Update on dengue in Africa

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Abstract

Dengue fever is a major public health problem worldwide, being considered one of the most important re-emerging diseases of today. Dengue viruses and their mosquito vectors, while being widely spread across all tropical and subtropical regions of the world, have recently emerged in temperate regions as well. In Africa, both the virus and the vector mosquitoes exist, but, unlike in Asia or South America, human dengue cases have been identified only occasionally, without reports of severe outbreaks, until a few years ago. Recent episodes in the African continent evidenced the lack of effective and reliable programmes for surveillance and control of dengue outbreaks. This paper tries to give a brief overview of the current status of dengue in Africa and to assess the main risk factors for any massive outbreaks in the future, while outlining the currently envisaged strategies to face this emergent threat.

Keywords: Africa; Dengue virus; Aedes; Endemic; Vector control.

Introduction

Dengue disease is one of the most important arthropod-borne viruses of today. It affects millions of people worldwide and is considered an emergent disease in both the developing and developed worlds. Symptoms range from relatively mild dengue fever (DF) to the life-threatening, severe haemorrhagic fever (DHF) or dengue shock syndrome (DSS). There are four antigenically-related serotypes of DENV (DENV-1-4), all of them causing illness. WHO reclassified ‘DHF’ as ‘severe dengue’ in an attempt to consider the frequent haemorrhagic manifestations also observed in mild disease. During the past millennium, dengue sylvatic viruses were consistently and independently spread around the world, probably from south-east Asia, and introduced into human urban cycles. Dengue disease has been notified in Africa since the early 20th century. Apart from the relatively few reported cases, outbreaks
in Africa have often been poorly documented, with no reliable data about the disease incidence or prevalence. The scanty information sources available about dengue presence and distribution in Africa include sporadic publications about local outbreaks, travellers’ infection cases and serosurveys, these being of very limited usefulness to determine the true incidence and the epidemiological aspects of the disease in the continent. Human population growth has been traditionally associated with increased dengue occurrences and outbreaks; sustainable endemic transmission may require, at least, dozens of thousands of people agglomerates,[2] thus occurring mainly among urban populations and in the presence of domestic anthropophilic mosquitoes, able to transmit the infection among humans within urban centres. Yet, even in urban African settings, severe DHF has been only occasionally reported.[3]

Unlike in the Americas and Asia, the sylvatic transmission cycle of DENV seems to predominate in West Africa. Despite the lack of systematic epidemiological and serosurveillance data, several African countries have registered, over the past decades, significant increases in the number of dengue epidemics, although at a much smaller scale than in south-east Asia or in the Americas,[4] with few deaths and reduced morbidity. Vectorial capacity, host genetics and virulence of viral strains have been implicated in this epidemiological pattern. Ultimately, adequate dengue surveillance will be crucial to implement suitable vaccination programmes, as expected for the near term.[5] This paper aims to assess the current status of dengue disease in Africa and, from the epidemiological, entomological and genetic perspectives, to evaluate the risk of the occurrence of severe dengue outbreaks as a major public health problem in the continent.

