Chikungunya Virus Infections Among Travelers—United States, 2010–2013

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Abstract. Chikungunya virus is an emerging threat to the United States because humans are amplifying hosts and competent mosquito vectors are present in many regions of the country. We identified laboratory-confirmed chikungunya virus infections with diagnostic testing performed in the United States from 2010 through 2013. We described the epidemiology of these cases and determined which were reported to ArboNET. From 2010 through 2013, 115 laboratory-confirmed chikungunya virus infections were identified. Among 55 cases with known travel history, 53 (96%) reported travel to Asia and 2 (4%) to Africa. No locally-acquired infections were identified. Six patients had detectable viremia after returning to the United States. Only 21% of identified cases were reported to ArboNET, with a median of 72 days between illness onset and reporting. Given the risk of introduction into the United States, healthcare providers and public health officials should be educated about the recognition, diagnosis, and timely reporting of chikungunya virus disease cases.

INTRODUCTION

Chikungunya virus is a mosquito-borne alphavirus that causes an acute febrile illness with severe polyarthralgia. Mortality is rare but the joint pains can be debilitating. The acute symptoms typically resolve within 7–10 days. However, some patients experience persistent joint pains for months to years.^{1,2} Chikungunya outbreaks were previously documented in countries in Africa, Asia, Europe, and the Indian and Pacific Oceans.² In 2013, the first locally acquired cases in the Americas were reported on islands in the Caribbean.³ As of September 5, 2014, > 650,000 suspected cases had been reported from 31 countries or territories in the Americas, including the United States.

Chikungunya virus is transmitted to humans primarily by *Aedes aegypti* and *Aedes albopictus* mosquitoes, the same vectors that transmit dengue virus. These mosquitoes are found throughout much of the Americas, including parts of the United States where they are most active from April through September.⁴ Humans and other primates are the primary amplifying hosts, and infected travelers can potentially introduce the virus into non-endemic areas leading to local transmission and outbreaks of the disease.⁵ The viremic period typically lasts 4–6 days, but can be as long as 12 days after illness onset.^{6–9} From 1995 through 2009, a total of 109 laboratory-confirmed cases of chikungunya were identified in travelers visiting or returning to the United States.¹⁰ None of these imported cases resulted in local virus transmission.

In the United States, chikungunya virus testing is available at the Centers for Disease Control and Prevention (CDC), a few state health departments, and one commercial laboratory. Through 2014, chikungunya virus disease was not a nationally notifiable condition, but state health departments have been able to report cases to ArboNET, the national arboviral disease surveillance system, since 2006. Chikungunya virus disease will become a notifiable condition starting in 2015. We reviewed the epidemiology of all chikungunya virus infections identified in the United States from 2010 through 2013 and evaluated completeness and timeliness of reporting of identified cases to ArboNET.

METHODS

Case finding. We identified all positive chikungunya test results from 2010 through 2013 at CDC, the New York State Department of Health, the California Department of Public Health (CDPH), and Focus Diagnostics. Since 1995, clinical specimens submitted to CDC have been tested for evidence of chikungunya virus infection upon request or if a patient had a history of recent travel to an endemic area. Specimens are tested by enzyme-linked immunosorbent assay for anti-chikungunya virus immunoglobulin (Ig) M and IgG antibodies.^{11,12} Specimens with a positive, equivocal, or indeterminate result for IgM antibodies are evaluated for virus-specific neutralizing antibodies using plaque reduction neutralization tests (PRNT) with a 90% cutoff value.^{13,14} Serum specimens collected < 7 days after onset of illness are also tested for chikungunya virus RNA by reverse transcriptase-polymerase chain reaction (RT-PCR) and virus isolation using Vero cell culture.⁸ Since 2005, the New York Department of Health laboratory has performed chikungunya virus PRNT, RT-PCR, and isolation in Vero cell culture. Since 2008, Focus Diagnostics has performed an immunofluorescence assay (IFA) for anti-chikungunya virus IgM and IgG antibodies and RT-PCR for chikungunya virus RNA. The CDPH has performed an IFA for anti-chikungunya virus IgM and IgG antibodies since 2010. Samples determined to be positive for chikungunya virus antibodies at CDPH are confirmed by PRNT or referred to CDC for further testing.

