



COMMENTARY

# An imported case of Chikungunya fever from Madagascar: Use of the sentinel traveller for detecting emerging arboviral infections in tropical and European countries

Thierry Pistone<sup>a,b,1</sup>, Khaled Ezzedine<sup>a,b,\*,1</sup>, Isabelle Schuffenecker<sup>c</sup>,  
Marie-Catherine Receveur<sup>a,b</sup>, Denis Malvy<sup>a,b</sup>

<sup>a</sup> Travel Clinics and Tropical Disease Unit, Department of Internal Medicine, Infectious Diseases and Tropical Medicine, University Hospital Center, Bordeaux F-33075, France

<sup>b</sup> Centre René Labusquière (Tropical Medicine and Hygiene Branch), EA 3677, University Bordeaux 2, Bordeaux F-33076, France

<sup>c</sup> Centre National de Référence des Arbovirus, Institut Pasteur, IFR128, Lyon F-69386, France

Received 9 July 2008; received in revised form 27 August 2008; accepted 14 October 2008  
Available online 18 November 2008

## KEYWORDS

Chikungunya virus  
infection;  
Sentinel;  
Returning traveller;  
Emerging arboviruses

**Summary** A major Chikungunya virus (CHIKV) epidemic affected the South-Western Indian Ocean islands in 2005. This major outbreak raised concerns about the possibility of the emergence of CHIKV infections in Europe as an autochthonous CHIKV outbreak occurred in the Ravenna region of Italy during the summer of 2007 and was linked to a viraemic index case originating in Kerala, India. This report highlights the need for surveillance in countries where such emerging infections could be introduced by returning travellers.

© 2008 Elsevier Ltd. All rights reserved.

Early in 2005, a major Chikungunya virus (CHIKV) epidemic affected the South-Western Indian Ocean islands, including

Comoros, Mauritius and Réunion, and also involved India.<sup>1,2</sup>

A few cases were also reported on the East Coast Madagascar in 2006. This major outbreak raised concerns about the possibility of the emergence of CHIKV infections in Europe, as *Aedes albopictus*, the mosquito vector of CHIKV in Réunion, is present in twelve countries, including Italy, where it was first recorded in 1990 and is particularly common.<sup>3</sup> Indeed, this concern was born out by documentation of an autochthonous CHIKV outbreak in the Ravenna region of Italy during the summer of 2007, which was linked to a viraemic index patient

\* Corresponding author at: Unité de Médecine tropicale et Pathologie d'importation (Prof. D. MALVY), Service de Médecine interne et des Maladies tropicales, Hôpital Saint-André – CHU Bordeaux 1, rue Jean Burguet, F-33 075 Bordeaux Cedex, France. Tel.: +33 5 56 79 58 28; fax: +33 5 56 79 58 15.

E-mail address: [kezzedin@ulb.ac.be](mailto:kezzedin@ulb.ac.be) (K. Ezzedine).

<sup>1</sup> Both authors have equally contributed to this work.

originating in Kerala, India.<sup>4</sup> In addition, a large number of imported cases has been seen in Metropolitan France accounting for 808 imported cases confirmed serologically between April 2005 and August 2006.<sup>5</sup> The diagnosis of exotic imported infections is therefore a challenge for travel medicine, particularly when patients return from an area where adequate diagnostic facilities are not available for the detection of emergence of such infections, and highlight the need for surveillance in countries where they could be introduced by returning travellers. In this context, the Americas are particularly at risk given the abundance and widespread of susceptible and competent vectors, i.e. *Aedes aegypti* and *Aedes albopictus*.

A 23-year-old man presented to the University Hospital department of Tropical Medicine in Bordeaux, France with a febrile acute dengue-like syndrome, on January 18, 2007, four days after he returned from a five-week trip to Madagascar on a humanitarian mission. During his trip, he remained permanently in the vicinity of Sambava village located in the North-East of the island (Sava district). His mission took place during a three-week period of heavy rains which followed a disastrous hurricane. He had been taking antimalarial chemoprophylaxis with chloroquine–proguanil. He reported a two-day history of sudden acute febrile illness (temperature 40.5 °C) with severe asthenia, headache, disabling pain in multiple joints involving the knees, hips, shoulders, the left elbow and the lumbar region. He also presented with a diffuse maculo-papular erythematous exanthema predominantly on the trunk and the extremities with intense pruritus and palmo-plantar hyperaesthesia. Upon admission, laboratory findings included negative blood smears for malaria and a normal blood cell count. Blood chemistry values were within normal limits except for raised hepatic enzymes and C-reactive protein; 68 IU/L aspartate aminotransferase (normal values, 12–35 IU/L), 65 IU/L alanine aminotransferase (normal values, 8–45 IU/L), 247 IU/L gamma glutamyl transferase (normal values, 7–55 IU/L) and C-reactive protein at 30 mg/L (normal values, <7.5 mg/L). CHIKV RNA was detected by RT-PCR on the third day after the onset of symptoms. Comparison of glycoprotein E1 partial sequences (890 bp) (GenBank accession number: EU244646) revealed a 100% homology with sequences from Chikungunya patients collected during the second period of the Reunion outbreak.<sup>2</sup> The patient was seronegative for Dengue virus (DENV)-specific immunoglobulin M (IgM) and IgG antibodies as well as for CHIKV by IgM-antibody capture (MAC-ELISA) and IgG (ELISA). The serological follow-up detected seroconversion to CHIKV for IgM. One week later, the patient remained firmly asthenic with anorexia, persistent arthralgia, burning sensation of the skin and intense desquamative features of the palms and soles. Furthermore, two additional confirmed infections were diagnosed in the department within the following two weeks in travellers returning from the same area.

