Dengue fever/Dengue haemorrhagic fever (DF/DHF) is on the increase in the countries of the South-East Asia and Western Pacific Regions, notably in Indonesia, Myanmar the Philippines, Singapore, Thailand and Viet Nam. Epidemics of DHF are now recurring in a 2-3 year cycle. The increasing trend has been facilitated by increased water storage due to the lack of adequate water supply and facilities for solid waste disposal, rapid uncontrolled urbanization, population movement and increased commercial activities. The infection, earlier restricted to urban/semi-urban centres, has now invaded rural areas as well.

The regional dengue control strategy envisages selected integrated mosquito control with community and intersectoral participation. The countries of the SEA Region have developed various modules of community-based control programmes with varying degrees of success.

An Intercountry Consultation of Programme Managers of DF/DHF from endemic countries and scientists/experts from the South-East Asia and Western Pacific Regions was held at Batam Island, Indonesia in July 2001. It reviewed the latest developments related to case management and prevention and control of DHF and recommended a “Revised Regional Strategy - July 2001”.

Starting with Volume 26, a section on “Letters to the Editor” will be introduced to encourage comments, and discussions related to the management, prevention and control of DF/DHF in view of the hands-on-experience perspective of different workers.

Volume 26 is fully subscribed. **However, the deadline for the receipt of contributions for Volume 27 (2003) of Dengue Bulletin is 30 April 2003.** Contributors are requested to follow the instructions carefully while preparing the manuscript. Contributions accompanied by computer diskettes using MS Word for Windows should be sent to the Editor, Dengue Bulletin, WHO/SEARO, Mahatma Gandhi Road, I. P. Estate, Ring Road, New Delhi-110 002, India, or by e-mail as a file attachment to the Editor at dengue@whosea.org.

Readers desirous of obtaining copies of the Dengue Bulletin may contact the respective WHO Regional Offices in New Delhi or Manila or the WHO Country Representative in their country of residence.

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New Initiatives in Dengue Control in Singapore

by

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Abstract

The incidence of dengue in Singapore follows the trend in other countries in the region very closely. However, efforts are being made to minimize the number of cases in the country. This is being achieved by the introduction of new tools such as the geographical information system (GIS) for the management of databases and spatial identification of “hotspots” and the use of hand-held terminals (HHT) for the collection of field surveillance data. New initiatives include regular mosquito surveillance of housing estates and crowded places, redesigning of structural habitats, incorporation of heating elements in roof gutters and tracking behavioural changes.

Keywords: DF/DHF, new initiatives, GIS, hand-held terminals, ovitraps, Singapore.

Introduction

Singapore is situated in a geographical region which is endemic for DF/DHF[1,2]. The incidence of dengue in Singapore follows very closely the trend in other countries in the region. Although we are affected by the peaks and troughs of dengue in the region, we are making all efforts to minimize the peak (magnitude of the cases) within Singapore.

Aedes control strategies

Broadly, our strategies for Aedes mosquito control include:

(1) Source reduction;
(2) Health education;
(3) Law enforcement, and
(4) Chemical control

Source reduction remains the main focus of our control strategies and the approach is preventive rather than reactive. For example, all construction sites, schools and condominiums are required to engage pest control operators to do regular mosquito control. These are places where activities usually create mosquito-breeding problem, or where there is high density of people to support disease transmission. We also identify certain residential estates as dengue-sensitive areas, and check the

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premises and educate the householders on mosquito prevention regularly on a two-monthly cycle. These sensitive areas are reviewed periodically as mosquito population is dynamic.

**New tools used for Aedes control operations**

**Geographical Information System (GIS)**

Since 1998, we have developed and made use of the PC-based geographical information system (GIS) to manage the huge databases on cases and Aedes mosquitoes island-wide. Examples of information stored on the GIS are: patients’ particulars, locations of Aedes breeding, larval densities, species of vectors, habitat types, premises types, and ovitrap locations. The GIS enables us to visualize at a glance “hotspots” where cases or breeding are concentrated so that early control operations can be implemented (Figures 1 and 2). We can also perform spatial and temporal analyses of the data for future planning, such as the review of dengue-sensitive areas; and for day-to-day operation planning such as the boundary of control operations in outbreak areas, the progression of an outbreak, etc.

