Dengue Virus Seroconversion in Travelers to Dengue-Endemic Areas

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Abstract. We conducted a prospective study to measure dengue virus (DENV) antibody seroconversion in travelers to dengue-endemic areas. Travelers seen in the Boston Area Travel Medicine Network planning to visit dengue-endemic countries for ≥ 2 weeks were enrolled from 2009 to 2010. Pre- and post-travel blood samples and questionnaires were collected. Post-travel sera were tested for anti-DENV IgG by indirect IgG enzyme-linked immunosorbent assay (ELISA) and anti-DENV IgM by capture IgM ELISA. Participants with positive post-travel anti-DENV IgG or IgM were tested for pre-travel anti-DENV IgG and IgM; they were excluded from the seroconversion calculation if either pre-travel anti-DENV IgG or IgM were positive. Paired sera and questionnaires were collected for 62% (589/955) of enrolled travelers. Most participants were 19–64 years of age, female, and white. The most common purposes of travel were tourism and visiting friends and relatives; most trips were to Asia or Africa. Median length of travel was 21 days. DENV antibody seroconversion by either anti-DENV IgM or IgG ELISA was 2.9–6.8%; lower range percent excluded potential false-positive anti-DENV IgG due to receipt of yellow fever or Japanese encephalitis vaccines at enrollment; upper range percent excluded proven false-positive anti-DENV IgM. Eighteen percent of those with seroconversion reported dengue-like symptoms. Seroconversion was documented for travel to Africa as well as countries and regions known to be highly dengue endemic (India, Brazil, southeast Asia). Given widespread risk of dengue, travel medicine counseling should include information on risk of dengue in endemic areas and advice on preventing insect bites and seeking prompt medical attention for febrile illness.

BACKGROUND

Dengue is the most common arboviral disease in the world.^{1,2} Vectors for transmission of dengue virus (DENV) include *Aedes aegypti* and *Aedes albopictus* mosquitoes, which are common in tropical and subtropical areas. Four DENV viruses, or serotypes, are known to cause human infection: DENV-1, DENV-2, DENV-3, and DENV-4. Primary infection or first infection with DENV provides long-lasting immunity to the infecting serotype and transient protection against other serotypes. Secondary infections can occur with other DENV serotypes. Clinical manifestations of dengue range from asymptomatic infection to severe disease.³

Travel-associated dengue infections have been increasing.⁴ From 1996 to 2005, 1,196 suspected dengue cases were reported in U.S. travelers, 334 (28%) of which were confirmed.⁵ From 2006 through 2008, the annual average of confirmed and probable travel-associated dengue cases recorded in ArboNET and by the U.S. Centers for Disease Control and Prevention (CDC) was 244, compared with an annual average of 33.5 confirmed and probable cases during 1990–2005.⁶ Although most of this increase was likely due to the 2003 addition of dengue reporting to the ArboNET surveillance system, increased dengue incidence in subtropical and tropical areas and increased travel to these regions were also responsi-

ble. Passive surveillance systems potentially underestimate dengue incidence. Five prospective studies, two in Dutch, one in Israeli, one in Swiss, and one in Australian travelers, reported DENV seroconversion in 1.0–6.7% of adults traveling to dengue-endemic areas.^{7–11} No prospective study of DENV antibody (DENV-Ab) seroconversion has been conducted in travelers from the United States. The objective of this study was to measure DENV-Ab seroconversion in travelers to dengue-endemic countries.

METHODS

Patient population. Participants were recruited from the Boston Area Travel Medicine Network (BATMN), a research collaboration of five travel clinics in the greater Boston area that sees approximately 7,500 travelers per year in a variety of practice settings. Travelers ≥ 2 years old were eligible for enrollment if they attended the clinics from January 6, 2009 to September 29, 2010 for pre-travel consultations and planned to visit dengue-endemic countries (as categorized by the World Health Organization [WHO]) for ≥ 2 weeks.¹ Information about travel beyond the country level was not available.

Institutional support and participant consent. The study was reviewed and approved by the institutional review boards of each institution and by CDC Human Subjects Advisors. We obtained written consent from participants ≥ 18 years of age, written assent and parental consent for ages 7–17 years, and parental consent for those younger than 7 years.

