MINI-REVIEW

The interplay between environmental factors, vector competence and vaccine immunodynamics as possible explanation of the 2019 yellow fever re-emergence in Nigeria

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Abstract

Throughout the year 2019, Nigeria had sporadic outbreaks of yellow fever (YF), which began in the northern region of the country. Indeed, controlling the bites and population of *Aedes* mosquitoes and vaccination are the only effective means of preventing YF. Vectorial migration, sylvan-to-urban spillover, immunization failure and, perhaps, genetic modification of YFV could be reasons for the re-emergence of YF at the community, state and national levels. This article offers a critical review of the vector biology, YF vaccine immunodynamics and environmental drivers of YFV infections, with the aim of understanding the interplay of these factors in the re-emergence of YF and risk assessment of living in or travelling to areas where YF is endemic.

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Introduction

In the year 1969 yellow fever (YF) disease was first reported in Charleston, South Carolina, Philadelphia and Pennsylvania [1]. The most recent outbreak was reported in Brazil, Angola and the Democratic Republic of Congo from 2015 to 2018 [2,3]. Yellow fever virus (YFV), the causative agent of YF, is an arbovirus that belongs to the genus *Flaviviridae*. The virus has a single-stranded RNA genome that is transmitted mainly by mosquitoes, identified by Walter Reed in the year 1900 as *Aedes aegypti* [4].

Based on the virus genotype, YFV is classified into Eastern and Western region of African, Southern region of American I, and Southern region of American II [5]. The commonest virus route of transmission was categorized into three: (a) sylvatic cycle, involving non-human primates (NHP), which are infected by arboreal mosquito mechanical carriers, including *Haemagogus* spp. and *Sabethes* spp.; (b) intermediate cycle, involving peri-domestic *Aedes* species, which act as a bridging point between humans and NHP and; (c) urban cycle, which involves viral transmission between humans and urban *Aedes* mosquitoes [6].

Despite the success of the vaccines developed against YFV, it remains a threat to the global population because of the relatively low coverage of the vaccination in regions where YF is endemic and exposure to the mosquito vector. These suggest that YF outbreaks can effectively be controlled through adequate and appropriate vaccine administration and vector population control [7]. Recently, about 200 000 cases of YF have been reported across the African and South American regions with 30 000 deaths. Furthermore, the sudden re-

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emergence of YF has been associated with travel of individuals to different parts of the world [1].

This article offers a critical review on the vector biology, YF vaccine immunodynamics and environmental drivers of YF, with the aim of understanding the interplay of these factors in the re-emergence of YF, and a risk assessment of living or travelling to areas where YF is endemic.

Global epidemiology and genotype distribution of YF

Periodic outbreaks of YF are known to occur in regions of the tropics and subtropics located within Southern America and Africa. About 0.08% of the world's population are estimated to reside in areas where YF is endemic [8]. The World Health Organization reported that sub-Saharan Africa experiences the highest incidence of YF outbreaks and associated mortality. Indeed, YF is of great public health concern and affects millions of urban residents in 32 African countries [8].

Yellow fever is endemic in South Central American countries, and several Caribbean islands are now considered high-risk areas of future epidemics. Yellow fever is known to affect all urban dwellers of the American tropics where *Ae. aegypti* primarily acts as the mechanical vector to enhance the risk of viral transmission due to low immunization coverage. The Latin American region is presently most vulnerable to future urban epidemics when compared with the last 50 years [8].

The density and habitats of *Ae. aegypti* have extended to both urban and rural areas, and regions that had previously eradicated *Aedes* mosquitoes are now becoming re-infested. Yellow fever was reported to have originated from Africa and to have been imported into the Americas where it became extensively established [9]. Yellow fever is not known to occur in several developed countries. Still, circumstantial importation of the YFV by chance can lead to outbreaks because of the presence of an appropriate mosquito vector [9].

It has been estimated that about 90% of the outbreaks of YF are recorded on the African continent [9]. In 2008, Togo recorded the largest incident rate. In 2016, Angola experienced a large outbreak which spread to neighbouring countries before the adoption of a massive vaccination campaign that contained the disease. In March and April 2016, China recorded and reported 11 YFD cases; this was the first report for Asia [8,10].

