

## Chikungunya fever in the Emilia Romagna region: what is the public health message?

Giuseppe La Torre<sup>1</sup>, Maria Daniela Gliubizzi<sup>1</sup>, Cinzia Marano<sup>2</sup>, Angelo G. Solimini<sup>1</sup>, Antonio Boccia<sup>1</sup>

<sup>1</sup>Department of Experimental Medicine, Unit of Clinical Medicine and Public Health, Sapienza University of Rome, Italy; <sup>2</sup>Division of Global Migration and Quarantine, Travelers' Health and Animal Importation Branch, Centers for Disease Control and Prevention, Atlanta, Georgia, USA

Correspondence to: Giuseppe La Torre, Department of Experimental Medicine, Unit of Clinical Medicine and Public Health, Sapienza University of Rome, Viale Regina Elena 324, 00161 Rome

**Key words:** Chikungunya, Italy, outbreak, Public health

### Introduction

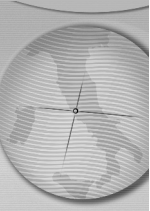
Chikungunya virus (CHIKV) is a mosquito-borne alphavirus indigenous to African countries, the Indian Subcontinent, and Southeast Asia, where it causes endemic and epidemic chikungunya (CHIK) fever [1]. Chikungunya infection is transmitted by biting mosquitoes belonging to the genus *Aedes*. Since the identification of the virus in the 1950s [2] in Africa, transmission to humans has been usually associated with bites of *A. aegypti* mosquitoes. In recent outbreaks occurring in the South-eastern islands of the Indian Ocean, transmission has also been associated with *A. albopictus*, also known as the "tiger mosquito." This species is indigenous to Southeast Asia, the Western Pacific, and the Indian Ocean, but has recently spread to Africa, the Middle East, Europe, and the Americas. [3]. Although tropical forests are considered to be their original habitat, *A. aegypti* and *A. albopictus* have developed the capacity to exploit artificial environments [4]. Besides the natural habitat consisting of tree holes filled with water and other small natural pools, they are capable of breeding in any artificial habitat with small reservoirs of stagnant water, such as vases, buckets, tires and other containers found around houses in urban and periurban areas.

Many Southern European countries have a temperate climate and ecologic conditions potentially propitious for local establishment of *A. albopictus* [5]. Unlike *A. aegypti*, *A. albopictus* can permanently establish populations in temperate areas by overwintering in the egg stage through a diapausing embryo mechanism induced by a short photoperiod in the female [6]. In Italy, *A. albopictus* was introduced in 1990, through the importation of used tires [7]. The presence of

high densities of individuals of this species is particularly threatening, given the suggestion that the strain CHIKV in the Indian Ocean is better adapted to *A. albopictus* than it is to other *Aedes* [8].

Chikungunya infection is characterized by abrupt onset of fever, severe arthralgia, rash, and other constitutional symptoms lasting for about a week. Generalized myalgias with back and shoulder pain, lymphadenopathy, and maculopapular rash are common. Symmetrical, small joint arthritis occurs frequently and can last for many months. The incubation period is 2-10 days, and most infections are asymptomatic or present with a mild self-limited illness. No specific antiviral treatment is available, and symptomatic therapy includes nonsteroidal anti-inflammatory agents and, occasionally, corticosteroids [9-11]. Although it is not a life-threatening disease, high morbidity rates and prolonged polyarthritis leading to considerable disability of some patients can cause substantial socioeconomic impact in affected countries. Chikungunya is known to produce more severe disease in elderly and debilitated patients.

With increasing international travel, returned infected travelers can represent a reservoir for the virus and initiate new epidemics during the summer in countries where replication-competent vectors are present [1, 8, 12], as reported recently for Europe and United States. Considering that the spread of such vector-borne diseases requires only a host reservoir and a specific vector, if humans are the host reservoir and the vector is widely distributed, globalization of the disease is just a matter of time. The 1999 emergence of West Nile virus in the United States in 1999 and its subsequent rapid spread throughout the country



provides evidence that arboviruses can represent a threat in developed countries with temperate climates and in the absence of herd immunity. To date, no vaccine is available, and vector control is the only way to prevent outbreaks.

In August 2007, the simultaneous presence of a high concentration of competent vectors, infected travelers returning from epidemic areas, and favorable environmental conditions were factors responsible for local mosquito-borne disease transmission for the first time in northeastern Italy [8, 12, 13]. This paper briefly reports a summary of the CHIK fever outbreak (detailed elsewhere by others) [14], and highlights the efficient and coordinated response of several parties with different levels of involvement in the management of the emergency.