**Figure 1. Distribution of dengue cases in Singapore in 2001 shown on GIS**
Cluster of cases identified using GIS in Singapore during 2001

The use of the GIS has helped us to be more precise in defining problematic areas and in decision-making and we can respond faster to a bad mosquito situation before cases occur. We are in the process of developing GIS models as early-warning indicators of dengue transmission.

**Hand-held terminals (HHT) for field surveys**

Since 2001, our field officers have begun using hand-held terminals (HHT) to input field surveillance data in the field. Previously, they filled in such information on paper forms, which then needed to be keyed into the computer and converted into formats readable by the GIS software. With the HHT, the information is stored in the HHT and then downloaded into a server and read directly by the GIS software. This cuts down time in transferring data and we can analyse the information collected from all field officers on the same day of the survey or by the next day the latest. This has enhanced our capabilities to be prompt in control operations. We are looking into exploiting wireless technologies to send or request information on the HHT wirelessly to or from the server. For example, field officers will be able to retrieve past enforcement or breeding records for any premises without having to return to the office to search for such records.

**Ovitraps**

Ovitraps are autocidal traps which attract Aedes mosquitoes to breed in them, but the adult mosquitoes are unable to emerge and therefore drown in the traps. It has been used mainly as a monitoring tool so far. We are using ovitraps both as a monitoring tool and a control tool. About 2,000 ovitraps are placed in dengue-prone areas all over Singapore to serve as sentinel or monitoring stations. They are useful as we are unable to check every part of Singapore regularly. About 10 ovitraps are placed in each of the monitored areas, and weekly readings of the number of eggs laid, larval counts and...
species breeding are recorded. If there is an increase in prevalence or change in the species breeding in the ovitraps from Aedes albopictus to Aedes aegypti, control operations will be launched in the area immediately.

In some outbreak areas where transmission has started spreading outwards, we use ovitraps to contain the outward spread of mosquitoes from the foci of transmission. We have found that cases tend to spread outwards after we removed or neutralized all potential breeding sites within the initial focus, as the remaining surviving infected adult Aedes mosquitoes would fly further out to look for breeding habitats. We now put ovitraps back into the outbreak area to continue providing the mosquitoes a place to breed within the area, and to reduce their population eventually.

We are in the process of researching the optimal layout distribution of ovitraps in the field to give us a better indication of mosquito population. We are also improving the design of the ovitrap to make it tamper-proof so that it does not need to be serviced or checked weekly in areas which are already well under control.

**New Initiatives**

We are constantly looking for ways to improve our effectiveness in Aedes control. Several new initiatives have been or will be taken soon; these are described below:

**Regular surveillance of outdoor areas in public housing estates and crowded places**

Traditionally, it is assumed that the Aedes aegypti mosquitoes breed indoors and people are infected in the home. However, the profile of our cases in Singapore showed that the most prevalent age groups are the teenagers and young adults\(^4\) (Figure 3). These are very mobile groups who do not spend more time at home during daytime most of the days. Children and the elderly people who are not very mobile and are most likely to spend their time in the home, are not the ones most affected. This led us to suspect extradomiciliary transmission. We have also found Aedes mosquitoes breeding in many outdoor habitats, whereas the House index is generally very low (1-2%). Based on these observations, we have implemented, since September 2001, fortnightly checks on outdoor areas in public housing estates where more than 82% of the population reside, and crowded or popular places where people hang out and congregate.

![Figure 3. Age-specific morbidity rates of local DF/DHF cases (31.12.2000 to 06.10.2000)](image)

Previously, these outdoor areas were checked on an ad hoc basis only in response to complaints or cases. This new scheme is implemented in the south-eastern, north-eastern and southern parts of Singapore which contribute about 82% of all cases reported. After a month of implementation, we saw quite a sharp decline in the number of cases reported, but it is still too early to draw any conclusion.
Morbidity rates are highest amongst teenagers and mobile adults.

