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LETTER TO THE EDITOR

RESURGENCE OF YELLOW FEVER IN BRAZIL: OVERVIEW AND POSSIBLE CONTROL OPTIONS

ABDUL WAHEED KHAN[1,2]*, ZEESHAN NASIM[3], FAZLI ZAHIR[3], MUHAMMAD ADIL KHAN[3], ABID ALI[4], SHAHID ALI[2] and ABDUL HALEEM KHAN[5]

[1]Institute of Information Sciences, Academia Sinica, Taipei, Taiwan
[2]Center of Biotechnology and Microbiology, University of Swat, Odigram, Pakistan
[3]Institute of Biotechnology and Genetic Engineering, The University of Agriculture, Peshawar, Pakistan
[4]Department of Zoology, Abdul Wali Khan University, Mardan, Pakistan
[5]Department of Zoology, Islamia College Peshawar, Peshawar, Pakistan

Dear Editor,

Brazil is one of the few countries with warm humid tropical weather, offering conducive environment to the nourishment of tropical pathogens [1, 2]. Following the footprints of dengue [1] and Zika virus [2], yellow fever has recently emerged as the new public health menace. The responsible agent of the infection is an RNA virus of genus *Flavivirus* known as yellow fever virus. Prominent symptoms comprise fever, loss of appetite, fatigue, nausea, and in severe cases, bleeding and jaundice.

Since December 2016, Brazil is confronted with a new wave of yellow fever outbreak [3]. The reckoned affectees include 586 confirmed cases along with 190 confirmed deaths (Table I) [4] (as of April 5, 2017). Furthermore, 450 incidence cases and 49 suspected deaths are under investigation, making the ongoing outbreak as the deadliest in the history of Brazil. In addition, 1,324 epizootic deaths in primates have been reported to Ministry of Health, Brazil [5]. By now, human yellow fever cases have originated in multiple states including Minas Gerais, Espirito Santo, Rio de Janeiro, and Sao Paulo. All cases reported till date have been associated with jungle mosquitoes *Haemagogus* and *Sabethes* [5]. With the preexisting burden of Zika virus [2] and dengue [1], yellow fever outbreak is another setback for country's health and economic sector. The immunization pace has been amplified and a total of 18.8 million doses of yellow fever vaccine have

*Corresponding author; E-mail: khan_ibge@yahoo.com

Table I. Distribution of yellow fever cases in various states of Brazil [4]

State	Cases			Deaths		
	Suspected	Confirmed	Total	Suspected	Confirmed	Total
Minas Gerais	287	426	713	38	138	176
Espirito Santo	98	142	240	6	43	49
Rio de Janeiro	19	9	28	1	1	2
Sao Paulo	8	5	13	1	4	5
Para	5	4	9	1	4	5
Parana	9		9			
Bahia	8		8			
Santa Catarina	6		6	1		1
Rio Grande do Sul	4		4			
Amapa	1		1			
Distrito Federal	1		1			
Goias	1		1			
Mato Grosso	1		1			
Mato Grosso do Sul			1			
Tocantins	1		1	1		1
Total	**450**	**586**	**1,036**	**49**	**190**	**239**

been distributed since January 2017 [5]. An extra 3.5 million doses requested by Brazil have successfully arrived to address the vaccine-shortage issue [5].

