Epidemiology and vector efficiency during a dengue fever outbreak in Cixi, Zhejiang Province, China

Tianci Yang1, Liang Lu2, Guiming Fu1, Shi Zhong3, Gangqiang Ding1, Rong Xu4, Guangfeng Zhu4, Nanfeng Shi5, Feilong Fan5, and Qiyong Liu2

1Institute of Vector Control, Zhejiang Center for Disease Control and Prevention, 630 Xincheng Road of Binjiang Area, Hangzhou, Zhejiang Province 310051, P.R. China
2National Institute for Communicable Disease Control and Prevention, Chinese Center for Disease Control and Prevention, Post Box 5, Changping, Beijing, 102206, P.R. China
3Zhejiang Academy of Agricultural Sciences, 198 Shiqiao Road, Hangzhou, Zhejiang Province 310021, P.R. China
4Department of Disinfection and Vector Control, Ningbo Municipal Center for Disease Control and Prevention, 237 Yongfeng Road, Ningbo, Zhejiang Province 315010, P.R. China
5Cixi Municipal Center for Disease Control and Prevention, 1141 Eastern Road of Southern Second Ring, Cixi, Zhejiang Province 315300, P.R. China

Received 18 November 2008; Accepted 29 Mar 2009

ABSTRACT: An emigrant worker returning from Southeast Asia triggered the outbreak of a DF epidemic in Zhejiang province, China, in October, 2004. Eighty-three cases, mainly young and middle-aged people between 20 and 50 (78.3%), were reported in the area of Cixi. There were no obvious occupational patterns. The majority of cases were female, with a sex ratio of 1:1.86 (m:f). The dengue virus (DENV) strains from the epidemic area were isolated and identified as DENV-1, which belongs to Asian strain 1. According to the epidemiological investigation, the incidence of DF had no relationship to temperature, humidity, or precipitation, and the Breteau index of larvae showed a clear relationship only with the House Index and Container Index. Recent dengue problems in the town have been associated with the complex social factors and hygienic conditions for endemic villagers and immigrant workers. Some hygienic measures should be taken by the local government to reduce the risk of mosquito-borne disease. These measures should aim to eliminate the breeding sites of the vector Aedes albopictus in indoor and outdoor containers filled with rainwater and thus reducing the risk of DF transmission.

INTRODUCTION

Dengue fever (DF) is the most common arboviral disease in the tropics and subtropics, especially in Africa, Latin America, Oceania, and Southeast Asia. Its incidence has increased dramatically, with up to 100 million cases of DF estimated to occur annually on a world-wide basis, which result in 250,000 to 500,000 cases of dengue hemorrhagic fever (DHF) and approximately 24,000 or more deaths each year in recent decades (WHO 1997, Shu and Huang 2004, WHO 2005). DF or DHF has thus become one of the most important and escalating health problems for the management of public health. In Asia, epidemic DHF has expanded geographically from Southeast Asian countries west to India, Sri Lanka, the Maldives, and Pakistan and east to China (Gubler 1998, Jamil et al. 2007).

With the rapid increase of trade and travel between Southeast Asian countries and China, imported cases of dengue virus (DENV) infection have increased and were reported from the southern coastal provinces of China, such as Guangdong, Guangxi, Hainan, and Fujian provinces (Lu 1999, Fang et al. 2005). The most recent outbreak was reported from the Cixi area, Zhejiang Province, in 2004. Previous outbreaks occurred in the Yangtze River delta area and north of 30°N in China, following the great epidemic of Hankou city, Hubei province, in 1945 (Lu 1999).

DENV, a single-stranded RNA virus, belongs to the family Flaviviridae. Four serotypes are known and are transmitted by Aedes aegypti and Ae. albopictus (Ashford et al. 2003). Typical infection symptoms are an acute febrile illness that can develop into a life-threatening syndrome (dengue shock syndrome, DSS). The predominant serotypes reported from China are DEN-1 and DEN-2. This epidemiological study has been carried out to identify the factors determining the DF outbreak in Cixi and to recommend measures to avoid additional epidemic outbreaks in the same region.