### The Italian outbreak

#### Summary and Clinical manifestation

Outbreaks of CHIK fever during the summer of 2007 occurred in the provinces of Ravenna, Forlì-Cesena, Bologna and Rimini; this represents the first documented local vector-borne transmission of CHIKV within Europe. The presumed index case was a resident of the region who had travelled to India in June. The first locally transmitted case occurred on July 4; onset of symptoms for the last case occurred on September 28. Since the first case occurred, 337 suspected cases were reported to the local health authorities; 217 of them were confirmed by PCR laboratory test, 30 were classified as probable (as the persons involved denied blood samples), and 89 were negative. The majority of cases (142 of those confirmed as positive) were reported from two neighbouring villages separated by a small river (Castiglione di Cervia e Castiglione di Ravenna). The outbreak successively spread to several small secondary centres of infection. Distribution of confirmed cases was rather homogeneous among males (45%) and females (54, 4%). Approximately 42% of the patients were older than 65 years. Presenting symptoms in confirmed cases were similar to those presented by cases during the outbreak in La Réunion, with 94.5% having fever, 93.6% arthralgia, 94.5% asthenia, 53.5% skin rash, 50.2% headache, and 49.8% muscle pain. The disease was fairly mild in almost all cases; only one patient (an 83-year-old) died. [14].

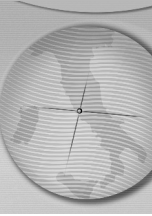
#### Public Health Response

On August 9, the Department of Public Health of the Local Health Unit (AUSL) of Ravenna was notified of the first case of CHIKV. An epidemiologic investigation was initiated in the

following days, and the first intervention of disinfection of the whole urban centre of Castiglione di Cervia took place during the night of August 18-19. From August 23 to 27, the disinfection was methodically extended to the entire epidemic area. Following the initial warning, local health authorities contacted the Ravenna hospital as well as the general practitioners (GPs) of Castiglione to enhance surveillance for early detection of new suspected cases. On August 24 epidemiologic surveillance was extended to all GPs in the province, inviting them to report all suspected cases (defined as the presence of high body temperature [ $> 38.5^{\circ}\text{C}$ ], joint pain, asthenia, and/or rash, and living or having visited one of the two affected villages [even if only for a few hours] or with a history of travel to endemic areas) [14]. On August 29 the Emilia-Romagna Region developed and issued the first guidelines to control and prevent CHIKV in the Region. Guidelines were disseminated to all the Local Health Units, GPs, and emergency units of the Region, with the aim to implement an active surveillance system involving the whole regional area. The following criteria were defined and included in the guidelines:

- a) *clinical*: acute onset of fever  $>38.5^{\circ}\text{C}$  and severe arthralgia not explained by other medical conditions;
- b) *epidemiologic*: residing or having visited epidemic areas;
- c) *laboratory*, including at least one of the following tests on blood samples in the acute phase: virus isolation of viral RNA by RT-PCR; virus-specific antibodies in a single sample serum collected in the acute phase.

Based on the aforementioned criteria, three case definitions were established: possible case (patient meeting clinical criteria); probable case (patient meeting both clinical and epidemiologic criteria); and confirmed case (patient meeting the laboratory criteria but not necessarily having the clinical presentation). On August 30, after National Health Institute (Istituto Superiore di Sanità, ISS) laboratory verification, further regional indications were published, and all the procedures for the specific emergency management were fully activated. On the same day, the Italian Ministry of Health notified the EU Member States, the European Centre for Disease Prevention and Control and the IHR point of contact at the World Health Organization regional office for Europe, of a laboratory-confirmed outbreak of CHIK fever in the region of Emilia-Romagna. Finally, on August 31 the Istituto Zooprofilattico Sperimentale of Lombardia and



Emilia-Romagna isolated CHIKV from a sample of tiger mosquitoes taken from the area of Castiglione di Cervia and Ravenna.

### **Prevention of CHIKV outbreaks**

Based on the experience gained during this CHIK fever outbreak, the Emilia Romagna Region developed a Regional Plan for the prevention and control of Chikungunya and Dengue Fever. The Regional Plan is based on existing national and international guidelines; it focuses on a mandatory notification system, on the surveillance and control of communicable diseases, on rules for blood, organ and tissue donation, and on international measures for the prophylaxis and control of the international movement of persons and goods.

