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Japanese Encephalitis in Travelers from Non-Endemic Countries, 1973–2008

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Abstract. Japanese encephalitis (JE) is a severe disease and a risk for travelers who visit JE-endemic countries. We reviewed all published JE cases in travelers from non-endemic areas from 1973 through 2008, and assessed factors related to risk of infection. There were 55 cases that occurred in citizens of 17 countries. Age range of case-patients was 1–91 years (median = 34 years). Ten (18%) persons died and 24 (44%) had mild to severe sequelae. In a detailed risk assessment of 37 case-patients, 24 (65%) had spent ≥ 1 month in JE-endemic areas, and most had factors identified that may have increased infection risk. The estimate of overall JE risk was low, < 1 case/1 million travelers to JE-endemic countries. Nonetheless, for each traveler, a careful assessment of itinerary and activities, a decision on vaccination, and information on mosquito precautions are needed to reduce the risk of this disease.

INTRODUCTION

Japanese encephalitis virus (JEV) is a mosquito-borne flavivirus and a leading cause of encephalitis in Asia.[1] Clinical illness develops in less than 1% of persons infected with JEV. However, when neurologic infection occurs, it is usually severe, with a case-fatality rate of up to 30% and sequelae in 30–50% of survivors.[2–4]

Transmission of JEV occurs throughout much of Asia and parts of the Western Pacific region. The risk of JEV infection varies among countries, in different areas within countries, and from year to year. In temperate regions, there is usually a seasonal pattern of JEV transmission, and large and explosive outbreaks can occur. In tropical regions, transmission usually occurs year-round, often with a peak during the rainy season.[5,6] Japanese encephalitis virus is transmitted in an enzootic cycle between mosquitoes and vertebrate hosts, primarily pigs and wading birds. The main mosquito vector, *Culex tritaeniorhynchus*, commonly breeds in flooded rice fields and ground pools. It is an evening-biting and nighttime-biting mosquito that feeds most often in the outdoors, with peak biting times after sunset and again after midnight.[7] The risk of infection is greatest in rural, agricultural areas, where all elements of the JEV transmission cycle are present. However, JE cases are occasionally reported from urban and peri-urban areas.[8,9]

There is no specific treatment for JE, but the disease is preventable by vaccination. A mouse brain–derived vaccine has been available for many decades, and a live, attenuated JE vaccine is increasingly available in Asia.[5,10] An inactivated Vero cell-derived vaccine was licensed in 2009 for use in adult travelers in the United States, Europe, and Australia.[11] In some JE-endemic countries, immunization programs have substantially reduced the incidence of JE among the local population. However, because JEV is maintained in an animal–mosquito cycle in nature, unvaccinated travelers to these countries are still at risk for infection.

The risk of JE in travelers to Asia is generally considered to be low, with previous estimates for U.S. and European travelers suggesting that its frequency is less than one case per one million travelers.[12,13] Higher rates have been estimated for travelers from some countries to particular destinations, with risk estimates for Finnish and Swedish travelers to Thailand of 1 case/257,000 and 1 case/400,000 travelers, respectively.[14,15] Risk for the individual traveler depends on many factors including length and season of travel, itinerary, type of accommodations, and activities. We reviewed all published cases of JE in travelers who originated from non-endemic countries, occurring during 1973–2008. Before 1973, publications focused on cases among military personnel, with more than 300 cases described among soldiers from the United States, the United Kingdom, Australia, and Russia.[16–24] In 1993, summary information on travel-associated JE cases during 1978–1992 was published.[12] We included and expanded on the previous data and assessed factors related to risk of infection.

MATERIALS AND METHODS

Data sources. The PubMed database, the Global Health database, and the EMBASE database were searched for articles published up until June 30, 2009. The search strategy used was "Japanese encephalitis" and "travel+" or "journey". If one of the selected articles referred to another article in which a case of travel-associated JE was described and was not captured in the database search, then that article was also included. Communicable disease-related publications available on the internet from Australia (Communicable Diseases Intelligence), Canada (Canada Communicable Disease Report) and Europe (Eurosurveillance, United Kingdom Communicable Disease Report Weekly, United Kingdom Communicable Disease and Public Health, United Kingdom Health Protection Report) were searched for any additional published case reports. The authors were aware of one article "in press" at the time, which has subsequently been published and was also included.[11] If any case reports required clarification or additional information, we attempted to contact the article's author or the clinician.