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Sample size. We used information from previous prospective studies showing rates ranging from 1.1% to 6.7% to assume a rate of 5% DENV-Ab seroconversion.^{7–11} A sample size of 1,166 participants would allow calculation of the proportion of travelers with DENV-Ab seroconversion with 1.25% margin of error, using a 95% confidence interval (CI). We aimed to enroll 240 participants at each site, but expiration of grant funding limited recruitment of the desired sample size.

Data collection. Questionnaires were administered at enrollment and again at 1–4 months after the return date. Pre-travel questionnaires included demographics (sex, age, country of origin, race/ethnicity) and trip characteristics (purpose of travel, itinerary, travel dates). We collected self-report of prior receipt of yellow fever (YF) and Japanese encephalitis (JE) vaccines and previous diagnosis of dengue, YF, JE, or West Nile virus infections.

Information collected at follow-up included verification of travel dates and other trip characteristics, including mosquito bite avoidance practices, symptoms of illness (fever, headache, muscle pain, other) during travel, and whether a diagnosis of dengue, YF, or JE was made during or after travel. We determined retrospectively whether participants with DENV-Ab seroconversion by ELISA had received YF or JE vaccine at enrollment. Participants who traveled for < 14 days because of changes in travel plans were kept in the analysis.

Laboratory methods. Pre-travel blood samples were collected at enrollment and post-travel samples at the follow-up appointment, which was intended to be 1–4 months after return from travel. Sera were stored at –80°C until testing was performed in batches. All post-travel specimens were tested for anti-DENV IgG by indirect ELISA and for anti-DENV IgM by capture ELISA (Focus Diagnostics Inc., Cypress, CA). To assess for presence of preexisting anti-

DENV IgG or IgM, post-travel specimens positive for anti-DENV IgG or IgM were paired with the corresponding pre-travel specimen and tested together for anti-DENV IgG or IgM.

Participants were identified whose sera tested positive for post-travel anti-DENV IgM, but negative for pre-travel anti-DENV IgM, and who had received either YF or JE vaccine at their enrollment visit. Given the potential cross-reactions of dengue with other arboviral infections when tested by ELISA for anti-DENV IgM result, these samples were tested for DENV and YF by plaque-reduction neutralization test (PRNT) at the CDC Arboviral Diseases Branch according to a protocol based on WHO guidelines; PRNT for JE was planned but could not be performed.¹² Funding limited number of samples that could be confirmed by PRNT; we were not able to test samples of subjects with seroconversion of anti-DENV IgG who received JE or YF vaccines.

Definitions. “DENV-Ab seroconversion” was defined as occurring when a post-travel sample was positive for either anti-DENV IgG or IgM, but the corresponding pre-travel sample was negative for both (Figure 1). “Prior infection samples” were defined as pre- and post-travel sample pairs that were either positive for anti-DENV IgG or IgM; these were excluded from the seroconversion calculation. “False-positive IgM samples” were defined as those positive by anti-DENV IgM testing, but negative for dengue by PRNT. “Potential false-positive IgG samples” were defined as those positive by anti-DENV IgG and negative by anti-DENV IgM, which were from travelers who had received either YF or JE vaccine at their pre-travel enrollment visit.

DENV-Ab seroconversion percent was first calculated by adding the number of participants who were anti-DENV IgG negative pre- and positive post-travel to the number who were anti-DENV IgM negative pre- and positive

FIGURE 1. Dengue antibody seroconversion according to enzyme-linked immunosorbent assay results of 589 paired sera.

post-travel, divided by the total number of participants. The "DENV-Ab seroconversion incidence rate (IR)" was first calculated by dividing the number of participants with DENV-Ab seroconversion by the total person-time of travel (in months). The final calculations of DEN-Ab seroconversion included the upper range values for the seroconversion percent and IR, which excluded the proven false IgM positives, and the lower range for DENV-Ab seroconversion percent and IR, which excluded the potential false-positive IgG samples.

Data management and statistical analysis. Participant information and laboratory results were entered into Census and Survey Processing System version 4.0 (U.S. Census Bureau, Washington, DC). Chi square tests were conducted to ascertain differences in proportions, and Wilcoxon rank-sum tests were conducted to test differences in continuous variables. Data were analyzed by using SAS Version 9.1.3 (SAS Institute Inc., Cary, NC).

