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Review

Deconstructing "malaria": West Africa as the next front for dengue fever surveillance and control

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ABSTRACT

Presumptive treatment of febrile illness patients for malaria remains the norm in endemic areas of West Africa, and "malaria" remains the top source of health facility outpatient visits in many West African nations. Many other febrile illnesses, including bacterial, viral, and fungal infections, share a similar symptomatology as malaria and are routinely misdiagnosed as such; yet growing evidence suggests that much of the burden of febrile illness is often *not* attributable to malaria. Dengue fever is one of several viral diseases with symptoms similar to malaria, and the combination of rapid globalization, the long-standing presence of *Aedes* mosquitoes, case reports from travelers, and recent seroprevalence surveys all implicate West Africa as an emerging front for dengue surveillance and control. This paper integrates recent vector ecology, public health, and clinical medicine literature about dengue in West Africa across community, regional, and global geographic scales. We present a holistic argument for greater attention to dengue fever surveillance in West Africa and renew the call for improving differential diagnosis of febrile illness patients in the region.

Contents

1. Introduction

The burden of malaria persists even amid substantial expansion in funding and implementation of global malaria control programs (World Health Organization, 2012). Eradication has returned to the global agenda (Tanner and de Savigny, 2008) while malaria control and elimination continue to stabilize at national and regional scales (Chiyaka et al., 2013). Population growth, urbanization, and human mobility have been increasingly recognized as driving the heterogeneity of malaria transmission (Pindolia et al., 2012; Tatem et al., 2008), with urbanization generally associated with control over the disease (Pond, 2013; Tatem et al., 2013). Yet in sub-Saharan Africa, and particularly in West Africa, the sub-region that will experience the highest rates of population growth over the next half-century (United Nations, 2011), health resource constraints result in the majority of febrile illnesses still being presumptively treated as malaria, despite growing evidence that in some contexts, malaria may only be responsible for a minority of illnesses. The diversity

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of etiological agents leading to clinical febrile illness is exemplified by a recent study of 870 hospital admissions in Tanzania in which malaria was the clinical diagnosis given to 528 (60.7%) patients, but was only the laboratory-confirmed cause of fever in 14 (1.6%); ten different types of infections, ranging from bloodstream infections to bacterial zoonoses and arboviruses, were all presumptively diagnosed as malaria (Crump et al., 2013).

These findings underscore the heterogeneity of Africa's infectious disease burden and beckon questions about the interplay between demographic forces, malaria control, and other emerging diseases. The forces of urbanization and globalization have driven the global emergence of arboviral diseases in developing cities, particularly dengue fever (Gubler, 2002, 2011). Recent studies suggest that dengue transmission occurs over a far wider geographic scale than previously thought (Brady et al., 2012), and that the actual global infection burden may be triple the estimate of the World Health Organization (Bhatt et al., 2013). This paper presents a synthesis of current evidence for dengue in West Africa drawn from the region-specific literature on vector ecology, public health, and clinical medicine, and framed by three contextual geographic scales (community, regional, and global) as summarized in Fig. 1. We argue that national health authorities would be able to strengthen malaria control strategies once underlying causes of febrile illness are better understood, and that West Africa is particularly poised to be the next front for the surveillance and control of dengue—one of many diseases that appears to be categorically misdiagnosed as malaria while remaining a neglected tropical disease in every sense of the phrase. Previous reviews have provided more in-depth discussion on quantifying dengue endemicity (Anders and Hay, 2012), global dengue distributions (Bhatt et al., 2013; Rogers et al., 2014), the economic burden of dengue (Beatty et al., 2011; Stahl et al., 2013), dengue vaccine progress (McArthur et al., 2013; Wan et al., 2013), and the impact of climate change on dengue (Åström et al., 2012; Morin et al., 2013), but none have integrated these issues into a single discussion that is specific to any region of sub-Saharan Africa. This review presents a holistic argument for greater attention to dengue in West Africa, using Ghana as a case study, and calls for a more comprehensive focus on, and commitment to, improved diagnosis of the disease across the region.

