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Trends in Imported Chikungunya Virus Infections in Germany, 2006–2009

Christina Frank,[1,2] Irene Schöneberg,[1] and Klaus Stark[1]

[1]Department for Infectious Disease Epidemiology, Robert Koch Institute, Berlin, Germany.
[2]Institute for Hygiene and Public Health, University of Bonn, Bonn, Germany.

Address correspondence to:
Christina Frank
Department for Infectious Disease Epidemiology
Robert Koch Institute
DGZ-Ring 1
D-13086 Berlin
Germany
E-mail: frankc@rki.de

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Abstract

Chikungunya virus (CHIKV) has been previously reported in many African and Asian areas, but it recently reemerged strongly in countries bordering the Indian Ocean as well as caused an outbreak in northern Italy. In Germany, where potential CHIKV vectors are not yet established, CHIKV infection is mandatorily notifiable. Cases reported from 2006 through 2009 were analyzed for travel characteristics and demographic factors. 152 cases of symptomatic CHIKV infection were notified. Both sexes were affected, with a median age of 46 years. Over the years, countries of infection largely followed the outbreaks reported from various travel destinations. India and the Maldives were the countries of infection most frequently named. In Sri Lanka, India, and Thailand, which are also frequently named countries of infection for dengue virus, the median age of CHIKV-affected patients was higher than that of dengue fever patients. Taking traveler numbers into consideration, risk of CHIKV infection was higher in the Seychelles and Mauritius than in Thailand and India. Even though substantial underdiagnosis is suspected, this assessment of CHIKV importation to Germany offers valuable information about the details of travel-associated cases. Between 17 and 53 notified cases per year signify that CHIKV would be occasionally available for local transmission in Germany once a vector becomes present. Although CHIKV most often causes a comparatively mild disease, the high median age of notified cases and the higher age than dengue patients support more severe disease courses in older adults. Travelers to all CHIKV endemic areas should protect against mosquito bites. In Germany, CHIKV surveillance will be continued to monitor ongoing importation of the virus and to detect early potential autochthonous cases.

Introduction

Chikungunya virus (CHIKV) infections were first described in the mid-1950s in Africa (Lumsden 1955, Robinson 1955, Ross 1956). The disease has resurged in recent years, with major epidemics reported from countries surrounding the Indian Ocean (Table 1). Although frequently a comparatively mild disease, individual severe cases have been observed (Economopoulou et al. 2009, Tandale et al. 2009) and waves of CHIKV infections have been linked to a subsequent rise in overall population mortality (Beesoon et al. 2008).

From a European perspective, chikungunya fever was a rarely diagnosed imported travel-associated infection, until the outbreaks on Réunion and Mauritius rendered European tourists to these islands at a suddenly increased risk of infection. Consequently, in 2005 and 2006, especially mainland France (Cordel et al. 2006, Krastinova et al. 2006), but also other European nations (Depoortere and

Coulombier 2006), reported a sudden increase in imported CHIKV infections. The need for CHIKV surveillance in Europe was driven home by the autochthonous outbreak of CHIKV infections in central Italy in 2007 (Rezza et al. 2007, Angelini et al. 2008). There, after introduction of the virus by a traveler from India, abundant local *Aedes* (*Ae.*) *albopictus* transmitted the virus and caused an outbreak of 337 suspected cases (217 confirmed) including one fatality. *Ae. albopictus* has been introduced to coastal Europe in recent decades, established themselves in Mediterranean countries and appear to spread further. Consequently, vigilance both of this potential vector and regarding importations of the virus is sensible (Straetemans 2008).

Parts of Germany are considered potential colonization areas for *Ae. albopictus* (European Centre for Disease Prevention and Control 2009). Published case series of German CHIKV cases imported since 2005 have focused mainly on clinical and diagnostic features (Taubitz et al. 2007, Panning et al. 2008, Pfeffer et al. 2008). As CHIKV infections are notifiable in Germany under the Protection Against Infection Act of 2001, from 2006 the German national-level database for notifiable infectious disease registered cases of CHIKV infections. Laboratories have to notify any diagnosed acute infection to the patient's local health department, who then investigates symptoms, dates of onset, possible hospitalization, travel details including country of infection, etc. This study aimed to describe all notified cases and to interpret the time trends of the infection's importation since its resurgence in the Indian Ocean.

