minimum temperature are independent predictors of RRV. Therefore, predicted increases in these factors due to global climate change (Intergovernmental Panel on Climate Change 2007) could translate into increases in RRV infections. Furthermore, climate change may lead to increases in numbers of all four vectors implicated for transmission of RRV in tropical northern Australia, increasing RRV infections. Nevertheless, temperature increases without adequate humidity may actually decrease mosquito numbers. While it is predicted that in the tropical north of the Northern Territory of Australia, there will be increased rainfall with climate change, many other areas of Australia are predicted to have decreased rainfall (CSIRO 2001; Hennessy *et al.* 2004). The implications of this are that there may be very geographically specific alterations in RRV infection rates across the continent. For instance, global climate change is likely to affect transmission dynamics in semi-arid, temperate and cool temperate parts of the country. The potential for RRV to enter and proliferate in temperate locations and New Zealand under future global warming scenarios has also been raised (Derraik & Calisher 2004).

A limitation of this study is the 'location' classification of cases based on usual place of residency, rather than confirmed location of disease acquisition. Although the data resulted in a model to accurately predict RRV infections, it cannot be assumed that targeting only the Darwin area for mosquito control efforts will prevent cases in the Darwin population who have extensive recreational or work-related pursuits in rural areas. The surveillance data only reflect notified RRV infections, not the full range of RRV infections, which includes asymptomatic infections and people with infections not presenting for blood testing, or not being considered for testing by health staff. Another limitation of the study is that local mosquito control activities in Darwin varied over the study period and are not accounted for in the analysis. Despite these activities, the models still accurately predict RRV infections. This reflects the primary importance of absolute mosquito numbers irrespective of how mosquito numbers are influenced by control activities, or by climate factors.

Another limitation of our study is the lack of data available on the putative major reservoirs of RRV in the region, *M. agilis* and *R. colletti*. Furthermore, when considering the potential effects of global warming on arboviral infections, it is imperative that the critical role of host animals in the complex cycles of virus activity be recognized (Russell 1998).

In summary, we have produced a predictive model of RRV infections in urban Darwin. The lag times used in the global model enable real-time predictions for the upcoming month. This enables the development of accurate early warning systems of potential RRV disease outbreaks, providing the opportunity to implement control measures such as timely and efficacious spraying of mosquito breeding sites and public education about personal protection (Whelan *et al.* 1997), especially with regards to travellers and new residents. Further research should focus on other local high risk areas within the Northern Territory and elsewhere in tropical Australia to ascertain the best local climatic and vector predictive RRV models for each region. As climate-only models are 'sufficiently cheap and simple' (Hu *et al.* 2006) our future research aims to produce accurate climate-only models, where possible. This methodology can also be tested for assessing the utility of predictive models for other endemic mosquito-borne diseases in locations outside Australia and to predict the geographically specific effects of global climate change.

Acknowledgements

The authors wish to acknowledge the support provided by Nina Kurucz and Tamara Pearce from the Medical Entomology Branch, Northern Territory. Thank you to all staff at the Medical Entomology Branch, Northern Territory past and present, for their tireless collection and identification of mosquitoes, and entering weekly data over the last 15 years. The authors wish to acknowledge the Department of Planning and Infrastructure, Northern Territory for Figure 1. The authors also thank Joseph McDonnell for statistical advice. This work was supported by an Australian Research Council Linkage Grant.

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