INTRODUCTION

Chikungunya fever is an arboviral infection transmitted by *Aedes aegypti* and *Aedes albopictus*. “Chikungunya” means “that which bends up” in the language of the Makonde ethnic group from northern Mozambique where it was first described in 1952 and in reference to the stooped posture of chikungunya patients experiencing severe joint pain. It is an acute illness most commonly characterized by fever and joint pain and less commonly, joint swelling, headache and rashes. In some cases, chronic arthralgia may persist for months. There is currently no vaccine or antiviral treatment for chikungunya.

After the isolation of chikungunya virus (CHIKV) in southern Tanzania in 1952, it continued to circulate in West and East Africa at relatively low levels. It subsequently spread throughout South and Southeast Asia in three waves with the first wave during the 1960s and 1970s (involved mainly South Asian countries such as India and Sri Lanka); the second wave during the 1980s and 1990s (involved mainly Southeast Asian countries, namely Philippines, Thailand, Myanmar and Indonesia); and the most recent wave during the last decade (involved mainly South Asia). This wave was heralded by successive outbreaks involving the Indian Ocean islands (Comoros, Madagascar, Mayotte, Mauritius, La Reunion and the Seychelles) in 2005. Subsequently, Sri Lanka reported outbreaks in 2006 and 2007. India saw a surge in cases in 2006 which continued into 2008, 2009 and 2010. Southeast Asia also experienced outbreaks in Indonesia from 2001 to 2003 and in Thailand from 2008 to 2009.
Three distinct genotypic clades [West African, Asian, and East/Central/South African (ECSA)] of CHIKV are recognized. However, in the last decade, the ECSA strain alone has been implicated in almost all major outbreaks involving Africa, South Asia and Southeast Asia.

Malaysia reported its first outbreak of chikungunya fever from 1998 to 1999 in Port Klang, Selangor State, and the second outbreak in Bagan Panchor, Perak State in March 2006. Genetic studies of CHIKV isolates from both outbreaks showed clustering with known Asian lineages distinct from those of the ongoing epidemics in India and the Indian Ocean Islands, suggesting endemic transmission of CHIKV in Malaysia. The third outbreak in Malaysia occurred in Ipoh (Perak State) in December 2006. The index case was found to have travelled to India and this outbreak marked the first time the ECSA strain was isolated in Malaysia. More recently, Malaysia experienced a nationwide outbreak of at least 7000 cases of chikungunya fever from 2008 to 2009. The CHIKV isolates from the outbreak which began in Johor State were linked to the ECSA strain.

In view of the regional resurgence of chikungunya fever, Singapore took a pre-emptive approach to prevent its introduction into the country. The medical community in Singapore was alerted of the regional chikungunya situation and advised to consider chikungunya fever as a differential diagnosis for dengue fever. By December 2006, an active laboratory-based surveillance system was set up among a sentinel network of general practitioners (GPs) and in two restructured hospitals. With this system, blood samples found to be negative for dengue PCR were routinely tested for CHIKV by reverse-transcriptase-polymerase chain reaction (RT-PCR) at Environmental Health Institute (EHI), National Environment Agency (NEA). Laboratory diagnosis of chikungunya fever by PCR and serology was also made available at the Defence Medical and Environmental Research Institute (DMERI), Defence Science Organisation (DSO). In addition, chikungunya fever was made a legally notifiable disease on 19 December 2008, and a passive surveillance network was established.

After the surveillance system was put in place, sporadic imported chikungunya cases began to appear in Singapore. The first local outbreak occurred in January 2008 and was successfully contained. However, the success was short-lived as clusters of locally-acquired cases began to erupt island-wide throughout 2008 and 2009. The situation took a turn for the better in 2010 with the lowest number of 26 cases reported in the year.

We conducted a review of the chikungunya fever situation from 2006 to 2010 in Singapore to determine the epidemiological characteristics and progression of the outbreak. We also described the measures taken to prevent chikungunya from establishing itself as an endemic disease in Singapore.

Materials and methods

All the relevant epidemiological data and outbreak reports maintained by the Communicable Diseases Division, Ministry of Health (MOH) from 2007-2010 were collated and analysed. We defined a case of chikungunya fever as one who presented with an acute febrile illness of at least 37.5°C, with or without joint pain, and whose blood sample was either tested positive for CHIKV by RT-PCR or showed a four-fold rise in anti-CHIKV IgG antibody titres from acute and convalescent samples taken at least...
14 days apart. We also included clinically-compatible cases with a positive anti-CHIKV IgM result if they were epidemiologically-linked to a laboratory-confirmed case.

A chikungunya cluster was defined as two or more laboratory-confirmed cases epidemiologically linked by person, place and time. Cases were further classified as imported if they had a history of travel to a known outbreak or endemic area up to 12 days prior to the onset of symptoms. Those who had no prior history of travel were classified as locally-acquired/indigenous cases.

At the NEA, the location of all notified cases and Aedes breeding sites were plotted using the Geographic Information System (GIS) to identify foci of transmission to facilitate vector control. When cases or clusters were notified, trained environmental health officers were mobilised to carry out our vector surveillance and “search and destroy” operations which included indoor ultra low volume insecticide misting and outdoor thermal fogging. The principal vector of each cluster was defined as the predominant larval species recovered and identified in cluster areas.