The virus

Arbovirus infections presumably constitute a high proportion of undiagnosed febrile illnesses in Africa. The existence of the disease, the prevalence of anti-dengue antibodies in the scarcely reported serosurveys and their higher abundance with increasing age indicate dengue endemicity in most regions of the continent.[5,6] The prevalence of dengue in Africa seems to be lower than in Asia and in the Americas, but it is unclear if its emergence in the last few years results more from real enhanced occurrence of the disease or from improved reporting. The apparent low incidence and prevalence can still be ascribed to the increased vulnerability of local populations to diseases as malaria, tuberculosis and AIDS (due to socioeconomic and environmental determinants) than to dengue, or simply to the small sample sizes usually tested in the few existing surveys.[5] Unlike the virus of yellow fever (YF), which presents a well-known sylvatic transmission cycle, DENV evolved preferentially to a human-to-mosquito-to-human urban cycle.[7] However, unlike in South America, sylvatic cycles of DENV have been detected in West Africa and south-east Asia.[8] Here, forest vector-mosquitoes are only moderately anthropophilic and a dominant sylvatic transmission cycle, while occasionally affecting some humans, is most likely maintained by several Aedes spp. mosquitoes and non-human primates.[9]
Nevertheless, the true role of non-human primate as hosts for DENV remains questionable, as shown by a serological survey on Senegalese monkeys, where 100% of infected isolates were tested negative for anti-dengue IgM and 58% positive for IgG, the latter probably due to cross-reactivity with other flaviviruses. The lack of reported human dengue outbreaks caused by DENV sylvatic strains suggests that they are confined to the forests – given their absence from pools of peridomestic mosquitoes from endemic dengue – or that they yield relatively mild human disease. The first genetic evidence of a sylvatic cycle probably arose from a genome sequencing and profiling study of several isolates of DENV-1 and DENV-2 genotypes, where a single genotype (from DENV-2) represented an isolated forest virus cycle that has evolved independently in West Africa. In parallel, it is now known that DENV urban strains infect sinantropic mosquitoes (e.g. *Aedes aegypti* and *Aedes albopictus*) more easily than ancestral sylvatic DENV strains. The existence of a permanent sylvatic cycle constitutes an unlimited source of viral traffic to human hosts in urban environments, making dengue eradication almost impossible. Experimental studies with different surrogate human model hosts have shown no differences in the mean replication rates of sylvatic and endemic DENV-2 strains, thereby suggesting that the presumable evolution of DENV sylvatic into urban strains may not have required adaptation to replicate more efficiently in humans than in ancestral animal hosts. Thus, there is a considerable risk for dengue reintroduction into the endemic urban cycle from the sylvatic circulation.

In fact, the first human case of DHF in Africa associated to a sylvatic DENV strain, of DENV-2, was reported recently, in a patient from Guinea-Bissau returning to Spain. It is possible that cases of sylvatic dengue have been underreported as clinical diagnosis, which has largely constituted the predominant diagnostic approach for dengue in Africa, frequently shows identical symptoms caused by endemic and sylvatic DENV strains. Since DENV is endemic in West Africa and DENV-2 is largely the predominant circulating serotype (of endemic and sylvatic lineage as well), a secondary infection is unlikely to explain this case’s disease severity. Unfortunately, serological diagnosis (mainly via the IgM/IgG ratio) is inconclusive in distinguishing a secondary infection from a primary infection concomitant with previous immunity to other flavivirus, strongly suggesting a primary infection with a highly virulent sylvatic strain. Nevertheless, the potential of sylvatic strains as serious threats to public health has been questioned.

Some authors focus on reports about dengue infections with similar severe symptoms caused by endemic and sylvatic strains and on present DENV circulation in primates, despite the ongoing deleterious human interventions in the tropical ecosystems to support the hypothesis about the risk for the emergence of human outbreaks caused by sylvatic dengue viruses. On the other hand, some writers claim that because of the only few number of human dengue outbreaks reported in several decades that were caused by sylvatic DENV strains, and the unlikelihood of the virus spillover from the sylvatic to the human cycle – in accordance with the non-African origin of the strains that have caused human outbreaks in the continent – make such emergence unlikely to occur. Meanwhile, the interpretation
about the significance and implications of clinical data, viraemia levels and human-driven environmental disruption is not consensual.\[16,18\] Nevertheless, caution must be exercised about the possible emergence of human dengue from sylvatic viral strains with enhanced host and vector ranges.\[17\]