Case definition. We defined a case as a patient with one or more of the following: 1) chikungunya virus or viral RNA detected by culture or RT-PCR, 2) ≥ 4 -fold rise in anti-chikungunya virus neutralizing antibodies between acute- and convalescent-phase specimens, or 3) anti-chikungunya virus IgM antibodies with either anti-chikungunya virus IgG or neutralizing antibodies. Patients with chikungunya virus or RNA detected in serum were considered viremic.

Data collection. For chikungunya virus infections identified at CDC and the state health departments, information was typically collected on sex, age, state of residence, date of illness onset, date of specimen collection, travel destinations, and dates of travel. For cases identified at Focus Diagnostics, information was routinely available on sex, age, and date of specimen collection; state of residence and information on travel history were available for some cases. For cases without a specific onset date noted, the sample collection date was

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TABLE 1
Characteristics of case-patients with chikungunya virus infection identified in the United States, 2010–2013

	Cases (N = 115)	
	No.	(%)
Female sex	63	(55)
Age group		
< 20	6	(5)
20–39	37	(32)
40–59	53	(46)
60 +	18	(16)
Unknown	1	(1)
Country where infection was acquired		
India	37	(32)
Indonesia	7	(6)
Philippines	7	(6)
Cambodia	2	(2)
Madagascar	1	(1)
Nigeria	1	(1)
Unknown	60	(52)
Days from illness onset to return to the United States		
< 7 days	21	(18)
≥ 7 days	10	(9)
Unknown	84	(73)
Positive chikungunya virus laboratory test		
Immunoglobulin M antibodies*	106	(92)
Reverse transcriptase-polymerase chain reaction	6	(5)
≥ 4-fold rise in neutralizing antibodies	3	(3)

* Positive for immunoglobulin M (IgM) antibodies with either immunoglobulin G (IgG) or neutralizing antibodies in the same or later specimen.

used as a surrogate for the month of illness onset. A state was considered to have chikungunya virus vectors if *Ae. aegypti* or *Ae. albopictus* was identified and reported to ArboNET from anywhere in the state during 2000–2013.

Data analysis. Data were analyzed using SAS statistical software, version 9.3 (SAS Institute, Cary, NC). Categorical variables were described as proportions, and continuous variables were described by median and interquartile range (IQR). To assess the risk for local chikungunya virus trans-

mission, we compared states that reported the presence of chikungunya vectors to states that had residents with laboratory-confirmed chikungunya virus infections. We evaluated the completeness and timeliness of national chikungunya surveillance by comparing cases identified through the diagnostic laboratories with those reported to ArboNET.

RESULTS

Overall, 115 laboratory-confirmed chikungunya virus infections were identified in the United States from 2010 through 2013, with a median of 23 cases identified per year (range, 5–65 cases per year). Sixty-three (55%) case-patients were female (Table 1). The median age of case-patients was 44 years (IQR 34–54 years); only 4 (3%) were children < 18 years of age. Cases occurred in every month, but only 39 (34%) had illness onset from April to September (Figure 1), the months when *Ae. albopictus* and *Ae. aegypti* are most likely to be active in the United States.

Of the 55 case-patients with known travel history, all traveled outside the United States during or immediately before their illness onset. Fifty-three (96%) reported travel to Asia and 2 (4%) to Africa. The most commonly reported travel destinations were India, Indonesia, and the Philippines (Table 1). Of the 31 cases with known dates of travel and illness onset, 21 (68%) returned to the United States < 7 days after illness onset or had illness onset in the United States.

Of the 115 chikungunya virus infections identified, 86 (75%) had testing performed at Focus, 38 (33%) had testing performed at CDC, and 1 (< 1%) had testing performed at CDPH. Ten cases had testing at more than one location (nine tested at Focus and CDC and one tested at CDPH and CDC). No positive cases were identified through the New York Department of Health. Chikungunya viral RNA was detected by RT-PCR in 6 (5%) of the 115 cases. All viremic cases were tested < 6 days after illness onset and had illness onset in the months of September–November. Three cases had a ≥ 4-fold

FIGURE 1. Month of illness onset* of chikungunya cases identified in the United States, 2010–2013. * If date of illness onset was missing, the collection date for the earliest specimen was used as a surrogate for month of illness onset.

rise in anti-chikungunya virus neutralizing antibodies between acute- and convalescent-phase specimens. For the remaining 106 (92%) cases, the diagnosis was determined on the basis of the detection of anti-chikungunya virus IgM antibodies with either anti-chikungunya virus IgG ($N = 79$) or neutralizing antibodies ($N = 27$).

