

Field Action Report

Incidence of Chikungunya Fever in Singapore: Implications of Public Health Measures and Transnational Movements of People

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Abstract: In addition to Dengue virus infection, another mosquito-borne viral infection has become a significant health hazard. After the first domestic case of Chikungunya fever was reported in the Republic of Singapore, the outbreak was brought under control in 18 days. Despite the quick and thorough public health measures including intensive vector control, this country known as a developed island state could not stop the subsequent outbreaks as both domestic and imported cases surged. Our in-depth investigation benefiting from field activities recapitulates the governmental interventions to control the re-emerging infectious disease. We discuss potential factors contributing to the subsequently increased cases in Singapore and then review strategies that other governments may consider in controlling vector-borne infectious diseases in urban areas with transnational movements of people.

Key words: Chikungunya, vector control, public health measures, transnational movements, Singapore

BACKGROUND

Chikungunya fever (hereinafter abbreviated as CF) is a mosquito-borne viral infection that is expanding its geographic distribution worldwide. Chikungunya virus (CHIKV) was first isolated in Tanzania in 1953; several African and Asian countries then experienced sporadic outbreaks of CF. The large-scale re-emergence in this century appears to have been triggered by outbreaks in Kenya in 2004. CF further spread to Indian Ocean islands in 2005, India in 2005 [1, 2] and Sri Lanka in 2006 [2]. As of March 2008, 35 countries including ten Southeast Asian countries have reported local CHIKV transmission [3], and some European [4] and North American countries have reported imported cases [5]. In addition, fatality and severe complications resulting from CF were documented from Italy [6], India [7], Reunion Island [8, 9] and Mauritius [10]. Since CF is typically self-limiting, far less attention has been paid to CF than other infectious mosquito-borne diseases such as malaria, dengue fever (DF) and dengue hemorrhagic fever (DHF).

Singapore is often described as a tropical “city-state” because of its role as an urban hub in the region with frequent movements of people and goods. The city-state is generally congested and its climate hot and humid, condi-

tions that allow the propagation of mosquitoes (*Ae. aegypti* and *Ae. albopictus*) serving as vectors of CHIKV and DF/DHF throughout the year [11]. The population of Singapore in 2008 was estimated to be 4,839,400, and the population density was 6,489 people per km². Approximately 80% of the population resided in public flats built by the Housing and Development Board of Singapore (known locally as HDB flats), 8% in private condominiums, 6% in landed property or compound houses, and the remaining 6% in other types of housing such as shop houses. The average annual temperature is 27 °C ranging from 23 °C to 34 °C; the average humidity is about 84%; and the average annual rainfall is 2,400 mm with the wettest months from November to January.

The Republic of Singapore is recognized for its comprehensive dengue vector surveillance and control system [12, 13]. The well-organized interventions by the government were reinforced after the 2005 dengue outbreak [14] and thus seem to have contributed to the current success [Yoshikawa, MJ, manuscript in preparation]. Fortunately, Singapore was able to quickly control the first domestic CF outbreak in January 2008, but it has suffered from subsequent domestic outbreaks as well as a large number of imported cases. This paper, therefore, retrospectively describes CF cases reported in the country for the first nine months of

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2008, reviews the governmental interventions in public health measures to control CF, and then attempts to discuss some possible strategies that may be relevant to the control of vector-borne diseases in developed urban areas like Singapore.

FIELD RESEARCH ACTIVITIES

This research benefited not only from literature but also from fieldwork such as interviews and on-site findings in Singapore: a series of meetings with personnel at the head office and its laboratory of the National Environment Agency (NEA) and the Ministry of Health (MOH) were carried out in March, May and September 2008. For example, we scrutinized Singapore's vector control tools by observing one of the regular on-site inspections including larval surveillance and adult trapping operations by the South East Regional Office of the NEA. The inspection on the day covered private houses and public high-rise residential buildings (HDB flats). The regular inspection provides the NEA with the necessary vector and environmental data to evaluate its vector control strategy and public education programs. At private houses, the inspectors climbed roofs to check gutters because choked gutters with stagnant water can produce attractive egg-laying sites for mosquitoes. In compliance with the NEA's community outreach efforts, the plates providing potential mosquito breeding sites were removed from the bottom of flower pots. Inspectors applied larvicide to the water drains between houses and streets as a preventive measure. At the HDB flats, problematic areas like the multi-story parking lot and other places shared by residents were carefully checked in addition to the rooftop and water tanks. The NEA inspectors took note of trays underneath air conditioners used by some residents as they tend to collect water. At both the individual houses and the HDB flats, public education measures were implemented to remind the residents of precautionary measures against mosquito-borne diseases. Additional details of the half-day inspection are available in a separate report [15].