MATERIALS AND METHODS

Investigations on the index case and case finding

After the primary outbreak of DF in Xiaolin town of Cixi city, the epidemic districts were isolated by a clear demarcation within a radius of 100 m from the center of
each patient’s residential building or workplace. Everyone who had to enter these districts for business and work had to strictly follow the regulations set by the health authorities. Epidemiological surveys were carried out under the guidance of a panel of experts from the province, municipalities, and county councils. This expert panel was set up at the end of September 2004, at the time of the outbreak. The first investigations included a detailed analysis of the situation of the first patient. We collected information on the traveling activities of the subject to explore the underlying mechanism of spread of DF in the local district.

Laboratory and clinical diagnosis of DF

Blood samples of suspect cases, border-line cases, and patients with overt DF symptoms were drawn and detected by routine blood tests. An indirect immunofluorescence assay (IFA) was used to detect positive IgG and IgM, using dengue virus-specific enzyme-linked immunosorbent assay (ELISA) (Balmaseda et al. 2003). DENV was further isolated from the patients’ serum added to C6/36 monolayer cells. The virus was then isolated and identified and its DNA sequence was amplified by RT-PCR to construct the phylogenetic tree of the local DF agents.

Surveillance of Ae. albopictus

Within the epidemic area, permanent or temporary water containers around the village were searched for larval Ae. albopictus. Mosquito traps were set and measures were taken to control the density of mosquito adults and larvae, to study the dynamics of the vectors, and to initiate mosquito control measures. Conventional Aedes larval indices (Breteau index: BI = number of positive containers per 100 houses; house index: HI = percentage of positive houses divided by the total inspected houses; and container index: CI = percentage of positive containers divided by the total inspected containers) were used to describe the risk of DF transmission. The BI is an important measure for evaluating mosquito control using the WHO standard threshold (< 20), based on the daily recording of mosquito frequencies.

Ecological and meteorological factors

Rainfall, relative humidity (RH), and average daily temperatures from July to October 2004 were obtained from the Archives of Meteorology, China Meteorological Administration. Information on the social conditions in the epidemic area was provided by the local government.
Figure 1. Map on the left: Distribution of the epidemic areas (shadowed) of dengue fever in China before 2004 and the geographic position of Cixi (★). Map on the right: three villages (black filled and open circles) in Xiaolin town, Cixi, where most of the patients lived. The black and blue lines indicate the road networks and the river system, respectively.

Table 1. Monthly meteorological data between July and October during the DF outbreak.

<table>
<thead>
<tr>
<th></th>
<th>Highest temperature (°C)</th>
<th>Lowest temperature (°C)</th>
<th>Average temperature (°C)</th>
<th>Average humidity (%)</th>
<th>Minimum humidity (%)</th>
<th>Total precipitation (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>July</td>
<td>38.1</td>
<td>22.0</td>
<td>30.3</td>
<td>68.4</td>
<td>59.0</td>
<td>93.0</td>
</tr>
<tr>
<td>August</td>
<td>39.6</td>
<td>23.6</td>
<td>29.1</td>
<td>74.3</td>
<td>58.0</td>
<td>228.7</td>
</tr>
<tr>
<td>September</td>
<td>33.3</td>
<td>18.1</td>
<td>24.0</td>
<td>82.9</td>
<td>68.0</td>
<td>201.0</td>
</tr>
<tr>
<td>October</td>
<td>26.4</td>
<td>10.0</td>
<td>18.7</td>
<td>71.3</td>
<td>50.0</td>
<td>20.2</td>
</tr>
</tbody>
</table>
Figure 2. Emergence of cases of dengue fever in relation to temperature, humidity, and precipitation in the epidemic area from July to October.