Seven genotypes of YFV have been identified through phylogenetic analysis that are adapted in different ways to their mechanical carriers and human hosts. Five genotypes—Angola, Central & Eastern Africa, Eastern Africa, Western Africa I and Western Africa II—have been reported within the African continent. Nigeria and its surroundings are reported to harbour the West Africa genotype I [11]. This strain appears to be often associated with major outbreaks and is especially virulent and infectious. However, the other three genotypes reported within the Eastern and Central regions of Africa are seen in locations where widespread transmission of YF is seldom experienced. Two previous widespread transmissions of YF were reported in Kenya (1992–1993) and Sudan (2003 and 2005), which demonstrated the presence of the genotype of East African origin that continued to be transmitted unnoticed before the widespread transmission of the virus [12].

A South African study reported the existence of two YFV genotypes within the country, which include genotypes I and II of South American origin [13]. The phylogenetic investigation identified two YFV genotypes that are of West African origin [14] but were imported into Brazil [15]. The year 1882 appears to be the date of introduction into South America (95% CI 1701–1911) [15]. Between 1685 and 1690, the historical record demonstrates the widespread transmission of YFD in Recife, Brazil. Following this period, YFD was not observed until 1849 when the next epidemic occurred. Slave trade across continents may have paved the way for the introduction of YF in the region. The classification of genotype I revealed five subclades (A to E) [16].

Towards the end of 2016, Minas Gerais in Brazil experienced a huge outbreak that was alleged to have originated in brown howler monkeys from whom the virus was transmitted to humans who had contact with the animals within the forest [17,18]. There is no reported incidence that suggests the transmission of the virus from *Ae. aegypti* mosquito to humans that is known to withstand the rapid widespread viral infection within the urban setting. The widespread sylvan transmission progressed towards the Brazilian coast in April 2017, a place where most of the population were unvaccinated [19]. By the end of May 2017, the mortality and case fatality rates for YF were reported as 8.8% and 34.8%, respectively [20]. In addition to the statistics at the time, the outbreak appeared to be declining [20] but the concern for subsequent waves of infection pressured the CDC to trigger a level 2 response [21]. This response was supported by a vaccination campaign launched by the Health Ministry in order to prevent the spread of YFV during the Carnival period [22].

According to the Bayesian phylogenetic investigation of YF genotypes I and II, it was revealed that genotype I was responsible for most infections in Brazil, Trinidad, Colombia and Tobago, and Venezuela. In contrast, genotype II was implicated in most cases in Peru [23]. Genotype I has been documented to have originated around the year 1908 in the Northern Brazilian region, whereas Genotype II originated in Peru during the 1920s. They both (Genotype I and II) have an estimated rate of mutation of about 5×10^{-4} substitutions per

site per year, which is peculiar to that seen in other RNA viral pathogens [21].

The tropical and subtropical areas of Australia, Asia and countries of the Pacific also harbour *Ae. aegypti*. However, no YF outbreaks or cases had ever been reported there, until the 11 imported YF cases introduced by immigrants from Angola and the Democratic Republic of Congo. There have been attempts to explain the reasons for the absence of YF outbreaks in such areas [24]. These include the sterile *Aedes* mosquitoes, which hamper their ability to transmit YFV, the cross-protection immunity in individuals against YF that is conferred by other related flaviviruses such as dengue virus, and the absent or insufficient YF viral load introduced by immigrants from epidemic regions [24]. Another possible explanation could be the absence of slave trading from epidemic countries to Asia, which occurred for the Americas. The trans-Atlantic slave trade perhaps encouraged the transmission of YF into countries of the western region from African countries where YFV was endemic [25].

Yellow fever transmission

The *Ae. aegypti* mosquitoes are among the most anthropophilic mosquitoes, so contribute to the viral transmission cycle within the urban settings [26]. Humans are the reservoir for this cycle; but mosquitoes can also serve as a reservoir for YFV because of their ability to transmit it transovarially [27].

The sylvan, or forest, cycle constitutes of two mosquito genera: *Aedes* and *Haemagogus* [8]. These genera of mosquitoes mainly spread YF to NHP, the reservoir host. There are some NHP that could be affected, and so serve as aberrant hosts in the survival of YFV during sylvan transmission [27]. The viral cycles within the urban and jungle settings take place in South American and African countries; this makes such regions vital locations for the maintenance of YFV [28]. The jungle cycle in African countries requires that *Aedes africanus* preserves the viral ecological habitat. Unlike the jungle cycle in Africa, the transmission cycle in South American countries does not include *Aedes* mosquitoes [28].