Study selection criteria. A case of travel-associated JE was defined as a published report of JE in a traveler from a non-endemic country who had visited or lived in an Asian or Western Pacific country with JEV transmission. A traveler was defined as a tourist, expatriate or soldier. We selected articles that described travel-associated cases occurring during 1973–2008.

Japanese encephalitis case review and risk analysis. For each case, we recorded information on age, sex, country of origin, year and places of travel, traveler type, vaccination

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status, laboratory testing performed, and outcome of illness. Sequelae were assessed as severe if the author described them as serious or severe, if the case-patient had permanent neurological sequelae at ≥ 3 months, or if there were physical and cognitive/intellectual sequelae.

We also conducted a more detailed descriptive risk analysis on a subset of cases with more complete information available. This analysis included a review of the length of time in country, season of travel, and potential risk-related exposures during the period in the JE-endemic area.

RESULTS

Over the 36-year period from 1973 through 2008, we identified 55 published cases of travel-associated JE among tourists, expatriates, or soldiers who had visited one or more countries in Asia or the Western Pacific region (Table 1). A small increase in the number of published cases occurred in each of the three most recent decades: 1979–1988 (n = 14), 1989–1998 (n = 17), and 1999–2008 (n = 20). Two cases were reported from 1973–1978, and two cases had unknown dates of onset but occurred before 1993. Since 1980, most years had one or two reported cases, with a maximum of six cases in 1991 (Figure 1). Among the 46 cases for which age was recorded, patients ranged from 1 to 91 years of age (median = 34 years) (Figure 2). Overall, 29 (53%) of 55 cases were in males, 22 (40%) were in females, and 4 (7%) were in persons whose sex was not known. Laboratory confirmation was available for 38 (69%) cases, diagnosis was epidemiologically based for 1 (2%) case, and diagnostic test information was unavailable for 16 (29%) cases.

Overall 33 (60%) of the cases were in tourists, 9 (16%) were in expatriates, 6 (11%) were in soldiers, and the type of travel was unknown in 7 (13%). The tourist category included three persons who were visiting friends and relatives (VFRs), and two students on study-abroad programs. None of the 29 travelers for whom information on vaccination status was available had been vaccinated.

The 55 cases occurred in citizens of 17 different non-JE-endemic countries. Only two non-endemic countries had more than five published cases over the 36-year period: the United States (n = 15) and Sweden (n = 7). Of the 15 published cases in U.S. citizens, nine occurred in tourists or expatriates and six occurred in military personnel. The countries where JE was likely acquired included at least ten different JE-endemic countries. Travel-associated cases of JE were most frequently reported from Thailand, which had 19 cases overall, including nine cases during the last 10 years, followed by Indonesia (n = 8), China (n = 7), and the Philippines (n = 5) (Table 2).

The case-fatality rate was 18% (10 of 55 cases). There were 24 (44%) patients who survived but had sequelae, 12 (22%) who recovered completely, 1 (2%) who survived but for whom the presence of sequelae had not been determined, and 8 (14%) who had an unknown outcome. Of the 24 patients with sequelae, 10 (42%) had severe sequelae, 7 (29%) had non-severe sequelae, and 7 (29%) had no detailed sequelae information. Severe sequelae included major neuropsychologic disturbances and serious physical sequelae, including total incapacitation. Less-severe outcomes included a mild residual tremor, poor concentration, and memory problems. One woman was infected in the sixth month of pregnancy and recovered; however, mild pyramidal signs were detected in her infant at one year of age.[16]

Detailed case review and risk analysis. More complete information regarding travel itineraries and activities was available for 37 (67%) of 55 cases, and was included in the detailed descriptive risk analysis. Many reports documented exposures that would have increased the risk of JEV infection, including rural travel, residence on or near a farm, staying in unscreened accommodations, and participating in trekking or other outdoor activities (Table 3). Duration of travel or residence in a JE-endemic country ranged from 10 days to 34 years, and was ≥ 1 month in 24 (65%) cases.