Table 2. Breteau index (BI), house index (HI), and container index (CI) during the outbreak of DF and the vector control in Xiaolin town in October, 2004.

<table>
<thead>
<tr>
<th>Date</th>
<th>Temperature (° C)</th>
<th>Relative humidity (%)</th>
<th>Breteau index (%)</th>
<th>Container index (%)</th>
<th>House index (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10.6</td>
<td>23.5 17.0 19.5</td>
<td>71</td>
<td>326.0</td>
<td>42.0</td>
<td>62.0</td>
</tr>
<tr>
<td>10.7</td>
<td>22.0 17.4 19.0</td>
<td>80</td>
<td>315.0</td>
<td>38.2</td>
<td>58.0</td>
</tr>
<tr>
<td>10.8</td>
<td>24.4 15.8 19.2</td>
<td>80</td>
<td>261.0</td>
<td>56.4</td>
<td>90.7</td>
</tr>
<tr>
<td>10.9</td>
<td>26.2 16.4 20.4</td>
<td>69</td>
<td>112.2</td>
<td>34.2</td>
<td>40.1</td>
</tr>
<tr>
<td>10.10</td>
<td>26.3 15.8 20.5</td>
<td>62</td>
<td>36.3</td>
<td>40.8</td>
<td>28.8</td>
</tr>
<tr>
<td>10.11</td>
<td>26.4 16.2 20.7</td>
<td>58</td>
<td>6.5</td>
<td>15.6</td>
<td>6.5</td>
</tr>
<tr>
<td>10.12</td>
<td>24.2 17.7 20.0</td>
<td>67</td>
<td>15.0</td>
<td>15.7</td>
<td>11.7</td>
</tr>
<tr>
<td>10.13</td>
<td>23.7 13.9 19.0</td>
<td>64</td>
<td>15.2</td>
<td>21.1</td>
<td>9.8</td>
</tr>
<tr>
<td>10.14</td>
<td>23.7 13.6 18.3</td>
<td>63</td>
<td>11.0</td>
<td>11.2</td>
<td>7.6</td>
</tr>
<tr>
<td>10.15</td>
<td>22.3 15.4 18.2</td>
<td>66</td>
<td>2.8</td>
<td>10.9</td>
<td>2.8</td>
</tr>
<tr>
<td>10.16</td>
<td>22.2 13.8 17.7</td>
<td>71</td>
<td>6.9</td>
<td>12.1</td>
<td>5.4</td>
</tr>
<tr>
<td>10.17</td>
<td>24.1 16.2 19.1</td>
<td>78</td>
<td>4.8</td>
<td>11.3</td>
<td>4.4</td>
</tr>
<tr>
<td>10.18</td>
<td>25.5 17.0 20.6</td>
<td>81</td>
<td>3.4</td>
<td>9.8</td>
<td>3.4</td>
</tr>
<tr>
<td>10.19</td>
<td>23.9 18.3 20.3</td>
<td>72</td>
<td>2.5</td>
<td>11.4</td>
<td>2.5</td>
</tr>
<tr>
<td>10.20</td>
<td>23.3 16.6 19.4</td>
<td>69</td>
<td>3.9</td>
<td>9.3</td>
<td>3.9</td>
</tr>
<tr>
<td>10.21</td>
<td>24.3 15.2 18.7</td>
<td>66</td>
<td>2.5</td>
<td>10.9</td>
<td>2.0</td>
</tr>
<tr>
<td>10.22</td>
<td>22.3 14.8 17.9</td>
<td>76</td>
<td>2.5</td>
<td>3.8</td>
<td>2.5</td>
</tr>
<tr>
<td>10.23</td>
<td>22.4 13.8 18.2</td>
<td>71</td>
<td>1.0</td>
<td>7.4</td>
<td>0.5</td>
</tr>
</tbody>
</table>
Discussion

Observed.