Black plastic devices known as ovitraps are placed on selected floors of some HDB flats to attract female mosquitoes. The ovitraps are designed to collect eggs laid by female mosquitoes and then trap emerging adults within the containers. These devices are deployed in dengue-prone areas across the island to monitor *Aedes* mosquito activities. The use of ovitraps as a monitoring tool forms part of NEA's preventive surveillance regime. Checking them weekly enables NEA to detect the presence and types of mosquitoes and determine any increase in mosquito activities in a particular area. Indeed, NEA has been able to proactively remove mosquito breeding habitats in many areas

even before dengue cases were reported. Thus, it provides an early warning signal. Geographical information on the distribution of mosquito breeding sites is captured by NEA in Geographical Information System (GIS) maps for planning and analytical purposes. These activities of surveillance and rigorous "search and destroy" mosquito operations of NEA may explain why it is not very common for visitors from neighboring countries to complain of mosquito bites in Singapore.

FINDINGS

When Singapore identified the first domestic case of CF that progressed to an outbreak in January 2008, the outbreak was quickly controlled. Prior to the arrival of the new disease, Singapore implemented a laboratory-based surveillance network consisting of general practitioners and hospitals, and began an active surveillance as early as late 2006 during which blood samples testing negative for dengue virus by PCR were tested for CHIKV [11, 16]. Such a careful and thorough preparation, partly in response to the outbreaks in other countries, could account for Singapore's swift reaction in January 2008. As soon as the clinical network of surveillance detected the first domestic case, the MOH and the NEA initiated public health measures by collecting 2,626 blood samples and detected 12 additional cases [11; Table 1, press release on February 6]. The patients were treated at the Communicable Disease Centre, Singapore, which enabled the healthcare institution to monitor CHIKV in the patients to determine the timing of patient discharge and thus to prevent further transmission [11, 17], ensuring that the patient is no longer viraemic. The NEA examined the periphery of the patients' residences and destroyed over 87 mosquito breeding sites [11] with more than 4,800 inspections conducted. Five additional governmental and one private organizations with premises or land in the vicinity also participated to enhance intergovernmental efforts to prevent transmission of CF. These were the Urban Redevelopment Authority, Land Transport Authority, Singapore Land Authority, Ministry of Manpower, Public Utilities Board, and Singapore Construction Association Ltd. The strength of intersectoral collaboration among different agencies is an important component in integrated vector management. This allowed swift and thorough actions in Singapore but is relatively lacking in many other countries. The timely control strategy in Singapore appears to have resulted in termination of the first local outbreak at only the 13th case within 18 days in the area known as Little India.

However, a new outbreak with two cases occurred after five months and sporadic cases and outbreaks at various lo-

Table 1. Domestic and imported CF cases in Singapore from January to September 24, 2008*.

Date of press release	Breakdown of domestic cases		No. of cumulative cases	
	No. of new cases reported	Cases detected by active surveillance	Domestic cases	Imported cases
Feb 6	13	0	13	0
Jun 7	2	0	15	8
Jun 12	1	0	16	8
Aug 1	1	0	17	31
Aug 2	3	0	20	31
Aug 6	1	18	39	35
Aug 8	10	0	49	46
Aug 13	5	0	54	49
Aug 16	7	2	63	54
Aug 19	4	0	67	61
Aug 25	10	3	80	70
Sep 5	12	0	92	86
Sep 12	11	0	103	97
Sep 17	13	0	116	102
Sep 25	7	0	123	108
Total	100	23	123	108

* Source: National Environmental Agency, Singapore and Ministry of Health, Singapore.

cations followed thereafter; amounting to 123 domestic cases by September 24, 2008 [18]. Table 1 summarizes the chronology of the domestic cases and imported cases. The new outbreak started with two cases reported to the MOH on June 3 and June 5 [Table 1, press release on June 7]; both individuals resided within the same household in the Teachers Housing Estate [19]. Soon, the screening of persons living or working in the estate and laboratory tests of blood samples began. The Environmental Health Department of the NEA inspected more than 100 premises and identified 10 breeding sites, while the health authorities advised those who visited the estates to consult doctors upon developing fever [19]. Hence, the control measures applied in June were essentially the same as the ones in January, but these did not succeed in stopping the subsequent domestic cases. Concurrently, there was continual importation of cases following outbreaks in neighboring countries; 108 imported cases were recorded for the January 1 to September 24, 2008 period. These patients arrived in Singapore from (the patient numbers in parentheses): Johor (87) and other states of Malaysia (12), Indonesia (4), Sri Lanka (2), India (2) and the Maldives (1) [18].