Haemagogus mosquitoes are the critical vectors of YF in the jungle cycle for YFV transmission in South America. The tropical forest is the ecological habitat for these mechanical vectors [8]. These vectors lay their eggs on the water surface, where they develop and mature during the rainy season [8]. These mosquitoes transmit the virus primarily to NHP that inhabit the forest canopy. Besides NHP, humans can also be exposed to YFV infections during their forest activities (e.g. deforestation, resource derivation and farming), which interferes with the jungle cycle of the virus [29]. The *Ae. africanus* and *Haemagogus* mosquito vectors are analogues in the African jungle cycle of the virus (Fig. 1) [27]. The *Ae. africanus* and the South American mosquito *Haemagogus* species have a similar ecology and live within the jungle, where they feed on NHP (YFV reservoirs). Besides deforestation and agricultural activities, humans are also exposed to the jungle cycle of the viral transmission during conflicts and war in some sub-Saharan Africa countries where YF is endemic. This consequently enhances the widespread transmission of YFV [30].

The transmission of the YFV within rural settlements has mainly been observed in endemic regions of Africa [31]. Similar to the case of the sylvan cycle, the rural cycle involves a mechanical vector that feeds on both humans and NHP. Landscapes influence the viral transmission path in this cycle from one ecological niche to another [27,31].

Yellow fever vector and their association with landscape

The breeding sites of choice for YF vectors are based on the presence of water puddles and other water sources for laying and development of their eggs. Unlike other species, *Ae. aegypti* has no preference for water sources, so it does not require water surfaces to lay its eggs [20]. This species of vector lays its eggs on the internal wall of a vessel that contains water. This enables the eggs to become submerged when the water level in the vessel rises, which induces further development and maturation of the eggs while underwater before the period of desiccation of the water source within the vessel [20]. *Aedes aegypti* adapts well to a jungle niche where it seeks a crevice within trees where water subsequently gathers during the rains [32]. Human exposure to these mosquito species increases during forest encroachment, deforestation, agriculture and urban development [32].

Human forest activities enhance the rapid adaptation of the vector species from a forest setting to an urban eco-environment where it thrives in the presence of water-collecting vessels. Unlike other vector species, whose transmission cycle is easily altered during human interference, *Ae. aegypti* not only adapts to its new ecological niche within the urbanized area, but consistently survives by feeding on human blood during the night and day as they continue to co-habit and have unrestricted access to humans in their homes. During the vector's blood meals, the YFV are transmitted to uninfected and unvaccinated humans [33].

Resurgence of yellow fever in Nigeria

Yellow fever is endemic in the western African country of Nigeria, but it has assumed the level of an epidemic outside this