No relationship with temperature and relative humidity was

Relative coefficients being 92.4% and 82.8% (P<0.0001), but

BI showed a positive relationship with HI and CI, with the

Change indicates that the transmission risk of DF was very

To only 20% and stabilized below 5% after October 17. This

In China, especially in urban and semi-urban areas with

Complex social factors and inadequate hygienic conditions


First record of DF in the Cixi district, in Zhejiang province,

Have been mainly located in the southeastern coastal areas

Emigrant workers returning from southeast Asian countries

Anopheles sinensis, Armigeres obturans, and other minor species. The density of

Ae. albopictus was about 20.3%. At the same time, the BI value of

larvae was greater than 300 on October 6 and 7 (see Table

2) and therefore above the standard threshold set by WHO.

HI and CI were 95.2% and 65.3%, respectively, before the

Introduction of control measures on October 6. The density of

Ae. albopictus larvae sharply declined and the BI dropped to

only 20% and stabilized below 5% after October 17. This

Change indicates that the transmission risk of DF was very

Low after the larval habitats were eliminated. Moreover, the

BI showed a positive relationship with HI and CI, with the

Relative coefficients being 92.4% and 82.8% (P<0.0001), but

No relationship with temperature and relative humidity was

observed.

Analysis of vector efficiency of Ae. albopictus for DF

Due to the large number of local industries, waste

Materials and tires accumulated throughout the villages, providing perfect larval habitats for Ae. albopictus, a species

Well adapted to life in urban settings and a known vector of
dengue virus. This mosquito feeds preferentially on human blood in the daytime and feeds on multiple hosts

Over short periods. According to our investigations, Culex pipiens pallens and Ae. albopictus were the dominant species, clearly outnumbering Anopheles sinensis, Armigeres obturans, and other minor species. The density of

Ae. albopictus was about 20.3%. At the same time, the BI value of

larvae was greater than 300 on October 6 and 7 (see Table

2) and therefore above the standard threshold set by WHO.

HI and CI were 95.2% and 65.3%, respectively, before the

Introduction of control measures on October 6. The density of

Ae. albopictus larvae sharply declined and the BI dropped to

only 20% and stabilized below 5% after October 17. This

Change indicates that the transmission risk of DF was very

Low after the larval habitats were eliminated. Moreover, the

BI showed a positive relationship with HI and CI, with the

Relative coefficients being 92.4% and 82.8% (P<0.0001), but

No relationship with temperature and relative humidity was

observed.

Discussion

In recent years, dengue infections have been increasing in China, especially in urban and semi-urban areas with

Rapid economic development and increasing tourism. Emigrant workers returning from southeast Asian countries

Are frequent carriers. Since the 1980s, the epidemics of DF

Have been mainly located in the southeastern coastal areas

Of China and initiated by imported cases. We report here the

First record of DF in the Cixi district, in Zhejiang province,

With the isolated DENV identified as the serotype DEN-1


Recently, DF cases have also been associated with the

Complex social factors and inadequate hygienic conditions

For endemic villagers and immigrants. The local population

Pays little attention to environmental protection. The

Overpopulation of the region is very high and the lack of

Vector control, compared to that of adjacent towns, is evident. Substandard housing, crowding and deterioration of water,
sewer, and waste management systems associated with unplanned urbanization were favorable to the propagation of

Mosquitoes and created ideal conditions for an increased transmission of mosquito-borne diseases.

In addition, the BI of Ae. albopictus larvae in the

Endemic district was very high before control of this vector

Began (Tables 1 and 2). In July, the density of Ae. albopictus

Should be very low because of the high temperatures and

Low RH. Alto and Juliano (2001) suggested that climate

Changes are likely to extend the northern distribution of

Ae. albopictus and further limit its establishment in arid regions, with the variability of precipitation contributing

Relatively less to variation in production of adults. Yi et

Al. (2003) concluded that the density of Ae. albopictus is

A primary factor in dengue incidence, while average air

Temperature, rainfall, and RH have a large but less important influence. Watts et al. (1987) suggested that the pattern of
temperature-induced variation in the vector efficiency of