POTENTIAL FACTORS CONTRIBUTING TO RECENT INCREASE IN CF CASES IN SINGAPORE

The initial outbreak in January was brought under control in 18 days, but the same intervention measures did not stop the subsequent outbreaks. We analyze and discuss the factors responsible for the ineffectiveness of the intervention which was successful initially.

The first factor is the ongoing expansion of areas infected by CHIKV across continents. In March 2005, researchers reported an outbreak on French Reunion Island in the Indian Ocean, with over 150,000 CF cases in 12 months [20]. Imported cases were reported in Canada, the Caribbean, Guyana in South America and the United States [5, 21]. An imported case in Italy was followed by domestic cases [22, 23]. CF also reached South Asia, India and Sri Lanka suffering outbreaks in 2005-2006 [1, 2]. In East Asia, Hong Kong confirmed an imported case [24] while Japan recognized two imported cases in December 2006 [25]. CHIKV has thus expanded its geographical distribution rapidly in the past five years. As Singapore is a traveling hub with millions of visitors arriving and departing yearly, the geographical expansion of CHIKV poses a serious threat to the island state.

The second factor is the grave situation in countries neighboring Singapore since 2006. Intensive and coincidental outbreaks of CF have been observed in Southeast Asia. For example, Malaysia appears to have renewed the record of CF cases in 2008 [26]. In Johor, Singapore's immediate neighbor, 771 cases were reported by August 16 [27] and 1,169 CF cases by September 2008 [28]. Not all Malaysian cases, however, may have originated abroad. As for the outbreaks in the west of Ipoh in Perak, Malaysia where 200 villagers were infected between March and April 2006, researchers have suggested the re-emergence of CF of domestic origin, tracing Malaysia's first known CF outbreak to 1998-1999 when more than 50 cases were recorded in Port Klang [29]. These findings suggest that more than one strain of CHIKV is spreading in Southeast Asia: one introduced from the Indian Ocean recently, other(s) persisting since the last century, and perhaps many more. Each day, thousands of Malaysians commute to Singapore. Likewise, hundreds of Singaporeans cross the border into Malaysia for business and social visits. Such large and frequent transnational population movements are another possible route of CHIKV transmission between and around the two countries.

The third factor is the increase in reported cases in Singapore due partly to active surveillance. The cases reported as a result of the active surveillance in Singapore make up almost 19% of the 123 domestic cases (Table 1). Similarly,

the imported cases up to September 2008 showed a sharp rise to 108 from 10 in 2007. It can be inferred that the reported cases in Singapore increased in part due to health-seeking behavioral changes among residents viewing frequent press releases and warnings from MOH and NEA as well as media reports. It is possible that asymptomatic and even some symptomatic cases went undetected before CF attracted much attention. This is probably because of the self-limiting nature of the majority of cases, not misdiagnoses as DF/DHF, since laboratory confirmation of all reported DF/DHF cases is conducted in Singapore. It is highly probable that local transmissions had already existed before the outbreak in Little India in January 2008. Researchers in Taiwan submitted an intriguing phylogenetic tree analysis of a CHIKV isolated from a 13-year-old Taiwanese student who had been identified as an imported CF case returning from Singapore on November 20, 2006 [30]. The result suggested that he had been infected with East/Central/South African genotype of CHIKV in Singapore.

The fourth factor is mutations that may increase the virulence of CHIKV to humans and/or increase the competence of the vector mosquitoes. It has been suggested that the large outbreak in Reunion Island was the result of A226V mutation in the genome of the CHIKV and adaptation to an additional vector, *Ae. albopictus* [11, 31]. The mutated virus might have brought a scourge to Singapore as well. The first domestic outbreak in the Little India area in January was transmitted by *Ae. aegypti* [16]. An interview at NEA in September 2008, however, revealed an important change; CHIKV in Singapore could now be mediated by *Ae. albopictus*. The subsequent outbreaks showed that the virus with the A226V mutation has spread and that most of the breeding sites uncovered were those of *Ae. albopictus*. Achieving substantial reduction of the native species or *Ae. albopictus* on the island by interventions over the short-term is extremely difficult since the vector population exists in a wide range of outdoor environments, unlike *Ae. aegypti* which inhabits the interior and periphery of buildings and therefore is more manageable. As shown in Table 2, the 123 domestic cases were reported from more than 11 work/residential locations [18] including the vegetated areas conducive for breeding and harborage. After NEA confirmed the additional vector of CHIKV, the agency modified the strategy against CF, including wider geographical target area for surveillance and control as well as more frequent use of outdoor fogging. The control of *Ae. albopictus* will, however, continue to be a big challenge for a country like Singapore that places strong emphasis on greenery in its urban planning policies.

