Bridget Barber
MBBS, DTM&H, is an infectious diseases registrar, Victorian Infectious Diseases Service, Royal Melbourne Hospital, Victoria. bridgetbarber@hotmail.com

Justin T Denholm
BMed, MBioethics, is a research registrar, Victorian Infectious Diseases Service, Royal Melbourne Hospital, Victoria.

Denis Spelman
MBBS, FRACP, FRCPA, MPH, is Head of Microbiology and Deputy Director, Infectious Diseases Unit, Alfred Hospital, Melbourne, Victoria.

Ross River virus

Background
Ross River virus is Australia's most common and widespread arbovirus. It causes epidemic polyarthritis and is associated with significant morbidity and cost to society.

Objective
This article aims to increase clinicians' awareness of the epidemiological and clinical features of Ross River virus and provide information regarding prevention, diagnosis and management.

Discussion
Ross River virus occurs throughout Australia and numerous outbreaks have occurred. Most cases occur in northern Australia during the wet season, and individuals with high exposure to mosquitoes are most at risk. Arthralgia is the most common presenting symptom and is usually associated with rash, fever and lethargy. No treatment alters the course of the illness, although patients may benefit from simple analgesics or nonsteroidal anti-inflammatory drugs. Symptoms usually resolve within 6 months. Personal protective measures against mosquitoes are an important prevention strategy.

Ross River virus (RRV) is a mosquito transmitted alphavirus that causes epidemic polyarthritis and arthralgias, with about half of patients also experiencing fever and rash. It is Australia's most common arbovirus with about 5000 cases notified every year (*Figure 1*).[1]

The first documented outbreak of RRV occurred in 1928 in Narranderra and Hay in New South Wales[2,3] with subsequent outbreaks described during World War II among troops in the Northern Territory[4] and Queensland.[5] The virus was isolated in 1959 from an *Aedes vigilax* mosquito along the Ross River near Townsville in Queensland,[6] although it was not until 1985 that it was isolated from an Australian patient with polyarthritis.[7] Outbreaks have since occurred in all Australian states, including Tasmania, and have occurred in metropolitan areas of Sydney (New South Wales),[8] Perth (Western Australia)[9] and Brisbane (Queensland).[10] Most notifications are from Queensland, with high case rates also reported from Northern Territory and the Kimberley region in Western Australia (*Figure 1*).

Risk factors for outbreaks include higher rainfalls and higher maximum tides,[11] and in northern Australia most cases occur during the months January to April.

The largest ever RRV outbreak, affecting more than 60 000 people, occurred in the western Pacific in 1979–1980 and involved the islands of Fiji,[12] Samoa,[13] the Cook Islands,[14] and New Caledonia.[15] The virus apparently disappeared from the region, although was recently reported again in travellers returning from Fiji,[16,17] suggesting the probable reintroduction of RRV to Fiji from the neighbouring endemic regions of Australia, Papua New Guinea or the Solomon Islands.

Over 30 mosquito species have been implicated as possible vectors of RRV, but those most strongly associated with transmission include the tidal breeding *Ae. vigilax* (*Figure 2*) and *Ae. camptorhynchus*, found along the northern and southern Australian coastlines respectively, and the freshwater *Culex annulirostris*, found throughout all of Australia, except Tasmania (*Table 1*). *Ae. notoscriptus* has also been implicated as a likely vector. Kangaroos and wallabies are the main reservoir hosts of RRV, although in urban areas possums and horses, and possibly birds and flying foxes, may play a role.[18] During epidemics, human-

mosquito-human transmission has almost certainly occurred.[18] Vertical transmission in mosquitoes can occur, and desiccation resistant Ochlerotatus eggs may allow maintenance of the virus throughout drought conditions. As yet there has been no documented case of transfusion transmitted RRV, however, the occurrence of asymptomatic viraemia suggests that this risk cannot be excluded.[19]

Prevention

Ross River virus occurs more commonly in people who have participated in outdoor activities, and camping is a particular risk factor. Personal protective measures against mosquitoes including wearing light coloured clothing, using insect repellents, and burning citronella candles and mosquito coils all significantly reduce the risk of RRV and are particularly important at dawn and dusk when mosquitoes are most active. Screens should be fitted to windows and doors in high risk areas and mosquito breeding should be minimised by removing open water containers and water holding plants (*Figure 3*) from around homes.