Data analysis was conducted using Statistical Package for Social Sciences (SPSS) Version 17.0 (SPSS Inc., Chicago, IL). The incidence rates of indigenous cases, expressed as per 100,000 population, were calculated using the estimated mid-year population of the corresponding year obtained from the Department of Statistics, Singapore. The annual risk of acquiring travel-associated CHIKV among residents from 2007 to 2009 was calculated based on the number of resident departures to the destination country in that year and expressed as per 100,000 departures. The annual rate of CHIKV imported into Singapore by foreigners from 2007 to 2009 was calculated based on visitor arrivals from specific countries for that year. Differences in proportion of demographic variables were compared using 2-sample independent z-tests, with standard error estimated using pooled value of the independent proportions. A p value less than 0.05 was considered as statistically significant.

Results

Epidemiological features

On 6 November 2006, Singapore reported its first case of chikungunya fever. On further investigation, the case was found to be imported from India. Since then, sporadic imported cases continued to surface until the first indigenous case occurred on 14 January when a GP from the sentinel surveillance network notified MOH of a case with no travel history out of Singapore for several months and working and living in Little India. Subsequently, another 12 indigenous cases clustering around the same locality were reported. The outbreak was successfully contained and declared over on 21 February 2008.

This was followed by a quiescent period of three months until May 2008 and June 2008 when local transmission was reported in two suburban areas (Teachers’ Estate, 2 cases and Farrer Road, 1 case). No further cases were detected in these locations despite extensive case surveillance which included mass blood screening of the household, neighbourhood and close contacts. Following this period of sporadic local transmission, July 2008 heralded the occurrence of two large outbreaks in the northwestern rural industrial areas of Singapore (Kranji Way, 42 cases, 14 July 2008 to 3 September 2008 and Sungei Kadut, 61 cases, 3 August 2008 to 18 January 2009). Chikungunya subsequently spread towards the central and southwestern areas of Singapore.
Chikungunya was sporadically imported into Singapore in late 2006, followed by sporadic local transmission and subsequently, sustained local transmission, and back to sporadic local transmission since third quarter of 2009 (Fig 1). A total of 1,098 cases comprising 280 (25.5%) imported cases and 818 (74.5%) indigenous cases were reported between 2006 and 2010 (Table 1). Together with the Kranji Way and Sungei Kadut clusters, the clusters at Tanjong Kling (61 cases, 25 December 2008 to 28 February 2009), Jalan Papan (49 cases, 11 November 2008 to 20 January 2009) and Leedon Heights (26 cases, 19 November 2008 to 13 February 2009), made up the five largest clusters in Singapore and accounted for about a third of all the indigenous cases.

**Imported cases**

All age groups were affected, with most of them aged 55 years and above (25.3%), and 25-34 years (23.9%). Majority (59.6%) of the cases were males. More local residents (62.9%) than foreigners (37.1%) were affected (Table 1).

Among local residents, 59.7% were Chinese; 19.9%, Malays; and 16.5%, Indians. Most residents had travelled to Malaysia (76.7%), followed by India (16.5%) and Indonesia (4.5%). Other countries implicated included Myanmar (1 case), Philippines (2 cases) and Thailand (1 case). The most common reasons for travel among residents were vacation (75.0%), social visits (17.6%) and work (4.5%). Among residents, the rate of importation of cases for travels to India increased from 5.4 per 100,000 departures in 2007 to 12.2 per 100,000 departures in 2009 (Table 2). In the case of travels to Malaysia, the rate decreased from 1.03 per 100,000 departures in 2008 to 0.18 per 100,000 departures in 2009.

Most imported cases brought into Singapore were from Malaysia (55.8%), followed by India (23.1%) and Indonesia (9.6%). Other countries im-
Table 1
Epidemiological characteristics of reported chikungunya fever cases in Singapore, 2006-2010

