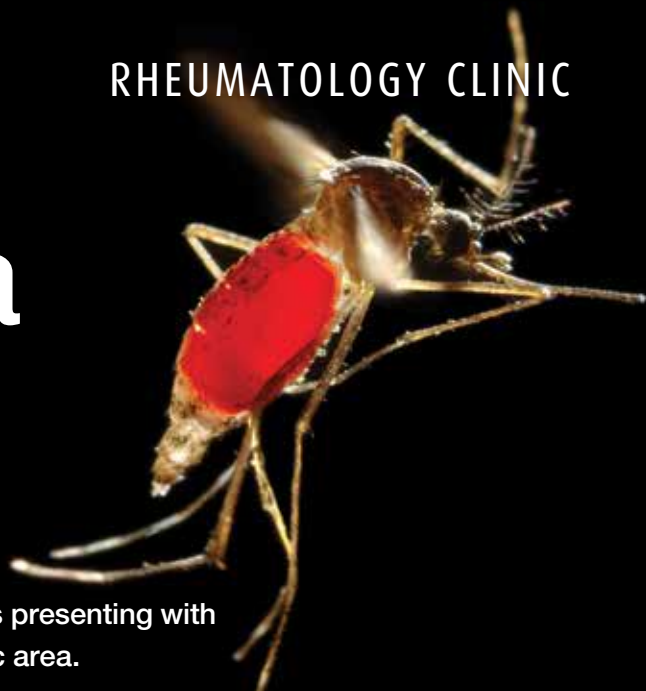


Chikungunya

A cause of persistent arthritis in Australia

ARVIN KUMAR DAMODARAN BSc, MB BS(Hons), MMedEd, FRACP

Chikungunya infection should be considered in patients presenting with persistent arthritis, particularly after visiting an endemic area.



Mosquito-borne viruses can cause fever, rash and arthritis. In Australia, Ross River, Barmah Forest and dengue viruses are familiar. Recently, Chikungunya and Zika viruses have emerged in countries near Australia, with cases confirmed in Australian travellers. Patients infected with these viruses can present with painful, sometimes protracted, debilitating arthritis.

CASE SCENARIO

In April 2013, Ms KP, an active 70-year-old woman with type 2 diabetes, presented to an emergency department in Sydney on return from a trip to Bali, with a three-week history of worsening arthralgia and myalgia. A diffuse pruritic rash had resolved over the first week with accompanying fever and arthralgia that initially responded incompletely to NSAIDs. A doctor she had seen in Bali suspected that she was infected with either dengue or Chikungunya virus, as both were endemic to the area. Before presenting to hospital, Ms KP experienced worsening severe neck pain that prevented her lifting her head off the bed and left hip pain so severe she was unable to walk. She also had generalised myalgia, profound lethargy, headache and abdominal pain.

MedicineToday 2015; 16(1): 56-58

Dr Damodaran is a Rheumatology Specialist and Director of the Clinical Teaching Unit at Prince of Wales Hospital, Sydney; and a Senior Lecturer at Prince of Wales Clinical School, University of New South Wales, Sydney, NSW. SERIES EDITORS: Dr Bethan Richards MB BS(Hons), FRACP, MMed(ClinEpi),

MSportsMed, Director of Medical Education, Network Director of Physician Training and Senior Clinical Lecturer, The University of Sydney, and Staff Specialist Rheumatologist at the Institute of Rheumatology and Orthopaedics, Royal Prince Alfred Hospital, Sydney, NSW. Professor Lyn March, MB BS, MSc, PhD, FRACP, FAFPHM, Professor of Medicine, The University of Sydney, Department of Rheumatology, Royal North Shore Hospital, Sydney, NSW.



Investigations showed Ms KP's inflammatory markers were raised (erythrocyte sedimentation rate, 66 mm/h; C-reactive protein level, 70 mg/L). A viral arthritis was considered and blood samples were sent for serological testing. Other differential diagnoses considered at presentation were polymyalgia rheumatica and a septic process.

Over Ms KP's 10-day hospital admission, blood cultures remained negative; a bone scan and an MRI of the neck did not demonstrate any localised infection. Various analgesic strategies were ineffective, but Ms KP ultimately responded to prednisone, commenced at 20 mg/day, although this complicated the control of her diabetes.

Some weeks after Ms KP was discharged, the results of the serological tests returned positive for Chikungunya virus. One year later, Ms KP continues to experience intermittent inflammatory joint pain, but she is no longer taking corticosteroids.

CHIKUNGUNYA CLINICAL FEATURES

Chikungunya means 'that which bends up' in the Makonde language of Tanzania.¹ Like Ross River and Barmah Forest viruses, it is a mosquito-borne RNA virus of the *Alphavirus* genus, and infection is associated with the triad of fever, arthritis and rash.

