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Chikungunya Outbreak — Cambodia, February–March 2012

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What is already known on this topic?

The East/Central/South African strain of chikungunya has been emerging in Asia since 2006, first in the Indian Subcontinent, then Thailand. Little is known of the transmission dynamics of this chikungunya reemergence in Asia.

What is added by this report?

This report describes the epidemiology of a Chikungunya outbreak in a Cambodian village. The outbreak occurred 3 weeks after rains and lasted 3 weeks. The outbreak affected the entire village and all age groups; 44.7% of the population tested had evidence of infection by chikungunya virus (CHIKV). The investigation found an end-of-outbreak clinical attack rate of 73.4%, and a 5.3% proportion of asymptomatic infections.

What are the implications for public health practice?

Awareness of the location and extent of CHIKV infection can help guide health planning efforts and prioritization of resources for control, both in Cambodia and nearby, currently unaffected countries such as Laos or Vietnam.

Chikungunya virus (CHIKV) is an alphavirus transmitted to humans through the bite of infected *Aedes* mosquitoes (1). CHIKV causes fever and usually is not fatal, but can cause debilitating joint pains or, in rare instances, severe illness. The East/Central/South African strain of chikungunya has been emerging in Asia since 2006, first in the Indian subcontinent, then Thailand. This report describes the characteristics of a local outbreak linked with chikungunya reemergence in a rural Asian setting. Sporadic cases of chikungunya were identified in Cambodia in 2011 (2). Antibodies to CHIKV have been detected in serum collected in Cambodia in 2007, but the strain could not be identified for those cases (U.S. Naval Medical Research Unit 2, unpublished data, 2012). On March 7, 2012, several cases of rash with fever were reported among village residents of Trapeang Roka in Kampong Speu Province, Cambodia. Subsequent field investigation revealed that four of six blood samples from affected persons were positive for CHIKV by polymerase chain reaction (PCR) at U.S. Naval Medical Research Unit 2 in Phnom Penh. Investigators from the Cambodian Communicable Disease Control Department, National Malaria Center, Institut Pasteur du Cambodge (IPC), local health centers, and village authorities conducted a seroprevalence study of village residents on March 26 to gather information for response planning and control efforts. The outbreak affected families throughout the village, and 44.7% of the population tested had evidence of infection by CHIKV, which affected all age groups. Public health agencies and policymakers in affected and nearby unaffected areas of Asia and elsewhere should be alert to the potential spread and reemergence of CHIKV.

Trapeang Roka has a population of approximately 695 persons in 134 houses; most adults are farmers or factory workers. For the survey, the village was divided into six sectors created by the roads crossing through it. One team of investigators was assigned to each sector, and a central blood-sampling station was established. Teams worked outward from the center of the village, going from house-to-house. In each house, all occupants present were interviewed. Those who were in the field or factory rather than at home were interviewed when they returned to the village in the evening. Informed consent was obtained in the Khmer language from all adult residents and

parents or guardians of children; none refused to participate. A standardized questionnaire was used to gather information on demographics and recent (since the February 14–15 rains) or current self-reported symptoms including joint pains, fever >38°C (axillary or subjective), and rash. A clinical case was defined as one or more of these symptoms in a person from this village with onset after February 14 through March 26, 2012. Blood specimens were obtained for serologic testing; dried blood spots were collected from all persons surveyed and venous samples were collected from febrile patients. Confirmed cases had a positive laboratory test.

At IPC's Virology Unit, immunoglobulin M (IgM) antibody capture enzyme-linked immunosorbent assay (MAC-ELISA) testing was performed to detect anti-CHIKV IgM (3). Serologic testing also was performed by MAC-ELISA for recent infection by dengue (DENV) and Japanese encephalitis B (JEV) viruses (4). Positive serology for DENV and JEV pointed to recent flavivirus infection, which might present similar symptoms. Patients who were febrile at investigation also were tested by real-time reverse transcriptase PCR for CHIKV and also DENV and JEV. The 91 persons with recent or current symptoms who were negative for CHIKV IgM were screened for malaria by PCR.

The survey included 98 (73.1%) households distributed throughout the village. The team interviewed 425 persons (61.1% of village population; male:female ratio = 0.82); mean age was 26.4 years (range: 1 month–87 years; interquartile range: 10–39 years). Among the 425 persons interviewed were 96 (22.6%) farmers, 89 (20.9%) students, 91 (21.4%) factory workers, and 73 (17.2%) persons who stayed at home; the remaining 76 persons were preschool-aged children, construction workers, vendors, or pig farmers.

Of the 425 persons interviewed, 312 (73.4%) reported that they had at least one of the three defining symptoms since the rains of February 14–15, 2012 (Table). Among those 312 persons, 173 (55.4%) took leave from school or work. One death during that period was identified retrospectively in a woman aged 33 years with no known underlying disease. The woman had fever and intense joint pain, developed neurologic signs, and died within 2 hours of hospital admission. No samples were available for testing. Her two children were symptomatic, CHIKV IgM-positive, and seronegative for dengue and JEV.