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Imported cases</th>
<th>n (%)</th>
<th>Indigenous cases</th>
<th>n (%)</th>
<th>Incidence per 100,000</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>2008 (n=537)</td>
<td>2009 (n=275)</td>
<td>2010 (n=6)</td>
</tr>
<tr>
<td>Total</td>
<td>280 (100)</td>
<td>818 (100)</td>
<td>11.1</td>
<td>5.5</td>
<td>0.1</td>
</tr>
<tr>
<td>Age group (yrs)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-4</td>
<td>1 (0.4)</td>
<td>4 (0.5)</td>
<td>1.4</td>
<td>0.5</td>
<td>0</td>
</tr>
<tr>
<td>5-14</td>
<td>11 (3.9)</td>
<td>18 (2.2)</td>
<td>2.0</td>
<td>1.6</td>
<td>0</td>
</tr>
<tr>
<td>15-24</td>
<td>17 (6.1)</td>
<td>119 (14.5)</td>
<td>9.0</td>
<td>6.0</td>
<td>0.1</td>
</tr>
<tr>
<td>25-34</td>
<td>67 (23.9)</td>
<td>237 (29.0)</td>
<td>14.6</td>
<td>7.5</td>
<td>0.4</td>
</tr>
<tr>
<td>35-44</td>
<td>52 (18.6)</td>
<td>202 (24.7)</td>
<td>17.2</td>
<td>6.4</td>
<td>0</td>
</tr>
<tr>
<td>45-54</td>
<td>61 (21.8)</td>
<td>118 (14.4)</td>
<td>11.2</td>
<td>6.1</td>
<td>0.1</td>
</tr>
<tr>
<td>55+</td>
<td>71 (25.3)</td>
<td>120 (14.7)</td>
<td>10.5</td>
<td>4.8</td>
<td>0</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>167 (59.6)</td>
<td>640 (78.2)</td>
<td>16.9</td>
<td>8.1</td>
<td>0.1</td>
</tr>
<tr>
<td>Female</td>
<td>113 (40.4)</td>
<td>178 (21.8)</td>
<td>4.7</td>
<td>2.7</td>
<td>0.1</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-residents</td>
<td>104 (37.1)</td>
<td>519 (63.4)</td>
<td>28.4</td>
<td>13.9</td>
<td>0.4</td>
</tr>
<tr>
<td>Residents</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chinese</td>
<td>105 (37.5)</td>
<td>253 (30.9)</td>
<td>6.1</td>
<td>3.1</td>
<td>0.04</td>
</tr>
<tr>
<td>Malay</td>
<td>35 (12.5)</td>
<td>8 (1.0)</td>
<td>1.0</td>
<td>0.6</td>
<td>0</td>
</tr>
<tr>
<td>Indian</td>
<td>29 (10.4)</td>
<td>25 (3.1)</td>
<td>5.3</td>
<td>2.3</td>
<td>0</td>
</tr>
<tr>
<td>Others</td>
<td>7 (2.5)</td>
<td>13 (1.6)</td>
<td>7.8</td>
<td>4.2</td>
<td>0</td>
</tr>
<tr>
<td>Housing type</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Compound house</td>
<td>-</td>
<td>203 (24.8)</td>
<td>31.8</td>
<td>22.1</td>
<td>1.1</td>
</tr>
<tr>
<td>Public housing apartment</td>
<td>-</td>
<td>200 (24.5)</td>
<td>3.7</td>
<td>1.8</td>
<td>0.1</td>
</tr>
<tr>
<td>Condominium</td>
<td>-</td>
<td>50 (6.1)</td>
<td>10.0</td>
<td>5.0</td>
<td>0</td>
</tr>
<tr>
<td>Others**</td>
<td>-</td>
<td>365 (44.6)</td>
<td>41.9</td>
<td>17.3</td>
<td>0</td>
</tr>
</tbody>
</table>

* There were no indigenous cases prior to 2008.
** Refers to temporary residences and dormitories
Table 2
Number of imported cases and rate of importation of chikungunya fever per 100,000 departures among residents in Singapore, 2007-2009

<table>
<thead>
<tr>
<th>Country visited</th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>Rate</td>
<td>n (%)</td>
</tr>
<tr>
<td>Indonesia</td>
<td>0 (0)</td>
<td>0</td>
<td>4 (3.3)</td>
</tr>
<tr>
<td>Malaysia</td>
<td>0 (0)</td>
<td>0</td>
<td>114 (93.4)</td>
</tr>
<tr>
<td>Thailand</td>
<td>0 (0)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>India</td>
<td>5 (100)</td>
<td>5.38</td>
<td>3 (2.5)</td>
</tr>
<tr>
<td>Others**</td>
<td>0 (0)</td>
<td>-</td>
<td>1 (0.8)</td>
</tr>
</tbody>
</table>

* Number of outbound travels to India in 2009 was calculated based on average percentage change from 2006 to 2008.
** Refer to Philippines (2008), Myanmar (2009)

complicated included Sri Lanka, Maldives, Myanmar and Cambodia. The rate of importation by foreigners from Malaysia increased from 0.15 per 100,000 arrivals in 2007 to 7.88 per 100,000 arrivals in 2008 and subsequently declined to 0.92 per 100,000 arrivals in 2009 (Table 3). On the other hand, the rate of importation from India increased from 0.13 per 100,000 arrivals in 2007 to 2.34 per 100,000 arrivals in 2009.

Indigenous cases

All age groups were affected with the incidence rates increasing with age, peaking in the 25-34 years and 35-44 years age groups and gradually declining thereafter. The incidence rates were highest among non-residents and males had three or more times higher incidence rate than that of females. Residents of compound houses and temporary housing had higher incidence rates compared with residents of public housing apartments and private condominiums (Table 1).

Comparing the demographic characteristics between imported and indigenous cases, a greater proportion of males were affected and there were more non-residents among the indigenous cases. Significant differences were observed in the age groups 15-24 years, 35-44 years, 45-54 years, and 55 years or older (Table 1).

Entomological features

When local transmission of CHIKV first occurred at Little India in January, 2008, the principal vector implicated was *Aedes aegypti*. However, at the Teacher’s Estate cluster, as well as the large clusters at Sungei Kadut and Kranji Way, *Aedes albopictus* was the main vector implicated and CHIKV was isolated from field caught adult female mosquitoes. *Aedes albopictus* accounted for 57 (60.6%) of the 94 clusters identified in 2008 and 2009; *Aedes aegypti*, 6.4%; and both species, 3.2%. No *Aedes* larvae were detected for the remaining clusters. The highest larval counts for *Aedes albopictus*, numbering 73,993 and 19,923 were recorded at the Sungei Kadut and Kranji Way clusters, respectively. The clusters were distributed mainly in the northwestern, central and...
southwestern parts of Singapore where *Aedes albopictus* was the more prevalent vector (Fig 2).