Materials and Methods

In Germany, acute CHIKV infections are notifiable by law. Physicians and laboratories finding evidence for an acute infection notify the case to the local health department of the patient's residence. Information from both sources, as well as the patient, is collated and recorded. The case file—minus name and address information—is passed on to state- and national-level health departments electronically within a few days. At the national level, the resulting database is hosted by the Robert Koch Institute. Available information on CHIKV infections notified from January 2006 through December 2009 was extracted and analyzed descriptively with respect to sex, age, type of laboratory confirmation, hospitalization, seasonality, and country of infection. Data on dengue virus cases from the same period and data source were used for comparisons. Chikungunya fever case data were compared with data on the number of travelers embarking to important contributing countries of CHIKV infections [source: German Statistical Office (DESTATIS 2006–10)—data available monthly through October 2009].

Results

In the years 2006 through 2009 (as of January 5, 2010) 152 cases of symptomatic CHIKV infection (at least fever) were notified in Germany (17–53 per year): 8 (5.3%) were confirmed by polymerase chain reaction, 49 (32.2%) by a significant increase in IgG in between two serum samples, and the remainder (62.5%) by a single elevated IgM result. All infections were imported from outside mainland Europe (travel within the incubation period). Twenty percent reported hospitalization for between 1 and 28 days (median: 7 days), but none of the case patients died.

Earliest onset was on December 29, 2005 and latest was on November 18, 2009. For 110 cases, onset could be calculated relative to their return to Germany (for the others, travel history was available but without dates): 38 (35%) fell ill upon or after their return, and additional 36 (33%) had symptom onset within 7 days before returning to Germany and could have been viremic while back in Germany.

Among the patients, 57% were female. Age ranged from 6 to 77 years (median: 46 years, similar for both sexes). Month of disease onset had to be extrapolated for 16 cases—for 14, date of the first diagnostic sample was used as a proxy, and for 2, the month of notification. Most cases fell ill in 2006 (n=56), much fewer in 2007 (n=28) and 2008 (n=20), and an upsurge again in 2009 (n=47). Cases occurred throughout the year, with an overall minimum in December and January. There was no clear overall seasonality, with peaks shifting from year to year: in 2006 there was one in February through May and in 2007 from June through August. There was no peak discernable in 2008. In 2009, case numbers increased from July through November.

The countries most frequently named as the origin of the infection were India (*n*=37), Mauritius (*n*=34), and the Maldives (*n*=20) (Table 2). However, notifications came in distinct waves (Fig. 1).

Duration of travel was known for 116 cases and ranged from 4 to 1034 days (median: 19.5 days), although only two patients stayed more than a year in the country of infection. Median travel duration was notably longer in Sri Lanka, India, the Seychelles, and Thailand than in Mauritius and the Maldives. Peak months also varied by country.

Median age was higher than the overall median in Mauritius and Sri Lanka. It was lower in the Maldives and Thailand. As Sri Lanka, India, Thailand, and the Maldives also are frequent countries of infection for dengue fever imported to Germany, median age of the notified affected patients with the two infections can be compared. For these countries, median age for dengue fever cases is between 4 (Thailand) and 15 years (India) lower than that of chikungunya fever cases from the respective country.

Taking the annual number of air travelers to the most frequently named countries of infection into consideration, the risk to become infected with CHIKV in the 4-year period from 2006 through 2009 was higher in the Seychelles and Mauritius than in the other countries studied—they were lowest in India and Thailand. Even broken down by month, short-term risks reach higher levels in island destinations (Fig. 2).

