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First cases of autochthonous dengue fever and chikungunya fever in France: from bad dream to reality!

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Following the outbreak of autochthonous chikungunya fever in humans in northern Italy, first reported 3 years ago [1] we have now witnessed two independent cases of autochthonous transmission of dengue fever and two cases of chikungunya fever in south-eastern France during September 2010. This worrying trend has raised serious concern among the health authorities, as *Aedes albopictus*, the Asian 'tiger mosquito', is the most likely transmission vector of both viruses, and this mosquito species is known to be spreading widely throughout many regions of southern Europe. The two cases of dengue fever occurred in patients (a 64-year-old male and an 18-year-old male) living in Nice in the same neighbourhood and knowing each other. The two cases of chikungunya fever occurred in 12-year-old female patients also living in the vicinity of each other in Fréjus, and attending the same high school. Both presented with high fever, headache, lombalgia and arthralgia. These two patients lived in the same neighbourhood as the unique laboratory-documented imported case of the county, affecting a 7-year-old female patient returning from Asia. All four cases resulted in mild, self-resolving infections.

The virological identification of these four cases of arboviral disease, with no travel history, and within the recorded area of dissemination of *A. albopictus*, along the 180-km region of the Mediterranean coast from Menton to Toulon [2]: (i) demonstrates the first cases of autochthonous transmission of both viruses (dengue and chikungunya) in France; (ii) implies that *A. albopictus*, which is resident in this region, is the most likely competent vector for dengue virus (http://www.sante-sports.gouv.fr/apparition-des-premiers-cas-autochtones-de-dengue-en-france-metropolitaine.html); and (iii) raises important issues to be resolved in time for the next 'mosquito season', namely the adaptation of surveillance systems and the implementation of countermeasures to limit dispersal of the viruses and to limit the number of human cases of dengue or chikungunya fever.

How alarmed should we be in Europe? Imported cases of dengue and chikungunya fever have long been reported in infected viraemic travellers [3] returning from tropical regions where the viruses are endemic or transiently epidemic. Indeed, dengue virus ranks second only to the malarial parasite as an agent of systemic febrile illness in travellers to the tropics who are returning to Europe [4]. However, during the past 5–10 years, the perceived risk of infection in Europe, particularly with these two arboviruses, has increased. This is because a competent mosquito vector was not previously present at a sufficient density in Europe to be able to initiate and generate secondary human cases of chikungunya or dengue fever among human populations. With the establishment and amplification of *A. albopictus* in Europe, and these cases of dengue and chikungunya fever in France, the perceived risk of epidemics caused by these viruses or other emerging arboviruses has increased dramatically. Consequently, in an attempt to prevent and monitor the appearance of autochthonous cases, the French authorities have elaborated a surveillance programme targeting both viruses in returning travellers during the summer period of vector activity (http://www.circulaires.gouv.fr/pdf/2010/05/cir_31164.pdf). Among the 124 cases of laboratory-documented imported cases of dengue fever since May 2010, most were diagnosed in patients returning from the Caribbean (where unprecedented numbers of cases were observed in 2010 (>70 000 in Martinique and Guadeloupe)) and Southeast Asia (endemic dengue). The coincident seasonality of *A. albopictus* activity in France and endemic or epidemic dengue virus activity overseas was predicted to raise the likelihood of emergence of autochthonous cases in France [5]. As we have seen, two autochthonous cases of dengue fever have now been documented in Nice. The even more recent autochthonous cases of chikungunya fever in two children in Fréjus serve as an additional warning of the seriousness of the incursion of *A. albopictus* (presumed to be the vector of both of these viruses) into southern France. It is important to note that this occurred despite the fact that only two imported cases of chikungunya fever were recorded in trav-

