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Lessons learned from Chikungunya

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Chikungunya virus (CHIKV) is an Arbovirus belonging to the Alphavirus genus, which is transmitted by *Aedes* spp mosquitoes. Since late 2004, CHIKV caused several outbreaks in coastal Kenya, in the Indian Ocean (especially on the island of La Reunion), and on the Indian subcontinent, where it caused more than 1.5 million cases. Although *Aedes aegypti* is the most commonly involved vector, other *Aedes* spp mosquitoes, such as *Aedes albopictus*, appear to have a good vectorial capacity for CHIKV. The vectorial capacity of *Aedes albopictus* is of special concern, since this mosquito is widespread in several countries in Southern Europe and in other areas of the world, outside tropical areas.

In the summer of 2007, an unexpected outbreak of CHIKV fever, caused more than 200 human cases in the Emilia-Romagna Region of Italy; most of the cases were recorded in two villages in the Province of Ravenna, but smaller clusters were also detected in other towns in the same Region (i.e., the towns of Cervia, Cesena, Ravenna, Rimini, and Bologna). The tropical virus was introduced in Italy by a man from Kerala (an Indian district affected by a large outbreak) and sustained by local mosquitoes (*Aedes albopictus*, “the tiger mosquito”), which transmitted the infection to other persons. The epidemic can be said to have been the result of the globalisation of vectors and humans, which occurred through a two-step process: i) the introduction and adaptation of *Aedes albopictus* to a new environment (i.e., an area with a temperate climate); and ii) the introduction of Chikungunya virus (CHIKV) in a previously infection-free country, as a result of population movement. The CHIKV strains introduced in Italy contained a mutation in the E1 glycoprotein which was responsible for a single amino-acid substitution (A226V) able to increase the infectivity of the virus for *Aedes albopictus*. CHIKV outbreaks did not reoccur in the areas that had been affected by the 2007 outbreak. This was probably the consequence of three combined factors: i) the lack of

human cases during the winter season, due to extremely reduced *Ae. albopictus* activity; ii) the mosquito control activities performed during and after the outbreak; and iii) the extremely low rate of transovarial transmission of the infection (i.e., transmission from the adult mosquito to larvae). By contrast, on the island of La Reunion, although the number of human cases decreased during the dry season, they did not completely disappear, and a second epidemic wave ravaged the local population determining significant increase in mortality.

Investigations conducted during the recent outbreaks provided a unique opportunity to improve our knowledge on epidemiological, clinical and virological aspects of CHIKV infection (i.e., estimate of CHIKV infection R_0 , definition of the clinical spectrum of the disease, duration of viremia, antibody dynamics), and on evolutionary changes leading to virus adaptation to different vectors.

In conclusion, the re-emergence of CHIKV is paradigmatic of the infectious threat in the era of globalisation and emphasises the need for preparedness and response to vector-borne infections and other emerging infectious threats.

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