**Redesigning of structural habitats**

We have worked with other building authorities to redesign structural habitats so that these will be mosquito-proof in new developments. Examples are: gutters in bus shelters and houses, bamboo pole holders, gully traps.

**Heating elements in roof gutters**

Roof gutters have been found to contribute significantly to dengue cases and outbreaks in Singapore. Aedes breeding in gutters is usually profuse, and yet gutters are very difficult to reach and maintain. In recent years, we have convinced architects not to build houses or structures with gutters. Also, where gutters can be removed from existing houses, we try to get householders to do so. The problem is with concrete gutters which form part of the structure of the house; these cannot be removed and continue to pose a problem.

The use of heating coils in temperate countries to melt snow in roof gutters gave us the idea of heating up stagnant water in gutters to kill mosquito larvae/pupae. We have done pilot studies using a modified set-up to suit local conditions. Water in gutters was heated up twice a week to 45°C and maintained at this temperature for 3 hours, and the larvae/pupae were killed. The only impediment is the cost of installation, estimated at between US$ 6,000 to US$ 12,000 for a house with front and back gutters, depending on the size of the house.

The monthly electrical utility bill is estimated to cost S$ 12 – S$ 36. We are looking into ways to make it conducive for householders with gutters which cannot be removed to install such heating element system.

**Tracking behavioural changes**

Like most vector control authorities, we view public health education as an important ingredient for sustained dengue control. However, one common complaint is that health education efforts seem to be ineffective in eliciting sustained behavioural changes. There could be many reasons why this is so; for example, the message might not be clear; there is a gap in the perception or understanding of the seriousness of the disease; there are too many things to remember; the measures recommended are difficult to carry out; people are too busy; they don’t know how to do it; etc. Very often, mosquito-breeding is a result of negligence rather than commission. Our health education is generally one-way, i.e. we give out information and expect people to receive it. But there is no feedback mechanism to check whether the message is understood and why people do not act if they have understood the message. We will be carrying out a market survey soon to get the feedback from householders on the level of knowledge and action taken in mosquito prevention, and to find the emotive motivators which will make them sustain the efforts. This will help us come up with more effective education strategies.

The aim of public health education is ultimately to change behaviours. Getting the message across to the community is not
enough. There should also be mechanisms to track whether behaviours have been changed and desirable habits formed. We are planning to do a three-month campaign to show residents in landed properties in the south-eastern and north-eastern parts of Singapore what the potential habitats are, and what they must do to remove or prevent breeding. A checklist of all habitats and their number in the premises will be given to the householders to follow-up. During subsequent visits, the habitats and their number will be recorded again. A reduction in or removal of habitats by the householders will be an indication of actual behavioural changes. To sustain the efforts after the 3-month campaign, reminders must be sent periodically as part of the total education and publicity plan.

We will be looking into a publicity plan package for dengue to send out messages at the right time and in a tone that will produce confidence and cooperation and not panic in the public.

**Research initiatives**

In 1999, we launched research initiatives on Aedes mosquitoes to answer questions we have about Aedes mosquitoes and its control.

One very critical need is the development of a good indicator for mosquito population which is easy to obtain or compute at the operational level. Future projects being planned include evaluation of current control methods and tools, life-table studies, behavioural studies on Aedes mosquitoes, GIS models for forecasting dengue, etc.

**Conclusion**

In this paper, I have outlined some of our new initiatives and tools for improving Aedes control, health education and for solving breeding problems. This is by no means the end of our efforts, as the situation on the ground is dynamic and changing all the time. Some of the tools and initiatives would need to be fine-tuned and improved over time, and other new ones introduced to deal with problems that arise. Singapore is fortunate as dengue control efforts do receive a relatively high level of support from the management and politicians. By and large, we are also able to work with other authorities to solve vector breeding problems. Such high-level support and inter-agency cooperation and understanding are very crucial to the success of the dengue control programme, and emphasize the need for vector control authorities to convince and to engage people outside of vector control area, even the private sector (e.g. PR firms), into the programme.