**Outbreak response and vector control**

The strategy adopted in the early stages of the outbreak was that of containment. Every reported case was isolated in hospitals until no longer infectious. Active case detection, including mass blood screening exercises, was also conducted in response to every suspected and confirmed case. Extensive ‘search and destroy’ vector control operations were carried out in the cluster areas. This all-out approach was successful in containing the first cluster at Little India where *Aedes aegypti* was the primary vector. However, as more clusters began to emerge, the increasing number of indigenous cases made it logistically impossible to continue this all-out approach. The strategy was shifted to mitigating the public health impact of chikungunya by channelling all available resources to high-risk areas.

**Table 3**

<table>
<thead>
<tr>
<th>Country of origin</th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>Rate</td>
<td>n (%)</td>
</tr>
<tr>
<td>Thailand</td>
<td>0 (0)</td>
<td>0.00</td>
<td>0 (0)</td>
</tr>
<tr>
<td>India</td>
<td>1 (20.0)</td>
<td>0.13</td>
<td>1 (1.7)</td>
</tr>
<tr>
<td>Sri Lanka</td>
<td>0 (0)</td>
<td>0.00</td>
<td>3 (5.1)</td>
</tr>
<tr>
<td>Others*</td>
<td>2 (40.0)</td>
<td>-</td>
<td>1 (1.7)</td>
</tr>
</tbody>
</table>

*2007: Maldives (2); 2008: Cambodia (1); 2009: Myanmar (1), Maldives (2)

**Figure 2**

Distribution of chikungunya clusters and (a) *Aedes aegypti* and (b) *Aedes albopictus* breeding sites, 2008-2009
The passive surveillance network was enhanced by alerting and updating medical practitioners of the latest situation, especially GPs operating in clinics close to the cluster areas. Using GIS, localities where foreign workers congregated, such as work places and dormitories with high *Aedes albopictus* population were marked out for intensive vector surveillance and control operation. All potential *Aedes* breeding habitats were either destroyed or treated with larvicides and outdoor thermal fogging and residual spraying of internal walls of premises were stepped up. Residents and foreign workers were educated on the common peridomestic and outdoor breeding habitats of *Aedes albopictus*, and the measures to be taken to destroy the habitats.

**Comments**

CHIKV might have been introduced into Singapore as early as the 1960s, when the disease first emerged in the Southeast Asian region. During an outbreak of viral hemorrhagic fever in Singapore in 1960, one patient was incidentally tested positive for antibodies to CHIKV. Subsequently, in a serological study conducted on 531 young healthy adults at the DMERI in 2002-2003, two (0.4%) were tested positive for antibodies against CHIKV. Despite suggestions of the presence of CHIKV in Singapore, it was not recognized as a public health problem until laboratory diagnostic methods were available in late 2006. Coincidentally, at around the same time, Taiwan reported its first imported case of chikungunya fever in a student who was returning from Singapore, whose fever was detected by thermal scanners at the airport.

Malaysia and India were the biggest sources of imported cases. Malaysia’s most recent outbreak occurred from 2008 to 2009, at the same time when cases were exported from Malaysia to China and Japan. Singapore, located within close proximity to Malaysia, recorded about 11 million outbound travels to Malaysia (including about 9 million same-day travels) in 2008. Genetic findings in viral isolates confirmed the importation of cases from Malaysia into Singapore. It is not surprising then that the chikungunya situation in Singapore mirrored that of Malaysia with the rate of imported cases among both residents and foreigners increasing and decreasing in tandem with the changing epidemiology of the disease there. Together with the marked decline in the disease incidence in the affected states in Malaysia (as indicated by the 9-fold reduction in the rate of importation by foreigners from 7.88 per 100,000 arrivals in 2008 to 0.92 per 100,000 arrivals in 2009), the rate of importation by local residents dropped by 6 times from 1.03 per 100,000 departures in 2008 to 0.18 per 100,000 departures in 2009.

The rate of importation of cases from India among residents and foreigners was highest in 2009, although the incidence in India had declined from 95,091 cases in 2008 to 73,288 cases in 2009, and further decreased to 22,356 in first 10 months of 2010. This could be due to increasing exposure of Singapore residents travelling to active CHIKV transmission localities in India, as well as foreigners coming to Singapore from these areas.

Based on the epidemiological data of the indigenous cases collected and analysed, foreigners working in high *Aedes albopictus*-infested areas and living in temporary housing quarters were identified as a high-risk population group. There are about a million foreign workers (about 36% of the total workforce), distributed in the service, manufacturing and construction industries. As a result, more vector surveillance and control efforts were directed at the
work places and living quarters of foreign contract workers to eliminate all potential *Aedes* breeding habitats. Health education on environmental hygiene and sanitation and good housekeeping efforts were focused in these high-risk areas to ensure that areas where foreign workers congregate are not receptive to the introduction and spread of CHIKV. All these measures helped to prevent the risk of CHIKV transmission to other parts of the country.