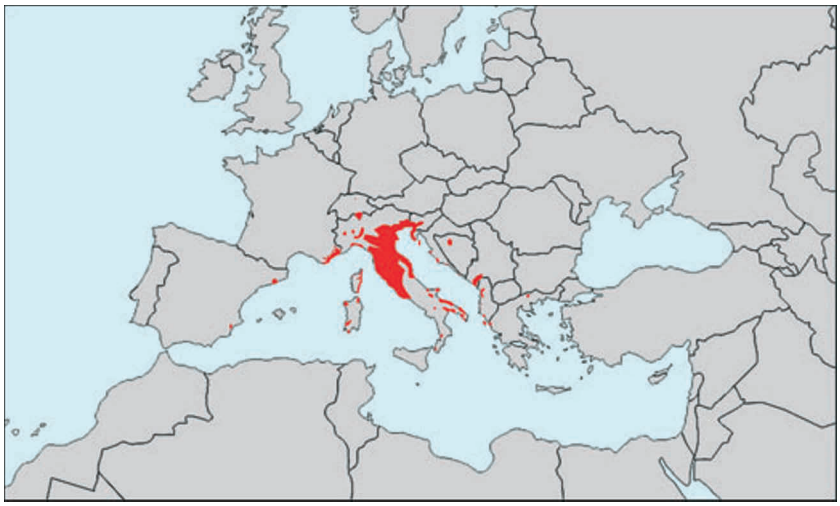

FIG. 1. Dissemination of *Aedes albopictus* in Europe and the Mediterranean countries (adapted from http://ecdc.europa.eu/en/publications/Publications/0905_TER_Development_of_Aedes_Albopictus_Risk_Maps.pdf).

ellers returning to France in 2010. Probably, the very high viral loads of clinically ill travellers returning to France [6] constitute a major factor in the success of this virus.

Strategic surveillance and appropriate countermeasures are urgently needed in anticipation of the possibility that dengue and chikungunya viruses will survive in overwintering mosquitoes or be re-introduced into French mosquitoes via clinically ill travellers, leading to further cases, and possibly even an epidemic of dengue or chikungunya fever during the summer of 2011. The countermeasures should consist of: (i) intensive surveillance at the medical, virological entomological and environmental levels; (ii) consideration of the possible consequences for the blood transfusion service (based on the experience of West Nile virus in North America); (iii) education of the general public, and helpful guidance on how to avoid mosquito bites; (iv) introduction of rapid diagnostic tests (RT-PCR and NS1 antigen detection) into the public health system, to enable timely implementation of entomological field countermeasures; and (v) isolation of viraemic patients, imported cases or autochthonous cases, as preventive measures to limit the risk of dissemination to active vectors.

In addition to all of these concerns, the detection of autochthonous cases of dengue and chikungunya virus infections in southern France raises the issue of the safety of the national blood transfusion system. For dengue virus worldwide, there are only two published laboratory-documented cases of infection related to transfusion [7,8], both resulting in mild infections. For chikungunya virus, no cases linked with transfusion have been published. Nevertheless, cases resulting from blood transfusion have almost certainly been significantly underestimated, as the documentation is extremely difficult to assess accurately in an endemic and epidemic context [9]. These four French documented cases raise specific questions concerning the screening procedures and the appropriate timing of their implementation in the blood bank system. Possible measures include nucleic acid testing for dengue and chikungunya virus on blood samples collected in regions where the presence of the tiger mosquito has been confirmed. However, whether or not this option is employed, many practical questions need to be resolved, for example: (i) the criteria that need to be fulfilled before we initiate nucleic acid testing detection (epidemic threshold, targeted area); (ii) how we should determine the at-risk geographical area in term of blood bank system; and (iii) whether we should accept and therefore act on the risk map predictions for *A. albopictus* distribution in Europe produced by the European Centre for Disease Prevention and Control (http://ecdc.europa.eu/en/publications/Publications/0905_TER_Development_of_Aedes_Albopictus_Risk_Maps.pdf) (Fig. 1).

The four very recent cases of autochthonous infection of humans by emerging arboviruses in southern France serve as an early warning of the potential dire consequences of the establishment of *A. albopictus* in Europe. As the summer season is now almost over, the immediate likelihood of an epidemic arising in 2010 is very low. This does not mean we should become complacent. Governments have a responsibility to act quickly and effectively. Additional measures that might temporarily alleviate the problem should mimic those implemented to reduce exposure to West Nile virus in North America, i.e. rapid diagnosis of acutely infected patients to enable the implementation of chemical and physical isolation from mosquitoes via the use of repellents and bed-nets in the areas where the mosquitoes appear to be established. However, in addition to implementation of these 'classic' measures, it is vital that appropriate measures should

be introduced and, if necessary, enforced to limit the dissemination of the tiger mosquito throughout the at-risk areas of Europe and ultimately to eradicate the mosquito. Even though such a policy is currently considered to be highly challenging, in terms of both cost and logistics, major and innovative measures should be urgently planned and introduced to effect a real reduction in terms of numbers and dissemination. Failure to achieve this objective could soon result in unimaginable levels of morbidity and mortality, particularly when we consider the other emerging viruses that might also be vectored by *A. albopictus*.

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Transparency Declaration

The authors have no conflicts of interest to declare.

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