2. Community challenges: malaria misdiagnosis, mosquito ecology

Misdiagnosis of malaria is a common problem not only in West Africa, but throughout sub-Saharan Africa (Bisoffi and Buonfrate, 2013; Chandler et al., 2008a,b; Crump et al., 2013; Font et al., 2001; Koram and Molyneux, 2007; Nankabirwa et al., 2009; Reyburn et al., 2004; Van Dillen et al., 2007; Ye et al., 2009), and tends to bear a greater burden on populations of lower socio-economic status (Amexo et al., 2004; Biritwum et al., 2000). This is unsurprising since malaria endemicity usually mirrors low levels of socioeconomic development and limited access to quality healthcare.

In areas of high malaria transmission, hospitals and health centers usually depend on clinical algorithms for case management (Chandler et al., 2008a). A clinical algorithm provides the clinician with predictor symptoms and signs, like intermittent fever, chills/rigors, and hepatosplenomegaly, which if present, point to a likely diagnosis of malaria (Chandramohan et al., 2002). Despite high sensitivity, clinical algorithms often have low specificity (i.e. ability to identify true-negatives) since symptoms and signs of uncomplicated malaria overlap with many other febrile illnesses, leading to a high probability of false-positive diagnoses (Chandramohan et al., 2002; Nankabirwa et al., 2009). In a study of Nigerian children, 83% of those under 5-years of age that tested negative for malaria via microscopy were still treated with artemisinin-based combination therapy (ACT) (Oladosu and Oyibo, 2013). This is a common practice in both clinical and home-based treatment of malaria and has somewhat obscured the decline in malaria transmission in several countries (Reyburn et al., 2007). The tendency to over-diagnose malaria in West Africa is also exacerbated by high patient-to-clinician ratios (i.e. clinical workload), substantial variation in health worker training and skills maintenance, slide preparation techniques, condition of the microscope, and quality of essential laboratory supplies (Wongsrichanalai et al., 2007). Furthermore, a large proportion of fevers are still treated at home, suggesting that hospital data alone greatly underestimate the enormity of malaria diagnosis in West Africa (Biritwum et al., 2000; Jombo et al., 2011; Nonvignon et al., 2012). The phenomenon of misdiagnosis must therefore be confronted using a holistic approach, beginning with a systematic effort to deconstruct not only the repertoire of etiologies that cumulatively cause febrile illness, but also some non-biomedical community perceptions of fever (Hertz et al., 2013).

Virtually all of Ghana's nearly 25 million residents comprise the population at risk of malaria infection, and the vast majority of local infections are due to *P. falciparum* (World Health Organization, 2012). Access to confirmatory diagnostic blood tests for malaria is limited, with the annual rate of blood examination for suspected malaria patients in Ghana estimated at less than 10% from 2007 to 2011 (World Health Organization, 2012). WHO (2012) also reports that 100% of cases were potentially treated with ACT in 2011, which is a troubling statistic in an era of increasing antibiotic resistance.

A recent Ghana Urban Malaria Study concluded that less than a third of malaria diagnoses are confirmed via blood analysis nationwide, and that clinical staff nationwide diagnose approximately 40–50% of all sick children—and about 40% of all outpatients—with malaria (JSI Research and Training Institute, 2013). A prior study produced similar numbers showing that between 2001 and 2006, 47% of healthcare facility visits by children in Accra, and 37% for adults, were due to clinical malaria (Donovan et al., 2012). The same data also demonstrated that the amount of rainfall during the one and two months prior to the clinic visit was a significant predictor of malaria morbidity. The link between rainy seasons, mosquito breeding activity, and malaria-like illness is certainly not new (Colbourne and Edington, 1954), and has resulted in an institutionalized view that lagged, seasonally concurrent spikes in febrile illnesses seen at clinics after the onset of rainy periods are predominantly attributable to malaria, and consequently are diagnosed as such. But rainy seasons amplify many vector species, particularly the various *Aedes* and *Culex* mosquitoes of public health importance, and also result in flooding that presents a host of health risks associated with poor sanitation infrastructure (Fobil et al., 2012). Mild cases of typhoid fever, which often initially present with fluctuating fevers, headaches and general malaise, may be particularly prone to misdiagnosis as malaria during these rainy periods. Child pneumonia has also been known to clinically overlap with malaria elsewhere in Africa (O'Dempsey et al., 1993; Yeboah-Antwi et al., 2010). In a 2009–2010 Accra study, blood microscopy was performed on 605 feverish children suspected of malaria but only 11% tested positive for parasites, yet 80% were diagnosed with malaria and treated with anti-malarials (Malm et al., 2012). All of these reports suggest that malaria incidence data in Ghana do not accurately capture the nation's malaria burden (JSI Research and Training Institute, 2013).

