

# The 2007 epidemic outbreak of Chikungunya virus infection in the Romagna region of Italy: a new perspective for the possible diffusion of tropical diseases in temperate areas?

Vittorio Sambri<sup>1,2,3</sup>, Francesca Cavrini<sup>2</sup>, Giada Rossini<sup>2</sup>, Anna Pierro<sup>2</sup>, Maria Paola Landini<sup>1</sup>

<sup>1</sup>Microbiology Section, Department of Haematology and Oncology;

<sup>2</sup>Regional Reference Centre for Microbiological Emergency;

<sup>3</sup>National Institute of Biostructures and Biosystems, University of Bologna, Faculty of Medicine, Bologna, Italy

The Chikungunya virus (CHIKV) belongs to the Togaviridae family and is characterized by a 70 nm spherical particle. The virus has a lipoprotein envelope and a monomeric (+) non segmented RNA genome. The whole length of the genome is 11824 nucleotides and the entire sequence is fully available. CHIKV was discovered in Tanzania in 1953 and since then the spectrum of the haematophagous arthropods able to act as vectors for the human transmission of this virus so far identified includes many species of mosquitoes belonging to the genus *Aedes*, including *A.albopictus* also known as "tiger mosquito" (Rezza *et al.*, 2007). The geographic area where *A.albopictus* is present has enlarged tremendously in the last two decades, including Asia, most of the Pacific Ocean, the Indian Ocean, Africa and southern Europe. In selected areas of southern Europe, like for instance the Romagna region of Italy, *A.albopictus* is now the most prevalent species of mosquito.

CHIKV is efficiently transmitted to humans by the tiger mosquito and after a short incubation period lasting 2-12 days, some 80% of infected subjects become acutely ill. The most prominent symptoms of CHIKV infection are: fever and arthralgia, myalgia, oedema and cutaneous rash.

The acute clinical picture usually lasts for less than two weeks, but prolonged arthralgia is present in some 65% of the patients after six months. The only possible prevention strategy to date has been to avoid being bitten by mosquitoes. In late July 2007, an epidemic outbreak of CHIKV infection started in a narrow area of the Romagna region in northern Italy. This is the first reported epidemic of CHIKV with local transmission by *A.albopictus* outside the tropical areas. The CHIKV virus was found by RT-PCR in mosquitoes collected in the site of local transmission and repeatedly isolated in cell cultures from blood of several patients. The sequence analysis of the gene for E1 protein showed the presence of the A226V mutation: this polymorphism was already described in CHIKV strains isolated from Indian patients in late 2006. This mutation in the E1 gene sequence has been demonstrated to be a major adaptive factor for efficient CHIKV transmission by *A.albopictus* and it has been hypothesized that the local transmission that occurred in Romagna in 2007 was also possible because of this mutation (Bordi *et al.*, 2008). The initial source of this focus of local transmission has now been identified in an Indian immigrant resident in Romagna who returned from his home country in late June 2007 during the viremic asymptomatic stage of the infection. The extremely large population of *A.albopictus* present in the area where this patient was resident during the acute phase of CHIKV infection, was the other side of the coin that precipitated the local transmission. Up to the end of September 2007 a total of 248 cases (including the index patient) were identi-

Corresponding author

Vittorio Sambri, MD

National Institute of Biostructures and Biosystems

University of Bologna

Faculty of Medicine

Via Massarenti, 9 - 40138 Bologna, Italy

E-mail: vittorio.sambri@unibo.it

fied following a laboratory diagnostic criterion over a geographical area that was enlarged to most of the Romagna region (including a small 5 cases cluster in the regional capital city of Bologna located some 70 kilometres away from the origin of the epidemic) (Seyler *et al.*, 2008). The laboratory diagnosis of CHIKV infection was achieved on peripheral blood samples by a RT-PCR test targeted at E1 gene within the first six days after clinical onset and by detection (by IFA) of the specific IgG and IgM antibody response after this first period.

The 2008 Emilia Romagna Regional Preparedness Plan for Chikungunya and dengue has been approved and released by the Health Authority. This plan increases the alert level of the whole public health system in the Romagna region and regulates activities to control the diffusion of *A.albopictus*.

In conclusion, the epidemic of CHIKV infection that occurred last summer in a temperate area of northern Italy constitutes a new model for the diffusion of a tropical disease outside the conventional locations. The outbreak mainly resulted from the "dangerous mixture" of the large population of a highly competent vector, the tiger mosquito, and the possibility that an individual returned from an area of normal diffusion of

CHIKV during the asymptomatic viremic stage of infection. Considering the difficulties in controlling the spread of *A.albopictus* and the large population travelling to and from the areas of normal diffusion of vector-borne tropical diseases we think that the 2007 epidemic may be only the first of a possible series of these outbreaks.

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