**The vectors**

The African-native *Aedes aegypti* mosquito species has been considered the main urban-cycle dengue vector and the one responsible for all major DHF outbreaks.\[19\] This species is composed by the subspecies *Ae. aegypti aegypti* and *Ae. aegypti formosus*. It is likely that the ancestral sylvatic *Ae. aegypti formosus* from sub-Saharan forest became domesticated by differentiating into the current *Ae. aegypti aegypti* urban subspecies. This original afrotropical mosquito then spread to other regions of the world, including the Mediterranean and the Americas.\[20\] *Ae. aegypti* mosquitoes were involved in the late 2009 dengue outbreak in Cape Verde islands.\[21\] Until a few decades ago, the physical isolation of the archipelago could justify the absence of endemic vector-borne diseases, e.g. dengue or malaria. However, the same factors that most likely explain the homogeneity of mosquito biodiversity between the islands, especially urbanization and increased human, vector and pathogen movements (apart differences in climate and vegetation), may favour, under appropriate environmental conditions, the emergence of more frequent and severe outbreaks.\[22\] The role of *Aedes* sp. mosquitoes other than *Ae. aegypti* in dengue transmission has been probably underestimated due to the non-existence of reliable entomological and epidemiological studies. Like *Ae. aegypti*, *Ae. albopictus* also infests urban environments,\[23\] thus acting as a secondary vector of urban, epidemic dengue in Africa. This species has lower *in vivo* than *in vitro* vectorial capacity for human infections. Human dengue is, indeed, the only disease known to be transmitted in nature in epidemic form by *Ae. albopictus*,\[19\] but this species has also been considered a less efficient epidemic vector than *Ae. aegypti* as a result of differences in host preferences.\[15\] However, as for *Ae. aegypti*, geographical variations influence susceptibility to dengue infection in these mosquitoes.\[24\] The general higher susceptibility of *Ae. albopictus* than of *Ae. aegypti* for dengue viruses, as suggested by experimental infection studies,\[25\] indicates a superior degree of adaptation as a result of longer historical contact.\[13\] *Ae. albopictus* is the main dengue vector in Asia, where *Ae. aegypti* (an efficient vector for both DENV and yellow fever virus (YFV)) is also abundant but in competitive disadvantage with *Ae. albopictus*. In Africa, the relatively low abundance of *Ae. albopictus* compared to that of *Ae. aegypti*, as well as the high cross-immunity between dengue and YF (by which recovering from one disease decreases susceptibility to the other), might fully explain the coexistence of both diseases in Africa and the absence of YF from Asia (even before the introduction of mandatory vaccination, in most countries, for incoming travellers), as recently demonstrated by mathematical modelling.\[26\]

In Africa, *Ae. albopictus* was first detected in South Africa in 1989, and, shortly afterwards, in West Africa.\[25\] The species has been implicated, for several decades, as the main or even sole
vector in several dengue outbreaks in Africa.[27] In recent years, West and Central Africa have experienced human co-infections of dengue and chikungunya (the last having Ae. albopictus as the main vector), simultaneously with the invasion of the continent by Ae. albopictus.[25,28] Even more surprising is the fact that such episodes of dengue epidemics have also occurred in regions previously occupied by Ae. aegypti, and phylogenetic analysis confirmed that this happened with urban rather than sylvatic DENV strains.[29] This phenomenon is probably related with the above-mentioned higher susceptibility of Ae. albopictus for the virus. Such highly probable association between Ae. albopictus territorial infestation and the emergence of human dengue transmission and disease has been recently confirmed in Europe, with the introduction of DENV in 2010 in the Mediterranean, where Ae. albopictus circulates, and the onset of autochthonous viral circulation thereafter.[14] Experimental assays showed that isolate pools of African mosquito species, tested for both DENV and CHIKV, were positive for both viruses in most of the isolates of Ae. albopictus and negative for many other species, e.g. Ae. aegypti.[29] In addition, well-succeeded experimental infection of African Ae. albopictus mosquitoes with sylvatic, but even more with urban/epidemic DENV strains, was achieved.[30] Unlike Ae. aegypti, Ae. albopictus has higher tolerance for temperate winters, thus presenting a high risk for dengue spreading to non-tropical regions.[31]

Given the strong evidences about the high compartmentalization of both sylvatic and urban dengue cycles, and apart from the suggestions about an eventual relevant role of Ae. aegypti[24] and Ae. albopictus[19] in this regard, Aedes furcifer is perhaps the strongest link for DENV exchange between the two cycles in view of its susceptibility to dengue viruses and presence in both environments.[30] Indeed, only sylvatic strains of DENV-2 have been reported, in association with the forest mosquitoes Ae. luteocephalus, Ae. taylori and Ae. furcifer.[10] In East Africa, since 1980, a high abundance of mosquito populations has accompanied the temperature increase observed in the highlands. In fact, the expected rise in DENV incidence and geographical expansion in the African continent, especially in eastern and central Africa, has been predicted by recent mathematical modelling based on premises and evidences about climate and ecological changes suitable for enhanced dengue transmission.[32] Nevertheless, the real impact of climate conditions on dengue incidence and prevalence remains unclear and controversial.