Ghana's urban ecology, with limited sanitation infrastructure, multiple rainy seasons, pervasive household water storage, and virtually no public awareness of dengue transmission, presents a similarly prime environment for breeding of *Aedes aegypti*, the primary vector for yellow fever and dengue fever, as observed around the world (Gubler, 2004; Monath, 1994). Entomological surveys have long documented *Ae. aegypti* in West Africa, and it has been

Community	Regional	Global
Limited public and vector control program awareness of dengue or the *Aedes* vector	Rapid population growth and intensifying globalization	Economic burden of misdiagnosis for both patients and health care systems
Urban ecology supports prime breeding environment for vector species	Mosquito vector presence established in entomology literature	Climate change implications for geographic changes to vector distributions
Inefficient consumption of health services due to over-diagnosis of clinical malaria	Etiology of febrile illness established in seroprevalence surveys	Potential for emergence of ACT-resistant *Plasmodium* beyond Southeast Asia
Unfamiliarity with dengue among local medical establishment, and ambiguity of field diagnostics	Local dengue acquisition established in international traveler case reports	Slow progress in development of vaccines against malaria and dengue

Fig. 1. Multi-scale considerations for increased surveillance and control of dengue fever in West Africa.

described in Ghana for at least one hundred years as Europeans struggled to contain yellow fever outbreaks along the Gold Coast (Patterson, 1979). Some of West Africa's richest entomological literature related to arboviral diseases originated in Ghana as a result of decades of work by William Addo Chinery (e.g. Chinery, 1970, 1984, 1991, 1995, 1999) building on his predecessors. As late as 2006, dengue fever was not reported in Ghana, though it has been reported in seven West African nations with a mortality rate of about 5% (World Health Organization, 1995). The vector has consistently reappeared in mosquito surveys throughout the twentieth century (Appawu et al., 2006; Chinery, 1970, 1995; Klinkenberg et al., 2008; Opoku et al., 2007), and a 2006 study found that *Ae. aegypti* breeding densities and biting rates in four northern Ghanaian communities were sufficient for facilitating an outbreak of dengue, though no flaviviruses were isolated from collected mosquitoes at the time (Appawu et al., 2006).

Improving differential diagnoses for febrile illness may be a matter of better physician training and clinical algorithms that pinpoint hallmark features (Eisenhut, 2013). But in some settings, the need for confirmatory tests may require reprioritization of limited health resources, as many febrile illnesses, such as chikungunya and dengue, may be clinically indistinguishable (Nkoghe et al., 2012). There may also be unknown issues of cross-reactivity within and between families of bacteria and viruses, particularly within the *Flaviviridae* family, which besides the dengue virus also includes yellow fever, hepatitis C, West Nile virus, and viruses causing several forms of encephalitis. Cross-reactivity is already a noted problem in some parts of the world among flaviviruses (Innis et al., 1989; Peeling et al., 2010), and has also been observed between dengue and both chikungunya and leptospirosis, as well as in some malaria-positive patients, though the relationship is not well-defined (Hunsperger et al., 2009). While these are not limitations of molecular methods, cross-reactivity issues with commercially-available serology kits and rapid diagnostic tests remain relatively uncharacterized and present an obstacle to rapid, cost-effective, geographically-scalable improvements to clinical diagnosis.

