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Yellow fever in the Americas: risks for the Caribbean islands

La fièvre jaune dans les Amériques : risques pour les îles de la Caraïbe

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Yellow fever (YF) is a viral hemorrhagic fever with a case fatality rate up to 50%. Yellow fever virus (YFV; *Flaviviridae*, *Flavivirus*) is an historical example of the first arbovirus identified as transmitted by a mosquito vector [1]. YFV is found in 44 countries in Sub-Saharan Africa and tropical South America, and seven virus genotypes have been identified, five in Africa and two in America [2]. First isolated in West Africa in 1927, YFV is primarily transmitted in a forest cycle between non-human primates and zoophilic mosquitoes. Urban cycle of YFV involves the anthropophilic mosquito *Aedes aegypti*. The virus was imported into the Americas during the slave trade, as was introduced the African mosquito *A. aegypti.* In the Americas, the disease caused devastating urban epidemics from the 18th to the early 20th century [3]. The development of two attenuated vaccines in the 1930s as well as a continental eradication program of *A. aegypti* initiated in 1916 by the Rockefeller Foundation, and then continued by the Pan American Health Organization from 1940, led to a clearance of urban YFV, which has not been reported in America since 1954 [4]. However, the relaxation of the control program in the early 1970s led to re-infestation by *A. aegypti* of most American countries [5]. As far as that goes, the Asian tiger mosquito, *Aedes albopictus*, was introduced in the Americas in the 1980s, 1985 in United States [6] and 1986 in Brazil [7]; the species is now present in 19 American countries [8].

Today, in continental America, human YFV infections are only acquired in the forest cycle. Humans are contaminated by the bite of forest canopy-dwelling mosquitoes of the genera *Haemagogus* (primary vectors) and *Sabethes* (secondary vectors). The steady spread of the vectors *A. aegypti* and *A. albopictus* is raising concern about the return of urban YFV epidemics in South America, as in the past [9]. In Brazil, between December 2016 and March 2018, more than 2,000 confirmed human cases were reported including more than 500 deaths, as well as more than 4,000 nonhuman primates)[1]. We showed that the anthropophilic mosquitoes *A. aegypti* and *A. albopictus* as well as the enzootic mosquitoes *Haemagogus leucocelaenus* and *Sabethes albiprivus* from the YFV-free region of the Atlantic coast of Brazil were highly susceptible to American and African YFV strains [10]. Therefore, the risk of reemergence of urban YFV epidemics in South America is major with a virus introduced either from a forest cycle or by a traveler returning from the YFV-endemic region of Africa. Moreover, the mosquito *A. albopictus* has all biological characteristics to play the role of "bridge vector" between the forest and the urban YFV cycles. We demonstrated using experimental selection assays that YFV can become adapted for an efficient transmission by *A. albopictus* [11].

The last documented large urban YF outbreak in the Americas was likely in Brazil in 1928. In Americas, there are regular epizootics, which emerge approximately every 5 to 10 years. In the Caribbean, the first epidemics began in 1640 in Guadeloupe then Jamaica in 1655 and Martinique in 1687. It was in Cuba that Carlos Finlay (1881) and later Walter Reed (1900) confirmed the role of the mosquito *A. aegypti* in the transmission of YFV [12]. In the French West Indies, Martinique experienced its last outbreak in 1908 [13]. Today, urban YF is no longer reported in the Caribbean but the mosquito *A. aegypti* is still predominant. In the region, the YFV only circulates in a sylvatic

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[1] Pan American Health Organization. *Yellow fever –epidemiological update 20 March 2018*. www.paho.org/hq/index.php?option=com_docman&task=doc_view&Itemid=270&gid=44111&lang=en.

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cycle on Trinidad island [14]. However, we cannot rule out that imported cases could initiate an urban cycle involving *A. aegypti* [15]. Imported cases are periodically reported in *Aedes*-infested countries [16] as exemplified by the 11 Chinese workers infected in Angola, who returned to China where they developed YF disease [17]. We showed that *A. aegypti* mosquitoes from Guadeloupe were susceptible to YFV, transmitting viral particles from day 14 post-infection [18].

The shortage of YF vaccines together with worldwide distribution of the main vector *A. aegypti* should call us about the means to combat YFV emergence. Travelers caused multiple importations into YFV-free countries without generating secondary infections until now. Improved knowledge on genetic characteristics of YFV circulating strains and mosquito vectors along with serological surveys of non-human primates may help in modeling of YFV activity, and predict the future sites of YF emergence. These predictions will then guide in targeting populations in high-risk areas, to whom will be offered vaccination and implementation of vector control measures.

Conflicts of interest : none.

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