In Africa, given the concurrence of various favourable conditions (including those of socioeconomic origin) for the rapid emergence of severe dengue disease outbreaks, it would be particularly interesting and useful to carry out prospective and/or retrospective studies about the presumable correlation between climate, urban infestation by vector mosquitoes and human epidemics, as well as entomological studies to assess the eventual implication of sylvatic DENV strains, in order to assess the influence and dimension of such factors in human dengue transmission. In particular, updates on the geographical distribution of mosquito populations, and comparative analysis of vector-virus interactions including the predominant Ae. aegypti and Ae. albopictus species, could clarify more properly the exact and relative role of each species, especially of the new-comer Ae. albopictus, in the current dengue emergence in Africa.[28]
Dengue in Africa


DENV-3 was initially reported in the continent during an outbreak in Mozambique in 1984-85,[50] where several secondary infections were reported. Shortly afterwards, in 1993, a mixed outbreak of DENV-2 and DENV-3 occurred in the US military troops stationed in Somalia.[38] Prior to DENV-3, DENV-1 and DENV-2 were reported as being endemic in the region, where dengue was identified as a dominant cause of fever.[51] In West Africa, apart from the recent large outbreak in Cape Verde (2009), and its co-circulation with YF in Ivory Coast (2008),[38] DENV-3 has been isolated only in European travellers returning from Benin (2010),[52] Comoros, Zanzibar (2010),[53] Cameroon (2006) and Senegal (2007 and 2009).[39,54] Senegal, in particular, has reported an unusual frequency of dengue outbreaks, but this may be biased by improved surveillance in this country compared to most of the others. The DENV-3 outbreak in Cape Verde, the largest dengue outbreak ever registered in West Africa, was most likely a consequence of the increased travel and trade that occurred between the archipelago and neighbouring African countries and, as such, a serious sign that the virus is still spreading in the continent.[39] DENV-3 was detected in early samples, ruling out the hypothesis of an escalation of the pandemic influenza A (H1N1) virus, which was also affecting Cape Verde at the time. After this outbreak, which caused a few deaths by DHF out of around 20 000 reported cases of dengue disease, the Cape Verde Health Ministry requested a multidisciplinary task force from WHO aimed to evaluate the risk of introduction of YF in the country. As a consequence, a stepwise vaccination programme and improved controls at the frontiers were implemented.

The circulation of DENV-4 was detected in Senegal in the 1980s[42] and remained poorly documented since then, indicating a negligible occurrence and impact. In Africa, DENV-2
accounts for most of the epidemics, followed by DENV-1. Although the correlation between dengue serotypes and disease patterns is uncertain, DENV-2 and DENV-3 seem to be the main contributors to disease severity and mortality worldwide. Owing to the scarcity of documented dengue outbreaks in Africa, the true burden of the disease in the continent is difficult to estimate, and therefore the scarcity of DHF episodes is not easy to interpret. Since dengue endemicity in sub-Saharan Africa seems to be increasingly evident, growing urbanization remains as a high-risk factor for large outbreaks of dengue in the continent. Although most of the African people still live in rural regions, the overall urban population in the continent increased 3-fold in the last 50 years. Cities provide many artificial, non-biodegradable containers that accumulate the necessary water for intense breeding of mosquito larvae. Yet, a very recent study in Viet Nam showed that DENV transmission may be more intense in rural than in urban regions owing to the existence, in rural areas, of higher mosquito-man ratios and higher proportions of horizontally- than vertically-aligned human habitations, creating higher risk for efficient DENV transmission than in tall buildings (which have higher overall rather than ground-floor human densities than horizontal settings). Given that, in Africa, more than 70% of the human population still lives in rural regions, a risk for large outbreaks becomes obvious. Even so, despite the unfavourable vector-host ratio for efficient dengue transmission in cities, the absolute number of cases is, most likely, higher in cities than in rural areas.

Despite all DENV serotypes have already been reported in the continent, the reasons for the apparent absence of severe dengue disease in Africa remain unclear. The available evidences suggest that this low severity of human disease is multi-factorial. Low virulence of viral strains, low genetic susceptibility of native black persons, high cross-protection conferred by other native flavivirus’ antibodies from previous infections or vaccinations (e.g. from YF) and low vectorial capacity of endemic mosquito populations, probably contribute to the scarcity of severe cases. Recent evidences have suggested that African sylvatic strains of dengue viruses are less virulent than those circulating in other parts of the world, thus explaining, at least in part, the historical lack of severe forms of dengue disease in Africa.