Clinical manifestations

Ross River virus most commonly occurs in adults aged 25–44 years, with males and females equally affected. The incubation period is generally 7–9 days, with a reported range of 3–21 days.[18] Subclinical infection probably occurs in up to 30% of those infected.[18]

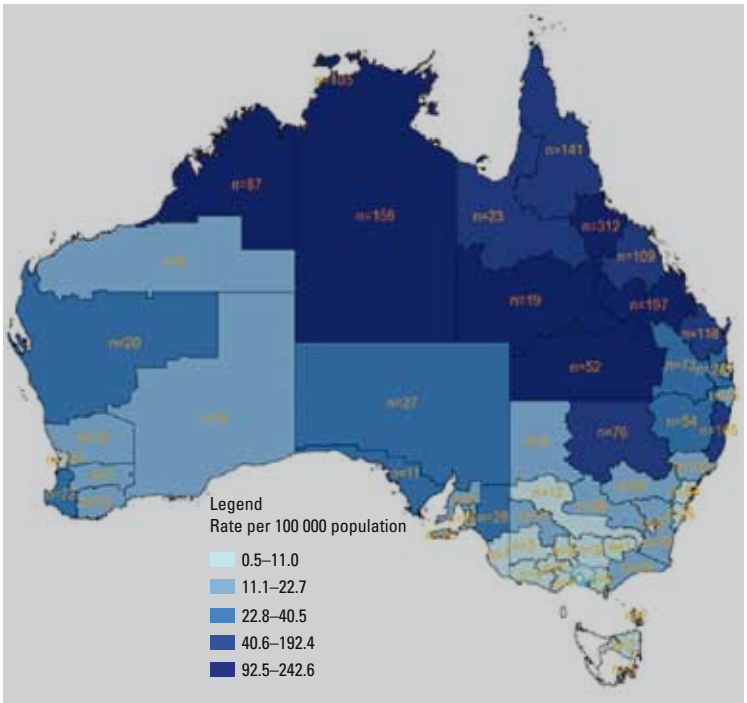
Acute symptoms and signs

Joint pain is the most common presenting symptom and is present in more than 95% of patients (*Table 2*). Joint manifestations are usually symmetrical and acute, and most commonly involve the fingers, toes, wrists, ankles, knees and elbows. About 50% of patients have associated joint swelling, while a minority have effusions, disorders of ligamentous or muscular attachments (enthesopathy) or other abnormal findings.[20] Tiredness is experienced by more than 90% of patients, and fever, myalgias or headache each occur in 50–60% of patients.[20–22] Rash occurs in about 50% of patients and may be the presenting symptom.[21] The rash is generally maculopapular and appears predominantly on the limbs and trunk, although it may also involve the face, hands and feet. Anorexia, nausea and decreased libido have been reported in about a third of patients,[21] and there are case reports of splenomegaly, haematuria, glomerulonephritis, meningitis and encephalitis.[18] In the acute setting, functional ability can be significantly impaired, with about half of patients requiring time off work.[21,23]

Chronic manifestations of RRV

Studies from the 1980s and 1990s suggested that the clinical manifestations of RRV disease could be prolonged, with reports of arthralgias, tiredness and depression persisting years after diagnosis.[21,22] These retrospective studies however, were limited by respondent bias and in some cases relied on patients recalling symptoms months to years after diagnosis. Some studies used inconsistent criteria to diagnose RRV disease and did not account for comorbid conditions.