Ae. aegypti for DEN-2 virus paralleled the seasonal cyclic

Pattern of the incidence of DHF cases. Chung and Pang

(2002) reported that DF epidemics were related to rainfall,

With weather variability identified as a meaningful and

Significant indicator for the increasing occurrence of DF. Wu et al. (2007) also considered that the incidence of DF

Was negatively associated with monthly temperature and

Inversely related to relative humidity. However, we could

Not observe any relationship between the incidence of DF

And temperature, humidity, and precipitation values during

This outbreak.

In recent years, the southeastern area of China has

Become warmer and more humid, especially in the summer season. The expansion of the epidemic areas of DF is

Potentially related to the warming climate in the endemic zone. Therefore, the adult populations of Ae. albopictus

In Cixi were likely to increase as long as the rainwater containers did not dry completely, even during the summer

Drought. The duration of the extrinsic incubation period is

Influenced markedly by environmental temperatures (Watts

Et al. 1987). DENV could also be transmitted to the offspring

Through the oviposition of mosquitoes and then to humans; the

Main transmission vector, Ae. albopictus plays indeed an important role in the maintenance of DENV in nature

(Ashford et al. 2003, Ponlawat and Harrington 2007).

Monath (1994) considered that virus transmission in

Its simplest form involves the ingestion of viremic blood by

Mosquitoes and the passage to a second susceptible human

Host. The DENV from the index case was misdiagnosed and

Could hardly have triggered the outbreak of a DF epidemic.

DF is often asymptomatic or causes a non-specific febrile

Illness during its initial infection with DENV serotypes I to

IV (Halstead 2007). During the first peak of DF epidemics,

Only 14 cases (16.9%) were infected by dengue virus after 34

days, since the index case displayed the syndrome of dengue

And was sent to local hygiene hospital, while the entire

Incubation period of DF does usually not exceed 20 days

possible explanation could be that the infected mosquitoes contained only low numbers of DENV and survived long enough to feed on the subjects, although it may take some time for the virus to be transmitted to mosquito progeny through transovarian infection and then to patients. Obviously, the transmission of DENV is determined by the magnitude and duration of viremia in the human host (WHO 1997) and is modulated by different cell types (Diamond et al. 2000), depending largely on the patient’s age and immunologic condition. The second observed outbreak (Diamond et al. 2000), depending largely on the patient’s age and immunologic condition. The second observed outbreak may be a good illustration to explain this situation: during the long latent phase of DENV in the subjects and field, *Ae. albopictus* had enough opportunity to transmit the DENV among the susceptible population and further expand its distribution in the adjacent villages.

Our investigation has shown that the spread of DF was very limited in this suburban area. It is, however, necessary to pay enough attention to imported cases to prevent any local outbreak of DF. The main strategy to control DF is to conduct mosquito vector surveillance and to introduce mosquito control programs in the areas around imported cases. Further, early detection of the disease should be enhanced by closely monitoring the onset of febrile illness and implementing early detection and diagnosis of potential DF cases (Yi et al. 2003, Rotela et al. 2007, Chowell et al. 2007). Public education should include handling of environmental factors with an emphasis on the frequent inversion of any artificial containers with stagnant water that should be emptied at least once a week to interrupt the mosquito breeding cycle. Unless mosquito control and sanitation programs are improved, the continued presence of multiple breeding sites created by domestic sources and high mosquito populations will increase the likelihood of DF outbreaks in the future.

Acknowledgments

We thank Dr. Orlando Petrini, Director of the Cantonal Institute of Microbiology, Canton Ticino, Switzerland, for helpful advice and intensive revision of the manuscript. We are grateful to Dr. Chunhui Ye from Card Building, Zhejiang University for his favorable support. This research was funded by Health Bureau of Zhejiang Province grant 2005B023.

REFERENCES CITED