Regarding host genetics, distinct clinical patterns of hospitalization between black and white people observed in the Caribbean, with almost nonexistence of DHF/DSS among blacks even in DENV hyperendemic regions, have suggested lower genetic predisposition of blacks to dengue, especially to its severe forms. This has been attributed to the existence of polymorphic genes, unequally distributed among different ethnic groups (as a result of different selective pressures exerted on geographically-split human ancestors), regulating disease severity and resistance to infection. The identification of human genes regulating infection susceptibility may render powerful tools for the combat and management of dengue disease.

Given the common historical origins of black people from both the Caribbean and Africa, it has been assumed that a common genetic profile between the two black people groups might be associated with the low incidence of severe dengue cases and fewer
outbreaks in both tropical regions.\cite{60,61} Genetically-controlled factors also regulate unequal predisposition to dengue infection among different \textit{Aedes} mosquito populations.\cite{62} Indeed, African \textit{Ae. aegypti} populations have shown lower vectorial capacity for both sylvatic and urban dengue viruses than Asian and American populations.\cite{24} Low vectorial capacity can be circumvented by relevant factors such as high local vector density, mosquito population longevity or anthropophilic behaviour. Adult mosquito survival rates and density, both crucial parameters for arbovirus transmission, are affected by eco-climatic factors. Even in the current context of low DHF/DSS incidence in Africa, the presumable low vector susceptibility in the continent may result, in the long term, on selection for higher viraemia and, in turn, to more frequent and severe disease.\cite{10} With respect to immunological factors, an eventual low rate of dengue infection in Africa may result from cross-protecting immunity from heterologous antibodies from other endemic flaviviruses in Africa.\cite{5} A similar hypothesis was already described to explain the absence of YF in Asia.\cite{8}

**Dengue control and surveillance**

There are several strategies already employed or under development for control of dengue disease, especially towards the production of a vaccine and new tools for control of vector mosquito populations. Since the occurrence of DHF/DSS may essentially depend on the well-known antibody-dependent immune enhancement effect (by which circulating antibodies from a primary infection confer lifelong protection against the infecting serotype but induce greater susceptibility to other serotypes in secondary infections and eventual haemorrhagic symptoms), vaccination not targeted at all four serotypes will likely enhance susceptibility to severe disease.\cite{63} If, however, as it has been more recently proposed, distinct DENV serotypes, and probably genotypes as well, may exhibit different virulence and/or transmissibility – both factors influencing proneness to severe and epidemic disease – then an efficient strategy to fight dengue would be direct control of the more virulent strains through vaccination. Assuming that the last condition predominates, a future dengue vaccine, in practice, should be effective against the four serotypes, and its use in African populations would be expected to eradicate one or more serotypes within the endemic regions. However, without vector control, this would not avoid the introduction of zoonotic strains into the human urban cycle,\cite{64} given the multiple forest niches of the virus. Only sustained vaccination programmes could prevent this scenario, assuming the development, with time, of a strong protective cross-reactivity between dengue urban strains used for vaccines and the zoonotic ones.\cite{31}

Given the known difficulties and limitations of the insecticide-treated nets for mosquito-bite prevention and the complexity and expensiveness of mosquito genetic control (e.g. by releasing, into the natural environment, sterile males or transgenic mosquitoes) for application in low-income countries and settings, the implementation and/or reinforcement of classical insecticide-based mosquito eradication programmes should be reinforced, together with continuous surveillance and monitoring, in order to prevent and/or minimize the emergence
of insecticide resistance. Data about insecticide susceptibility are essential to implement effective and long-lasting control measures, especially regarding the most common insecticides used for mosquito control in Africa. Yet, particularly in Central and West Africa, such data are not available for *Ae. albopictus*, in view of the recent introduction of this species in the continent, and outdated for *Ae. aegypti*. It is suspected that insecticides commonly used for other insects may also trigger selective pressure and thus insecticide-resistance in *Aedes* spp. As such, DDT treatments used 50 years ago to control malaria most likely caused a drastic reduction of *Ae. aegypti* populations in several African countries. Subsequent relaxation of vector control programmes led to latter reoccupation by this species, and, by competing colonization, by *Ae. albopictus*. A similar effect was observed in the 1950s–1970s campaign to eradicate YF, whose interruption provoked quick *Ae. aegypti* recolonization and, shortly afterwards, to the worldwide emergence of dengue disease.

