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Globalization of Chikungunya: 10 years to invade the world

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Considering the worldwide dissemination of *Aedes* mosquitoes, several years ago some of us anticipated the globalization of Chikungunya virus through invasion of the Americas, and stated that the question was not whether it can happen, but when it will happen [1].

Arboviruses present an ongoing challenge to medicine and public health. Chikungunya virus was first isolated in Africa in the 1950s at the border of Tanzania and Mozambique. Chikungunya fever is transmitted by *Aedes* mosquitoes. Clinically, it resembles dengue fever and several other arboviral diseases, but is more frequently associated with arthralgia [2]. For 50 years, the virus was confined to sub-Saharan Africa and Southeast Asia. Although it generally occurred in the form of large and brutal epidemics affecting non-immune populations, it was classified as a mildly pathogenic arthropod-borne virus, and was rated as 'emerging' by the Institute of Medicine in 1992. The situation changed abruptly in 2005–2006, when a strain of Chikungunya virus entered the South West Indian Ocean Islands and adapted rapidly to mosquitoes of the species *Aedes albopictus* through a mutation in the envelope gene of the virus. The E1 A226V mutation is associated with increased replication capacity in this worldwide-disseminated and invasive vector. Since 2005, the epidemics in the Indian Ocean, India and Southeast Asia have accounted for millions of cases locally, and have resulted in thousands of imported cases in Europe and the Americas. No autochthonous case was recorded there, most probably because of the seasonal asynchronicity with the southern hemisphere. The 2007 Italian outbreak of Chikungunya fever (205 laboratory-confirmed cases) was fuelled by a unique patient returning from northern India (north hemisphere) during the viraemic phase of the infection. Later, Chikungunya virus autochthonous transmission was demonstrated in south-eastern France, with two confirmed cases in September 2010 [3].

The first definitive evidence for autochthonous cases of Chikungunya virus infection in the western hemisphere was reported in December 2013 on the island of Saint-Martin, in the French West Indies [4]. Four months later, at the end of March 2014, there were >15 000 cases in nine Caribbean islands in the French West Indies, and the first documented cases inland in South America occurred in French Guyana. One month later, at the end of April 2014, there were cases in 15 islands of the Caribbean, and the count has reached 35 000. Six fatalities have been reported so far [5].

Although prediction of epidemics of transmissible diseases is a difficult art, Chikungunya virus has the potential to spread into new territories of America and Europe where competent insect vectors are widely disseminated [6]. The immense majority of human populations are immunologically naïve, which is a prerequisite for rapid and extended spread.

Accordingly, we believe that several points need to be raised and underlined for the public health community.

First, the situation is drastically different from that observed in 2006 in the Indian Ocean Islands. Seasonal synchronicity between Caribbean islands on the one hand and Europe and central–northern America on the other hand creates a high-risk situation: (i) for the introduction of Chikungunya virus into *Aedes* populations of new territories; (ii) for endemization; and (iii) for subsequent autochthonous clusters of cases of varying magnitude, up to large outbreaks [7]. This process may be aided by the fact that the Caribbean region is visited yearly by millions of tourists from Europe and the Americas.

Second, as previously shown during the La Reunion Island outbreak that affected approximately 40% of the island's population [2], laboratory capacity has permitted the identification and description of unprecedented clinical forms (respiratory failure, cardiovascular decompensation, meningoencephalitis and other central nervous system problems, severe acute hepatitis, severe cutaneous effects, and kidney failure) and previously unrecognized modes of transmission [2]. Approximately 200 severe cases who required medical assistance for vital functions were reported, with a 35% fatality rate [2]. Mother-to-neonate transmission was reported in 44 neonates aged <10 days [2].

Third, the question of safety in blood donation and the required procedure for testing must be addressed as an alternative to stopping blood collection. In particular, the demonstration that asymptomatic infections exist demands the implementation of a strategy for prevention relying on nucleic acid testing that can be complemented with other methods,

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such as quarantine and post-donation self-reporting of febrile illness [8].

Fourth, the media coverage of the Caribbean outbreak of Chikungunya fever is limited, and is overshadowed by the attention focused on the Middle East respiratory syndrome coronavirus cases in the Arabian peninsula or the Ebola outbreak in West Africa. However, it must be underlined that: (i) the potential for the worldwide spread of Chikungunya virus is much higher than the risk of dissemination of Middle East respiratory syndrome coronavirus or Ebola virus; (ii) the total number of cases to be expected from the introduction of Chikungunya virus into the Americas, Europe or even both is undoubtedly immeasurably higher; and (iii) attention and funding should be directed to building up or maintaining an efficient surveillance system, organizing for international coordination and information exchange in a timely manner, and rapidly developing countermeasures, as advocated by the American Committee on Arthropod-Borne Viruses [9].

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