As demonstrated by previous vector-borne disease outbreaks in other world regions, the risk of transmission of CHIKV is essentially linked to two factors: 1) introduction of the virus through an infected and viremic person and 2) transmission of the virus by the bite of an appropriate vector. Considering that neither factor can be totally eliminated, it is essential to operate simultaneously on both fronts, minimizing the chance that they combine. Besides, the risk of an outbreak not only depends on the presence and density of vectors but also on the population's lifestyle. In particular, individual and collective collaboration to prevent the presence of larval habitats (through the removal of water-filled containers) and minimization of vector-patient contact (using individual protection measures against mosquito bites) are both important preventive measures. For these reasons, the key measures for preventing Chikungunya epidemics include entomologic surveillance, peridomestic mosquito control, public education, detection of imported cases, and early recognition of local transmission, followed by efficient vector control.

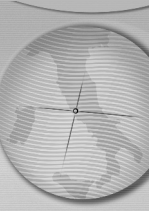
Accordingly, the prevention plan carried out by the regional authorities is based on two simultaneous actions: 1) entomologic surveillance of tiger mosquitoes and 2) early detection of suspected cases. The first action is conducted to quantify and minimize, as much as possible, the density of the vector population through the placement of ovitraps to evaluate the adult insect population and measure the infestation around the regional area, subdivided on the basis of the urbanized surface and subsequent larvicide and adulticide treatments. Early detection of suspected cases is based on an "alert notification system;" active surveillance is carried out by GPs,

pediatricians and Emergency Department physicians, any suspected case will be reported by the GPs to the Local Health Authorities within 12 hours; laboratory tests will be provided by a central laboratory. The Local Health Authorities will then coordinate the implementation of health protection measures.

Finally, each year in April detailed information will be disseminated to citizens, travelers and health-care workers regarding the prevention of the spread of mosquitoes and mosquito bites. The measures detailed in the regional plan required coordinated involvement of different authorities with specific tasks, such as the Regional Health System (health surveillance, diagnosis and control measures against the spreading of the disease) and municipal institutions (disinfestation activities). The strong coordination required was ensured by regional governments, provinces, social and health conferences which offered an ideal connection tool between the health system and the local government institutions [8, 15, 16].

### **Conclusions**

Climate change, increased globalisation including the growing volume of persons and goods moving around the planet, the aging population, the production of solid waste that can shelter *Aedes* mosquitoes, and the biological features of the vectors and of the viruses are all factors that increase the risk of the joint presence of a CHIKV host reservoir and a high density of the specific vector (*A. albopictus*). For this reason, many temperate countries are now more likely to develop outbreaks of vector-borne diseases and epidemics may be amplified [1]. Notably, environmental factors and community behaviours (e.g., the "social environment") play a significant role in Chikungunya outbreaks and spread. Adult mosquitoes usually breed and rest in cool and shady areas in domestic and peridomestic settings and bite during the daytime. Heavy rains, followed by stagnation of rain water in flower pots, broken and abandoned pots, and utensils in and around the houses, abandoned vehicle tires next to dwellings or workplaces or in any other container that allows stagnation of water, all promote the breeding of *Aedes* [17]. Moreover, the ability of *A. albopictus* to colonize new areas and its adaptability to the mild Italian climate allow vector populations to be active throughout the year or at least for 7-8 months in colder regions [18]. Recent observations of *A. albopictus* reported as low as 11.5 hours of light and an average temperature  $>10^{\circ}$  C, which is sufficient for the activation of the biological cycle [19].



However, even if adult mosquitoes do not circulate during winter, recent studies have demonstrated the possibility of transovarian virus transmission, which increases the risk of reappearance of infected mosquitoes in spring [16].

The Italian CHIKV outbreak of 2007, to some extent unexpected, demonstrated the possibility that CHIKV epidemics may occur even in a non-tropical environment. It provided health authorities the opportunity to improve their knowledge and awareness of all imported vector-borne diseases. In particular, this outbreak emphasised the need for all physicians and public health workers to be prepared to encounter and face this arboviral infection, which represents a new paradigm for emerging infectious threats in this era of globalization. Nonetheless, it highlighted the urgent need to strengthen national surveillance, response capacity and active participation of the communities to prevent and contain this emerging infectious disease [14, 18]. The operative method adopted by Emilia-Romagna region substantially consisted of a cluster of feedback-based competencies. It promoted the attainment of excellent and rapid results in a simple but punctual and efficient way, optimizing and coordinating different professional skills (political, administrative and health) at different levels (national, regional, provincial and municipal), representing an effective example that can be applied to other similar epidemiologic situations.