RESULTS

Participant characteristics. Paired blood samples and completed questionnaires were obtained from 589 of 955 (62%) enrolled travelers; 366 participants were lost to follow-up. Characteristics of participants who completed the study did not differ from those lost to follow-up, except that travelers ≥ 65 years of age and white travelers were more likely to complete follow-up (80% versus 60%, $P = 0.008$; 66% versus 51%, $P < 0.0001$, respectively), and travelers visiting friends and relatives (VFR) were less likely to complete follow-up (57% versus 67%, $P = 0.033$). Participants with available demographic data were mostly adults 19–64 years of age, female, and white (Table 1). Most foreign-born participants were born in dengue-endemic countries. The two most common purposes of travel were tourism and VFR (Table 2). Most participants traveled to Asia or Africa. Approximately 60% of participants traveled for 14–30 days, with a median length of travel of 21 days (interquartile range 15–35 days, range 0–340 days). Median length of time between return from travel and post-travel visit was 92 days, with several

TABLE 1

Demographic characteristics of 589 travelers to dengue-risk countries	
	<i>n</i> (%)
Age (years) (<i>N</i> = 584)	
2–11	4 (0.7)
12–18	13 (2.2)
19–64	514 (88.4)
≥ 65	51 (8.7)
Sex (<i>N</i> = 586)	
Female	338 (57.7)
Race (<i>N</i> = 566)	
White	434 (76.9)
Black	46 (8.1)
Eastern Asia	32 (5.8)
Indian subcontinent	17 (3.0)
Hispanic/Latino	15 (2.7)
Bi/Multiracial	10 (1.8)
Other	10 (1.8)
Country of origin (<i>N</i> = 575)	
U.S. born	453 (78.8)
Foreign born, from a dengue-endemic country	72 (12.5)
Foreign born, from a non-dengue-endemic country	50 (8.7)

Response rates differed for survey questions; denominators are listed for each characteristic.

TABLE 2

Travel characteristics of 589 travelers to dengue-endemic countries	
	<i>n</i> (%)
Purpose of travel (<i>N</i> = 405)	
Tourism	170 (42.0)
VFR	79 (19.5)
Education/research	65 (16.0)
Volunteer/missionary	50 (12.3)
Business	37 (9.1)
Other	4 (1.0)
Travel destination (<i>N</i> = 609)	
Caribbean*	21 (3.6)
Latin America†	155 (26.6)
Asia‡	216 (37.0)
Africa§	210 (36.0)
Other	7 (1.2)
Duration of travel (<i>N</i> = 583)	
0–13 days	56 (9.6)
14–30 days	348 (59.7)
31–90 days	135 (23.2)
≥ 90 days	44 (7.5)
	Median, interquartile range
Timing of blood samples (<i>N</i> = 573)	92 days (67–132)
Length of time from return to post-travel blood-draw	
Replied "yes" to receipt of YF vaccine before enrollment, of 542 survey responses	196 (36.2)
Replied "yes" to receipt of JE vaccine before enrollment, of 569 survey responses	27 (4.7)

JE = Japanese encephalitis; VFR = visiting friends and relatives; YF = yellow fever. Response rates differed for survey questions; denominators are listed for each characteristic.

*Caribbean: Anguilla, Antigua and Barbuda, Bahamas, Barbados, Dominica, Grenada, Haiti, Jamaica, Martinique, Montserrat, St. Kitts and Nevis, St. Lucia, St. Vincent and the Grenadines, Trinidad and Tobago, Turks and Caicos, Virgin Islands (British), Virgin Islands (United States), Puerto Rico.

†Latin America: Argentina, Belize, Bolivia, Brazil, Columbia, Costa Rica, Cuba, Dominican Rep., Ecuador, El Salvador, French Guiana, Guatemala, Guyana, Honduras, Mexico, Nicaragua, Panama, Paraguay, Peru, Suriname, Venezuela.

‡Asia: Bangladesh, Bhutan, Brunei, Burma (Myanmar), Cambodia, China, Hong Kong, India, Indonesia, Laos, Malaysia, Maldives, Mauritius, Nepal, Pakistan, Papua New Guinea, Philippines, Singapore, Sri Lanka, Taiwan, Thailand, Vietnam.

§Africa: Angola, Burkina Faso, Comoros, Congo, Congo (Democratic Republic), Djibouti, Equatorial Guinea, Ethiopia, Ghana, Guinea, Guinea-Bissau, Ivory Coast, Kenya, Madagascar, Mozambique, Nigeria, Senegal, Seychelles, Sierra Leone, Somalia, South Africa, Sudan, Tanzania.