One of the most efficient *Ae. aegypti* control methods relies on the elimination of the most common peridomestic breeding sites. It has been shown that, even in regions with high human host density and mosquito/man ratios, regular supply of tap water eliminates most of the mosquito breeding sites, with drastic reduction of dengue transmission. However, this strategy implies not only existing infrastructures but also a continuous and usually difficult engagement of local human populations. Concerning *Ae. albopictus*, and taking into account its non-African origin, an insecticide-resistance background cannot be excluded, an aspect deserving careful assessment. Considerable resistance of this species to pyrethroids has recently been demonstrated in Singapore, through detection of a knock-down resistance gene (*kdr*) mutation in these mosquitoes.

Apart from the most common mosquito-borne way of infection, dengue may also be occasionally transmitted by transfusion of contaminated blood. In many endemic areas, particularly in Africa, there is no routine practice in blood centres for DENV screening in blood donations. The importance of blood transfusion in dengue transmission is likely to increase due to the growing rates of infection among aged people which, unlike children, are potential blood donors. Accordingly, screening tests for dengue in blood supplies are becoming available. As more adults will understandably be deferred or denied as blood donors due to confirmed or suspected infection, the availability of blood supplies may decrease. The expected rise in the number of DHF/DSS cases due to secondary infections will increase the need for non-contaminated blood. A serious issue when considering diagnosis and surveillance of dengue viruses is the mandatory knowledge about the endemicity levels and prevalence of malaria. Febrile illnesses are not routinely diagnosed in laboratory in Africa and recent evidences suggest that malaria has been overestimated in the continent, with many of the reported fever cases being misdiagnosed as malaria rather than correctly diagnosed as other diseases. Among travellers returning from sub-Saharan Africa, malaria is surprisingly much more prevalent as a cause of illness than dengue. However, in addition to a possible high underestimation of the true dengue cases, the average overestimation rate of malaria by clinical diagnosis in low-transmission regions of Africa reaches 61%.
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Since many dengue infections are present subclinically or as fever of unknown origin, they may remain undiagnosed and thus treated presumptively as malaria or other common endemic fevers. Especially in the early acute disease, clinical symptoms may be indistinguishable, thus delaying the correct diagnosis and prompt therapeutic actions, which may be crucial to combat these life-threatening diseases. Plus, erroneous attribution of fever to malaria may lead to unnecessary exposure to the collateral effects of antimalarial drugs (including malaria resistance) and, in endemic populations, to prolonged and worsening illness, resulting in low labour productivity and avoidable burdening of national health systems. Moreover, the increasing expensiveness and hazardousness of antimalarial drugs make malaria presumptive treatment less acceptable than in the past. This clearly highlights the need for simultaneous specific diagnosis for dengue and malaria in patients living in or returning from regions where both infections are endemic, or during dengue outbreaks. Indeed, the possibility of undertaking mixed dengue-malaria field studies on native populations has been proposed. Due to the lack of dengue warning systems in Africa, returned travellers have served as important sentinels for possible ongoing or imminent outbreaks, and thus a crucial complement to the scarce local information. Although not being endemic in Europe, dengue is the most common cause of fever in returning travellers. As in North America, the presence of Aedes sp. mosquitoes, in parallel with massive human travelling and migration, put these continents at serious risk of severe outbreaks.

Most African countries have established systems for HIV and YF diagnosis and surveillance, but lack those for specific, rapid and accurate diagnostic tests for dengue. Indeed, as with other illnesses of short incubation periods and frequently mild and/or nonspecific symptoms, dengue may be underrepresented in epidemiological surveys. Although the tourist flow between Africa and Europe is still low compared to that arising from more popular touristic destinations in South-East Asia or South America, a significant increase of imported cases from Africa has occurred since the 1990s. Even so, it has been claimed that Africa seems underrated in relation to dengue, considering the ratio of dengue-affected returning travellers in relation to the overall number of returning travellers from Africa to Europe. Proper and prompt management of these suspected patients is urgently required to avoid costly and cumbersome biosafety measures since, very often, the presence of a BSL-4 pathogen cannot be ruled out in advance. The high tourist flow between certain parts of Africa and Europe highlights the need for early alerts about viraemic travellers and for entomological surveillance, especially since Ae. albopictus mosquito populations have become established in several European countries. Since a significant proportion of travellers may get ill during travel owing to the short incubation period of the disease, there is an increasing need for reinforcement of surveillance mechanisms in endemic countries.