In Africa, Chikungunya virus historically appeared to exist in a cycle involving humans, *Aedes* mosquitoes and primates or other animals. However, the emergent epidemic disease is hosted in humans and mosquitoes without any other animal required. Its major mosquito vectors, as for dengue virus, are now *Aedes aegypti* and *Aedes albopictus*. Human to human transmission does not occur without the mosquito vector.

Chikungunya virus has an incubation period of two to four days, up to 14 days. Fever and malaise generally last for three to five days, with polyarthralgia and rash occurring two to five days after the fever begins (Figure 1). The rash usually resolves within a week. Associated symptoms such as headache and abdominal pain may complicate the presentation. One in five patients may have persistent arthritis after one year, which can present a diagnostic conundrum to clinicians.²



Figure 1. Rash caused by Chikungunya virus.

The patient in the case scenario was older and, although very active, had uncontrolled type 2 diabetes. Outbreaks of Chikungunya infection over the past decade have demonstrated that patients older than 65 years, particularly those with underlying chronic medical problems, are more likely to experience severe disease with acute complications and persistent arthritis.

No vaccine or definitive treatment for Chikungunya infection is available. Supportive measures and simple analgesia, including NSAIDs, are generally advocated for infected patients. Although there is a lack of reported evidence supporting use, low-dose oral corticosteroids were helpful in this patient who was refractory to the conventional approach.

CHIKUNGUNYA REGIONAL EMERGENCE

The emergence of Chikungunya virus and its increasingly recognised global importance have recently been reviewed.¹ The virus was first isolated in Tanzania during an epidemic of polyarthralgia in the early 1950s. Before 2000, Chikungunya virus appeared to be fairly restricted to Africa before emerging in epidemic proportions in the Indian Ocean region (Figure 2).³

It is thought that rapid spread was enabled by a mutation that allowed Chikungunya virus to be carried readily by *A. albopictus* (Figure 3).⁴ This mosquito is also known as the 'Asian tiger mosquito' because of its stripes and aggressive human biting habits. It is well adapted to urban environments, is an able traveller as its eggs can withstand desiccation and can adapt to temperate climates. It has spread from Asia to Africa, Europe and the Americas. Although *A. albopictus* has been found sporadically in the vicinity of major



Figure 2. Countries and territories where cases of Chikungunya infection have been reported. Countries and territories where only imported cases have been documented are not included.³

Reproduced with permission from the Centers for Disease Control and Prevention.³

ports along Australia's northern borders, there are no persistent populations reported as yet.⁵

A well-studied outbreak in 2005/06 was on Réunion Island, in the Indian Ocean.¹ This outbreak heralded the re-emergence of the disease and affected more than one-third of the Réunion inhabitants (more than a quarter of a million reported cases). Although life-threatening disease is rare, deaths occurred particularly in elderly people with other comorbidities. In the Réunion outbreak, more than 200 deaths may have been at least partially attributable to the disease. Persistent and fluctuating arthritis was also documented in some patients.⁶ Since then, massive outbreaks, with cases estimated to be in the millions, have occurred in India and Sri Lanka. On the other side of the world, Chikungunya has become prevalent in the Americas, with more than half a million cases reported.⁷

Viruses such as Chikungunya can cause outbreaks when an infected person enters an area where vectors exist for local transmission. A small, illustrative outbreak of Chikungunya virus occurred in Italy in 2007.⁸ This was traced back to a single Indian traveller visiting family, and ultimately 292 people were infected.

Two-thirds of the patients from the Italian outbreak had musculoskeletal symptoms a year after infection, particularly affecting older patients, again demonstrating the frequency of chronic disease.

OTHER ARBOVIRAL ARTHROPATHIES IN AUSTRALIA

Suggestive symptoms in a returned traveller or a patient with a recent history of mosquito bites in Australia should prompt consideration of arbovirus infection. The clinical picture of infection with Chikungunya virus closely resembles that of



Figure 3. *Aedes albopictus* or Asian tiger mosquito is the vector for Chikungunya virus.

TABLE 1. ARBOVIRUS NOTIFICATIONS IN AUSTRALIA¹³

Arbovirus	Endemic regions	Prevalence		
		2012	2013	2014 year to 30 June
Chikungunya	Asia, Africa, Indo-Pacific	19	133	40
Ross River	Australia wide, Papua New Guinea, Pacific	4687	4307	3066
Barmah Forest	Australia wide	1730	4239	564
Zika	Africa, Asia, Pacific	Not reported	Not reported	Not reported
Dengue	Tropics and subtropics worldwide including Australia	1541	1840	1085

Australia's own endemic mosquito-borne alphaviruses, Ross River and Barmah Forest viruses. These still dominate the reported cases of arbovirus infection in Australia. Dengue and Zika viruses are also mosquito-borne arboviruses (as in ARthropod-BORne) that can present with fever, rash and arthritis and are prevalent in the Asia-Pacific region. In the appropriate travel context, malaria also needs to be considered.