3. Regional challenges: seroprevalence, population growth, urbanization

Case histories and seroprevalence surveys, vector population dynamics, and future human population dynamics within West Africa provide regional drivers for dengue emergence and expansion. Flaviviruses and other tropical viruses, particularly dengue, have occasionally been isolated from travelers returning from West Africa. In the 1970s, antibodies for chikungunya, o'nyong-nyong, dengue, ntaya, and zinga viruses were isolated from British travelers to West Africa, with the most common recorded symptoms being myalgia and/or fever (Woodruff et al., 1978). In the 1990s, chikungunya and dengue antibodies were detected in German aid workers who had returned from West Africa (Eisenhut et al., 1999). More recently, dengue antibodies were found in a Finnish traveler returning from Ghana (Huhtamo et al., 2008), in a French traveler to Côte D'Ivoire (Ninove et al., 2009), in a Spanish traveler to Guinea Bissau (Franco et al., 2011), and in a Japanese traveler to Benin (Ujiie et al., 2012). Given the anecdotal nature of these case reports, dengue fever has not previously been considered a significant public health threat in West Africa, though some national militaries have long known about dengue in the region (de Laval et al., 2012; Durand et al., 2000).

Although clinical reports of dengue date back to the 1880s, dengue virus was not isolated from human sera in West Africa until the 1970s (Carey et al., 1971; Fagbami et al., 1977). Seroprevalence studies demonstrating previous or active dengue infections in the region have reemerged over the last decade. In a survey of six pathogenic viruses, 29% of blood donors and pregnant women tested positive for a previous dengue infection in Burkina Faso, with higher rates in urban populations (Collenberg et al., 2006). Just 13 of 1948 febrile patients revealed anti-dengue IgM antibodies in a Nigerian trial, though the virus was isolated from 14 of 59 pools of *Aedes* spp. across multiple ecological settings (Baba et al., 2009). The first reported case of dengue (and several other arboviral infections) was confirmed in 2007 in a small seroprevalence trial in Guinea

Table 1
Evidence of dengue fever in 16 West African nations (adapted and expanded from Brady et al., 2012).