¶Middle East: Saudi Arabia; Oceania: Australia, French Polynesia, Guam, Kiribati, Marshall Islands, Micronesia, Nauru, New Caledonia, New Zealand, Palau, Samoa, Solomon Islands, Tonga, Tuvalu.

subjects having a lag in returning to a study site of greater than 4 months after return from travel due to their availability. Before enrollment, approximately one-third of participants had received YF vaccine, and 5% had received JE vaccine (Table 2).

DENV-Ab results. Anti-DENV IgG was detected in 97 post-travel samples; 68 of corresponding pre-travel samples were also positive for anti-DENV IgG (Figure 1). Anti-DENV IgM was detected in 12 post-travel samples; four of the corresponding pre-travel samples were also positive for anti-DENV IgM. Both anti-DENV IgG and IgM were detected in two participants whose pre-travel samples tested negative for anti-DENV IgG and IgM.

Characteristics of the 39 participants with DENV-Ab seroconversion by ELISA are listed in Table 3. At enrollment, 20 participants received YF vaccine and four received JE vaccine. The most common destinations for those with DENV-Ab seroconversion were India, Brazil, and Kenya. Seven participants with DENV-Ab seroconversion by ELISA

TABLE 3
Characteristics of participants with anti-DENV IgM and or IgG antibody seroconversion by ELISA

Type of SC*	Days of travel	Days from trip return to sample collection	Travel destination	Purpose of travel†	Accommodation type	Symptoms of dengue‡	Received YF or JE vaccine at enrollment?
G	14	73	India	VFR, T	Hotel		
G	20	165	India	T	Hostel, Home		
G	26	51	India	E/R	Dorm, Home		JE
G	16	253	India		Hotel		
G	22	205	India	VFR, V/M	Ship, Hotel	HA	JE
M	23	119	India, Vietnam	VFR, T	Dorm, Hotel		
G	81	71	India, Nepal, Thailand	E/R, T	Hostel		
M	67	67	India, China, Nepal	T	Hostel, Hotel		
M	13	129	Brazil	T	Hostel, Home		YF
G	15	95	Brazil	V/M, T	Home		YF
G	20	132	Brazil	T	Hostel, Hotel, Tent		YF
G	15	126	Brazil	VFR	Home		YF
G	184	333	Brazil	V/M	Home	F	YF
G	62	125	Brazil, Barbados, Argentina, Chile, Peru, Ecuador, Colombia	T	Ship		
G, M	63	42	Kenya	V/M	Home	F, HA, My	YF
G	38	85	Kenya	Missing	Tent, Hostel		YF
G	17	60	Kenya	T	Tent, Hotel		YF
G	16	147	Kenya	V/M	Home	F, My	YF
M	59	64	Uganda	VFR	Home		YF
G	16	139	Uganda	V/M	Hostel, Hotel		YF
G	65	176	Uganda, Sudan	VFR	Home, Hotel		YF
G	163	66	South Africa, Lesotho	E/R	Home		YF
G	18	65	South Africa, Botswana, Zimbabwe	T	Hotel		
G	78	60	South Africa, Mozambique, Lesotho, Swaziland	T	Tent, Hostel	F, HA	YF
G	74	44	Mozambique		Orphanage		YF
G	14	172	Ecuador	T	Ship, Hotel		YF
G	35	125	Ecuador	T	Tent, Farm		
M	136	114	Ecuador, Peru	E/R, T	Home, Hostel		YF
G	34	90	China, Gabon	B	Dorm, Hotel		YF
G	153	202	China, Ethiopia, Egypt	VFR, T	Home, Hostel	F, HA	
G	20	107	Cambodia, Vietnam	T	Hotel		JE
G	24	79	Cambodia, Laos, Thailand, Myanmar	T	Hotel	HA	
G	31	83	Indonesia	E/R	Hostel, Hotel		JE
G	58	227	El Salvador	VFR	Home		
G	15	60	Tanzania	T	Tent, Hotel		YF
G, M	17	146	Ghana	V/M	Hostel		
M	37	120	Australia				
M	4	86	Nicaragua				
M	137	17	Malawi, Zambia	V/M	Tent, Hostel		YF

DENV = dengue virus; ELISA = enzyme-linked immunosorbent assay; JE = Japanese encephalitis; YF = yellow fever.

*SC = seroconversion; G = positive on anti-DENV IgG ELISA; M = positive on anti-DENV IgM ELISA.

†VFR = visiting friends and relatives; T = tourism; V/M = volunteer/missionary; E/R = education/research.

