www.nature.com/clinicalpractice/rheum

Emerging viral infections and arthritis: the role of the rheumatologist

Leonard H Calabrese

LH Calabrese is a Rheumatologist at the Cleveland Clinic Foundation, OH, USA.

The role of the rheumatologist in the evaluation of ill travelers returning from exotic lands has never been a central one. Today, however, in an era of increasingly common foreign travel combined with our recognition that viral epidemics can spread precipitously in our global community, this role might be about to change.

Up until now, the arboviral infections[1] (Supplementary Table 1 online) have been considered as well-recognized but rare and arcane causes of virally mediated rheumatic complications, attention to which has largely been relegated to textbooks and advanced specialty examinations. Since late 2004, one arbovirus known as chikungunya has been responsible for millions of new infections in countries near the Indian Ocean; as a result, an increasing number of cases are being diagnosed among travelers returning to Europe and the US.[2–7] Chikungunya fever has prominent rheumatic manifestations—essentially 100% in clinically diagnosed cases. The symptoms associated with chikungunya fever are capable of lasting many weeks or months after the acute illness. The mere prospect of possibly establishing chikungunya in an enzootic cycle of spread in the industrialized West justifies a brief review of the essentials of this infectious disease.

Chikungunya is a mosquito-borne alphavirus of the family Togaviridae. It was identified in Africa during the 1950s, where it is maintained in an epizootic cycle involving man and primates but, like dengue fever, is maintained in an urban epidemiologic cycle without a known animal reservoir. The name 'chikungunya' comes from the Maconde language and literally means "that which bends up", reflecting the severe and often chronic joint pains that are an essential element of the disease. In a detailed clinical report of 47 patients prospectively confirmed with chikungunya in Marseilles, France,[2] the illness was described to have two identifiable phases. The first was noted early in the course of the illness (within 10 days of onset) and characterized by fever, conjunctivitis and a rash described as macular, papular or diffusely erythematous that lasts only a few days. Severe bilateral and symmetric arthralgia and/or arthritis were present in all patients during this stage. Temporomandibular, sternoclavicular and axial pains were also common, and large joint effusions were noted in 15% of patients. Among those who developed symptoms and were diagnosed upon return to their homes, the mean interval to symptoms was 2.4 days (range 0–7 days). A second and more chronic phase of the illness was noted in almost 82% of patients who presented with persistent or recurrent joint pain 10 days after the onset of symptoms, none of whom had rash or fever at the time. During this chronic phase, over half the group had tenosynovitis (most commonly involving the wrists and fingers). Proximal finger joints were still swollen in 50% of patients 1 month after onset of symptoms. Even more importantly to rheumatologists, 88%, 86% and 48% of patients were still symptomatic at 1, 3 and 6 months after disease onset, respectively. Two patients had persistent musculoskeletal symptoms up to 15 months and their last follow-up. Although data derived from observational studies of the duration and prevalence of symptoms following arboviral infection might often be misleadingly high, it is clear that these patients could easily be referred for rheumatologic evaluation long after their acute febrile illness, when only an alert clinician taking the appropriate epidemiologic history of high-risk travel might possibly make the correct diagnosis. Serological testing for specific IgM antibodies or detection of viral RNA in blood by polymerase chain reaction is useful early in the disease course,[2] but only clinical suspicion combined with the elicitation of an appropriate history and the detection of IgG-specific antibodies is useful in late-stage patients. Treatment for these complications is anecdotal, but usually involves NSAIDs and analgesics; the role of glucocorticoids and other remittive agents remains undefined.

Correspondence
Cleveland Clinic Lerner College of Medicine
Case Western Reserve University
Department of Rheumatic and Immunologic Diseases
Cleveland Clinic Foundation
9500 Euclid Avenue, Desk A50
Cleveland
OH 44195
USA
calabrl@ccf.org

Received 14 September 2007
Accepted 29 October 2007
Published online 27 November 2007
www.nature.com/clinicalpractice
doi:10.1038/ncprheum0679

One might consider this epidemic a 'tempest in a teapot', given that while the number of cases of chikungunya infection diagnosed in the US and Europe are high relative to previous outbreaks, chikungunya fever is still a rare disease in the industrialized West. Granted, but one must also consider that chikungunya is a virus capable of establishing itself in a human-mosquito-human lifecycle, and all that is needed is an infected patient and a capable vector. This scenario now seems more possible than ever, given recent mutations in this error-prone RNA virus that might have affected its capacity to be carried by *Aedes albopictus*, a New World mosquito widely found across the Globe.[8,9] Evidence for this mode of spread has been reported in a cohort of patients in Northern Italy in September 2007.[10] In this outbreak, a total of 197 patients were reported, with 166 meeting case-definition criteria and the index case believed to be a foreigner coming from an affected area in the Indian subcontinent. Based on the clinical presentation and epidemiologic features observed, heath authorities suspected an arbovirus; serologic testing and polymerase chain reaction confirmed the diagnosis of chikungunya fever. In addition, chikungunya virus was detected in *Aedes albopictus*. Thus, this outbreak represents the first reported occasion that chikungunya virus has been transmitted by mosquitoes within Europe. With a similar example of the rapid spread of an emerging viral infection throughout a population lacking herd immunity documented for West Nile virus, the prospects for the globalization of chikungunya might just be a matter of time. Thus, although solidly on the sidelines, the rheumatology community of this millennium will likely be called on increasingly to participate in the health care of afflicted travelers with new and emerging infections. We should, therefore, remain prepared and knowledgeable.

Supplementary information in the form of a table is available on the *Nature Clinical Practice Rheumatology* website.

Competing interests
The author declared no competing interests.

References

1 Suhrbier A and La Linn M (2004) Clinical and pathologic aspects of arthritis due to Ross River virus and other alphaviruses. *Curr Opin Rheumatol* **16:** 374–379
2 Simon F *et al.* (2007) Chikungunya infection: an emerging rheumatism among travelers returned from Indian Ocean islands. Report of 47 cases. *Medicine (Baltimore)* **86:** 123–137
3 Reiter P *et al.* (2006) *Aedes albopictus* as an epidemic vector of chikungunya virus: another emerging problem? *Lancet Infect Dis* **6:** 463–464
4 Borgherini G *et al.* (2007) Outbreak of chikungunya on Reunion Island: early clinical and laboratory features in 157 adult patients. *Clin Infect Dis* **44:** 1401–1407
5 Taubitz W *et al.* (2007) Chikungunya fever in travelers: clinical presentation and course. *Clin Infect Dis* **45:** e1–4
6 Parola P *et al.* (2006) Novel chikungunya virus variant in travelers returning from Indian Ocean islands. *Emerg Infect Dis* **12:** 1493–1499
7 Centers for Disease Control and Prevention (CDC) (2007) Update: chikungunya fever diagnosed among international travelers—United States, 2006. *MMWR Morb Mortal Wkly Rep* **56:** 276–277
8 Yergolkar PN *et al.* (2006) Chikungunya outbreaks caused by African genotype, India. *Emerg Infect Dis* **12:** 1580–1583
9 Charrel RN *et al.* (2007) Chikungunya outbreaks—the globalization of vectorborne diseases. *N Engl J Med* **356:** 769–771
10 Angelini R *et al.* (2007) An outbreak of chikungunya fever in the province of Ravenna, Italy. *Euro Surveill* **12:** E070906.1