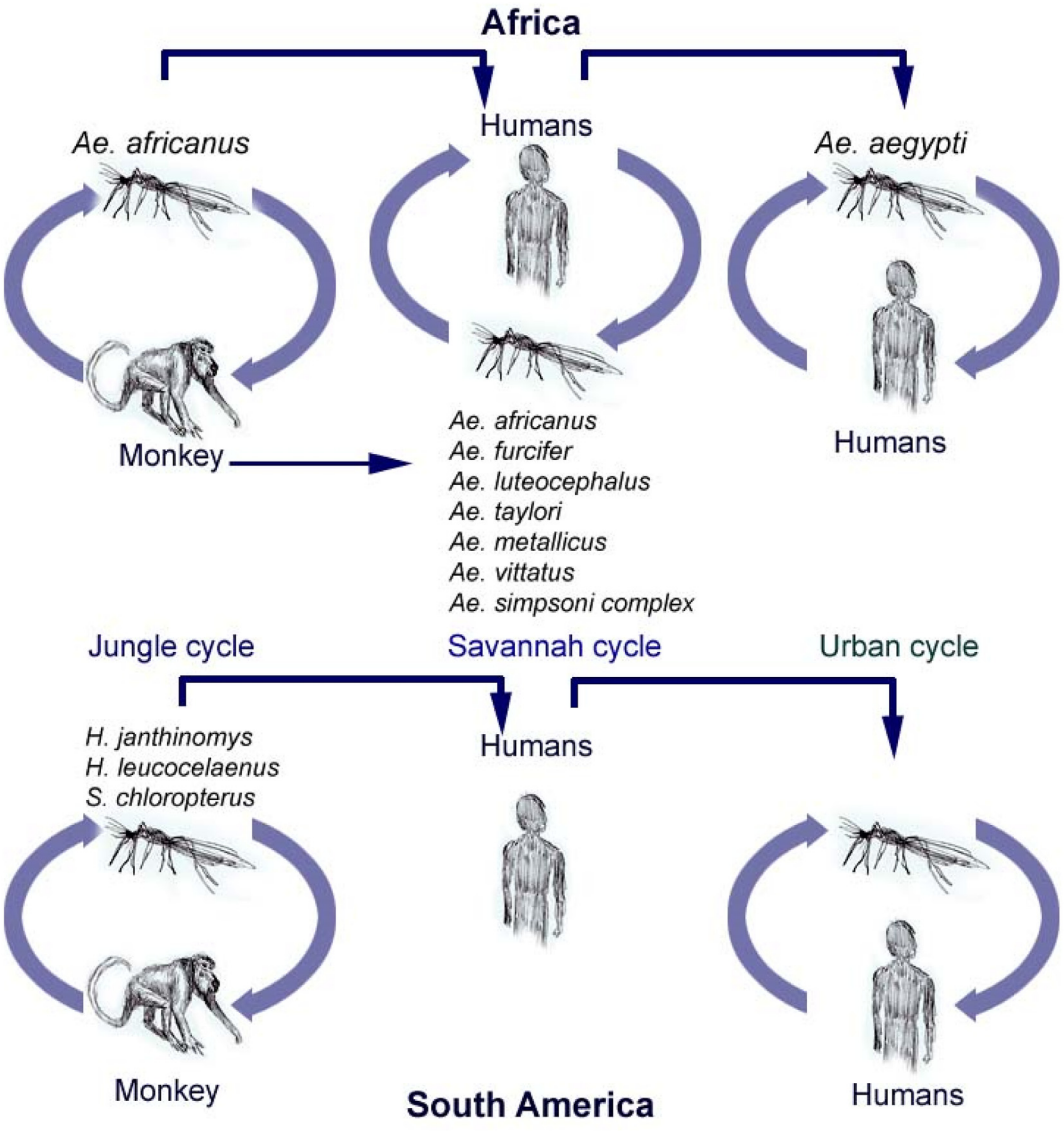

FIG. 1. Transmission cycle between yellow fever virus and its vector. Source: Walsh [27].

zone during previous years. The occasional re-emergence of YF transmission within the past decade has been attributed to an increased viral circulation observed throughout the country. Documented records dating back to January 2019 through December 2019 reported 4288 suspected cases and 231 deaths, of which 227 were laboratory confirmed; there was an increase in case fatality rate compared with 2018 (1.6% versus 0.0%) [34]. Out of the suspected YF cases in Nigeria, the most prominent was on 29 August 2019, when an individual with suspected YF was reported from Kano state and was traced to have travelled to Yankari game reserve in Bauchi State of Nigeria. Of the 231 YF-related deaths, the states of Bauchi (84; 36.6%), Katsina (36; 15.6%), Ebonyi (24; 10.4%) and Plateau (15; 6.5%) had the highest mortalities (Fig. 2). The predominant age groups affected were those <20 years and the male to female ratio among the confirmed cases was 1.3:1. The overall Case fatality rate was 5.4%, and 13.7% among confirmed cases [34].

Yellow fever vaccination protocol

Vaccination is the major available effective measure to prevent YF. In the quest to prevent future epidemics, prompt identification of YF outbreaks in high-risk locations and the achievement of between 60% and 80% vaccination coverage of the uninfected population is vital [35]. It is worth noting that only