The rapid spread of CHIKV in Singapore was due to the introduction of a mutated virus with substitution of alanine to valine at codon 226 (A226V) of the E1 gene. This phenomenon was also observed in outbreaks in Gabon, La Reunion Island, Italy, India, Thailand and Malaysia. When the first local transmission occurred at Little India in Singapore, the virus which was imported from India did not show such a mutation. However, CHIKV isolates from subsequent clusters where *Aedes albopictus* was the predominant vector showed the A226V mutation. Although this mutation has not been shown to increase disease virulence, it allows *Aedes albopictus* to supplant *Aedes aegypti* as the primary vector for CHIKV by lowering the oral dose required for the virus to infect *Aedes albopictus* and by increasing viral dissemination into its salivary glands. This means that infection of mosquitoes during blood meals could occur at lower threshold viremic levels, and hence for longer periods. The emergence of A226V mutation with *Aedes albopictus* as the primary vector, has implications on disease control as unlike *Aedes aegypti*, it is both endophagic and exophilic. As soon as this emerging trend was recognised, vector control strategy was revised to target at *Aedes albopictus*, rather than *Aedes aegypti* as in the case of the Little India cluster. By taking into consideration the flight range of *Aedes albopictus*, the area of vector operation was immediately extended from 150m to 300m radius from the foci of transmission. The successful control of the outbreak was evident in early 2009 when cases dropped sharply from January onwards (Fig 1).

It should be noted that chikungunya fever outbreaks globally have been observed to burn-out after a period of intense transmission, only to recur after years of quiescence. Although the period of quiescence can be explained genetically as the duration needed for the virus to acquire mutations which confer a survival advantage, it is not known why these outbreaks subsequently burn-out. Although non-human primates and avian hosts of CHIKV have been identified, a shift to sylvatic transmission cycles in an urbanized city such as Singapore is unlikely to occur. The A226V mutation has also not been shown to reduce the survival of the mosquito host. Infection with CHIKV is thought to confer life-long immunity. However, the acquisition of herd immunity is unlikely to account for the resolution of the outbreak, considering the extent of infections in Singapore is unlikely to approach the 38% seroconversion in the Reunion Islands.

Although it may be too early to conclude whether chikungunya fever will become endemic, be eradicated or later recur in an explosive outbreak, it is important to identify and address the systemic and demographic vulnerabilities in preparation for the next outbreak. Although these factors are not easily addressed, resources should be channelled towards understanding and alleviating these vulnerabilities. In addition, as the interplay of host, vector and viral factors continues to evolve dynamically, a high-level of vigilance should be sustained together with a robust system of surveillance to allow early detection and swift response to the resurgence of chikungunya.
Epidemiological News Bulletin

(Reported by Ho K1, Ang LW1, Tan BH1, Tang CS2, Ooi PL1, James L1, and Goh KT3).

1Communicable Diseases Division, Ministry of Health, Singapore, 2Environmental Health Department, National Environment Agency, Singapore, 3Office of the Director of Medical Services, Ministry of Health, Singapore)

References

Clusters of vivax malaria in Singapore, May-July 2009

Introduction

Between May and July 2009, a total of 29 vivax malaria cases were reported in Singapore. These cases were distributed in three distinct clusters (Fig. 3) epidemiologically linked by time, person and place of residence or work. The first cluster comprised nine cases at Jurong Island, the second cluster of 16 cases at Mandai-Sungei Kadut, and the third cluster of four cases at Sembawang. This report describes the epidemiological investigations and findings of these clusters.

Jurong Island

On 13 May 2009, the Ministry of Health (MOH) was notified of a vivax malaria case involving a 25-year-old Indian national construction worker who worked and resided in Jurong Island. The case developed symptoms on 3 May 2009 and had no known recent travel history outside Singapore or past malaria infection. Of 243 workers screened on 26 May 2009, two of them who developed symptoms between 24 May and 25 May 2009 tested positive for Plasmodium vivax. Both were also Indian nationals residing in the same dormitory as the index case.

A total of nine local cases with onset of symptoms between 3 May and 26 July 2009 were confirmed (Fig. 4). All were males aged between 24 and 46 years, with a median age of 30 years. Except for a Bangladeshi, all were Indian nationals. Seven stayed at one of the dormitories on the island (Fig. 5). All had no recent travel history outside Singapore or past malaria infection.

Another 500 workers living in the dormitory were screened on 11 August, but all tested negative for malaria parasite.
Figure 4
Time distribution of 9 reported vivax malaria cases in Jurong Island, 3 May-26 July 2009
Blood screening conducted for 243 workers. Two were positive for *P. vivax*.

Figure 5
Geographical distribution of 9 reported vivax malaria cases in Jurong Island, 3 May-26 July 2009

Blood screening conducted for 500 workers. None were positive.
No adult *Anopheles* vectors were detected. However, *An. separatus* larvae were found within 1km around the living quarters of the cases, and two larvae of *An. sinensis* in a drain more than 1km away from the living quarters.\(^1\)

Molecular analyses of *Plasmodium vivax* showed that most of the cases had a unique genetic profile.\(^1\)

The molecular and entomological findings could not confirm the occurrence of local transmission. The cases could have had an asymptomatic infection in their home country or they might not admit to a past history of malaria infection due to the fear of being repatriated.