Of the eight cases with known date of illness onset who had chikungunya virus RT-PCR performed, all five tested ≤ 3 days after illness onset were positive and 1 (33%) of three tested 4–5 days after illness onset were positive. Four (67%) of the six cases with chikungunya virus RNA detected also had virus isolation attempted; chikungunya virus was isolated in 3 (75%). All of the culture positive specimens were collected 1–2 days after illness onset. An additional 15 cases returned to the United States < 7 days after illness onset but did not have RT-PCR testing or virus isolation performed.

State of residence was available for 107 (93%) chikungunya case-patients. Case-patients were residents of 29 states; seven states (California, Illinois, Massachusetts, New Jersey, New York, Texas, and Virginia) had more than five cases (Figure 2). Ninety-one (85%) of the 107 cases were residents of states with reported chikungunya virus vectors. All six viremic case-patients were residents of states with reported *Ae. aegypti* or

Ae. albopictus (Figure 3), but only three of the patients had illness onset from April through September. Of the 15 case-patients who returned to the United States < 7 days after illness onset but did not have RT-PCR performed, 12 (80%) were residents of states with potential vectors.

Of the 115 chikungunya virus infections identified from 2010 through 2013, only 24 (21%) were reported to ArboNET. Seventeen (45%) of the 38 cases with laboratory testing performed by CDC were reported to ArboNET, compared with only 7 (9%) of the 77 cases with laboratory testing performed only by the commercial laboratory. The time between onset of illness and reporting of the case to ArboNET was a median of 72 days (IQR 52–117 days).

DISCUSSION

Before 2006, the diagnosis of chikungunya virus infection in a United States traveler was rare.¹⁰ However, in the past 8 years, a median of 26 chikungunya virus infections have been identified in the United States annually. No locally acquired infections were identified from 2010 through 2013, but many of the travelers became ill in the United States or returned to the United States within a week of becoming ill,

FIGURE 2. Number of chikungunya cases identified (2010–2013)* and presence of chikungunya virus vectors (*Aedes aegypti* and *Aedes albopictus*) reported to ArboNET (2000–2013) by state. * One hundred seven (93%) of the 115 identified cases had known state of residence.

FIGURE 3. Presence of *Aedes aegypti* and *Aedes albopictus* as reported to ArboNET, by state, 2000–2013. * No states reported *Aedes aegypti* in the absence of *Aedes albopictus*.

suggesting that they might have been viremic while in the country. Furthermore, some case-patients who may have been viremic returned to a state that has reported vectors capable of transmitting the virus. Although none of the cases identified through 2013 resulted in local virus transmission, they document a risk for the introduction and initiation of local transmission of chikungunya virus in the United States. This risk has recently been shown by the first autochthonous transmission in the Americas in December 2013.³ In the 8 months following the identification of the first locally acquired case, thousands of confirmed and suspected cases have been reported from Caribbean islands, and countries in North, Central, and South America.^{15,16} As of September 2, 2014, a total of 758 laboratory-confirmed chikungunya cases had been reported from the United States.¹⁷ Although most cases occurred in travelers, seven locally transmitted cases have been identified in Florida. An additional 222 laboratory-confirmed locally transmitted cases have been reported from Puerto Rico and the United States Virgin Islands. Given the similar ecology and vectors, dengue might provide the best predictive model for the expected course of chikungunya in the Western Hemisphere. In 2013, there were 2.4 million cases of dengue reported in the Americas.¹⁸ During the same year, 772 imported and 49 locally transmitted dengue cases were reported in the continental United States.^{19,20}