Discussion

These data provide a first assessment of imported symptomatic CHIKV infections in Germany over the course of 4 years. Because of the broad spectrum of disease, substantial underdiagnosis of imported CHIKV infections remains likely. However, a stable fraction notified to the surveillance system allows to monitor the trends of CHIKV importation into Germany and to estimate the risks for travelers to distinct regions. Based on our analysis, the absolute minimum of actual importations to be expected is currently 17–53 cases per year. Considering that approximately two-thirds of these cases likely experience some viremia while back in Germany (others may have already recovered upon their return), the presence of a competent vector mosquito would render local outbreaks, like the one in Italy, possible. *Ae. albopictus* has so far not established itself in Germany, although its ova have been found once (in 2007) in the German Southwest (Pluskota et al. 2008) and it has established itself in neighboring Switzerland (Wymann et al. 2008). The Netherlands to the West have repeatedly noted the importation of *Ae. albopictus* associated with plant shipments from overseas and, most recently, of *Ae. albopictus* and *Ae. aegypti* associated with tire shipments (Scholte et al. 2010).

Physicians ought to include the CHIKV infection in their differential diagnosis of travelers returning from subtropical and tropical areas in Africa and Asia who seek medical attention for fever and joint pains—regardless of the severity of these symptoms. Increased awareness for this infection among physicians would also be a prerequisite for early detection of potential autochthonous cases.

CHIKV infection is commonly described as a mild disease. That almost a fifth of the notified CHIKV infection case patients in Germany were hospitalized for a median duration of a week may be partially explained by more severely ill patients' higher propensity to be diagnosed and notified as cases. Quite possibly, the underdiagnosis of mild cases also explains a rather high median age of 46 years among those notified. A higher age in chikungunya fever patients than in dengue fever patients as found in this German group of patients has been previously described in a dual outbreak situation in Sri Lanka (Kularatne et al. 2009) and is likely due to more severe disease courses in older CHIKV-affected patients (Economopoulou et al. 2009). Similarly observed prolonged recovery in older patients (Soumahoro et al. 2009) would infer a higher likelihood of case notification, as among patients with disease onset during travel those with a longer duration of symptoms would be more likely to seek medical attention upon return to Germany and thus be notified as cases.

The risk to acquire CHIKV infection is largely driven by the local presence (and the intensity of the presence) of the infection. Temporal clusters of German patients coming from specific countries of infection are largely synchronous with epidemic waves described in the literature. Thus, the risk of a CHIKV infection is particularly high when visiting a small area with a known outbreak, i.e., a small island destination or a particular city. As potential areas of CHIKV activity are also frequently endemic

for dengue fever and malaria, travelers need to protect themselves from mosquito bites during the day and at night. For unexplained fevers, medical attention should be quickly sought, if only to exclude malaria. CHIKV surveillance in Germany will be continued to monitor continuing importation of the virus in viremic patients and to receive early notice of potential future cases of autochthonous transmission. Entomological surveillance needs to be strengthened in many European countries including Germany.

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Disclosure Statement

There are no conflicts of interest to disclose by any of the authors.

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Tables and Figures

Table 1. Chronology of Chikungunya Virus Infections Recently Spreading Around the Indian Ocean

Country/region	*Begin of outbreak*	*Source/reference*
Kenya	2nd half of 2004	(Chretien et al. 2007)
Comoros	Jan 2005	(Sergon et al. 2007)
Mayotte (adm. France)	April 2005	(Sissoko et al. 2008)
Reunion (adm. France)	April 2005	(Renault et al. 2007)
Mauritius	April 2005	(Beesoon et al. 2008)
Seychelles	November 2005	(Chretien et al. 2007)
Mainland India	December 2005	(Ravi 2006)
Andaman/Nicobar Islands (India)	July/August 2006	(Manimunda et al. 2007)
Madagascar	Early 2006	(Ratsitorahina et al. 2008)
Malaysia	March–April 2006	(AbuBakar et al. 2007)
Sri Lanka	October 2006	(Epidemiological Unit 2008)
Maldives	December 2006	(Yoosuf et al. 2009)
Singapore	January 2008	(Leo et al. 2009)
Southern Thailand	September/October 2008	(Theamboonlers et al. 2009)

Table 2. Features of Chikungunya Fever Cases and Median Age of Dengue Fever Cases Imported from the Most Named Countries of Chikungunya Virus Infection, 2006 to November 2009