**Mandai-Sungei Kadut**

On 24 May 2009, MOH was notified of a *vivax* malaria case involving a 40-year-old male Thai foreign worker who worked and resided in Mandai Estate. He developed symptoms on 16 May 2009. More cases were notified over the next few weeks and a total of 16 cases were finally confirmed to have *vivax* malaria with onset of symptoms between 16 May and 1 July 2009 (Fig. 6). All were males aged between 20 and 50 years, with a median age of 32 years. The cases comprised two Singaporeans, seven Indian nationals, three Thais, two Bangladeshis and two Malaysians. The two Singaporeans were a general worker who worked in Mandai Estate and a national serviceman who stayed at Mandai West Camp. The other cases were general labourers who resided or worked in Mandai-Sungei Kadut area (Fig. 7). All had no recent travel history or past history of malaria. All recovered after treatment in hospital.

None of these cases were picked up through blood screening of 165 workers from various companies conducted on 9 and 16 July 2009 at three different sites located within the area.
Anopheles sinensis was the predominant anopheline mosquito in the locality. Both larvae and adults were detected with the adults caught in well-lit busy road. However, all the Anopheles mosquitoes were negative for sporozites and oocysts.¹

Molecular analysis via restriction fragment length polymorphism (RFLP) based on the merozoite surface protein msp-3α and msp-1 genes showed similar profile among most of the cases.³ The findings are consistent with the results of epidemiological investigations which pointed to the occurrence of a local outbreak in Mandai-Sungei Kadut.

Sembawang

Four cases of vivax malaria with onset of illness between 12 June and 12 July 2009 were notified (Fig. 8). All the cases were hospitalized and recovered after treatment. There were two males and two females, aged between 24 and 49 years with a median age of 30 years. Among the cases, three were Singaporeans while one was an Indian foreign worker.

On 21 July 2009, a 24-year-old bartender who lived in Woodlands Ring Road and worked at night at a pub along Sembawang Road was notified to have vivax malaria. He developed symptoms on 30 June 2009 and had no known recent travel history or past malaria infection.

From a review of the records of notified vivax malaria cases working or living in the area, two with a recent travel history were previously classified as imported. However, further investigations showed that they had also frequented a coffee shop along the same stretch of Sembawang Road during the night (Fig. 9) and were subsequently re-classified as locally acquired malaria.

Figure 7
Geographical distribution of 16 vivax malaria cases in Mandai-Sungei Kadut, 16 May-1 July 2009

- One case
Blood screening on 97 workers working in the vicinity of the index case was conducted on 27 and 28 July 2009. A 24-year-old male Indian national working at a nearby nursery tested positive for *P. vivax*. He developed a fever on 12 June 2009 but did not seek medical treatment. He had not travelled out of Singapore and had no past history of malaria in his hometown.

*A. sinensis* (larvae and adults) was the predominant anopheline mosquito identified. The adult mosquitoes were caught in dimly-lit open-air restaurants. However, all were negative for sporozites and oocysts.¹

Molecular analysis also showed similar genetic profile among some of the cases,¹ indicating local transmission.

**Comments**

Although declared free of indigenous malaria by the World Health Organization in 1982,² Singapore is vulnerable to the threat of malaria from the introduction of cases arriving from or travelling to malaria endemic countries. The city state remains receptive to malaria transmission due to the presence of the *Anopheles* mosquitoes. *A. sundaicus³* and *A. macalatus⁴,⁵* were the main vectors identified in previous outbreaks.

Similar to the 2006 outbreak at Jurong Island, despite extensive vector surveillance, no adult *Anopheles⁶* mosquitoes were detected. Contrary to the 1998 outbreak in the Mandai/Sungei Kadut area where *A. maculatus* larvae were detected, only *A. sinensis*, were found in the 2009 outbreak. As *A. sinensis* is not a known vector in Singapore, this indicates a possibility of *A. sinensis* as an emerging vector in the country. *A. sinensis* is a known vector in Korea⁷,⁸ and China.⁹

We confirmed independent local transmission in Mandai-Sungei Kadut and Sembawang. Although molecular analysis could not confirm local transmis-

---

**Figure 8**

**Time distribution of 4 reported vivax malaria cases in Sembawang, 12 June-12 July 2009**

<table>
<thead>
<tr>
<th>Date</th>
<th>No. of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>31 May-06 Jun</td>
<td>1</td>
</tr>
<tr>
<td>07-13 Jun</td>
<td>1</td>
</tr>
<tr>
<td>14-20 Jun</td>
<td>1</td>
</tr>
<tr>
<td>21-27 Jun</td>
<td>1</td>
</tr>
<tr>
<td>28 Jun-04 Jul</td>
<td>1</td>
</tr>
<tr>
<td>05-11 Jul</td>
<td>1</td>
</tr>
<tr>
<td>12-18 Jul</td>
<td>1</td>
</tr>
<tr>
<td>19-25 Jul</td>
<td>1</td>
</tr>
<tr>
<td>26 Jul-01 Aug</td>
<td>1</td>
</tr>
<tr>
<td>02-08 Aug</td>
<td>1</td>
</tr>
</tbody>
</table>

**Timeline:**
- **Notification of first case**
- **Blood screening conducted on 97 workers. One was positive for malaria.**
- **Vector control implemented**

---

*Epidemiological News Bulletin*
sion in Jurong Island, more studies need to be conducted to fully understand the dynamics of possible malaria transmission there. Understanding transmission of vivax malaria is made more complex since the parasite has the propensity to hide in the liver. It can subsequently induce another bout of malaria when it moves back into the bloodstream. Molecular techniques are important tools that can be used to assist outbreak investigation. Nonetheless, epidemiological investigations to determine case movements and previous infection remain the mainstay in outbreak prevention and control.