So far, limited resource allocation for surveillance and research of dengue in Africa has resulted from the underrating of the disease extension and burden, but this may be about to change as climatic and socioeconomic factors will continue to favour its dissemination in the continent. Except for some noticed local outbreaks, the more frequent reports about dengue among travellers returning from Africa than in natives, and the fact that only half of the
African countries, where travellers have acquired dengue, reported local disease transmission, strongly suggest the underestimation of dengue in the continent and the urgent need for its improved diagnosis and surveillance.\[^5\] It is known that human travelling and trade have put in close contact geographically-separated mosquito populations, thus homogenizing their genetic differences. In this regard, regular monitoring of *Aedes* mosquitoes’ geographical distribution, especially through the integration of early detection systems into national disease control programmes, will be crucial to accurately and timely assess the risk of dengue transmission.

The US Army has recently implemented a complex multidisciplinary surveillance programme, in order to build a predictive model for prevention, control and urgent response to disease outbreaks.\[^77\] The programme, which integrates datasets from satellite remote sensing and geospatial mapping of eco-climatic events, as well as clinical and laboratorial data, for the identification of critical detection points to assess the risk of outbreaks (Figure), has proved its efficacy with the Rift Valley fever and is being extended to other infectious diseases, including dengue. Recently, another theoretical model applied to DHF cases in Thailand successfully identified, for the first time, a repeating spatial-temporal incidence wave in a human vector-borne disease,\[^78\] probably related with the above-mentioned effect of discrepant transmission rates between urban centres and rural areas (probably peaking most often when crossing rural regions). By accounting for the complex interaction between

**Figure:** Scheme of the Predictive Surveillance Program from The Armed Forces Health Surveillance Center, Division of Global Emerging Infections Surveillance and Response System Operations (AFHSC-GEIS)\[^77\]. Data sources fill and enrich the warning system framework. After reaching pre-established critical values, each model component triggers partial alerts that, upon inter-communication and coordination, yield reliable predictions about disease outbreaks aimed to produce prompt responses.
the eco-climatic factors that influence the pattern of DHF incidence, the model rendered accurate predictions about the location and times of high incidence, allowing more efficient allocation of resources to fight disease outbreaks. In conclusion, increased and improved laboratorial diagnosis and surveillance are required to evaluate the epidemiological patterns and public health burden of dengue in Africa.

**Conclusion**

Under a scenario of non-existence of effective drugs and vaccines, and given the well-known difficulties in timely and accurately diagnosing the dengue disease, vector control for disease prevention rather than responding to emergencies seems to be the best option available to combat the illness, although more efficient insecticides and methods of application are also needed. Unfortunately, the lack of infrastructure, health planning and economic affordability in most African countries does not allow them to implement simple and effective means which are available in richer tropical regions of the world, viz. window screening, air-conditioning and simple hygienic practices. In the last few years, several institutions and initiatives have been created to help WHO and governments fight dengue through new strategies and tools for improved diagnosis, as well as to develop candidate drugs and vaccines. These include the Paediatric Dengue Vaccine Initiative (PDVI), the Asia-Pacific Dengue Prevention Partnership and the Consortium for the Study of Dengue Disease (DENFRAME). The European Network for Imported Viral Disease-Collaborative Laboratory Response Network (ENIVD-CLRN), the European Network on Imported Infectious Disease Surveillance (TropNetEurop) and the Network of Medical Entomologists and Public Health Experts (VBORNET) of the European Centre for Disease Prevention and Control (ECDC) are important assets to assist the European Union (EU) and other countries in detecting, investigating and responding to dengue outbreaks and even isolated cases, especially in returning travellers. In Africa, the building of a sustainable research, diagnostic and surveillance capacity has been successfully implemented through tight collaborations between WHO and the Pasteur Institute in Paris for technology transfer to their African counterparts, namely, the Pasteur Institute in Dakar, a WHO Collaborating Centre for arbovirus and viral haemorrhagic fevers, and a partner of the Global Outbreak Alert and Response Network (GOARN), aimed at providing rapid response to dengue and other arboviral outbreaks. This may certainly constitute a sustainable model intervention to follow in the future.

**Acknowledgements**

The author most sincerely acknowledges the valuable contributions and helpful suggestions made by Professor Aida Esteves and Professor Carla Sousa, from IHMT, which enabled him to write this paper.
References


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