Country	Peer-reviewed evidence and case data	Entomological evidence
Benin	Returning aid workers from Germany 1987–1993 tested positive (14.8%) (Eisenhut et al., 1999). DENV-3 isolated (Franco et al., 2010). Travelers from France returning with dengue (Moi et al., 2010b).	Other arboviruses present (Powers and Logue, 2007). *Ae. aegypti* present (N'Guessan et al., 2007).
Burkina Faso	Virus identified in *Ae. aegypti* 1983–1986 (Robert et al., 1993). Dengue in sylvatic cycles (Hervy et al., 1985). 9.2% of aid workers returning from Burkina Faso seropositive for dengue (Eisenhut et al., 1999). 36.5% seropositive in urban areas (Collenberg et al., 2006). 2006 outbreak, 683 cases in Ouagadougou, Nouna (GIDEON, 2011).	–
Cape Verde	DENV-3 in Cape Verde 2009 (Franco et al., 2010). DENV-3 isolated from 5 French military personnel in 2010. 2009 outbreak with 21,304 cases including DHF and deaths, subsequent lower case load in 2010 (GIDEON, 2011).	–
Cote d'Ivoire	Dengue reported in mosquito catchers (Akoua-Koffi et al., 2001).Isolation of DENV-1 from a single patient (Durand et al., 2000). Imported cases to Japan and France (Moi et al., 2010a; Ninove et al., 2009). 28 DENV-2 isolates from 4 possible vectors (Cordellier et al.,1983). 2008 outbreak in Abidjan, with serosurvey of 800 people in Abidjan on-going (commenced December 2011) (Veronique, 2012).	–
The Gambia	Dengue reported in returning U.K. traveler (Stephenson et al., 2003).	*Ae. aegypti* and other arboviruses present (Monath et al., 1980).
Ghana	DENV-2 isolated from Finnish traveler to Ghana (Huhtamo et al., 2008).	*Ae. aegypti* present (Appawu et al., 2006; Chinery, 1970; Patterson, 1979).
Guinea	Dengue accounts for 2% of febrile illness (Jentes et al., 2010). Some dengue serologically detected in a wide viral survey (Butenko, 1996). DENV-2 isolated in 1981 (Vasilakis et al., 2007).	–
Guinea-Bissau	Dengue reported in returning Spanish traveler (Franco et al., 2011). Dengue outbreaks have occurred recently in Guinea-Bissau and at least 2 expatriots working in the country have presented with dengue back in Scandinavia (Aaby and Bandim Health Project, 2011).	*Aedes* spp. present (Palsson et al., 2004). Other arboviruses in Guinea-Bissau (Posey et al., 2005).
Liberia	Small outbreaks reported (Gubler, 2004).	Other arboviruses present in Liberia (Van der Waals et al., 1986). *Ae. aegypti* present (Surtees, 1967).
Mali	Seroprevalence survey reveals 93% of febrile illness patients are seropositive for dengue (Phoutrides et al., 2011). DENV-3 in suspected 2008 outbreak (World Health Organization, 2009). Imported case into France 2008 (Bai et al., 2008). 2008 suspected outbreak with 70 unconfirmed cases (GIDEON, 2011).	–
Mauritania	–	*Ae. aegypti* present (Amarasinghe et al., 2011). Multiple other circulating arboviruses (Diallo et al., 2005).
Niger	–	*Ae. aegypti* present (Amarasinghe et al., 2011). Multiple arboviruses present (Mariner et al., 1995).
Nigeria	DENV-1 and DENV-2 isolated (Carey et al., 1971). Seroprevalence to DENV-2 was 46% in Kainji lake area (Adekolu-John and Fagbami, 1983) 63% seroprevalence to multiple arboviruses (Fagbami et al., 1977). DENV-3 isolated (Franco et al., 2010). DENV-1 and DENV-2 isolated from human sera, all serotypes isolated from *Ae. Aegypti* collections, and seroprevalence ranged from 32 to 82% (Baba et al., 2009). Dengue isolated from European travelers 1999–2002 (Wichmann et al., 2003).	*Ae. albopictus* identified in Nigeria in 1991 (Centers for Disease Control and Prevention (CDC), 1991). Many other arboviruses also present (Adekolu-John and Fagbami, 1983; Fagbami et al., 1977).
Senegal	DENV-2 isolated from 1990 outbreak (Zeller et al., 1992). DENV-2 isolated from a variety of *Aedes* vectors (Diallo et al., 2003). Isolation of DENV-2 and 4 and serological evidence that dengue is widespread (Saluzzo et al., 1986). First report of DHF in West Africa (Franco et al., 2011). Outbreaks reported 2009 (ProMED-mail, 2009).	–
Sierra Leone	Blood donors found seropositive for dengue among many other arboviruses (Tomori and Fabiyi, 1976).	–
Togo	Dengue detected in French returning traveler (Moi et al., 2010b). Seroprevalence test revealed presence of multiple arboviruses (Ebke and Schafer, 1971).	*Ae. aegypti* present (Pichon et al., 1969).

(Jentes et al., 2010), and a similar trial in Bamako, Mali, revealed 93% prevalence of anti-dengue IgG (Phoutrides et al., 2011). The evidence suggests that most West African nations are now capable of supporting dengue outbreaks, which have hitherto gone undetected, and that Africa's dengue burden may be similar to that of the Americas (Bhatt et al., 2013). The evidence for dengue in West Africa, including case reports, seroprevalence surveys, and supporting entomological literature, is adapted and expanded in Table 1 from the supplemental data published by Brady et al. (2012).

