

# Dengue Gaining Ground

## Editorial

Virus outbreaks tend to evoke fear among people around the globe, and the recent Ebola outbreak in West Africa has more than ever shown how potent highly contagious viruses can be. The rapid spread of the virus and the vast number of fatalities, combined with the initially suboptimal aid response, has shed light on the pressing issue of how to prevent and minimize another outbreak, may it be of Ebola virus origin, or another potent virus. It would be naïve to assume that outbreaks of viral origin would be limited to areas with poor infrastructure, and lack of basic health care facilities. In an era when air travel is assumed to be part of basic transportation facilities, viruses and their vectors can rapidly expand and reach new territories within 24 hours. Travelers, tourists as well as of labor flow nature, are important vehicles for viral transmission. Of rising concern is the continuous geographical expansion of the dengue viruses, which are endemic in more than one hundred countries, and second only to malaria to cause tropical fever in travelers [1].

The dengue viruses, enveloped positive-sense RNA viruses with a genome of approximately 11 kb, and consisting of four related but anti genetically distinct serotypes, cause the most common arthropod-borne viral disease in man. In most cases, dengue virus infection is asymptomatic, but can potentially cause an acute febrile disease ranging in severity from classical dengue fever to a life-threatening hemorrhagic condition with shock syndrome. Its mode of transmission is by the mosquito species *Aedes aegypti* and *Aedes albopictus*, both species notoriously known as intermittent feeders of human blood, and with ecological niches well-adapted to human habitation [2]. It has been assumed for many years that there are approximately one hundred million dengue infections per year, but recent estimate indicates 390 million per year, of which 96 million manifests clinically [3]. Still, there are no anti-viral drugs against dengue disease, and neither prophylaxis nor vaccines exist. An effective dengue virus vaccine would need to provide a balanced immune response against all four serotypes. This has proven difficult to achieve despite considerable efforts. A number of dengue vaccines candidates are in pipeline, but it remains to be seen when there will be a well-tolerated and effective vaccine licensed and available on the market [2].

Being endemic in the tropical and sub-tropical belt, dengue virus infections are constantly imported into non-endemic territories by international travelers, and European countries frequently report on rising numbers of tourist-acquired dengue infections. Most cases are imported from Latin America and Asia, but serologic surveys suggest endemic dengue virus infection in several African countries, implying that dengue virus transmission may also follow with travelers from the African continent [4]. In several European countries, dengue is the second most frequent cause for hospitalization after malaria in patients arriving from tropical regions, and there are no indications implying that the trend would level off [1,5,6].

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In late 2012, Europe suffered its first sustained outbreak since the Greek outbreak in the 1920's with 2,000 people infected on the island of Madeira, Portugal [1,7], and dengue virus infections imported to the European mainland by travelers returning from Madeira have been confirmed [8]. Central Europe has also had sporadic cases of autochthonous dengue virus infections since 2010 when two cases were reported in metropolitan France [1]. Since one of the two major vectors species, *Ae. albopictus* is established in the Southern parts of Europe, a breeding ground already exists for establishing an autochthonous disease cycle and new regional outbreaks in previously non-endemic regions. The situation, however, is not unique for Europe. After have been free from the dengue viruses for a long period of time, the continental United States reported autochthonous dengue cases in 2009, and the vector is confirmed to be (re-) established in 26 states [9].

It is therefore strongly recommended that in a pre travel health consultation prior to departing to a dengue virus endemic area, information about the virus and its mode of transmission are discussed, and that practical recommendations for prevention are given. In regard to returning travelers, it is important that physicians who practice outside of traditionally dengue endemic areas are adept at the recognition of potentially fatal reemerging infectious diseases such as dengue. A Dutch study has estimated that >1 % of adult short-term travelers to dengue-endemic areas sero converted [10], and an American study identified anti-DENV IgG antibody in almost 7 % of travelers born in non-endemic countries, and who traveled to a dengue-endemic country for ≥2 weeks but <1 year [11].

These significant numbers are of major concern, but despite that and the presence of the vector in some of the non-endemic countries, there is little epidemiological surveillance for dengue anywhere outside endemic areas [7]. In order to reduce the risk of importation and establishment of dengue in such new areas, primary prevention measures to limit interaction of the virus, vector and human, combined with rigorous surveillance, are of crucial importance. This, however, would require a comprehensive and multisectoral plan of action, intensifying some activities in the areas of greatest risk.

Apart from bringing infectious disease agents back home, travelers are also efficient transmitters of disease within the endemic countries, providing an important route of transmitting virulent strains and outbreaks as they travel. The dengue viruses have for decades been known to benefit from human migratory behavior, as well as activities such as deforestation, urbanization and increase in volume of solid waste [1]. In addition to being transmitted by a potent vector, the sylvatic variants of dengue virus, assumed to be circulating among non-human primates in the jungles of South-East Asia, exhibit little or none barrier to be transmitted to humans. A new, fifth, serotype of dengue viruses originating in macaques with a spillover into humans, was announced in late 2013 [12]. This discovery of a fifth serotype of dengue viruses poses a new public health dilemma in dengue virus control, as well as it raises concerns regarding vaccine development against dengue.

Considering the health and economic impact of dengue, both on a societal level as well as on an individual basis, there are reasons for concern regarding the ongoing as well as the future spread and establishment of the dengue viruses. More than two-thirds of the world's population lives in endemic areas, and both the virus as well as its vectors is gaining access to new non-endemic territories. Continuous surveillance for identifying areas with ongoing transmission, or areas where transmission is likely to occur, combined with an integrated response plan for vector-borne diseases such as dengue, are critical measures to effectively limit transmission of the virus and its vector. The time to act cannot come too soon, only too late.

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