Of the 13 travelers with a shorter trip duration < 1 month, 10 (77%) traveled for 2 to < 4 weeks and 3 (23%) traveled for 10—12 days. The travel destinations for these shorter-term travelers were Thailand (n = 7), Indonesia (n = 4), China (n = 1), and Vietnam (n = 1). Three (23%) travelers spent most of their time in rural areas, 6 (46%) stayed in coastal or non-rural areas but took day trips to rural areas or national parks, 1 (8%) stayed in a coastal area and took day trips to unspecified destinations, and 3 (23%) had no exposure-related information. There were no cases among business or other short-term travelers who visited only urban areas.

Disease onset occurred in all months of the year, except November. Fourteen (61%) of the 23 travelers who visited a country that is considered to have a recognized peak JE transmission season were infected during that season. Two tourists acquired JEV infection in February in northern Thailand, where most JE cases occur during May–October. Although six other tourists to Thailand and one tourist to Vietnam acquired infection in the period during December–April, outside what is typically considered the peak transmission season, they visited only tropical, southern parts of these countries where the hotter climate typically means there is year-round JEV transmission.

DISCUSSION

The 55 travel-associated JE cases identified over the 36-year period from 1973 through 2008 represent an average of 1.5 published cases per year. Although there was a small increase in case frequency over time, this may reflect the increase in overall tourist numbers during the same period, or possibly clinicians more frequently considering the diagnosis of JE. The majority of cases occurred among expatriates or tourists who visited JE-endemic countries for at least one month.

The risk of JE for travelers is clearly low, although the precise risk is unknown. Among U.S. citizens, only 15 travel-associated JE cases were identified during 1973–2008. The annual number of entries of U.S. citizens to Asia was approximately 2–3 million earlier in this period and increased to approximately 5.5 million entries in 2004.[12,49] On the basis of these data, the approximate risk estimate was < 0.2 cases/1 million U.S. travelers. However, this figure does not differentiate between the lower risk for short-term travelers with low-risk itineraries and the greater risk for expatriates, travelers on long trips, or short-term travelers with high-risk itineraries. In addition, the JE vaccine licensed in the United States in 1992 undoubtedly has prevented cases. However, a recent survey in the United States found that only 47 (11%) of 415 travelers to JE-endemic countries with at-risk itineraries were vaccinated with ≥ 1 dose of JE vaccine (Duffy M and others, unpublished data). Despite this low rate of vaccination, only four cases have been reported

TABLE 1
Published cases (n = 55) of travel-associated Japanese encephalitis, 1973–2008*