Among all world regions, West Africa is projected to have the fastest-growing population growth rate (by a thin margin over East Africa) between now and mid-century (United Nations, 2011). A recent comparison of three global dengue risk maps reveals limited geographical consensus for dengue risk in Africa, although the geographically-largest consensus area on the continent is a coastal stretch of West Africa, roughly between Abidjan and Yaounde (Rogers et al., 2014). This study also notes that Africa's lower population density (relative to India or Southeast Asia) may be historically linked to the lower projected risk for dengue hemorrhagic fever, perhaps contributing to the underreporting of dengue in the region. But population growth and high rates of poverty in this urban strip of West Africa, a region which may ultimately prove to be the biggest urban poverty footprint on earth (Davis, 2006), underscore the inevitability of an expansion in dengue incidence in lieu of robust surveillance and control measures.

4. Global challenges: economics, ACT resistance, vaccines, climate change

Four global health drivers implicate urgency for attention to dengue fever in West Africa: the economic burden of malaria, emerging ACT resistance, the promise of a dengue vaccine, and the impact of climate change.

In 2009, malaria was thought to cost African countries over US$12 billion annually in direct losses (Kokwaro, 2009). Malaria over-diagnosis is considered costly both financially and in terms of morbidity and mortality from missed diagnoses (Chandler et al., 2008a). Misdiagnosis results in a greater number of healthcare visits and associated costs for adult patients (Hume et al., 2008). Additionally, since the burden of malaria is higher among rural health facilities (Mosha et al., 2010), the poorest individuals are paying more proportionally for their healthcare (Amexo et al., 2004). The implications range from individual to regional in scale: a malaria-stricken family may sacrifice up to a quarter of its income for treatment, and up to 40% of African health budgets are spent on malaria each year (Kokwaro, 2009). The looming threat of ACT-resistant parasites is poised to make malaria treatment even more expensive.

Recent studies have demonstrated significantly reduced *in vivo* susceptibility to artesunate among *P. falciparum* in western Cambodia (Dondorp et al., 2009). Scientists have explained this phenomenon as partial artemisinin-resistant *P. falciparum* malaria, and it is currently confined to the Cambodia-Thailand border due to place-specific conditions including decades-long use of artemisinin mono-therapies in sub-therapeutic doses, and the availability of substandard artemisinins (Dondorp et al., 2010). ACT resistance would potentially be devastating in Africa. Research in Tanzania showed that after an antimalarial was promoted and used as a first-line treatment following policy changes, the frequency of mutant genes increased by 37–63%, suggesting that such policies, which consequently increase drug pressure in endemic regions, ultimately increase the emergence of resistance even when drugs are used in combination (Malisa et al., 2010). New classes of medicines are required to avoid the emergence of ACT resistance in Africa; there are currently at least seven new compound families that have been discovered in the past few years, though all are far from entering phase I trials (Anthony et al., 2012). ACT resistance would almost certainly result in a reallocation of African health care spending and detract from efforts to control other causes of febrile illness whose local epidemiology is still not fully understood.

Several malaria vaccine candidates are currently in development, but the RTS,S construct was the only one successful at providing immunity in rodents, and the only one to reach phase III clinical trials (Greenwood and Targett, 2011). In 2011, RTS,S was thought to be very promising, but phase III trials reported 4-year efficacy of just 16.8%, declining over time and with increased malaria exposure (Olotu et al., 2013). More recently, the attenuated sporozoite vaccine model has shown some promising results in phase I clinical trials (Seder et al., 2013), but the level of protection was modest, and the vaccine was administered via intravenous infusion, which raises questions about the practicality of a large-scale deployment. The ongoing challenges to an efficient malaria vaccine are both financial and technical, the latter related to finding the compound that provides appropriate long-term protection from the parasite.