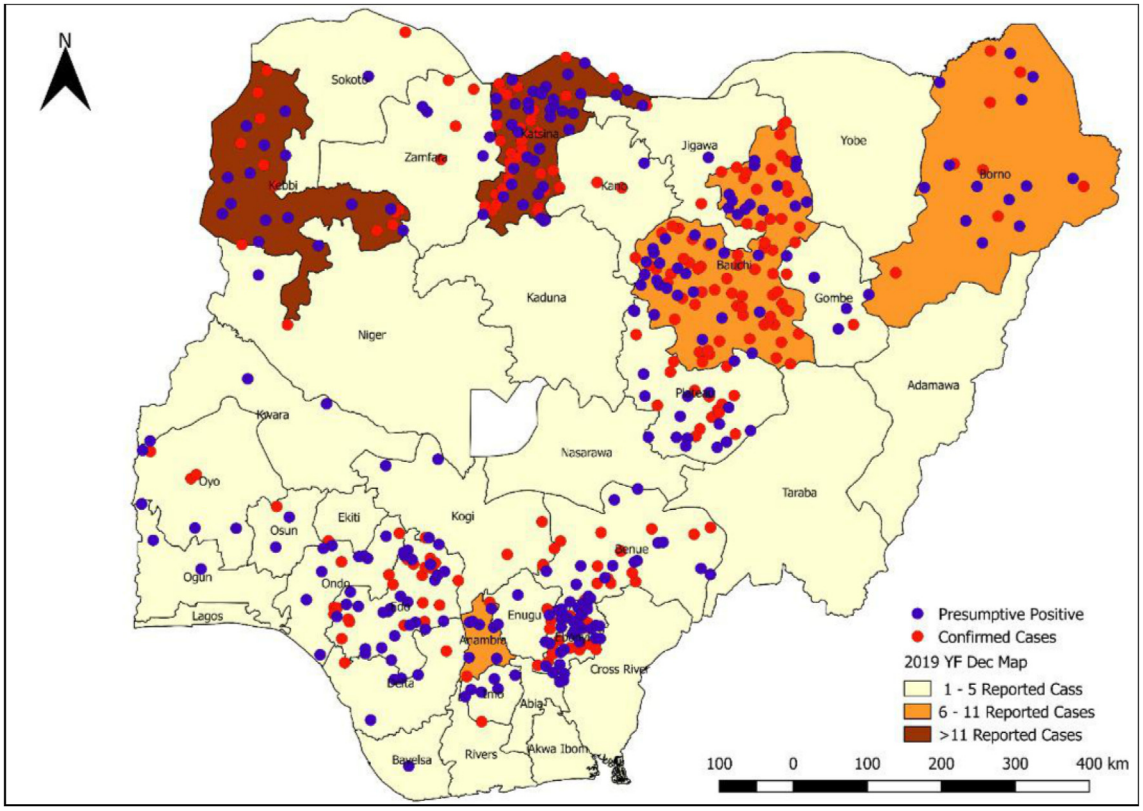

FIG. 2. Suspected/presumptive/confirmed yellow fever cases in Nigeria as at week 52, 2019 (As reported by the Nigeria Center for Disease Control).

two vaccines are available against YFV infection: YFV 17DD and 17D-204 [36]. The current Nigerian immunization schedule proposes a 0.5-mL dose administered subcutaneously at 9 months of age. However, the schedule is contraindicated in the follow age groups [37]:

(a) Below 9 months for regular vaccination or less than 6 months during disease outbreak;
(b) Expectant mothers or children below 6 months of age who are being breastfed, with exception for YF outbreaks due to the high risk of exposure;
(c) Severe allergic reactions to egg protein and/or other vaccine components;
(d) History of severe side effects to previous vaccine doses;
(e) Persons who have undergone surgery for organ transplantation;
(f) Early history of thymus disorders; and
(g) Persons with severe immunodeficiency disorders [37].

The live-attenuated viral strain of the 17D vaccine is currently the main commercially available YF vaccine that provides effective and sustained immunity against infection when administered to individuals at high risk of exposure to the wild-type YFV, especially tourists and inhabitants of endemic regions of Africa and South America. Those eligible for the vaccine are usually given either a single subcutaneous injection or an intramuscular injection [33,38].

The vaccine (17D-204 strain) can be given either to infants (paediatric dosage) above 9 months or adults (adult dosage) using one dose of subcutaneous injection ($\geq$4.74 $\log_{10}$ PFU/0.5 mL) not later than 10 days before regional migration. The single dose of the vaccine is usually sufficient to confer prolonged immunity against YFV infection but booster doses are required in some countries and in the following circumstances:

(a) Migrants or travellers who intend to spend long periods in highly endemic rural regions of West Africa, especially during outbreak or peak transmission periods [37].
(b) Medical laboratory professionals who frequently work on wild-type YFV. Based on regular exposure to this virus on a routine basis, the neutralizing antibody titres against YFV are usually assessed every 10 years to determine the necessity for booster doses of the 17D vaccine.

Irrespective of the knowledge of neutralizing antibody titres for YFV, vaccination every 10 years is recommended, especially for individually at risk of contracting YFV. These recommendations aid in effectively controlling YF re-emergence and transmission to regions of low risk for infection [39].