Figure 1. Notifications and notification rates of Ross River virus infections, Australia 2006–2007



Reproduced from: Liu C, Begg K, Johansen C, et al. Communicable Diseases Network Australia National Arbovirus and Malaria Committee Annual Report, 2006–2007. Map 2 – Notifications and notification rates of RRV infections, Australia, 2006–07. Comm Dis Intell 2008;32:1. ©Commonwealth of Australia. Reproduced with permission

Figure 2. Ae. vigilax

Photo courtesy Stephen Doggett, Department of Medical Entomology, Westmead Hospital, Sydney

More recent prospective studies have provided a clearer picture of the clinical sequelae and long term prognosis of RRV. Certainly the disease is associated with significant morbidity during the first few months following diagnosis, with one study reporting arthralgias more than 3 months after diagnosis in over two-thirds of patients.[20] A steady improvement in symptoms over this time however was demonstrated in most patients, with use of nonsteroidal anti-inflammatory drugs (NSAIDS) decreasing from 63% at 1 month

to 15% at 3 months. Arthralgias resolved for the majority of patients by 5–7 months, with the median number of painful joint groups decreasing from four to one over 4 months, and then to zero by 5–7 months. Psychological and physical functioning returned to normal by 2–5 months and 4–6 months respectively.

Premorbid and concurrent conditions may influence the course of RRV disease. One study found that at 6 months after diagnosis nearly half of patients had a comorbid condition, with rheumatologic conditions and depression being the most common.[23] While the prevalence of these conditions was not greater than expected in the RRV disease cohort, the impact on clinical outcome was significant. Among patients with RRV disease alone, the majority had almost completely recovered their physical and mental health by 6 months, whereas those with a comorbid condition had significant illness up to 12 months after diagnosis. Only one of 60 patients had persisting symptoms at 12 months in the absence of any diagnosis other than RRV disease. Another study evaluated the association between RRV and chronic fatigue syndrome and followed 250 patients for 12 months following a diagnosis of RRV, Ebstein-Barr virus or Q fever.[24] The incidence of chronic fatigue was 12% at 6 months and 9% at 12 months, and did not differ between infective agents. Its onset was predicted only by the severity of the acute illness and not by premorbid psychiatric or medical disorders.

Figure 3. Bromeliads are a breeding site for Ae. notoscriptus and their presence in gardens is associated with an increased risk of RRV in coastal areas of northern Queensland[26]

Diagnosis

Ross River virus should be suspected in patients presenting with acute polyarthritis and/or rash and with a history of travel to, or residence in, an endemic area. Differential diagnoses may include infectious mononucleosis, rubella, Q fever, other rheumatic conditions such as rheumatoid arthritis and systemic lupus erythematosis, and other arboviruses such as Barmah Forest virus (*Table 2*).

Diagnosis is confirmed by serology. Immunogobulin M (IgM) is produced early in the course of infection and hence its detection in an acute phase sample, collected within 7 days of symptom onset, provides a presumptive diagnosis of recent infection. However, IgM can persist for months to years after infection, and false positives may be caused by Barmah Forest virus, rubella, Q fever or rheumatoid factor. Confirmation of the diagnosis therefore requires demonstration of immunoglobulin G (IgG) seroconversion. A convalescent sample should be collected 10–14 days later and tested in parallel by the same laboratory. Diagnosis is confirmed by a four-fold increase in IgG antibody titre. Ross River virus can be detected by polymerase chain