Likewise, the challenge for dengue vaccine candidates under development is producing long-lasting immunity against all four dengue virus serotypes. Phase III clinical trials to test for efficacy among human subjects have been in planning stages for years (Guy et al., 2011), and have only recently been stalled by the recent failure of a leading candidate, CYD-TDV from Sanofi Pasteur, to provide tetravalent protection in a phase 2b trial in Thailand (Sabchareon et al., 2012). CYD-TDV has continued to perform well in other phase II trials in Latin America (Dayan et al., 2013; Villar et al., 2013), while promising results were also reported from a phase II trial using the TDEN candidate (Thomas et al., 2013), and from a phase I trial using the TV003 combination of the TetraVax-DV candidate (Durbin et al., 2013). Given the encouraging progress of these programs, the lack of knowledge in West Africa about local *Aedes* distributions and dengue incidence could be an obstacle to efficient vaccine rollout, particularly given the emphasis on cost-effectiveness of vaccine research ideas among vaccine economics experts (Lieu et al., 2002). In the short-term, improved diagnostic technology using filter paper blood spots or saliva (Balmaseda et al., 2003, 2008; Smit et al., 2014), could reduce the cost of differential diagnosis for dengue fever and aid the establishment of baseline rates and risk factors.

Layered on top of all of these concerns is the uncertainty of climate change, which may produce a dynamic African epidemiological profile of dengue (and many other infectious diseases) just as we uncover it. Climate variability may produce interactions between the environment, vector, and virus that influence virus replication, vector ecology, and disease occurrence (Morin et al., 2013). While recent studies have explored the impact of climate change on dengue in the Asia-Pacific region (Banu et al., 2011) and the Americas (Colón-González et al., 2013), global assessments of climate variability on dengue (Åström et al., 2012; Hales et al., 2002; Thai and Anders, 2011) have generally ignored the sub-regions of Africa. This is understandable given the lack of reliable dengue case data for the continent, though it remains unclear to what extent the web of climate, sociodemographic, economic, and immunological determinants of dengue will mimic patterns observed in other regions of the world.

5. Conclusion

Part of the reason why dengue has not been considered a threat in Africa is the historical absence of confirmed dengue hemorrhagic fever (DHF) cases on record. This gap may be attributable to many factors, the most obvious being clinical misdiagnosis. As with mild dengue, a patient surviving dengue shock syndrome, which is often a one-day period with varying degrees of hemorrhagic phenomena, may attribute the illness to any number of diseases with overlapping symptoms (malaria, influenza, etc.). A DHF fatality is similarly likely to be recorded as undifferentiated fever or malaria when dengue is not considered. Genetic factors may also play a role, as some studies have suggested that Africans, and people of African descent, may have some genetic resistance to severe dengue (Halstead et al., 2001; Sierra et al., 2007), a phenomenon that has re-emerged in recent vaccine trials (Durbin et al., 2013). Transmission may also be influenced by the complex coevolution of sylvatic and human dengue strains with their mosquito vectors, as well as variations in vector competence among *Aedes* subtypes (Kyle and Harris, 2008). Increased surveillance for dengue is likely to reveal the presence of DHF as experienced elsewhere in the world, although with potentially different manifestation.

As the global health community pivots toward non-communicable diseases in the developing world in recognition of the growing double burden of disease (e.g. Bygbjerg, 2012; Marquez and Farrington, 2013), it is becoming increasingly clear that we still have much to learn about infectious disease morbidity and mortality in sub-Saharan Africa. The increased threat of dengue due to climate change has spurred ongoing interest in mapping dengue risk among Western nations. Geospatial technology and Big Data will continue to play an important role in modeling the ecologies of neglected tropical diseases (Hay et al., 2013; Ratmanov et al., 2013), while participatory and mHealth innovations should

simplify traditional shoe-leather epidemiological data collection (Free et al., 2010; Lwin et al., 2014) and enable efficient deployment of appropriate vector control resources. As community, regional, and global drivers motivate the West African medical community to deconstruct "malaria" into a more accurate understanding of febrile illness, the region will likely join Latin America, the Indian sub-continent, and Southeast Asia as an important front for dengue surveillance and control.

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