Table 2. Location and number of domestic cases of CF in Singapore from January 1 to September 24, 2008*.

Location	No. of domestic CF cases
Little India	13
Kranji Way	41
Sungei Kadut	21
Lim Chu Kang	10
Bah Soon Pah Road	8
Pasir Panjang Wholesale Market	5
Mandai Estate	4
Teacher's Estate	2
Seletar Farmway	2
Bangkit Road	2
Others	15
Total	123

*Source: Ministry of Health, Singapore; news press release on September 25, 2008.

IMPLICATIONS OF SINGAPORE'S EXAMPLE

The challenges faced by the Singapore authorities in controlling CF testify to the difficulty of eliminating the importation of infectious diseases and the necessity for continuous improvements in the response to additional vectors and other epidemiological changes in today's globalized world. Any country inhabited by *Ae. albopictus* must quickly establish control measures. One imported case of CF into *Ae. albopictus*-inhabiting Italy was enough to cause a local outbreak of more than 200 cases [32]. This example is significant for Japan where *Ae. albopictus* species exist and where it remains rather uncommon for residents to associate mosquitoes with risks of infectious disease. Much more attention and cooperation are required especially from the individuals traveling to endemic areas to ensure precautionary measures. Two imported cases of CF were already recorded in Japan in December 2006; one was a Japanese female in her 30s living in Sri Lanka, and the other was a Japanese female in her 50s who visited Sri Lanka for one week [33]. A 37-year-old Japanese male returning from India was detected as the third case when he sought medical consultation in Osaka in September, 2008 [34]. As for DF/DHF, imported cases exceeded 375 in Japan between April 1999 and July 17, 2007 including 18 DHF cases [25]. Fortunately, 5,442 mosquitoes captured in the vicinity of four Japanese international airports between 2004 and the first five months of 2007 were found to be negative for flavivirus [25]. Prevalent mainly in summer from the southern prefecture of Okinawa to the northern prefecture of Akita, *Ae. albopictus* is said to be the most probable species that bite humans living west of the Kanto region [35]. Indeed, this par-

ticular mosquito species mediated DF outbreaks in the prefectures of Nagasaki, Hiroshima, Hyogo and Osaka [36, 37] in western Japan between 1942 and 1945 [25]. The statistics reported by health authorities at the time show 17,000 cases, but the true disease incidence could have reached 100,000 [36, 38]. A few signs have already emerged indicating that history repeats itself. The Kansai Airport Quarantine Station in western Japan alone detected eight imported cases of dengue virus infection out of 158 blood samples between 2005 and 2007 [39].

Establishing an effective monitoring system of imported cases remains a difficult and sensitive task for any government. The mobility of people in Singapore is characterized by transnational movements, especially huge influxes of foreign labor. Notably, the large number of domestic cases in Singapore was represented by foreign workers according to the details published by the authorities in press releases. The Kranji Way cases in Singapore, for example, involved a number of foreign workers who crossed the border every day [40]. According to a molecular epidemiological study conducted by Singapore's reference laboratory for Chikungunya, Environmental Health Institute, CHIKV isolated from the patients in Singapore were genetically heterogeneous. The strain that caused the first local outbreak in Little India was related to the one that had spread to India, but the strain in Farrer Road cases seemed to have the same origin as that isolated in Sri Lanka. The strains isolated from the cases in the Teacher's Housing Estate, Jalan Jelita, Kranji Way, and Miltonia Close were identical to those observed among patients in Malaysia [26]. The laboratory findings suggest that the termination of continuous flow of CHIKV hosts may not be achievable unless labor movements and overseas travel are prohibited. Clearly, neither option is realistic, while the cost of no action is obviously high. As far as outbreaks exist in the neighboring region, Singapore cannot be liberated from this dilemma. The struggle of the well-prepared and rapidly responding Singapore indicates that governments should establish, review, and strengthen capacity to respond to and minimize the impact by, for example, implementing effective vector control systems and measures to prevent subsequent outbreaks originating from imported cases. DF occurred in 1779-1780 and DHF first appeared in the 1950s [41]. Although it took dengue virus more than 170 years to develop into the more severe form, CHIKV might mutate and further increase in virulence or adapt to additional vectors much faster in today's highly populated and urbanizing environment.

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the potential factors contributing to the recent increase in CF cases in Singapore that we discussed above, especially multiple strains of CHIKV in circulation, mutation of viruses, and additional vector competence.

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