The periodic outbreaks of malaria remind us of the ever-present threat of reintroduction of malaria into Singapore due to the presence of anopheles vectors, high volume of travellers to and from malaria-endemic countries and influx of foreign workers from these areas. We should therefore be vigilant at all times.

Figure 9
Geographical distribution of 4 reported vivax malaria cases in Sembawang, 12 June-12 July 2009

(Contributed by Suhana S1, Tien WS, Chan PP, Foong BH, Hishamuddin B, Ooi PL, and Lin R. 1Surveillance & Response Branch, and 2National Public Health Laboratory, Communicable Diseases Division, Ministry of Health)

References
Rubella is a mild febrile viral exanthematous disease with a diffused punctuate and maculopapular rash.\textsuperscript{1,2} It is caused by the rubella virus which is classified under the family Togaviridae, genus \textit{Rubivirus}.\textsuperscript{3} Rubella is transmitted through droplets or direct contact with nasopharyngeal discharges of an infected person.\textsuperscript{1,4} Outbreaks of rubella are known to occur in settings where unvaccinated susceptible population congregates, such as boarding schools, colleges, universities, factories, offices, prisons and institutions.\textsuperscript{5-9}

On 26 Nov 2009, the Ministry of Health (MOH) was notified of a suspected outbreak of rubella infection among foreign workers staying in a dormitory on an off-shore island of Singapore. We report herein the epidemiological investigations into this outbreak.

**Epidemiological investigations**

There were a total of 7000 foreign workers involved in a construction project on the island. They were housed in the same dormitory.

Active case detection was carried out from the second week of 2010 onwards with twice daily fever surveillance.\textsuperscript{10,11} Febrile cases detected were isolated and tested for recent rubella infection by polymerase chain reaction (PCR) and/or serological assays.

In addition, a blood screening exercise was conducted on 260 asymptomatic foreign workers on 15 Jan 2010.

Sequencing of E1 gene of the virus was carried out at the National Public Health Laboratory, Communicable Diseases Division, MOH, according to US CDC protocol (personal communication). The 739 bp region in E1 coding region was compared with references strains as recommended by the World Health Organization.

The cases were categorized as either clinically diagnosed or laboratory confirmed. A clinical case was defined as one with symptoms of fever and rash.

and epidemiologically linked to a known laboratory-confirmed case. A person with compatible clinical signs and symptoms and whose blood tested positive for IgM antibody against rubella was considered a laboratory confirmed case.

**Findings**

A total of 53 workers, 49 symptomatic and 4 asymptomatic, were found to be infected with rubella. Of these, 28 were laboratory confirmed and 25 were clinically diagnosed. None of them had a past history of vaccination against rubella or recent travel history outside Singapore. The 4 asymptomatic cases reported no contact with any of the known rubella cases.

The onset of illness was from 15 Nov 2009 to 6 Apr 2010 (Fig. 10). The attack rate of the outbreak was 0.7%.

All the 53 infected cases were males between the ages of 22 and 44 years. They were from Thailand, India, Bangladesh, and Myanmar (Fig. 11).

Sequencing of E1 gene showed that the virus strains in the outbreak were of the same genotype and closely linked to each other in terms of genetic sequencing (Fig. 12).
Figure 12

Phylogenetic tree showing the sequence of the outbreak samples and reference sequences
Comments

This outbreak in the foreign worker dormitory lasted over a period of 6 months. Genetic sequencing confirmed that it was a common source propagated outbreak. It is unclear how the source of infection was introduced into the dormitory population because up to 50% of infected adults are known to be asymptomatic. The high dormitory occupancy turnover of hundreds per month presented the opportunity for rubella to be introduced by an infected person into the susceptible population.

Since the workers’ activities were mainly limited to the off-shore island with controlled access, the public health risk to the community at large was deemed to be low.

This outbreak illustrates the vulnerability of foreign workers staying in congregated settings to droplets and contact transmissible infectious diseases. More studies are needed to understand the various aspects of vulnerability to disease outbreaks among foreign workers staying in dormitories.

References

Risk assessment on monkeypox

Introduction

Background

Human monkeypox is a sporadic zoonotic viral disease caused by an orthopoxvirus. Monkeypox virus (MPXV) was first recognized as a pathogen of humans during the early 1970s in west and central Africa, during a time of intensification of smallpox eradication efforts.\(^1\)\(^,\)\(^2\) Thereafter, sporadic cases have been reported in forested regions of west and central Africa, in countries such as the Democratic Republic of (DR) Congo, Central African Republic, Gabon, Liberia and Sierra Leone. In 2003, a monkeypox outbreak in the US involved 72 human cases.\(^3\)\(^,\)\(^4\)

Disease overview

Primates, squirrels and several rodent species are suspected to be the reservoirs for monkeypox in Africa. Humans can acquire monkeypox through direct contact with infected animals or humans. In the United States (US), monkeypox occurred in humans who had direct contact with infected animals or who were bitten or infected through open wounds.\(^5\) While the mode of transmission between infected animals and humans is not well defined, direct mucocutaneous contact and respiratory routes have been implicated in epidemiological and experimental research.\(^5\)\(^,\)\(^7\)

Symptoms include headache, fever, sweats, and severe lymphadenopathy. Subclinical or very mild infection can occur in humans.\(^8\) It has been noted that monkeypox is usually milder with lower numbers of deaths among African patients with a history of smallpox vaccination. The estimated mean incubation period in humans is 12 days.\(^9\) Cases are most infectious during the first week of rash, similar to that observed with smallpox or chickenpox.