Yellow fever virus transmission is maintained in tropical forests in a sylvatic cycle involving mosquitoes and non-human primates [6] (monkeys and apes). Generally, the infection spread in urban settings is facilitated by *Aedes aegypti*, while in wild settings, *Haemagogus janthinomys* is the leading invasive mosquito specie [7]. In prospect of the current outbreak, despite the rapid reactive targeted vaccination, the virus dissemination is on its way [4, 5]. Indeed, by the time reactive-targeted vaccination is completed, considerable numbers of susceptible people are affected already by an ongoing outbreak. The current outbreak is considered to be the deadliest in the history of Brazil with highest number of morbidities (Figure 1). To date, the role of *A. aegypti* has not been reported [5]; nevertheless, if the infection is spread to urban settings, *A. aegypti* may become active. In view of the present outbreak, there is a dire need of precautionary measures to dilute the intensity of new cases. First, the practice of fumigation should be conducted in the surroundings of residential colonies to curb the nurturing of mosquitoes. Furthermore, use of mosquito repellents, safety nets, and screens should be preferred to nullify chances of mosquito bite. Along with the locals, travelers visiting Brazil should also take the vaccine for protection to restrict the possible spread of infection to new regions [4, 5]. On part of the government, awareness programs and campaigns should be started to convey

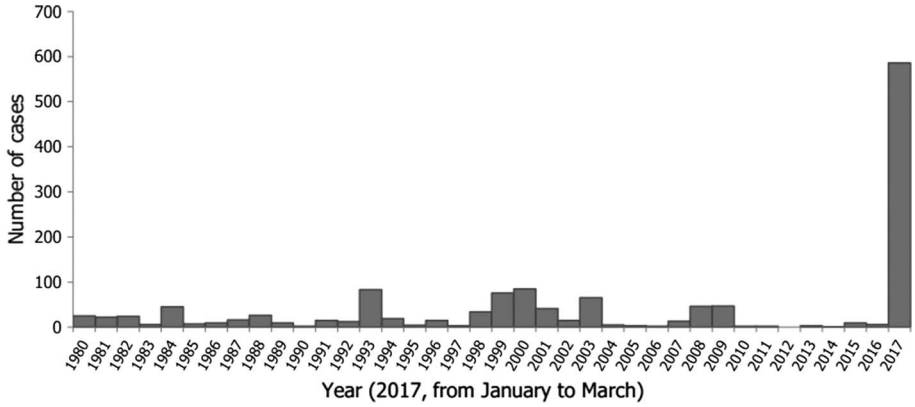

Figure 1. Yellow fever morbidities in Brazil from 1980 till March 2017 [4]

precautionary measures and related information to the dwellers effectively. It is of vital importance to inquire immune deficiencies (primary immune deficiency and HIV-infected individuals) before vaccine administering.

In broader perspective, the world is now confronted with more infections compared with the past. This is possibly due to global climatic changes and gradual adaptation of the vector mosquitoes to a range of environmental factors [7]. Interestingly, vector control is now an emerging area and hot topic for infection control. Fortunately, many infectious diseases may share common/related potential vectors. Therefore, hindering the potential vector would ensure significant decline in a range of vector-borne diseases. Along with conventional vector control strategies, novel schemes are under evaluations recently. Some of these practices have shown immense success in the past few years. These include the new technique, i.e., release of insects carrying dominant lethal genes (RIDL) genetic control strategy [8], which includes *A. aegypti* mass rearing. In this strategy, genetically transformed *A. aegypti* expresses a repressible lethal gene. During growth period, the supplied food supplement is not available in environment (e.g., tetracycline). The provided supplement represses the activation of lethal gene. To mate with wild female, RIDL males are introduced in competition with wild male. The resulting progeny mosquitoes perish as they lack dietary supplement in wild. Another novel strategy involving infection of *A. aegypti* with *Wolbachia* bacteria [9] has revealed remarkable decline in transmission capability of *A. aegypti* for range of arboviral infection including yellow fever. Recently, a similar study [10] revealed striking outcomes of pyriproxyfen (synthetic analogue of insect juvenile hormone) in curtailing the transmission capacity of *A. aegypti*. From the preliminary trials and studies on

innovative vector control techniques, it is evident that there is a scope of further improvement. Compared with the conventional chemical control, innovative vector control techniques are environment-friendly. Therefore, along with practice of immunization for routine outbreaks, there is a need of attention toward enhancement in innovative vector control strategies for long-term goals. Hopefully, these novel strategies would reduce the current burden of vector-borne diseases in future years.

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