**References**

Epidemiology and New Initiatives in the Prevention and Control of Dengue in Malaysia

by
Ang Kim Teng* and Satwant Singh
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Abstract
Dengue continues to be a public health problem in Malaysia showing an upward trend from 27.5 cases/100,000 population in 1990 to a high of 123.4 cases/100,000 population in 1998 during the global pandemic, declining to 31.99 cases /100,000 population in the year 2000 based on notification of clinically-diagnosed cases. There is a predominance of dengue fever (DF) over dengue haemorrhagic fever (DHF), with the highest incidence among the working and school-going age groups. Major sources of Aedes breeding are at construction sites, solid-waste dumps, open spaces and in factories.

Several initiatives have been taken to strengthen dengue control. Some of the initiatives include reprioritizing Aedes surveillance aimed at new breeding sites; strengthening information system for effective disease surveillance and response; legislative changes for heavier penalties; strengthening community participation and intersectoral collaboration; changing insecticide fogging formulation, mass abating and, lastly, reducing case fatality.

Keywords: DF, DHF, Aedes, new initiatives, surveillance information system, legislative changes, Malaysia.

Introduction
Dengue fever (DF) was first reported in Malaysia in 1902 and is now one of the major public health problems in Malaysia, especially with the emergence of dengue haemorrhagic fever (DHF) in 1962. Notification of DF and DHF was instituted in 1971, requiring all medical practitioners to report any case of confirmed or suspected dengue or dengue haemorrhagic fever to the nearest health office. Prevention and control of DF and DHF was further strengthened with the enactment of the Destruction of Disease-Bearing Insects Act 1975 which was amended in 2001 for heavier penalties.

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Epidemiology and New Initiatives in the Prevention and Control of Dengue in Malaysia

Dengue situation in Malaysia

Dengue infection is predominant in urban areas where 61.8% of the country’s population lives, as compared to only 34% in 1980. Rapid industrial and economic development over the last two decades has brought about massive infrastructure development and a very active construction sector for housing and commercial development, creating many man-made opportunities for Aedes mosquito breeding. This, coupled with rural-urban migration and pockets of illegal settlements, indiscriminate solid-waste disposal and a tropical rainfall, provide fertile grounds for Aedes breeding and the rise of dengue transmission in the country.

Epidemiological characteristics

Incidence

The number of clinically-diagnosed DF and DHF reported cases has been steadily increasing from below 1,000 cases a year to over 5,000 cases since 1991. There were outbreaks in 1974 and 1982, and a major outbreak in 1998 with 27,381 cases reported.

Serologically-confirmed cases ranged between 40-50% over the last five years (1996-2000). The rate was much higher in 1994 and 1995 due to pilot studies to notify only confirmed cases. The gap between clinically-diagnosed and laboratory confirmed cases remain high due to over-reporting, especially during the last major dengue outbreak in 1997-98, and also the fact that many laboratory results are inconclusive due to technical reasons. Figure 1 includes distribution of clinically and serologically-diagnosed cases per 100,000 population for the year 1991-2000.
Age distribution

Most of the reported cases were from the young and middle-age groups. These were people who were active outdoors, whether working, schooling or playing outside their homes. Aedes breeding in the homes is low, where the Aedes index is less than 1%. Figure 2 shows the age-specific morbidity rate per 100,000 population, 1991-2000.

Clinical entity

Dengue fever was the predominant type with the DF/DHF ratio of 16-25:1 over the last 5 years (Table 1), based on the notified clinically-diagnosed cases. For cases notified in the first 8 months of 2001, about 47.7% were serologically positive for dengue. From these serologically-confirmed cases, the predominance of dengue fever over dengue haemorrhagic fever was also noted where the ratio was 21.3:1, as compared to a ratio of 17.9:1 for all notified cases in the same period in 2001.