Since 2008, the majority of diagnostic testing for chikungunya virus has been performed at the one commercial laboratory offering testing. Less than 10% of cases identified at the com-

mercial laboratory from 2010 through 2013 were reported to ArboNET. This is likely related to the fact that chikungunya has not been a nationally notifiable disease condition in the United States. Among cases that were reported to CDC through ArboNET, reporting was often delayed by months. Incomplete and delayed reporting limits potential public health interventions to reduce the risk of local transmission following imported cases. Efforts are underway to improve the completeness and timeliness of reporting for all identified chikungunya virus disease cases, including improved communications between the commercial laboratory and state and local health departments and outreach to healthcare providers regarding recognition, diagnosis, and reporting of cases. In addition, chikungunya virus disease will be classified as a nationally notifiable condition starting in 2015.

The median age and sex distribution of case-patients identified from 2010 through 2013 were similar to what has been previously described.¹⁰ There were four cases identified in children from 2010 through 2013 compared with no children among the 109 cases identified from 1995 through 2009. Illness onset among cases identified from 2010 through 2013 occurred later in the calendar year from what has been previously described. Of cases identified from 2010 through 2013, only 26% of cases had illness onset during July–September, compared with the 48% reported previously.¹⁰ The reasons for this difference are unknown. The seasonality of identified cases may reflect travel patterns or seasonal patterns of chikungunya virus outbreaks in Asia where most of these travel-associated cases were acquired.

Additionally, illness onset date was missing for a large proportion of cases identified from 2010 through 2013. For those cases, the specimen collection date was used to approximate the month of illness onset. However, specimens may be collected weeks or months after the onset of the acute illness. Travel history among cases with available data showed the majority of cases with travel to India and other countries in Southeast Asia. Travel history was missing for a large proportion of identified cases; it is not known how representative the available data are for all cases.

There are several limitations to this analysis. It is likely that the number of chikungunya virus infections in the United States is underestimated for a number of reasons. Patients with chikungunya virus infection may not seek medical attention, particularly those patients with mild symptoms. Healthcare providers may not recognize the clinical features of chikungunya virus disease or submit specimens for appropriate testing. Diagnostic testing may not detect cases depending on when the specimen was collected and what testing was performed (e.g., specimen collected very early in the course of the illness but tested only for IgM antibodies). Studies have shown that anti-chikungunya virus IgM antibodies can persist for up to 18 months^{21,22}; therefore, some positive IgM results may reflect past rather than recent infections. We only identified cases tested at CDC, two state public health laboratories, and one commercial laboratory. As far as we are aware, these were the only laboratories in the United States that offered chikungunya virus testing during this time frame; however, it is possible that additional laboratories offer testing. There are no data comparing the relative sensitivity or specificity of the available diagnostic tests to further inform how the testing at different locations might have impacted the case ascertainment. For the purposes of this analysis, we presented data on the detection of chikungunya virus vectors at the state level. In fact, the distribution of the vectors may be limited to small geographic areas within a state. Additionally, the detection of vectors in some locations may reflect erroneous, single, or seasonal observations rather than established populations; these locations would presumably have lower risk of local chikungunya virus transmission following introduction by an infected traveler.

With the recent outbreaks in the Western Pacific and the Americas, the number of chikungunya cases among travelers visiting or returning to the United States from affected areas will likely continue to increase. These imported cases could result in additional local spread of the virus in the continental United States. Clinicians and public health officials should continue to be educated about the recognition, diagnosis, management, and timely reporting of chikungunya cases. Chikungunya virus infection should be considered in patients with acute onset of fever and polyarthralgia, especially those who have recently traveled to destinations with ongoing outbreaks. Because chikungunya and dengue viruses can circulate in the same area and cause similar clinical illnesses, these patients also should be evaluated and managed for possible dengue virus infection.^{1,23} Healthcare providers are encouraged to report suspected chikungunya infections to their state or local health department to facilitate diagnosis and to mitigate the risk of local transmission. Public health officials should perform surveillance for chikungunya cases in returning travelers and be aware of the risk of possible local transmission in areas where *Aedes* species mosquitoes are currently active. Further research is needed to better quantify the clinical,

economic, and public health impact of cases of chikungunya virus disease.

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