MAC-ELISA tests identified CHIKV IgM in 188 (44.2%) of the 425 persons. Of the six febrile persons, venous blood samples could be analyzed from four: two had positive PCR results for CHIKV, bringing the total that were laboratory confirmed to 190 (44.7%) CHIKV-positives (Table). One person with fever and joint pains was positive for DENV-4. PCR results found traces of *Plasmodium* spp. nucleic acid indicative of incubating or recent malaria in one afebrile person. Of the 190 CHIKV-positive persons identified, 10 (5.3%) reported having none of the three defining symptoms.

The onset of the epidemic was protracted. Among 140 persons with self-reported fever who recalled an onset date and who had positive results for CHIKV (IgM or PCR), most reported onset occurring approximately 3–5 weeks after a 2-day period of rain (Figure 1). The epidemic curve suggested that the CHIKV outbreak began 3 weeks after the rains, lasted about 3 weeks, and was on the verge of ending when this serosurvey was conducted on March 26, 2012.

Laboratory results were analyzed by age group (Figure 2). The analysis revealed a 40% IgM seroprevalence among persons aged ≤5 years; for persons aged 6–45 years, IgM seroprevalence was approximately 50%, declining sharply for each age group after that. Circulation of at least two other viruses was identified, including 11 cases of DENV, seven cases of JEV, and 15 cases of undistinguishable flaviviruses (among these, 10, four, and eight cases, respectively, occurred among CHIKV-positive cases).

During a small-scale entomologic assessment conducted during March 29–30, 2012, 123 mosquitoes were collected in Trapeang Roka and 651 mosquitoes were collected from a wider area, including two nearby villages that also reported cases, based on syndromic data. *Aedes aegypti* comprised 41.4% and 53% of mosquitoes collected in the two areas, respectively, and *Culex* species comprised 21.1% and 13.8%, respectively; the rest were *Anopheles* species, and no *Aedes albopictus* were identified.

Editorial Note

The serosurvey in Trapeang Roka on March 26, 2012, documented a CHIKV outbreak in a medium-size rural Cambodian community of 695 residents. It is the first CHIKV serosurvey in Cambodia since the initial isolation of CHIKV in 1961, and the first known serosurvey conducted during a chikungunya outbreak in Southeast Asia. The experience of at least one symptom since the rains was reported by 73.4% of interviewees. CHIKV prevalence was 44.7%, and the prevalence of asymptomatic CHIKV infection was 5.3%. A temporal association was noted between

an unusually large rainfall on February 13–14 and the subsequent outbreak of cases of CHIKV beginning 3 weeks later and lasting for 3 weeks.

Most persons who were CHIKV-positive cases had clinical signs and symptoms consistent with chikungunya. The level of seroprevalence in this outbreak is consistent with levels from CHIKV serosurveys conducted during outbreaks (7), but lower than that of Lamu Island, Kenya (75%) (8). Seroprevalence was lower in persons aged ≥ 45 years. This might be the result of immunity acquired when the CHIKV Asian strain circulated in Cambodia in the 1960s. The only other published CHIKV serologic study from the Mekong region was conducted in the Bangkok area in 1998–1999 (9), before the emergence of the East/Central/South African genotype. In that study, the prevalence in mothers (using cord blood) was 31.6% and 45% in women aged >35 years. This new genotype, which emerged in Africa in 2004 and is emerging in Cambodia, is well known to have an E226V mutation that is more efficiently transmitted by *Ae. albopictus*.

The findings in this report are subject to at least four limitations. ~~First, cocirculating arboviruses (i.e., dengue and JEV) share the same vector and cause similar symptoms.~~ First, clinical cases of acute febrile illness might have been caused by other infectious etiologies, including other mosquito-borne viruses such as dengue and JEV, the incidence of which would have also risen after the rains. Some symptoms might have been caused by dengue or JEV infection. Some of the clinical cases, therefore, could have been caused by undetected viruses other than CHIKV, and this could explain why clinical cases outnumbered laboratory-confirmed cases. Second, CHIKV IgM seroprevalence might have been underestimated because of suboptimal sensitivity of tests performed on dried blood spots. Third, IgM screening might miss infection still in the incubation period. Finally, the presence of a large team of medical investigators in a rural village might have stimulated over-reporting of symptoms. These also might account for the difference between the clinical attack rate and CHIKV IgM-positive prevalence (approximately 30%).

CHIKV affects all age groups. While conducting the survey, investigators also provided education to help control the outbreak, which had nearly ended. The main vector identified in the historic Reunion Island outbreak was *Ae. albopictus*, the Asian tiger mosquito, but none were found in the current study area. The fact that *Ae. aegypti* were found, but not *Ae. albopictus*, is important for researchers working on biomolecular aspects of transmission of the new variant chikungunya. Awareness of the location and extent of chikungunya virus infection can help guide health planning efforts and prioritization of resources for control, both in Cambodia and nearby, currently unaffected countries such as Laos or Vietnam.