Mechanisms of action of 17D vaccines

The successful reputation of the 17D vaccine has allowed it to serve as a unique model to understand responses of the human immune system during the acute phase of viral infection. The antibodies, generated on exposure to these viruses, play dominant effector mechanistic roles in ensuring prolonged, vaccine-induced protective immunity [40]. Several innate [41,42] and cellular [43] mechanisms, as well as the helper ($CD4^+$) and cytotoxic ($CD8^+$) T lymphocytes, are known to respond in ways that contribute to the provision of lifelong protective immunity [38].

Although the mechanism of protective immunity against YF is not entirely understood, immunoglobulins are considered to be the major contributors in conferring the protective vaccine-induced mechanism [44] and their presence has been associated with protective immunity.

Following immunization with a dose of the D17 vaccine, pre-existing non-cognate $CD4^+$ T lymphocytes are induced to enhance the immunoglobulin response to the target antigens on the YF-17D vaccine particles. These vaccine particles coated with target antigen also engage the B cells with B-cell receptors.

The B cells internalize these antigen-coated vaccine particles within their endosomes with the release of proteases, which disintegrate both the antigens on the vaccine surface and those entrapped within the vaccine particle to generate peptide fragments. These fragments are presented on the major histocompatibility complex class II (Fig. 3) to cognate $CD4^+$ T lymphocytes (i.e. those that recognize the same antigen as the rare or weak B-cell epitomes) and non-cognate $CD4^+$ T lymphocytes (i.e. those that identify the strong helper major histocompatibility complex class II receptors) [45].

The pre-existing $CD4^+$ T lymphocytes that identify helper antigen generated either by YFV infection or pre-vaccination can induce co-stimulatory signals to B cells, which generates a plethora of neutralizing antibody titres, which are measurable in vaccinated individuals within 6–28 days after vaccination [46]. These signals drive the proliferation, differentiation, immunoglobulin synthesis, somatic hypermutation and isotype switching of B cells. As a result of the determination of the specificity of the immunoglobulin response at the point of B-cell receptor-induced antigen identification, the immunoglobulins generated will be uniquely directed only against the target antigen on the YF-17D vaccine particle surface (Fig. 3).

Neutralizing antibody titres are known to persist in those vaccinated for up to 45–60 years after immunization [47].

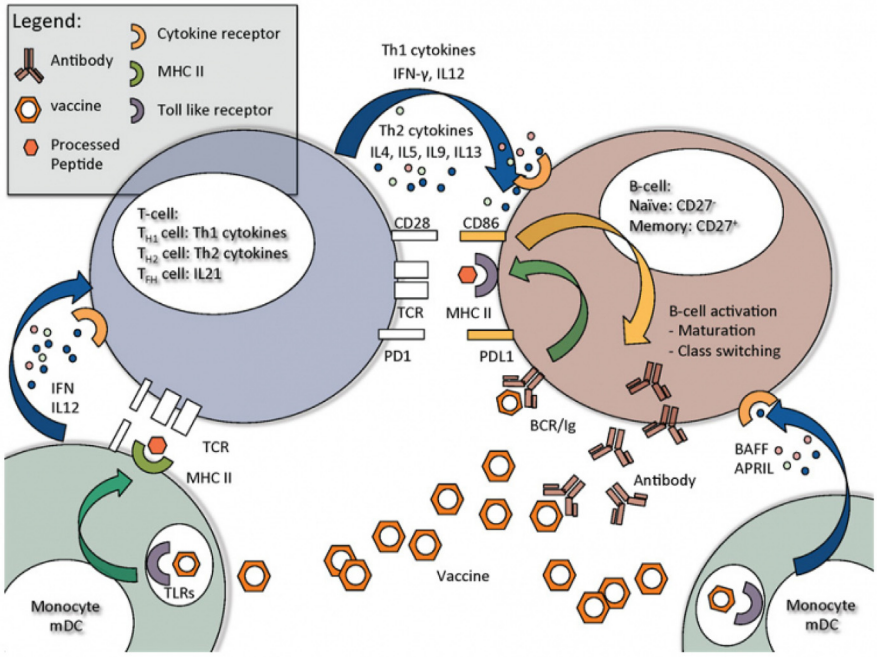

FIG. 3. Mechanism of action of yellow fever vaccine (Egli et al. [46]). Abbreviations: APRIL, a proliferation-inducing ligand; BAFF, B-cell-activating factor of the tumour necrosis factor family; BCR, B-cell receptor; IFN, interferon; Ig, immunoglobulin; IL, interleukin; mDC, myeloid dendritic cell; MHC II, major histocompatibility complex class II; PD-1, programmed cell death protein 1; PD-L1, programmed cell death ligand 1; TCR, T-cell receptor; Th1, T helper type 1; TLR, Toll-like receptor.