‡F = fever; HA = headache; N = nausea; V = vomiting; AP = abdominal pain; C = conjunctivitis; My = myalgia.

reported dengue-like symptoms, and five of these participants had been immunized with YF or JE prior to enrollment. Because of participant availability, there was a wide range of time (17–333 days) between return from travel and post-travel sample collection; 41% of participants with DENV-Ab seroconversion had post-travel sample collection beyond 4 months after their return. The longest duration between return from travel and anti-DENV IgM seroconversion was 129 days. Participants with DENV-Ab seroconversion had highly variable trip durations of 4–184 days.

PRNT results for participants immunized with YF vaccine at enrollment. Five participants positive for post-travel anti-DENV IgM and negative for pre-travel anti-DENV IgM received YF vaccine at enrollment; their post-travel sera were tested for DENV by PRNT. Four of five samples were positive for YF and negative for DENV, were therefore considered false IgM positive samples, and were removed from the DENV-Ab seroconversion calculation. The remaining

sample was positive for both YF and DENV on PRNT, so DENV-Ab seroconversion could not be excluded.

Final DENV-Ab seroconversion incidence. Participants who were anti-DENV IgM or IgG positive at baseline were excluded from the numerator and denominator and those with false-positive IgM from the numerator of seroconversion calculations. Therefore, 35 of 517 participants (6.8%) had DENV-Ab seroconversion. The number of person-months for travelers who completed our study was 596.5, yielding a seroconversion IR of 58.7 seroconversions per 1,000 person-months of travel (95% CI = 39.2–78.1). Because PRNT data supported cross-reactivity between administration of other flavivirus vaccines at the enrollment visit and presence of IgM DENV-Ab at follow-up, we also calculated DENV-Ab seroconversion after removing the 20 potential false-positive IgG samples from the numerator (e.g., 15/517, 2.9%). The corresponding seroconversion IR was 28.7 per 1,000 person-months of travel (95% CI = 14.7–42.8).

DISCUSSION

DENV-Ab seroconversion ranged from 2.9% to 6.8% and IR from 28.7 to 58.7 per 1,000 person-months based on ELISA data, with the lower ranges calculated after all travelers who received YF or JE vaccines at enrollment were assumed to have a false-positive dengue serology and were excluded from the numerator of the seroconversion calculations. Several other studies used similar methods to calculate DENV-Ab seroconversion in different populations of travelers and found similar results.^{7–11} Cobelens and others studied travelers to Asia for 1–13 weeks, excluding samples whose DENV-Ab titers were exceeded by JE-Ab titers, and found 2.9% seroconversion with an IR of 30 per 1,000 person-months.⁸ Potasman and others studied travelers who stayed at least 3 months in tropical areas and found that 6.7% seroconverted. Four of seven participants with DENV-Ab seroconversion had received JE or YF vaccine at an undefined time in the past; PRNT was not used to exclude cross-reactivity from receipt of a flavivirus vaccine.⁷ Baaten and others studied Dutch adults traveling to dengue-endemic countries for 1–13 weeks and found that 1.2% seroconverted, with a seroconversion IR of 146 per 1,000 person-months.⁹ Three of 14 participants with DENV-Ab seroconversion had received YF vaccine pre-travel.⁹ Ratnam and others reported that 1.0% of adult Australian travelers to Asia for at least 7 days had DENV-Ab seroconversion, and all subjects with evidence of DENV-Ab seroconversion were asymptomatic. There were three travelers with positive pre-travel anti-JE virus IgG who were not included in their DENV-Ab seroconversion calculation if their pre-travel anti-DENV IgG was positive. Most recently, Leder and others studied Swiss travelers to tropical areas and reported a DENV-Ab seroconversion rate of 1.1% with a seroconversion IR of 6.7 per 1,000 person-months. Two of three travelers with evidence of DENV-Ab seroconversion received YF vaccine before travel.¹⁰ These prior studies on DENV-Ab seroconversion along with our study demonstrate a rather consistent rate of seroconversion among travelers from multiple countries.