Although all of these arboviruses have become more prevalent, dengue virus has become a ubiquitous threat throughout the world's tropics and subtropics, including north Queensland resort destinations.⁹ The World Health Organization estimates that there are 50 to 100 million cases of dengue per year with half a million hospitalisations.¹⁰ 'Severe dengue' has a mortality rate of 2.5% with children at particular risk; however, early detection and supportive care can lower this to less than 1%.¹⁰

Zika virus deserves a special mention as a newly emerging issue in our region. Having been apparently confined to Africa before 2007, Zika virus is currently causing outbreaks in the Pacific, with the Australian state governments releasing health alerts in 2014.¹¹ There have been confirmed cases in travellers returning to Australia.¹² These include a 35-year-old man who was referred to this author after presenting to his GP in April 2014 with persistent, debilitating inflammatory arthritis after visiting a resort in the Cook Islands.

Although serologically confirmed cases of arboviral infection underestimate the true prevalence, Australia collects important information in its notifiable diseases database (Table 1).¹³

CONCLUSION

Infection with mosquito-borne arboviruses should be considered in patients presenting with fever, rash and transient or persistent arthritis. In nontravellers, a suggestive clinical presentation should prompt serological testing for Ross River and Barmah Forest viruses, which are widespread in Australia, and dengue virus, which is prevalent in the tropics. In travellers returning from destinations where other arthropogenic arboviruses are endemic (including popular tourist destinations in Asia, the Indian and Pacific Oceans and the Americas), consider serological testing for dengue, Chikungunya and Zika viruses as appropriate.

Although no specific treatments or vaccines are currently available for these arthropogenic arboviruses, early diagnosis and supportive and symptomatic treatment may benefit the patient and inform the public health response. Patients with persistent inflammatory musculoskeletal symptoms should also have arboviral arthropathy considered, and be referred to specialist care. **MT**

REFERENCES

1. Burt FJ, Rolph MS, Rulli NE, Mahalingam S, Heise MT. Chikungunya: a re-emerging virus. *Lancet* 2012; 379: 662-671.
2. Morens DM, Fauci AS. Chikungunya at the door — déjà vu all over again? *N Engl J Med* 2014; 371: 885-887.
3. Centers for Disease Control and Prevention. Chikungunya virus: geographical distribution. Atlanta: CDC; 2014. Available online at: <http://www.cdc.gov/chikungunya/geo/> (accessed December 2014).
4. Caglioti C, Lalle E, Castilletti C, Carletti F, Capobianchi MR, Bordi L. Chikungunya virus infection:

an overview. *New Microbiol* 2013; 36: 211-227.

5. Beebe NW, Ambrose L, Hill LA, et al. Tracing the tiger: population genetics provides valuable insights into the Aedes (Stegomyia) albopictus invasion of the Australasian region. *PLoS Negl Trop Dis* 2013; 7: e2361.
6. Borgherini G, Poubeau P, Jossaume A, et al. Persistent arthralgia associated with chikungunya virus: a study of 88 adult patients on Reunion Island. *Clin Infect Dis* 2008; 47: 469-475.
7. Staples JE, Fischer M. Chikungunya virus in the Americas — what a vectorborne pathogen can do. *N Engl J Med* 2014; 371: 887-889.
8. Moro ML, Grilli E, Corvetta A, et al. Long-term chikungunya infection clinical manifestations after an outbreak in Italy: a prognostic cohort study. *J Infect* 2012; 65: 165-172.
9. Queensland Health. Current dengue outbreaks. Brisbane: Queensland Government; 2014. Available online at: <http://www.health.qld.gov.au/dengue/outbreaks/current.asp> (accessed December 2014).
10. World Health Organization. Dengue and severe dengue. Geneva: WHO; 2014. Available online at: <http://www.who.int/mediacentre/factsheets/fs117/en> (accessed December 2014).
11. NSW Ministry of Health. Zika fever in the Pacific. Sydney: NSW Government; 2014. Available online at: http://www.health.nsw.gov.au/Infectious/alerts/Pages/Zika_virus_alert.aspx (accessed December 2014).
12. Pyke AT, Daly MT, Cameron JN, et al. Imported zika virus infection from the Cook Islands into Australia, 2014. *PLoS Curr* 2014; 6: pii: ecurrents.outbreaks.4635a54dbffba2156fb2fd76dc49f65e.
13. Australian Government Department of Health. National Notifiable Diseases Surveillance System. Canberra: Australian Government; 2014. Available online at: http://www9.health.gov.au/cda/source/rpt_1_sel_a.cfm (accessed December 2014).

COMPETING INTERESTS: None.