	Mauritius	*Seychelles*	*Sri Lanka*	*India*	*Thailand*	*Maldives*	*Overall*
Chikungunya							
Number of cases	34	16	17	37	10	20	152
% of overall cases	22.4	10.5	11.2	24.3	6.6	13.2	100.0
Median age	51.5	46	50	46	40	41.5	46
Starting year[a]	2006	2006	2006	2006	2009	2009	2006
Ending year[a]	2006	2008	2008	2009	2009	2009	2009
Peak month overall	March	May	April	June	July	September	n.a.
Minimal travel duration	8	13	16	5	15	7	4
Median travel duration	16	22	47	25	22	13	19.5
Maximum travel duration	93	181	1034	763	32	30	1034
No. of travelers to destination in 2008[b]	71,340	22,552	52,592	345,439	526,982	82,821	n.a.
Incidence/100,000 travelers in 2006–2009[c]	12.8	18.8	7.5	2.9	0.5	6.1	n.a
Dengue							
Number of cases	[d]	[d]	24	102	246	14	[d]
Median age	[d]	[d]	41.5[e]	31[e]	36	35.5	[d]

[a] First and last cases within the confines of the study period from January 2006 through November 2009.
[b] Persons embarking from a German airport to the ticketed destination in 2008 (DESTATIS 2006–10).
[c] As 2009 traveler numbers are incomplete, data for November and December 2008 were used as proxy for those months in 2009.
[d] Only isolated dengue cases imported from Mauritius and the Seychelles preclude calculation of a meaningful median age; similarly, as dengue fever is also common in South and Central America, a comparison of the overall median ages is inappropriate.
[e] Statistically significantly lower median age than the chikungunya cases from that country (Mann–Whitney *U* test, two-sided, $p<0.05$).

Figure 1. Major countries of infection named by German patients with chikungunya virus infection, 2006–2009 (number of cases per country).

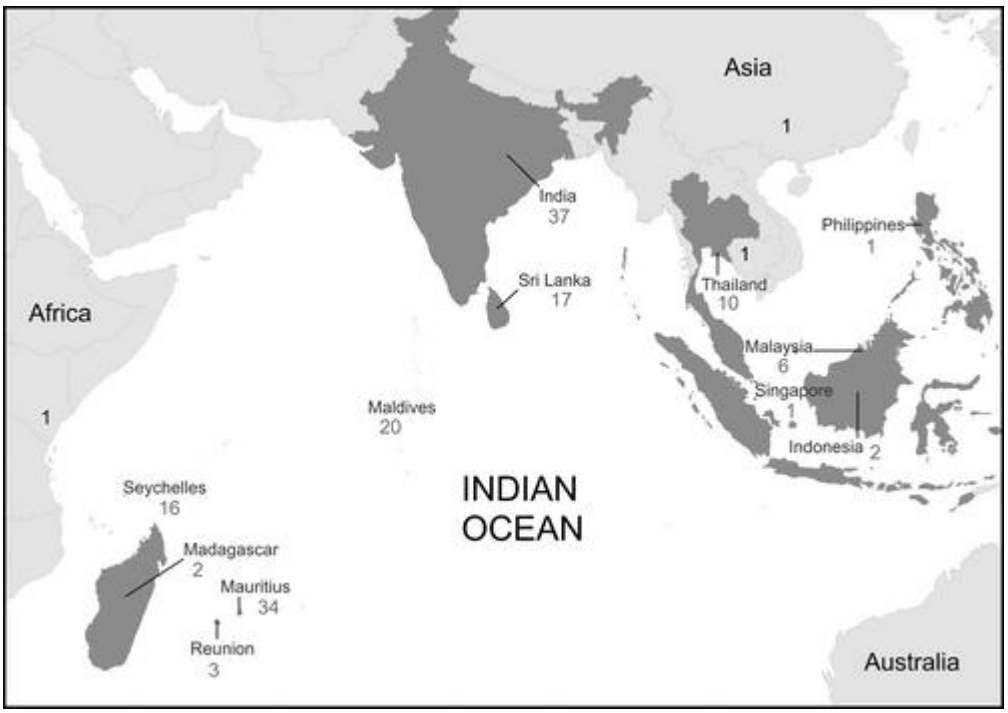

Figure 2. Absolute case numbers by month and year of infection, 2006–2009 **(A)**, and relative risk of infection (cases per 100,000 travelers to the country, January 2006 through October 2009) **(B)** by country/country group of infection.