Case	Year	Age (years)	Sex	Type	Citizenship	Probable country of JE virus acquisition	Outcome	Laboratory confirmed	JE vaccine	References
1	2008	9	M	Tourist–VFR	United States	Vietnam	Survived	Yes	No	11
2	2008	91	M	Tourist	Italy	Thailand	Died	U	U	15
3	2008	37	F	Tourist	Sweden	Thailand	Survived	Yes	U	15
4	2008	36	F	Tourist–VFR	Sweden	Thailand	Survived	Yes	U	15
5	2006	59	F	Tourist	Germany	China	Survived	Yes	No	25
6	2006	49	M	Tourist	Italy	Vietnam	Survived	Yes	No	26
7	2005	68	F	Tourist–VFR	United States	Philippines	Survived	Yes	No	11
8	2004	60	M	Tourist	Finland	Thailand	Survived	Yes	No	14
9	2004	29	F	Tourist	Netherlands	Indonesia	Survived	Yes	No	27
10	2004	49	F	Tourist	New Zealand	China	Survived	Yes	No	28
11	2004	22	F	Tourist–study abroad	United States	Thailand	Survived	Yes	No	29
12	2004	66	M	Expatriate	Germany†	Papua New Guinea	Survived	Yes	No	30
13	2003	30	F	Expatriate	United States	Thailand	Survived	Yes	No	11
14	2003	32	F	Tourist	New Zealand†	Malaysia	Survived	Yes	No	31
15	2002	65	F	Tourist	Sweden	Thailand	Survived	Yes	U	15
16	2002	41	M	Tourist	Sweden	Thailand	Survived	Yes	U	15
17	2001	U	M	Expatriate	Finland	China	Survived	Yes	No	32
18	2001‡	U	M	Tourist	Sweden	Thailand	Survived	Yes	No	33
19	2000‡	22	M	Tourist	France	Indonesia	Survived	Yes	No	34
20	2000	80	M	Tourist	Sweden	Indonesia	Survived	Yes	No	35
21	1998	57	M	Tourist	Norway	Philippines	Died	Yes	U	15
22	1998	65	M	Expatriate	Norway	Philippines	Died	Yes	U	15
23	1997	25	M	Tourist	Norway	Thailand	Survived	Yes	No	36
24	1997	30	F	Tourist	Netherlands	Thailand	Survived	Yes	No	27
25	1996	59	F	Tourist	France	Thailand	Survived	Yes	No	37
26	1995	51	M	Tourist	Denmark	Indonesia	Died	Yes	No	38
27	1994	60	F	Tourist	Sweden	Indonesia	Survived	Yes	No	39
28	1993	3	F	Expatriate	Australia	Indonesia	Survived	Yes	U	40
29	1992	21	F	Tourist	United Kingdom	Thailand	Survived	Yes	No	41
30	1992	19	M	Tourist	United States	Singapore	Survived	U	U	12
31	1991	20	M	Soldier	United States	Japan	Survived	Yes	No	42
32	1991	35	M	Soldier	United States	Japan	Survived	Yes	No	42
33	1991	28	M	Soldier	United States	Japan	Survived	Yes	No	42
34	1991	33	F	Expatriate	Russia	Japan	Survived	Yes	No	16
35	1991	U	U	U	Austria	Thailand	U	U	U	12
36	1991	U	M	U	Australia	Indonesia	Survived	Yes	U	12, 40
37	1989	22	F	Tourist	Israel	Thailand	Survived	U	U	12
38	1988	10	F	Tourist	Australia	Indonesia	Survived	Yes	No	43
39	1988	64	M	U	United States	U	U	U	U	12
40	1986	55	M	Soldier	United States	Philippines	Survived	U	U	12, 44
41	1986	U	M	Soldier	United States	Philippines	Survived	U	U	12, 44
42	1985	30	M	Tourist	Germany	Thailand	Died	U	U	12
43	1985	9	M	Tourist	Eastern Europe	Vietnam	Died	U	U	12
44	1983	1	M	Tourist	United States	U	U	U	U	12
45	1983	30	F	Tourist	Netherlands	Thailand	Survived	U	U	12
46	1982	35	F	Expatriate	United Kingdom	Hong Kong	Died	Yes	No	45
47	1982	35	F	U	Canada	China	U	Yes	U	12, 46
48	1982	32	M	Soldier	United States	U	U	U	U	12
49	1982	62	M	Tourist	United States	China	Died	No	U	12, 47
50	1981	21	M	Tourist–study abroad	United States	China	Died	Yes	No	12, 48
51	1981	U	U	U	Australia	U	U	U	U	12
52	1978	U	M	Expatriate	Italy	China	Died	U	U	12
53	1973	30	F	Expatriate	Russia	Myanmar	Survived	Yes	No	16
54	U§	U	U	U	Denmark	Thailand	U	U	U	12
55	U§	U	U	U	Germany	Thailand	U	U	U	12

* JE = Japanese encephalitis; VFR = visiting friends and relatives; U = unknown.
† Hospitalized in Australia.
‡ Year of onset not given but assumed from publication date and data in article.
§ Before 1993.

in U.S. travelers since 1992, reinforcing the fact that the overall risk of JE in travelers is low.

The percentage of the total number of JE travel-associated cases that these 55 published cases represent is unknown. Some indication is given by using available national data. In Australia, for example, JE has been a nationally notifiable disease since 2001. During 2001–2008, three JE cases were reported nationally; case reports were published for two of the cases and the third patient had a mild, self-limiting illness (Marich A, New South Wales Department of Health, unpublished data).[30,31,50] A recent review suggested that among Scandinavian patients, 7 (54%) of 13 cases that occurred during 1994–2008 were reported in the literature.[15] Documents from health departments in the United Kingdom and Canada in 2008 indicated that all known cases that had occurred in their travelers had been published.[51,52] These data suggest that at least 50%, and