Kongsgaard and colleagues [48] demonstrated an average neutralizing (Plaque Reduction Neutralization Test) antibody titre of 1:1280 (within 1:160 to 1:20 480) in those immunized after 9–40 days following vaccination with YF-17D vaccine. This finding is corroborated with animal studies involving either immunoglobulin transfers [49] or genetic induction of immune deficiencies [50]. In YF-17D-vaccinated mice, protection was demonstrated around 5–7 days—evident with the influx of specific cytotoxic ($CD8^+$) T cells. Reduction in the $CD8^+$ T-cell population was correlated with reduced protective immunity and elevated organ viral load [50]. These selected studies synergistically reveal the efficiency of the YF-17D vaccine in providing protective immunity in immunized individuals.

Demerits of yellow fever vaccines

Despite the successes of YF-17D, there are also limitations and adverse effects associated with the use of this vaccine. Adverse effects due to YF-17D vaccine include neurotropic and viscerotropic disorders but the YF-17D vaccine-associated viscerotropic disease is observed to be more lethal [38]. Two unique patterns of YF-17D vaccine-associated viscerotropic disease risk exist:

(a) Risk in younger individuals, which mainly involves females with innate immunity defects in whom mortality rate is higher.
(b) Risk in the elderly, especially in males with age-associated immune deterioration and relatively lower mortality rate.

Viscerotropic disease related to YF-17D vaccine is rarely observed after the initial immunization with the vaccine. Ten days after vaccination, severe multi-organ failure results with a mortality rate of >60%. The predisposing risk factors involve a previous history of thymectomy of thymoma and age of $\geq$60 years. Furthermore, neurotropic disease related to YF-17D vaccine that produces meningoencephalitis, acute disseminated encephalomyelitis and Guillain–Barré syndrome has been observed in infants $<$6 months and in individuals $\geq$60 years old [51].

Risk for travellers

Several factors come into play in exposing travellers to the risk of acquiring YF, such as their immunization status, travel location, season, time of exposure, recreational and occupational activities while migrating, and the virus transmission rate locally at the period of migration [34]. Even though suspected cases of human morbidity are the main indicator of disease risk, there may be no case reports because of a low level of transmission, failure of remote surveillance systems to identify cases or a high immunity level in the population (because of immunization, for example) [30]. Meanwhile 'epidemiological silence' does not imply risk absence, so travellers are advised to get vaccinated before going into areas where YFV is endemic or employing other protective measures [34].

Transmission of YFV is seasonal in rural parts of West Africa, with elevated risk towards the end of the wet season and also the commencement of dry season (between July and October) [34]. The *Ae. aegypti* mosquito may transmit YFV periodically, including during the dry season, in both rural and highly populated urban areas. Within the wet season (between January and May, with a high incidence experienced in February and March), the risk of exposure to infection by jungle vectors in South America is at its peak [34].

Between 1970 and 2015, YF cases reported in people with a history of travelling to West Africa or South America from the USA and Europe, were six and five, respectively, and a case fatality rate of 73% (8/11) was reported. Of all the travellers, one who had a previous record of YF vaccination survived. From the year 2016, there was a rise in the number of travel-associated YF cases, mostly as a result of widespread transmission in Angola and in Brazil. Between 2016 and mid-2018, over 35 travel-associated YF cases were observed in immigrants who were unvaccinated and also inhabitants of non-endemic areas or countries [34]; they included 13 European migrants and one American who journeyed to Peru [34].

It is difficult to predict the risk of acquiring YF during travel as a result of the variations associated with ecological factors of virus transmission. The predicted case fatality rate/mortality rate of YFD for an unimmunized migrant on a 2-week visit to endemic regions of West Africa and South America are 0.01/20% and 0.001/20%, respectively [34]. These estimates are built on the basis of risk to native populations, regularly during seasons recording peak transmission. However, travellers with a different immunity profile may not accurately reflect the risks mentioned above and may also have less outdoor exposure and take precautionary measures against mosquito bites. However, during an outbreak, there is a higher risk of infection for travellers, as demonstrated by the recent outbreaks in Angola and Brazil [52].