The diagnosis of the index patient was concomitant with an outbreak of dengue-like syndrome in Sava district (Sambava, Anthala, Vahemar, Andapa) which was reported in a local newspaper ("La Tribune de Madagascar", January 29th, <http://www.madagascar-tribune.com/index.php?JOURNAL=119&ART=21787>). The dispatch reported that hospitals and physicians in the Sava District were dealing

with an epidemic febrile illness condition affecting at least 50% of the inhabitants. Although the outbreak was not investigated locally, it may have been caused, at least in part, by Chikungunya virus. In 2006, indeed co-circulation of CHIKV and DENV-1 had been observed on the East Coast.<sup>2</sup> In such a context, the lack of information on the transmission and effects of arbovirus may also contribute to confusion between arboviral infections and endemic *Plasmodium falciparum* infection.<sup>6</sup> Thus, it can be postulated that this outbreak of dengue-like syndrome could be linked to a major episode of CHIKV dissemination in islands of the Indian Ocean.

This case of imported CHIKV illustrates how travellers can serve as a sentinel population providing information regarding the emergence or re-emergence of an infectious pathogen, particularly in countries where laboratory diagnosis is difficult to implement. In this respect, a single case of an imported new pathogen would be sufficient to raise the alert of potential unrecognised emergence or re-emergence of the pathogen in the source region. Websites and electronic bulletins, such as Promed, which were used in the present case, are useful information channels for communicating this risk to the source region. One advantage of using travellers as a sentinel population is that information on the denominator population is not an absolute requirement.<sup>7</sup> Another advantage of the use of sentinel travellers to indicate outbreaks of infectious disease is that an isolated case report can be sufficient to suggest the presence of infection and is quite independent of the magnitude of the event. Travellers can thus act as couriers who inadvertently ferry pathogens and microbial genetic material that can be used to map the location and movement of pathogenic strains and genotypes.<sup>8,9</sup>

Finally, with the increase in intercontinental travel, travellers can provide insights into the level of the risk of transmission of infections in other geographical regions.

## Conflict of interest

No conflict of interest.

## References

1. Bessaud M, Peyrefitte CN, Pastorino BA, Tock F, Merle O, Colpart JJ, et al. Chikungunya virus strains, Reunion Island outbreak. *Emerg Infect Dis* 2006;12:1604–6.
2. Schuffenecker I, Itean I, Michault A, Murri S, Frangeul L, Vaney MC, et al. Genome microevolution of Chikungunya viruses causing the Indian Ocean outbreak. *PLoS Med* 2006;3:e263.
3. Depoortere E, Coulombier D, ECDC Chikungunya risk Assessment Group. Chikungunya risk assessment for Europe: recommendations for action. *Eurosurveillance*, <http://www.eurosurveillance.org/ew/2006/060511.asp#2>; 2006 May 11.
4. Beltrame A, Angheben A, Bisoffi Z, Monteiro G, Marocco S, Calleri G, et al. Imported Chikungunya infection, Italy. *Emerg Infect Dis* 2007;13:1264–6.
5. Institut de Veille Sanitaire. Chikungunya in the world. Situation on September 3, 2007 (in French), <http://www.invs.sante.fr/surveillance/chikungunya> [accessed 04.12.07].
6. Gubler DJ. The global emergence/resurgence of arboviral diseases as public health problems. *Arch Med Res* 2002;33:330–42.
7. Guerin PJ, Grais RF, Rottingen JA, Valleron AJ, Shigella Study Group Ssg. Using European travellers as an early alert to detect emerging

- pathogens in countries with limited laboratory resources. *BMC Public Health* 2007;**7**:8. doi:10.1186/1471-2458-7-8.
8. Parola P, de Lamballerie X, Jourdan J, Røvery C, Vaillant V, Minodier P, et al. Novel chikungunya virus variant in travellers returning from Indian Ocean Islands. *Emerg Infect Dis* 2006;**12**: 1493–9.
9. Wilson ME. The traveller and emerging infections: sentinel, courier, transmitter. *J Appl Microbiol* 2003;**94**(Suppl.):1S–11S.