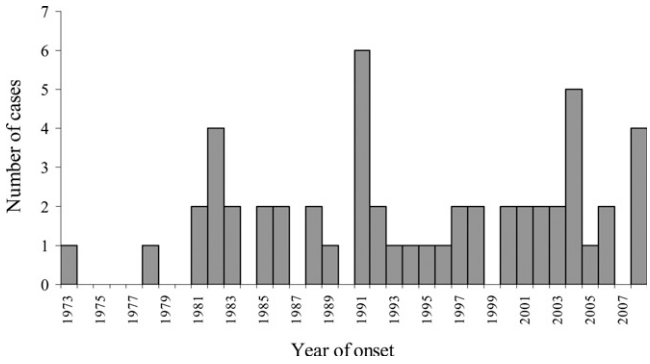

FIGURE 1. Year of onset of 53 travel-associated Japanese encephalitis cases. Dates of onset were not available for two cases, but both were before 1993.

TABLE 2

Number of travel-associated Japanese encephalitis cases by probable country of acquisition, 1973–2008

Country	Travel-associated cases (n = 55) No. (%)
Thailand	19 (35)
Indonesia	8 (15)
China	7 (13)
Philippines	5 (9)
Japan	4 (7)
Vietnam	3 (5)
Hong Kong (now China)	1 (2)
Malaysia	1 (2)
Myanmar	1 (2)
Papua New Guinea	1 (2)
Singapore	1 (2)
Not available	4 (7)

perhaps a higher percentage, of travel-associated JE cases that are diagnosed are published. It is likely that some travel-associated cases are never diagnosed as JE. Nevertheless, on the basis of the risk estimate calculated above of < 0.2 cases per 1 million travelers, and despite some degree of under-diagnosis and under-reporting, it is unlikely that the overall JE risk for travelers is > 1 case/1 million travelers.

The age groups represented among the reported cases ranged from young children to elderly adults. Before implementation of JE immunization programs in JE-endemic countries, the majority of cases characteristically occur in children less than 15 years of age because most of the older population has developed immunity from previous subclinical infection.[6] However, unvaccinated travelers who enter JE-endemic areas are usually immunologically naive with respect to JEV. As a result, travelers of all ages are susceptible to infection as clearly demonstrated in this review.

Cases among two particular subgroups of tourists, VFRs and students on study-abroad programs, were noted. Both groups are important in relation to risk of travel-associated JE because they frequently spend several months in JE-endemic countries, often in rural or remote locations. Despite potentially high risk itineraries, many may not seek pre-travel advice. It is well-recognized that the perception of risk among VFRs is often low, particularly in those traveling back to their country of birth.[53] Students may not always seek travel-related preventive medical advice, or receive appropriate interventions, for financial or other reasons.[54] Organized travel programs, including study-abroad programs, should ensure that their clients receive appropriate preventive health information.

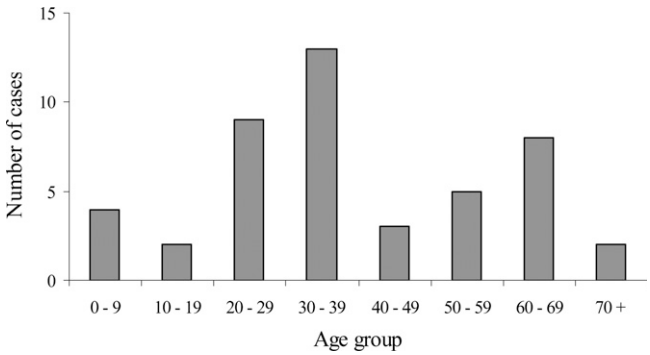

FIGURE 2. Travel-associated Japanese encephalitis cases by age group, 1973–2008 (n = 46).

Cases of JE were reported in travelers to countries where there is no ongoing surveillance for JE, including Papua New Guinea, Myanmar, and the Philippines. In countries where JE cases among the local population are not routinely recognized or reported, a tourist may act as a sentinel for the presence of JEV transmission. In the late 1980s and early 1990s, it was the reporting of JE in tourists to Bali that accelerated recognition by the Indonesian government that JE was a public health problem.[38,39,43,55] The lack of recognition and reporting of JE locally should not affect the decision to vaccinate tourists planning travel to areas considered to be JE-endemic.