Infectiousness

The basic reproduction number, R\(_0\), has been estimated to be less than 1.\(^10\) The secondary attack rate in household contacts is stated to be low, around 8 to 9\% from studies in Africa. However, secondary attack rates appear to be increasing in monkeypox-endemic areas due to increasing susceptibility of exposed populations. Notably, no human-to-human virus transmission was reported during the 2003 US outbreak.

Case-fatality rates

The case-fatality rates in African outbreaks range from 4\% to 33\% and are high among children.\(^11\)\(^,\)\(^12\) Case fatality is dependent on various factors such as exposure, susceptibility, and healthcare provision. However, the variability in case-fatality rates reported in Africa probably reflects incomplete assessment of the total number of cases, variations in case definition, and variability in the virulence of MPXV strains. The US outbreak in 2003 has been associated with a milder West African clade.

Treatment options

The US Food and Drug Administration (FDA) has not approved a treatment for monkeypox. Suggested treatment options include cidofovir, while the efficacy of vaccinia immune globulin in humans has not been established.\(^13\) Usually, supportive therapy is the recom-
mended treatment. Pre-exposure and post-exposure smallpox vaccine was used during the 2003 US outbreak, with only relatively minor adverse events reported.

**Outbreak in US in 2003**

A total of 72 human cases were reported in the 2003 outbreak in the US. About 51% of the cases were laboratory confirmed, and 35 met the case definition set by the Centers for Disease Control and Prevention (CDC). There were no human deaths in the 2003 outbreak but 2 children required intensive care. While the US outbreak was relatively large compared with most reported events in Africa, clinical features were milder than typically reported in Africa.

The monkeypox outbreak in the US in 2003 was traced to a consignment of rodents (Gambian giant rats) from Ghana that were kept in close proximity with 200 prairie dogs in a pet holding facility. The Gambian giant rats transmitted the MPXV to the prairie dogs which in turn transmitted the virus to humans. This event represents the sole instance whereby MPXV exported from virus endemic regions has resulted in human infections. Subsequently, the US banned the importation of all African rodents and the sale of prairie dogs as pets. To date, no new animal or human cases have been reported in the US.

**Recent increase in incidence in DR Congo**

Thirty years after mass smallpox vaccination campaigns ceased, there has been a 20-fold increase in human monkeypox incidence in nine rural Congolese districts surveyed (14.4 cases per 10,000, compared with an incidence of 0.7 cases per 10,000 in the early 1980s). Researchers studied 760 “laboratory confirmed cases” of monkeypox over two years starting in 2005. The conclusion was that after the eradication of smallpox in 1979, new generations of people who were ‘vaccine naive’ were exposed to the monkeypox virus in the DR Congo over time.

**Likelihood of spread to Singapore**

The most likely route of spread to Singapore is via import of infected animals and subsequent spread to humans. The Agri-Food Veterinary Authority (AVA) regulates the import of wild animals (including primates, rodents and squirrels) under the Animals and Birds Act (ABA) and Singapore’s veterinary import conditions. Under the ABA, an import permit from AVA is required for any import of animals. Through the ABA and veterinary import conditions, AVA has restricted the import of rodents, squirrels and primates from Africa.

AVA’s assessment is that the risk of introduction of monkeypox into Singapore through the import of animals is very low for the following reasons:

a) AVA does not allow commercial import of primates, rodents or squirrels from Africa.

b) Primates can only be imported from premises that have been free from monkeypox for at least 2 years.

c) Any import of primates or small mammals for laboratory use must be from approved facilities only. There is no approved facility in Africa;

d) All animals imported by the zoo must be quarantined for at least 30 days at the approved premises within the zoo. The zoo is required to report any illness or death of animals to AVA.

e) All small mammals brought in as personal pets must include a statement in the veterinary health certificate that the pet has been with the owner for at least 1 month. In addition, personal pets have to undergo 1 month of home quarantine.
**Consequences if spread to Singapore occurs**

Should the disease be imported into Singapore, the risk of a large outbreak occurring is low as:

1) Infectiousness of monkeypox is low with $R_0 < 1$ and secondary attack rate <10%.

2) Spread can be successfully contained via isolation of cases and quarantine of close contacts. No secondary spread occurred during the US outbreak in 2003.

3) Persons who have been vaccinated against smallpox (i.e. persons born before 1980) may still have immunity against monkeypox. The impact of any outbreak in Singapore can also be minimised as close contacts can be vaccinated with smallpox vaccine to minimise their chances of developing the disease.

**Conclusion**

Vigilance is maintained over the global monkeypox situation, as infected animals imported from endemic countries can spread the infection to humans as shown in the 2003 outbreak in the US. AVA has very stringent import requirements and no primates, rodents or squirrels are permitted to be brought into the country from Africa and areas where monkeypox is reported.\(^9\)

(Contributed by: Risk Analysis Branch, Communicable Diseases Division and Agri-Food and Veterinary Authority)

**References**