Table 1. Ratio of DF and DHF reported cases, 1996-2001 (August)

<table>
<thead>
<tr>
<th>Year</th>
<th>DF</th>
<th>DHF</th>
<th>DF:DHF Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>1996</td>
<td>13,723</td>
<td>532</td>
<td>25.8:1</td>
</tr>
<tr>
<td>1997</td>
<td>18,642</td>
<td>787</td>
<td>23.7:1</td>
</tr>
<tr>
<td>1998</td>
<td>26,240</td>
<td>1133</td>
<td>23.1:1</td>
</tr>
<tr>
<td>1999</td>
<td>9,602</td>
<td>544</td>
<td>17.6:1</td>
</tr>
<tr>
<td>2000</td>
<td>6,692</td>
<td>411</td>
<td>16.28:1</td>
</tr>
<tr>
<td>2001</td>
<td>9,375</td>
<td>524</td>
<td>17.9:1</td>
</tr>
</tbody>
</table>

Figure 2. Distribution of dengue cases by age-specific morbidity rate per 100,000 population, 1991-2000
Serotype

DEN-3 was the predominant serotype during the 1992-1995 period. This was replaced by DEN-1 and DEN-2 in the next 4 years from 1996-1999. Since the year 2000, DEN-3 has re-emerged with an increasing number of such serotypes, together with DEN-2. Figure 3 shows the distribution of circulating DEN serotypes in the last 10 years.

Mortality

The case-fatality rate (CFR) for DF and DHF is shown in Figure 4. The case-fatality for DHF was especially high but this was partly contributed by under-reporting of DHF where the initial notification as DF was not rectified when these cases subsequently were diagnosed as DHF. Thus, the denominator for DHF remains the old lower figure.

Figure 3. Circulating DEN serotypes 1990-2000

<table>
<thead>
<tr>
<th>Year</th>
<th>DEN-1</th>
<th>DEN-2</th>
<th>DEN-3</th>
<th>DEN-4</th>
</tr>
</thead>
<tbody>
<tr>
<td>1990</td>
<td>8.9</td>
<td>86.2</td>
<td>4.1</td>
<td>0.8</td>
</tr>
<tr>
<td>1991</td>
<td>11.9</td>
<td>54.2</td>
<td>32.5</td>
<td>1.4</td>
</tr>
<tr>
<td>1992</td>
<td>3.7</td>
<td>8.6</td>
<td>83.7</td>
<td>4</td>
</tr>
<tr>
<td>1993</td>
<td>0</td>
<td>4.1</td>
<td>93.1</td>
<td>2.8</td>
</tr>
<tr>
<td>1994</td>
<td>4.8</td>
<td>9.5</td>
<td>84.1</td>
<td>1.6</td>
</tr>
<tr>
<td>1995</td>
<td>14.7</td>
<td>29.5</td>
<td>54.6</td>
<td>1.2</td>
</tr>
<tr>
<td>1996</td>
<td>48.7</td>
<td>48.7</td>
<td>2.6</td>
<td>0</td>
</tr>
<tr>
<td>1997</td>
<td>63.5</td>
<td>33.4</td>
<td>2.1</td>
<td>0</td>
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<tr>
<td>1998</td>
<td>44.4</td>
<td>51.9</td>
<td>3.7</td>
<td>0</td>
</tr>
<tr>
<td>1999</td>
<td>28.2</td>
<td>69.2</td>
<td>2.7</td>
<td>0</td>
</tr>
<tr>
<td>2000</td>
<td>9.3</td>
<td>58.1</td>
<td>32.6</td>
<td>0</td>
</tr>
</tbody>
</table>

Figure 4. Dengue case-fatality rate according to DF/DHF and DHF in Malaysia 1984-2000 (August)
Aedes surveillance

Regular Aedes larval surveys and outbreak surveys provide the Aedes surveillance data in the country. The pattern of Aedes breeding is indicated by data from surveys for the year 2000 (Table 2). Residential premises had the lowest percentage of breeding at less than 1%.

