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Corresponding author mail id : remi.charrel@univ-amu.fr

Globalization of Chikungunya: 10 years to invade the world

Charrel RN,[1] Leparc-Goffart I,[2] Gallian P,[1,3] de Lamballerie X.[1]

1. Aix Marseille Université, IRD French Institute of Research for Development, EHESP French School of Public Health, EPV UMR_D 190 "Emergence des Pathologies Virales", & IHU Méditerranée Infection, APHM Public Hospitals of Marseille 13385, Marseille, France

2. National Reference Laboratory for Arboviruses, Institut de Recherche Biomédicale des Armées, Marseille, France

3. Etablissement Français du Sang Alpes-Méditerranée, Marseille, France

Considering the worldwide dissemination of *Aedes* mosquitoes, several years ago some of us anticipated the globalization of Chikungunya through invasion of the Americas, and alerted that the question was not if 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 1950's 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 (in particular small joints, *e.g.*, hand and wrist)[2]. For fifty years, the virus was confined to sub-Saharan Africa and South East Asia. Although it generally occurred in the form of large and brutal epidemic 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 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 an increased replication capacity in this worldwide disseminated and invasive vector. Since 2005, the epidemics in the Indian Ocean, India and South-East Asia accounted for millions of cases locally and resulted in thousands of imported cases in Europe and Americas. No autochthonous case was recorded there, most probably because of the seasonal asynchronicity with the southern

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hemisphere. The 2007 Italian outbreak of Chikungunya (205 laboratory confirmed cases) was fuelled from a unique patient returning from Northern India (north hemisphere) during the viremic phase of the infection. Later on, chikungunya virus autochthonous transmission was demonstrated in south-eastern France with two confirmed cases in September 2010 [3].

First definitive evidence for autochthonous cases of CHIKV infection in the Western hemisphere was reported in December 2013 on the island of Saint-Martin, in the French West Indies (FWI)[4]. Four months later, end of March 2014, 9 Caribbean islands were touched with more than 15,000 cases in the FWI and first documented cases inland in South America in French Guyana. One month later, at the end of April 2014, 15 islands of the Caribbean have claimed cases, and the count reaches 35,000. Six fatalities have been reported so far [5].

Despite prediction of epidemics of transmissible diseases is a dangerous art, Chikungunya virus has the potential to spread into new territories of America and Europe where competent insect vectors are largely 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 provides a high risk situation (i) for the introduction of Chikungunya virus into *Aedes* populations of new territories, (ii) for endemisation, and (iii) for observation of 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 touched ~40% of the island population [2], laboratory capacity has permitted to identify and describe unprecedent clinical forms (respiratory failure, cardiovascular decompensation, meningoencephalitis and other central nervous system problem, severe acute hepatitis, severe cutaneous effects, and kidney failure) and previously unrecognized modes of transmission [2]. Approximately 200 severe cases that required medical assistance for vital functions were reported with a 35%-fatality rate [2]. Mother-to-neonate transmission was reported in 44 neonates younger than 10 day-old [2].

Third, the question of safety in blood donation and required procedure of testing must be addressed as an alternative to blood collection stoppage. In particular, demonstration that asymptomatic infections exist demands to implement a strategy for prevention relying on nucleic acid testing that can be complemented by other means such as quarantine period and post donation self reporting of febrile illness [8].

Fourth, the media coverage of the Caribbean outbreak of Chikungunya fever is limited, and it is outreached by attention focused on the MERS Coronavirus cases in the Arabic peninsula or the Ebola outbreak in West Africa. However, one must underline *(i)* that the potential of worldwide spread of Chikungunya virus is much higher than the risk of dissemination of MERS Coronavirus or Ebola virus,

(ii) that the total number of cases to be expected from introduction of Chikungunya in the America, in Europe, or even in both is undoubtedly incommensurably higher, and *(iii)* that attention and funding should be considered seriously to build-up or maintain an efficient surveillance system, organize for international coordination and information exchange in a timely manner, and develop rapidly countermeasures as advocated by the American Committee on Arthropod-Borne Viruses [9].

References

1. Charrel RN, de Lamballerie X, Raoult D. Chikungunya outbreaks—the globalization of vectorborne diseases. *N Engl J Med* 2007; 356: 769-771.

2. Thiberville SD, Moyen N, Dupuis-Maguiraga L *et al*. Chikungunya fever: epidemiology, clinical syndrome, pathogenesis and therapy. *Antiviral Res* 2013; 99: 345-370.

3. Gould EA, Gallian P, De Lamballerie X, Charrel RN. First cases of autochthonous dengue fever and chikungunya fever in France: from bad dream to reality! *Clin Microbiol Infect* 2010; 16: 1702-1704.

4. Leparc-Goffart I, Nougairede A, Cassadou S, Prat C, de Lamballerie X. Chikungunya in the Americas. *Lancet* 2014; 383: 514.

5. PROMED-mail. Archive no. 20140519.2482881. Chikungunya (33): Caribbean [cited 2014 May 19]. http://www.promedmail.org.

6. Vega-Rua A, Zouache K, Girod R, Failloux AB, Lourenço-de-Oliveira R. High Level of Vector Competence of Aedes aegypti and Aedes albopictus from Ten American Countries as a Crucial Factor in the Spread of Chikungunya Virus. *J Virol* 2014; 88: 6294-6306.

7. Charrel RN, de Lamballerie X, Raoult D. Seasonality of mosquitoes and chikungunya in Italy. *Lancet Infect Dis* 2008; 8: 5-6.

8. Gallian P, de Lamballerie X, Salez N *et al*. Prospective detection of Chikungunya virus in blood donors, Caribbean 2014. *Blood in press*

9. American Committee on Arthropod-Borne Viruses (ACAV). Reaction to the Introduction of Chikungunya Virus in St. Martin, December 2013, http://www.astmh.org/Content/NavigationMenu/Publications/IntheNews/ACAV_Chikungunya_document.pdf