Although many of the persons who visited countries with recognized peak JEV transmission seasons were infected during these periods, some travelers to Thailand and Vietnam acquired infection at other times of the year. Thailand has year-round JEV transmission in much of the country with a seasonal peak during May–October, mainly in the northern part of the country.[56,57] Vietnam has seasonal transmission in its northern region but year-round transmission in the southern region.[3,58] Because of prominent seasonal peaks in some areas of these countries, the year-round disease risk in many parts of both countries is often under-appreciated. Travel medicine providers should review each traveler's itinerary in detail to provide the most appropriate preventive recommendations for JE.

The U.S. Advisory Committee on Immunization Practices recommends JE vaccine for travelers who plan to spend a month or longer in JE-endemic areas during the JEV transmission season. Japanese encephalitis vaccine should be considered for short-term travelers (< 1 month) to JE-endemic areas during the transmission season if their activities will increase the risk of JEV exposure. Japanese encephalitis vaccine is not recommended for short-term travelers whose visit will be restricted to urban areas or times outside of a well-defined JEV transmission season.[59] Although no minimum duration of travel eliminates a traveler's risk for JE, a longer itinerary increases the likelihood that a traveler will spend time in an area with active JEV transmission. Although a recent survey suggested that longer-term travelers comprise approximately 20% of U.S. travelers to JE-endemic countries (Duffy M and others, unpublished data), 65% of the cases included in this review were in expatriates and longer-term travelers, highlighting the increased JE risk in this group and need for protection by vaccination.

Among the 35% of case-patients who acquired infection during stays < 1 month, their itineraries, activities, or accom-

TABLE 3
Available exposure information for 37 published cases of travel-associated Japanese encephalitis, 1973–2008

Case	Probable country of Japanese encephalitis virus acquisition (other countries visited)	Month of onset*	Duration of travel	Exposures
12	Papua New Guinea	Jan	34 years	Lived on farm 20 km from Port Moresby
46	Hong Kong	Jul	22 years	Lived in Hong Kong, urban pig problem at that time
22	Philippines	Aug	3 years	No details
53	Myanmar	Jul	3 years	Lived in Myanmar, wife of Russian embassy staff member
28	Indonesia	Dec	2 years	Lived in Balinese jungle
34	Japan	Aug	12 months†	Lived in Chiba City near Tokyo, took business trips
13	Thailand	Aug	7 months	Lived on island off coast of southern Thailand
50	China	Sep	4 months	Stayed mainly in urban areas but traveled through China by train
2	Thailand	Dec	3 months	Stayed in Phuket, southern Thailand
7	Philippines	Jul	3 months	Stayed with family in Manila
21	Philippines	Sep	Months	Traveled around Philippines
29	Thailand (Malaysia)	Sep	9 weeks	Trekking in northern Thailand, beach resort in southern Thailand
3	Thailand	Feb	8 weeks	In northern Thailand
14	Malaysia (Thailand, Cambodia, Vietnam)	May	8 weeks	In Sarawak on a jungle trek, sleeping in longhouses
31	Japan	Jun	> 6 weeks	Military exercises in rural Okinawa
32	Japan	Sep	> 6 weeks	Military exercises in rural Okinawa
33	Japan	Oct	> 6 weeks	Military exercises in rural Okinawa
9	Indonesia	June	6 weeks	In small islands around Flores in two weeks prior to onset
4	Thailand	Feb	5 weeks	Traveled around northern Thailand
10	China (Japan)	Jul	5 weeks	Three weeks in rural and urban China
19	Indonesia (India)	Oct	5 weeks‡	No details
1	Vietnam (Cambodia)	Feb	4 weeks	Stayed with family in rural southern Vietnam
11	Thailand	Jun	4 weeks	Stayed in unscreened dormitory in Chiang Mai City and one night in rural Chiang Mai Valley, northern Thailand
17	China (Singapore)	Sep	4 weeks	Had relocated to China; lived 30km from Beijing with farms nearby
15	Thailand	Dec	< 4 weeks	Koh Lanta, southern Thailand
24	Thailand	Aug	> 3 weeks	Traveled through Thailand, including near Cambodian border
6	Vietnam	May	3 weeks	Much of trip in rural north Vietnam
20	Indonesia	Apr	3 weeks	Hotels on Java and Bali with day trips on the islands
16	Thailand	Apr	2 weeks	Stayed in Phuket, southern Thailand; occasional day trips
5	China	Sep	2 weeks	Stayed in suburb of northwest Beijing; rural trip for 2 days
8	Thailand	Dec	2 weeks	Coastal hotels in Khao Lak and Phuket, southern Thailand; day trips to rural areas
18	Thailand	Jan	2 weeks	Stayed in bungalow in Khao Lak, southern Thailand; day trip to national park with mangrove swamps
23	Thailand	Dec	2 weeks	Beach holiday in Thailand
38	Indonesia	Jan	2 weeks	Coastal hotel on Bali with a few day trips to rural areas
26	Indonesia	Jan	12 days	Coastal hotel on Bali with a few trips inland
25	Thailand	May	12 days	Hotels in Chiang Rai and Pattaya, northern and eastern Thailand
27	Indonesia	Mar	10 days	Coastal hotel on Bali with one day trip to countryside

