

# TRENDS IN THE EPIDEMIOLOGY OF DENGUE FEVER AND THEIR RELEVANCE FOR IMPORTATION TO EUROPE

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Dengue fever continues to spread globally, causing major epidemics and putting major strain on health systems in affected countries. For imported dengue in Europe, south east Asia is the most important region of origin, followed by Latin America, the Indian subcontinent, the Caribbean, and Africa. Information regarding mosquito protective measures is highly recommended for all travellers to affected areas.

### Introduction

Dengue fever has developed into one of the world's major emerging infectious diseases. The infection is by now seen as a global epidemic with recorded prevalence in more than 120 countries [1]. It appears that dengue originated from Africa and was introduced to Asia some 600 years ago. The first recognised dengue epidemics occurred almost simultaneously in Asia, Africa, and North America in the 1780s. Dengue is transmitted by *Aedes* mosquitoes, particularly *A. aegypti* and, less important, *A. albopictus*. These mosquitoes travel well, particularly in cargo ships and the four subtypes of dengue virus have spread to most tropical and subtropical countries in their wake. During the last 200 years, spread of the disease has increased, reaching epidemic proportions during the last three decades. Since the late 1990s, dengue is the most important mosquito-borne disease affecting humans after malaria, with around 40 million cases of dengue fever and several hundred thousand cases of dengue haemorrhagic fever (DHF) each year. The main endemic areas are Latin America, the Caribbean, Africa, south and southeast Asia, and parts of the Pacific Region. For Europe, dengue remains an imported disease, even though *A. albopictus* has become established in some parts of the continent.

The pathogenesis of DHF is not fully understood, but it has been well documented that secondary dengue infection is a major risk factor of the disease [2,3]. As a consequence, and maybe also under genetic control, European travellers rarely develop DHF [4]. A high percentage of dengue infections in travellers occur without any symptoms [5]. However, the important role of travellers is recognised to introduce more virulent dengue strains into endemic areas where usually only mild disease occurs [6], or into non-endemic areas but where the mosquito vector is common [7].

### Recent developments

While dengue activity remains quite high in Asia, Latin America has seen a particular increase of major epidemics during the last two years. Rio de Janeiro experienced serious outbreaks in 2002 and again in 2008, each straining the health infrastructure severely

[8]. A severe epidemic developed in Bolivia in early 2009 with several 10,000 patients, prompting the government to declare a state of emergency for the nation [9]. Most recently, Argentina declared a dengue outbreak in the northern provinces of Salta, Jujuy, Catamarca, Chaco, and Corrientes with more than 26,000 cases [10]. The disease has spread as far as the capital Buenos Aires. On the other side of the Pacific Ocean, an outbreak of dengue fever erupted in December 2008 in northern Queensland, Australia. Located around a focus in Cairns, it spread to other parts of the tropical north of Australia [11].

### Dengue importation into Europe

Reports on dengue in international travellers have increased, too. Both the increasing international air travel and the increasing activity of dengue in the tropics are responsible for the increased chance that healthcare providers, including those in western countries, are more and more likely to be confronted with imported dengue infections. In various studies at travel clinics, dengue infection was the most common cause for fever in returning travellers [4,12,13]. Since dengue surveillance, if performed at all, is passive, and since dengue infection presents either as a short and self-limiting viral disease or even asymptotically, it is certainly one of the under-diagnosed tropical infections in travellers.

The European Network on Imported Infectious Disease Surveillance (TropNetEurop) was founded in 1999 to detect emerging infections of potential regional, national, or global impact at their point of importation into the European area. The network currently consists of 57 collaborating centres in 17 European countries. Annually, the collaborating centres give approximately 220,000 consultations prior to travel, and treat 57,000 patients post-travel [14]. From comparisons between national notification numbers and patients reported to the network, it can be safely assumed that TropNetEurop is covering around 12% of the European patients with imported infectious diseases. Within this network, the number of reported dengue cases increased from 64 in 1999 to a maximum of 224 in 2002 and remained at 100–170 since then. For 2008, 116 cases have been reported. The median age in this population is 38 years (range 12–73 years). The median duration of travel during which patients acquired the dengue infection decreased from 38 days in 1999 to 21 days in 2008 [15].