The main challenges in serodiagnosis of dengue by ELISA are false-positive results due to cross-reactivity between DENV-Ab and other flavivirus antibodies.^{12–15} Many travelers to dengue-endemic areas receive a vaccine for YF or JE for travel to locations where they could encounter one of these flavivirus infections. Our PRNT results demonstrated false-positive anti-DENV IgM ELISA results due to cross-reactivity between flaviviruses. Because we collected information on receipt of JE and YF vaccine at the enrollment visit only in those who had DENV-Ab seroconversion by ELISA (this information was not obtained on all participants), we cannot determine to what extent receipt of a flavivirus vaccine at enrollment affects the ELISA results in our cohort. False-positive anti-DENV IgG results due to cross-reactions with other flaviviruses or prior receipt of YF or JE vaccines were not excluded in most studies of DENV-Ab seroconversion that used ELISA. Diagnostic tests for dengue infections with higher specificity such as PRNT and polymerase chain reaction were not feasible due to cost, and nonstructural protein 1 antigen testing is not commercially available in the United States.

We found 14 cases of DENV-Ab seroconversion in travelers visiting only countries in Africa; the most common desti-

nation was Kenya, and 12 of these travelers received YF vaccine at their enrollment visit (Table 3). Although dengue is recognized as a significant public health problem in the Asia-Pacific and Americas-Caribbean regions, it is underrecognized and underreported in Africa.¹⁶ As *Aedes* species are found widely throughout much of Africa, and given rapid population growth and unplanned urbanization, potential for DENV transmission in Africa is substantial.^{17,18} Recent global estimates indicate that Africa's dengue burden is nearly equivalent to that of the Americas.¹⁹

The only method of dengue prevention available currently in the United States is mosquito avoidance. Preventive measures include wearing long-sleeve shirts and long pants, using insect repellent, and staying in accommodations with air conditioning and screened windows.²⁰ A study of dengue seroconversion of people living along the Mexico–Texas border found use of air conditioning was protective; seroconversion was more common on the Mexico side, where there was substantially less use of air conditioning.²¹ The protective effect of air conditioning is plausible, as it may lead to keeping windows closed and staying indoors more often, but preventing *Ae. aegypti* bites is difficult, as the mosquitoes bite during the day, are often found indoors, and are widespread in urban areas.²²

Our study had several limitations. We did not perform PRNTs on samples of all participants with DENV-Ab seroconversion by ELISA to confirm both that seroconversion had occurred and there was no cross-reactivity with other flaviviruses. Our analyses did not detect statistically significant differences in travel-related risk factors (data not shown), and our sample size may have been too small to detect such differences. We excluded participants who were lost to follow-up, assuming they seroconverted at a similar rate as those who completed follow-up; having complete data on those lost to follow-up might have affected the findings of our study. In our study, seven of 39 participants with DENV-Ab seroconversion reported dengue-like symptoms. The report of dengue-like symptoms is subject to recall bias and is limited in several instances by a long duration of time between return from travel and administration of post-travel questionnaires. The interpretation of dengue-like symptoms is also challenging, as these symptoms are not specific for dengue infection. Some subjects were seen for follow-up well beyond the anticipated 1–4 month period; this may have resulted in missing IgM DENV-Ab in some subjects post-travel. We do not think we missed other exposures, as the travel history was confirmed at the time of the follow-up appointment and any changes in itinerary noted. We do acknowledge that, especially in participants with a long lag between return from travel and follow-up sera collection, local acquisition of West Nile Virus infection in the United States is possible and could have caused false-positive anti-DENV IgG or IgM results. A limitation of the commercial ELISA used in our study is that it is a qualitative assay, and therefore we were unable to assess for secondary infections by quantifying a rise in antibody concentration in pre- and post-travel specimens. Finally, we calculated seroconversion IR by using the entire travel time; this would result in the maximum possible exposure time (rather than removing each subject from the exposure time when they became infected), thus underestimating the seroconversion IR.

In conclusion, we confirm DENV-Ab seroconversion in travelers to dengue-endemic areas. As no preventive measures

are completely protective against DENV, there is an urgent need for a DENV vaccine. Travelers born in the United States were reported to be likely to accept a DENV vaccine with 75% efficacy and a low risk of minor adverse events.²³ Large trials of candidate dengue vaccines are in progress, a vaccine has been approved in Mexico, Brazil, the Philippines, and El Salvador, and the possibility of a vaccine available in the United States in the near future appears optimistic.^{24,25} Travel medicine providers should continue to counsel travelers on risk of dengue in endemic areas and provide advice on preventing insect bites and seeking prompt medical attention for any febrile illness. The finding of dengue seroconversion in travelers in this study combined with emerging information about dengue prevalence in Africa may require a shift from emphasis on “dusk to dawn” mosquito bite prevention (for malaria only) to round the clock prevention for travelers to this continent.

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