Novel control measures against yellow fever: prospects and drawback

Besides YFV, other viruses—including Zika, chikungunya and dengue viruses—are mosquito-borne and of public health

importance [53]. Despite the development of vaccine against these viruses, which has been a main focus, vector control still remains the best and most widely accepted mitigation strategy [53]. Failure to avoid current widespread disease transmission and to halt escalating widespread transmission of key arboviruses has increased the urgent need to further improve the available technological approaches for the control of arboviruses [53].

Synthetic chemical substances with lethal effect on adult vectors (such as dengue virus) using space sprays has been the main approach for arbovirus outbreak control [54]. Pyrethroid insecticides are frequently recommended in controlling mosquito population. However, a major challenge is how to prevent selection pressure on susceptible mosquito populations as well as the control of pyrethroid-resistant vectors [54]. In the population management of arbovirus vectors, specifically *Ae. aegypti*, larval control has long been implemented as a principal strategy [55], including the applications of chemical and bacterial toxins, microbial larvicides and insect growth regulators [56].

Other strategies employ the use of biological agents used against immature stages, which include predatory copepods, fish and *Toxorhynchites* larvae. Perhaps, the most significant challenge and an obstacle to the success of *Ae. aegypti* larval control has been the dependency to detect, access and eliminate or treat domiciliary, often cryptic, breeding sites, a challenging and costly task that is repeatedly responsible for low coverage. In addition, their widespread adoption is limited by their occasional reduced efficiency [57].

Possible environmental drivers of yellow fever resurgence

The resurgence of YFV infection in recent times (2016–2018) has been attributed to low vaccination coverage and the need for reconsideration of YFV as a serious threat to human health because of its re-emergence in both nonendemic and endemic areas with a history of low vaccination coverage [58]. Besides low vaccination coverage, other drivers exist that could result in the re-emergence of YFV in endemic and nonendemic areas. Global warming, increased temperatures, increased rainfall intensity, expansion of human activities to regions where YFV is endemic, and increase in human YFV circulation locally [58,59].

The sylvatic (*Haemagogus leucocelaenus* and *Sabethes albiprivus*) and urban (*Ae. aegypti*) transmission cycles are also important and crucial to the outbreaks [5,60]. Therefore, there is a need for further research elucidating the ecological connections between YFV, its vector and its environmental niche to quickly predict, anticipate and prevent future epidemics.

There is an opportunity to eradicate the disease from the human population but not from the NHP hosts. Children aged 9 months and older given the YF-17D vaccine have lifelong immunity [61]. YFV incidence has drastically reduced, and there were relatively few cases within a 25-year span, limiting outbreaks to countries where vaccines were inadequately administered.

The YF vaccine was not incorporated into childhood vaccination programmes; as a result, individuals born after the vaccination programmes were not vaccinated and young individuals who enter jungle areas for employment are vulnerable to infection. In the late 1950s and early 1960s, several YF outbreaks occurred in Africa, with the highest incidences in the western region [61]. The number of YF infections is on the rise as a result of the replacement of routine vaccination campaigns with emergency immunization campaigns immediately an outbreak has been detected. Once the epidemic ceases, so does the immunization. This mechanism has clearly proved not to be a cost-effective one in the control of vaccine-preventable infections. As for the YF resurgence in the Americas, the YF vector (*Ae. aegypti*) returned to South American countries after its elimination in the 1930s and 1940s as the result of abandoned control measures.

Currently, the vector transmits the virus to a larger area of the Americas and at a rate that is faster than that at which they are being eliminated; this is a result of global warming and political decisions to not continue vector-control programmes [13]. Densely populated coastal areas of Brazil have become reinfested with *Ae. aegypti*, which has resulted in concerns about the resurgence of the urban cycle of YF transmission. The southeastern region of Brazil has observed the highest occurrence of YF transmission in Latin America in decades, beginning in 2016 and it is spreading eastwards across the country.

Conclusion

An ongoing sporadic outbreak of YF in Nigeria commenced in 2018. It has now spread throughout the country. Reports have revealed that the YF has re-emerged in all the states of Nigeria. The large gap in YF prevalence and death that presently exists between Africa and the Americas is basically as a result of the massive vaccination campaigns and implementation of healthcare policies that have been practiced in several countries of South America. These have accordingly eradicated the urban cycle of the disorder in the western hemisphere. The same resources have not been available for large-scale vaccination in many African countries where YFV is endemic to attain reasonable coverage. This inadequate coverage, accompanied by further intermediate transmission cycle, has been significant

in contributing to the much higher YF disease burden in Nigeria.

Conflict of interest

All authors state that there is no conflict of interest.

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