In 2008, 43% of the dengue cases were acquired by patients who returned from travel to countries in south east Asia, 14% were

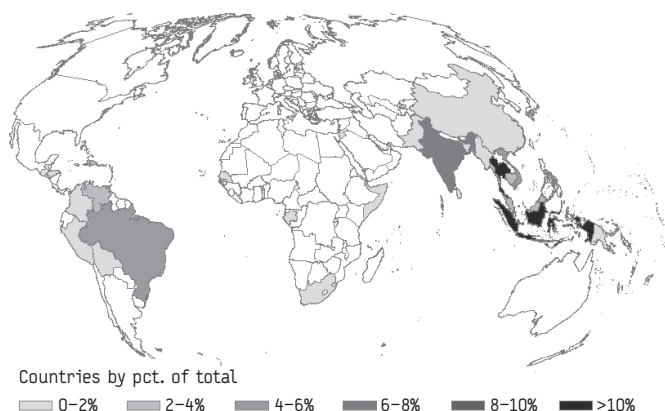
imported from Latin America, 12% from the Indian subcontinent, 11% from the Caribbean, and 4% from Africa (Figure 1).

This distribution reflects two different aspects: worldwide dengue activity and countries' popularity as tourist destinations. Thailand, Vietnam, and Indonesia are not only highly endemic areas for dengue viruses, but they are also very popular destinations for European tourists. Thailand alone is responsible for almost 30% of all travel associated dengue infections in our network over the past six years. Current developments mirror the epidemics in south America, with stronger reporting from Bolivia and Argentina. In addition, unusually strong signals come also from Eritrea, Jordan, Pakistan, Papua New Guinea, South Africa, Dominican Republic, and Suriname (Figure 2).

Reporting over the past years in Europe has shown that most dengue patients are European travellers (87% in 2008). Dengue

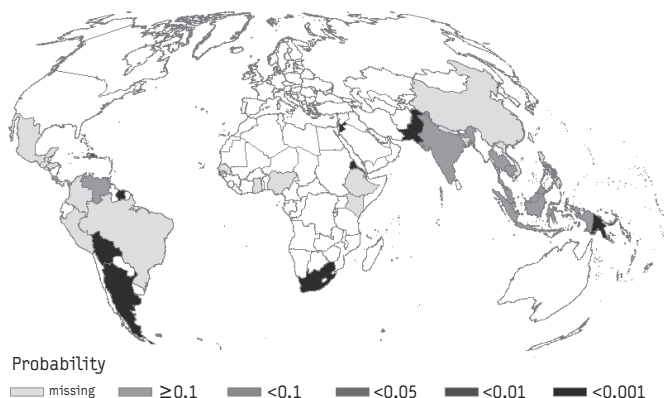
**FIGURE 1**

**Imported dengue fever cases in Europe in 2008 by country of origin (n=118)**



**FIGURE 2**

**Cases of imported dengue fever as of 1 June 2009, TropNetEurop data (n=1,419 entries in the database)**



Colourless = Cases were neither observed in the present months nor in the past reference period  
Missing = Cases were observed in the past reference period but not in the present months

haemorrhagic fever and death have remained rare events in European travellers but are being reported almost every year. In 2008, two out of 116 patients developed complications, and one patient died of DHF.

Overall, TropNetEurop has documented a clear increase of reported dengue cases during the early 2000s, reaching a plateau since 2002. This is in line with national reporting in most European countries, as documented by the World Health Organization (WHO) Europe centralized information system for infectious diseases (CISID) database [16]. The exceptions of the rule are France with several recent dengue outbreaks in its overseas territories, and Germany, with an increase from 218 reported patients in 2002 to 263 in 2007.

### Future outlook

It appears that the spread of dengue is only limited by the spread of its vector mosquitoes, in particular *A. aegypti*. Since *Aedes* spp. has proven to be exceptionally adapted to human habitation, its global spread cannot be controlled effectively. Dengue has moved to North America, Australia, east Asia, the Pacific, and eastern Africa. Its imminent spread to Europe has to be anticipated. However, a series of phase 2 trials for efficacy and reactogenicity of dengue tetravalent vaccines has been started in early 2009 [17]. Further trials are listed to follow soon, promising the availability of effective control tools within a few years. A dengue vaccine with high protective efficacy could change the whole picture of the current epidemic. However, as long as no effective vaccine is available, dengue viruses will present a serious threat to European travellers, to European countries with growing populations of potential vector mosquitoes, and an even greater threat to those living in already endemic countries.

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This article was published on 25 June 2009.

Citation style for this article: Jelinek T. Trends in the epidemiology of dengue fever and their relevance for importation to Europe. *Euro Surveill*. 2009;14(25):pii=19250. Available online: <http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19250>