Table 1. Arboviruses of importance to Australia

Genus	Species	Number of cases reported in Australia in 2008[1]	Geographical distribution	Clinical manifestations
Alphaviruses	Ross River virus	5650	Occurs throughout all of Australia, particularly in northern Australia	Acute onset of joint pains +/- rash, fever, lethargy and myalgia
	Barmah Forest virus	2103	Occurs throughout all of Australia, particularly in northern Australia	Similar to RRV, although joint pains less prominent and rash more prominent
	Chikungunya virus	9	Occurs throughout Africa and many areas of Asia. Imported cases occur in Australia	Acute onset of fever, headache, myalgia, nausea and vomiting, and severe arthralgia
Flaviviruses	Dengue virus	558	Endemic throughout tropical and subtropical parts of the world Transmission in Australia currently restricted to northeast Queensland	Acute onset of fever, lethargy, headache, rash and severe myalgias
	Japanese encephalitis virus	1	Endemic throughout Asia and the Pacific	>95% of cases are subclinical. Can cause encephalitis with a high mortality
	Murray Valley encephalitis virus	2	Endemic in northern Australia, although cases occasionally occur in southeastern Australia	Usually subclinical or mild disease consisting of fever, headache, nausea and vomiting. A small percentage progress to meningitis or encephalitis
	Kunjin virus	1	Endemic in northern Australia, although cases occasionally occur in southeastern Australia	Usually subclinical or mild disease consisting of fever, lymphadenopathy, lethargy and rash. May progress to encephalitis

Table 2. Frequency of symptoms and signs of Ross River virus[20–23]

Symptoms/sign	Frequency (%)
Joint pains	95
Tiredness	90
Fever	50–60
Myalgia	60
Rash	40–60
Headache	50
Joint swelling	50
Depression	45

reaction (PCR), however, the usefulness of this test is limited by the short duration of viraemia that follows infection.

Management

No treatment has been shown to shorten the duration or alter the course of RRV. In one study, 36% of patients reported that NSAIDS provided the most effective relief, while 16% found over-the-counter analgesics (aspirin or paracetamol) to be most effective.[21] Swimming, hydrotherapy, physiotherapy or massage was the most effective treatment for 10% of patients, while one-quarter found that rest provided the only relief. Eighteen percent found no relief from any form of treatment. Another study found that 58% of patients took NSAIDS at some stage of their illness and were largely satisfied with their effectiveness.[23] Corticosteroids have been used in some patients,[25] however, these is no evidence to support their effectiveness and they are not recommended.

Public health implications

Ross River virus requires notification to the appropriate state or territory health department, and notification rates are monitored to detect the occurrence of outbreaks. The outbreak potential of RRV has been clearly demonstrated by the 1979 Pacific epidemic and by smaller epidemics throughout Australia. Outbreaks tend to occur after rainy periods or flooding, and health practitioners should be particularly alert to the possibility of RRV at these times. Outbreaks may also follow urban development that occurs in or around wetlands or salt marshes and increases population exposure to mosquito breeding sites. It is also possible that increasing climate variability may affect mosquito breeding habitats and patterns and may increase the incidence of RRV. Outbreak control measures include identification of the important mosquito species involved and elimination of their breeding sites.

Summary of important points

- Joint pain is the most common presenting symptom of RRV and most commonly effects the fingers, toes, hands, feet, elbows and knees.
- Acute symptoms can be severe and debilitating and frequently last up to 3 months.
- Symptoms resolve over 4–6 months in the majority of patients.
- Symptoms are often more severe and prolonged in the presence of comorbid conditions.
- There is no specific treatment, although NSAIDs may provide relief.
- Personal protective measures against mosquitoes significantly reduce the risk of disease and should be recommended.

Conflict of interest: none declared.