*Month of illness onset or month Japanese encephalitis virus infection acquired.
†Japanese encephalitis occurred after 1 month.
‡Included travel time in Australia.

modations likely contributed to their risk of JEV exposure, despite their shorter lengths of stay. These cases demonstrate the complexity for both travelers and providers in assessing the risk presented by a specific travel itinerary. Decisions regarding the use of JE vaccine must weigh several factors. JE is a severe disease, no specific treatment is available, and disease outcome is often poor. Conversely, the overall risk of travel-associated JE disease is low, vaccination is costly, and there are potential side effects associated with vaccination.[60]

Because shorter-term travelers represent a much higher proportion of travelers overall, consideration of risk in this group is important. Among JE cases in our review with travel duration < 1 month, Thailand and Indonesia (Bali) were the two commonest destinations. On average, 4.5 million tourists from non JE-endemic countries visited Thailand each year during 2000–2008.[61] On the basis of survey data from U.S. travelers to Asia, which indicated 80% of all travelers have short-term (< 1 month) itineraries (Duffy M and others, unpublished data), and a conservative assumption that twice as many travel-associated JE cases occurred than were published, the JE risk was approximately 1 case/3.3 million short-term travelers since 1996, when the first case was reported. In 1988, the first reported JE case in a short-term tourist to Bali occurred; since then three additional such case reports have been published. The most recent case occurred in 2000 in a tourist who traveled to Java and Bali but likely acquired his JEV infection in Bali. On average, approximately 620,000 tourists from non–JE-endemic countries have visited Bali annually during the past decade.[62] Using conservative assumptions that annual tourists visits were half this amount in the 11 years before this decade, twice the number of cases occurred than were published, and 80% of Bali-visiting tourists had short-term itineraries, the JE risk in the 21-year period since 1988 was approximately 1 case/1.0 million short-term travelers.

The limitations of this review include that the 55 cases reported here cannot be considered a complete or representative sample of all travel-associated JE cases. Details of a case diagnosed and treated abroad may not be available in the person's home country. A case report is not published for every patient that is diagnosed, and the diagnosis may be missed. The reported cases may not be representative of all travel-associated JE cases, either diagnosed or undiagnosed. For example, publication may have been more likely if a case had a unique or more severe clinical presentation, unusual travel destination, or another noteworthy epidemiologic feature such as JEV infection associated with short-term travel. Our search strategy may not have detected all cases. Furthermore, we were unable to include 18 (33%) of the 55 cases in the detailed risk analysis because risk factor information was unavailable. Finally, we were able to conduct only a fairly simple, mostly qualitative description of possible risk factors for travel-associated JE. A more quantitative risk-factor study (e.g., a case–control study) would require a suitable comparison group of adequate size and composed of otherwise similar travelers who did not acquire JEV infection. Because constructing such a control group would be logistically extremely difficult, no analytic studies of this type have ever been published.

When consulted by a traveler planning to visit a JE-endemic country, travel medicine providers should perform a careful assessment of each traveler's itinerary, including destinations, duration and season of travel, and potential activities. All travelers should be advised of the risks of JE and the importance of personal protective measures to reduce the risk of mosquito bites. For some travelers who will be in a high-risk setting based on travel destination, duration, season, and activities, JE vaccine can further reduce the risk of infection.

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