## References

- 1) Pialoux G, Gaüzère BA, Jauréguiberry S, Strobel M. Chikungunya, an epidemic arbovirolosis. *Lancet Infect Dis* 2007;7(5):319-27.
- 2) Ross RW. The Newala epidemic. III. The virus: isolation, pathogenic properties and relationship to the epidemic. *J Hyg (Lond)* 1956;54:177-91.
- 3) Gratz NG. Critical review of the vector status of *Aedes albopictus*. *Med Vet Entomol* 2004; 18: 215-27.
- 4) Urbanelli S, Bellini R, Carrieri M, Sallicandro P, Celli G. Population structure of *Aedes albopictus* (Skuse): the mosquito which is colonizing Mediterranean countries. *Heredity* 2000; 84(3):331-7.
- 5) Straetemans M, on behalf of the ECDC consultation group on vector-related risk for chikungunya virus transmission in Europe. Vector-related risk mapping of the introduction and establishment of *Aedes albopictus* in Europe. *Euro Surveill* 2008;13(7):pii=8040.
- 6) Hawley WA, Pumpuni CB, Brady RH, Craig GB jr. Overwintering survival of *Aedes albopictus* (Diptera: Culicidae) eggs in Indiana. *J Med Entomol* 1989; 26(2): 122-9.
- 7) Knudsen AB. Global distribution and continuing spread of *Aedes albopictus*. *Parassitologia* 1995; 37: 91-7.
- 8) Charrel RN, de Lamballerie X, Raoult D. Chikungunya outbreaks—the globalization of vectorborne diseases. *N Engl J Med* 2007;356(8):769-71.
- 9) Laudati F, Zaratti L, Franco E. Chikungunya: a new epidemic for Europe. Is there a new vaccine coming soon? *Ig Sanita Pubbl* 2007;63(5):599-606.
- 10) Volpe A, Angheben A, Marchetta A, Caramaschi P, Biasi D, Carletto A et al. Chikungunya arthritis: report of 6 cases *Reumatismo* 2008;60(2):136-40.
- 11) Angelini R, Finarelli AC, Angelini P, Po C, Petropulacos K et al. An outbreak of chikungunya fever in the province of Ravenna, Italy. *Euro Surveill* 2007;12(9):E070906.1.
- 12) Depoortere E, Coulombier D; ECDC Chikungunya risk assessment group. Chikungunya risk assessment for Europe: recommendations for action. *Euro Surveill* 2006;11(5):E060511.2.
- 13) Charrel RN, de Lamballerie X. Chikungunya virus in north-eastern Italy: a consequence of seasonal synchronicity. *Euro Surveill* 2008;13(1). pii: 8003; author reply pii: 8004.
- 14) Rezza G, Nicoletti L, Angelini R, Romi R, Finarelli AC, Panning M, et al. CHIKV study group. Infection with chikungunya virus in Italy: an outbreak in a temperate region. *Lancet* 2007;370(9602):1840-6.
- 15) Piano Regionale dell'Emilia-Romagna per la lotta alla zanzara tigre e la prevenzione della Chikungunya e della Dengue- anno 2008 (Emilia Romagna Regional Health Plan for tiger mosquito elimination and Chikungunya and Dengue virus prevention 2008) Available from [http://www.saluter.it/wcm/saluter/news/il\\_fatto/2008\\_gennaio\\_aprile/20lotta\\_zanzaratigre/allegati/Piano\\_CHIK.pdf](http://www.saluter.it/wcm/saluter/news/il_fatto/2008_gennaio_aprile/20lotta_zanzaratigre/allegati/Piano_CHIK.pdf) [Accessed March 31, 2009].
- 16) ECDC Mission Report Chikungunya Italy, 2007
- 17) World Health Organization. Guidelines for prevention and control of Chikungunya fever, WHO. Available from [http://www.searo.who.int/LinkFiles/Chikungunya\\_Draft\\_Prevention&Control\\_CHIK\\_25\\_Nov.pdf](http://www.searo.who.int/LinkFiles/Chikungunya_Draft_Prevention&Control_CHIK_25_Nov.pdf) [Accessed March 31, 2009].
- 18) Beltrame A, Angheben A, Bisoffi Z, Monteiro G, Marocco S, Calleri G, et al. Imported Chikungunya Infection, Italy. *Emerg Infect Dis* 2007;13(8):1264-6.
- 19) Romi R. *Aedes albopictus* in Italy: an underestimator health problem. *Ann Ist Super Sanita* 2001; 37(2): 241-7.