References

1. Australian Government Department of Health and Ageing. National notifiable diseases surveillance system. Available at www9.health.gov.au/cda/source/cda-index.cfm [Accessed 3 June 2009].
2. Edwards A. An unusual epidemic. Med J Aust 1928;1:664–5.
3. Nimmo J. An unusual epidemic. Med J Aust 1928;1:549–50.
4. Halliday J, Horan J. An epidemic of polyarthritis in the Northern Territory. Med J Aust 1943;2:293–5.
5. Sibree E. Acute polyarthritis in Queensland. Med J Aust 1944;2:565.
6. Doherty R, Whitehead R, Gorman B, O'Gower A. The isolation of a third group of A arbovirus in Australia, with preliminary observations on its relationship to epidemic polyarthritis. Aust J Sci 1963;26:183–4.
7. Aaskov J, Ross P, Harper J, Donaldson M. Isolation of Ross River virus from epidemic polyarthritis patients in Australia. Aust J Exp Biol Med Sci 1985;63:587–97.
8. Brokenshire T, Symonds D, Reynolds R, Doggett S, Geary M, Russell R. A cluster of locally-acquired Ross-River virus infection in outer western Sydney. NSW Pub Health Bul 2000;11:132–4.
9. Lindsay M, Condon R, Mackenzie C, Johansen M, D'Ercole M, Smith D. A major outbreak of Ross River virus infection in the south-west of Western Australia and the Perth metropolitan area. Comm Dis Intel 1992;16:290–4.
10. Wenbiao H, Tong S, Mengersen K, Oldenburg B. Exploratory spatial analysis of social and environmental factors associated with the incidence of Ross River virus in Brisbane, Australia. Am J Trop Med Hyg 2007;76:S14–9.
11. Tong S, Dale P, Nicholls N, Mackenzie J, Wolff R, McMichael A. Climate variability, social and environmental factors, and Ross River virus transmission: research development and future research needs. Environ Health Perspect 2008;116:1591–7.
12. Aaskov J, Mataika J, Lawrence G, Rabukawaqa V, Tucker M, Miles J. An epidemic of Ross River virus infection in Fiji, 1979. Am J Trop Med Hyg 1981;30:1053–9.
13. Tesh R, McLean R, Shroyer D, Calisher C. Ross River virus (Togaviridae: Alphavirus) infection (epidemic polyarthritis) in American Samoa. Trans R Soc Trop Med Hyg 1981;75:426–31.
14. Rosen L, Gubler D, Bennett P. Epidemic polyarthritis (Ross River) virus infection in the Cook Islands. Am J Trop Med Hyg 1981;30:1294–302.
15. Fauran P, Donaldson M, Harper J, Oseni R. 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.
16. Klapsing P, MacLean D, Glaze S, MacLean K, Drebot M, Lanciotti R. Ross River virus disease reemergence, Fiji, 2003–2004. Emerg Infect Dis 2005;11:613–5.
17. Proll S, Dobler G, Pfeiler M, Jellnek T, Nothdurll H, Loseher T. Persistent arthralgias in Ross-River-virus disease. Dtsch Med Wochenschr 1999;124:759–62.
18. Harley D, Sleigh A, Ritchie S. Ross river virus transmission, infection and disease: a cross-disciplinary review. Clin Microbiol Rev 2001;14:909–32.
19. Dunstan R, Seed C, Keller A. Emerging viral threats to the Australian blood supply. Aust N Z J Pub Health 2008;32:354–60.
20. Harley D, Bossingham D, Purdie D, Pandeya N, Sleigh A. Ross River virus disease in tropical Queensland: evolution of rheumatic manifestations in an inception cohort followed for six months. Med J Aust 2002;177:352–5.
21. Condon R, Rouse I. Acute symptoms and sequelae of Ross River virus infection in South-Western Australia: A follow up study. Clin Diag Virol 1995;3:273–84.
22. Westley-Wise V, Beard J, Sladden T, Dunn T, Simpson J. Ross River virus infection on the north coast of New South Wales. Aust N Z J Pub Health 1996;20:87–92.
23. Mylonas A, Brown A, Carthew T, McGrath B, Purdie D, Pandeya N. Natural history of Ross River virus-induced epidemic polyarthritis. Med J Aust 2002;177:356–60.
24. Hickie I, Davenport T, Wakefield D, Vollmer-Conna U, Cameron B, Vernon S. Post-infectious and chronic fatigue syndromes precipitated by viral and non-viral pathogens: prospective cohort study. Br Med J 2006;333:575.
25. Mylonas A, Harley D, Purdie D, Pandeya N, Vecchio P, Farmer J. Corticosteroid therapy in an alphaviral arthritis. J Clin Rheumatol 2004;10:326–30.
26. Harley D, Ritchie S, Bain C, Sleigh A. Risks for Ross River virus disease in tropical Australia. Int J Epidemiol 2005;34:548–55.

AFP CORRESPONDENCE afp@racgp.org.au