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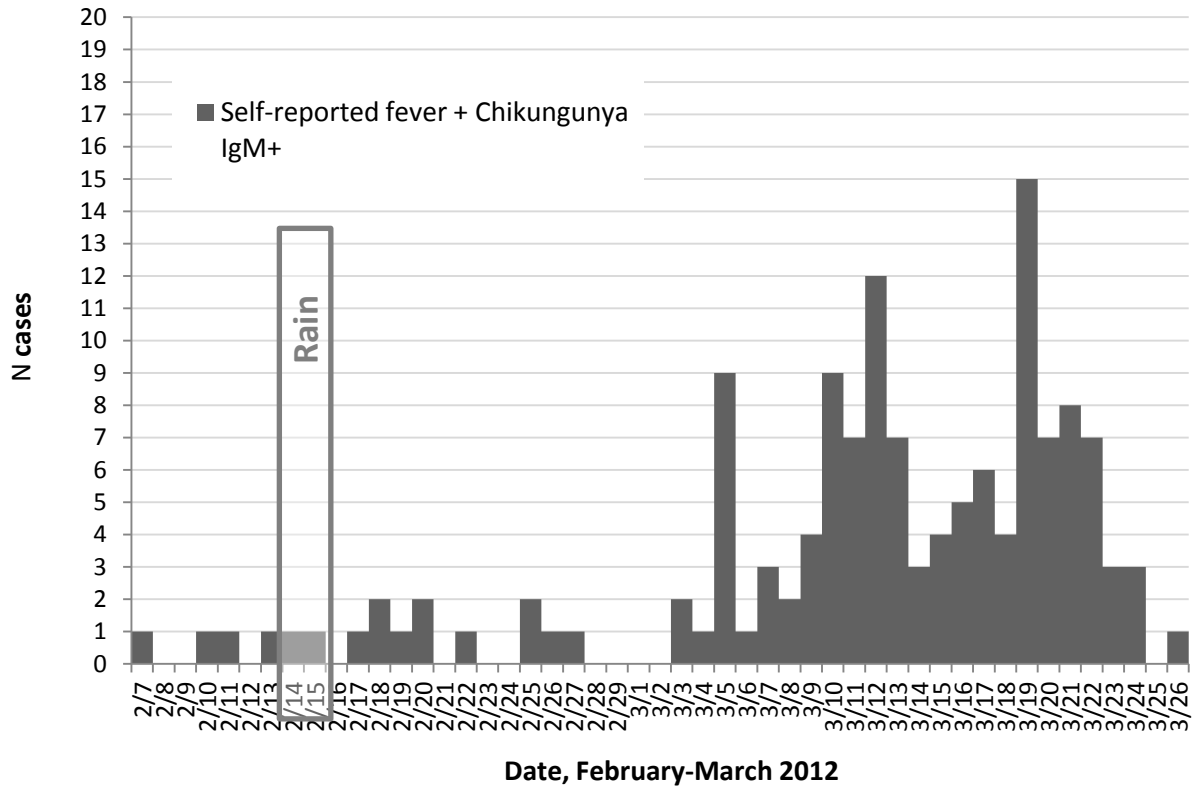
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TABLE. Chikungunya virus (CHIKV) serologic or polymerase chain reaction status and self-reported symptoms, recent or current, since February 14, 2012 — Trapeang Roka, Cambodia, March 2012

Symptoms	CHIKV-positive residents		CHIKV-negative residents		Total		Relative risk	
	(N = 190)		(N = 235)		(N = 425)		RR*	95% CI*
	No.	(%)	No.	(%)	No.	(%)		
Fever	163	(85.8%)	97	(41.3%)	260	(61.2%)	2.1	[1.8 – 2.4]
Skin rash	139	(73.2%)	52	(22.1%)	191	(44.9%)	3.3	[2.6 – 4.3]
Joint pain	159	(83.7%)	100	(42.5%)	259	(60.9%)	2.0	[1.7 – 2.3]
Any 2 symptom	178	(93.7%)	134	(57.0%)	312	(73.4%)	1.6	[1.5 – 1.9]
All 3 symptoms	126	(66.3%)	37	(15.7%)	163	(38.3%)	4.2	[3.1 – 5.8]

Abbreviations: RR = relative risk; CI = confidence interval. * Relative risk for self-reported symptom in CHIKV-positive residents and signs in CHIKV-negative residents.

FIGURE 1. Onset of fever among village residents who recalled an onset date and had laboratory confirmed cases of chikungunya virus (CHIKV) infection* — Trapeang Roka, Cambodia, February and March 2012



*Among these 140 persons with self-reported fever who recalled an onset date and who had positive laboratory results for CHIKV, most reported onset occurring approximately 3–5 weeks after a 2-day period of rain.

FIGURE 2. Prevalence of chikungunya immunoglobulin M (IgM) or polymerase chain reaction (PCR) positivity, by age group —Trapeang Roka, Cambodia, March 2012