Table 2. Aedes breeding by type of premises in 2000

<table>
<thead>
<tr>
<th>Type of premises</th>
<th>No. examined</th>
<th>Aedes breeding</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. positive</td>
<td>%</td>
</tr>
<tr>
<td>Factories</td>
<td>8,064</td>
<td>651</td>
</tr>
<tr>
<td>Abandoned housing</td>
<td>828</td>
<td>56</td>
</tr>
<tr>
<td>projects</td>
<td></td>
<td>6.80</td>
</tr>
<tr>
<td>Construction sites</td>
<td>6,335</td>
<td>398</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6.30</td>
</tr>
<tr>
<td>Vacant land</td>
<td>5,789</td>
<td>212</td>
</tr>
<tr>
<td>Garbage dump sites</td>
<td>3,439</td>
<td>110</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3.20</td>
</tr>
<tr>
<td>Offices</td>
<td>3,199</td>
<td>94</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2.90</td>
</tr>
<tr>
<td>Schools</td>
<td>22,464</td>
<td>576</td>
</tr>
<tr>
<td>Houses / Shops</td>
<td>1,916,604</td>
<td>11,187</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.60</td>
</tr>
</tbody>
</table>

Dengue control programme

Areas of focus

Dengue control forms part of the national Vector-Borne Disease Control Programme which encompasses malaria, dengue, Japanese encephalitis, filariasis, typhus, yellow fever and other new emerging vector-borne diseases. The dengue control programme(2) comprises the following aspects:

- Disease surveillance and control
- Vector surveillance and control
- Public education
- Inter-agency collaboration and community participation
- Quality assurance
- Research and training

Objective and targets of the dengue control programme

The main objective of the programme is to reduce the morbidity and mortality caused by DF/DHF so that it will no longer pose a public health problem.

The targets set under the Eighth Malaysia Plan (2001-2005) are as follows:

1. Not more than 50 cases of DF/100,000 population.
2. Not more than 2 cases of DHF/100,000 population.
3. Case-fatality rate of DF/DHF not more than 0.2%.
4. Case-fatality rate of DHF not more than 1.0%.
5. Aedes Premise Index not more than 1%.

Strategies

(1) Epidemiological surveillance through prompt case notification within 24 hours of clinical diagnosis via phone, fax or e-mail.
(2) Enhancing laboratory diagnostic support through the use of rapid screening tests and confirmation by standard laboratory technique.

(3) Improved clinical management through early case detection and quality assurance surveillance and audit.

(4) Case control through rapid response aimed at case investigation and destruction of vector by chemical fogging.

(5) Entomological surveillance through regular Aedes larval surveys.

(6) Legislative control on Aedes breeding through premises inspection and destruction of breeding sources.

(7) Public education through health education activities in the community and with community involvement.

(8) Inter-agency collaboration targeting at high-risk areas and population groups such as schools, construction sites, solid-waste dumps, factories and government facilities.

**Country initiatives and policy changes**

**Reprioritizing Aedes surveillance areas**

Prior to 1998, Aedes larval surveys were concentrated in residential areas. However, Aedes breeding was noted to be low, at around or below 1% of houses inspected. On the other hand, surveillance at construction sites indicated Aedes index to be very high (20.4% in 1995; 23.8% in 1996; and 15.6% in 1997).

In 1998, the approach was changed where dengue teams carried out regular inspections at construction sites, factories, abandoned housing projects, garbage dump sites, schools, government facilities and others, besides inspections at any site during case/outbreak investigations. Targets were set in terms of proportions of different premises and areas to be inspected, based on three classifications of priority areas.

**Strengthening information system for effective disease surveillance and response**

**Communicable Disease Control Information System (CDCIS)**

The Ministry of Health is in the process of developing a comprehensive national computerized communicable disease control information system (CDCIS) that would cover the following aspects:

- Disease notification
- Disease registration
- Case investigations
- Case follow-up
- Report generation
- Early warning system

A geographical information system (GIS) is in the early stage of development. This would initially be developed for vector-borne diseases before being expanded to other communicable diseases.
Legislative changes

Legislative control is an important means for dengue prevention and control in Malaysia. The Destruction of Disease-Bearing Insects Act, 1975, was recently amended and new provisions for heavier penalties became enforceable from 1st January 2001. This was aimed at big offenders like housing developers and factory owners where the earlier penalty was found to be not deterrent enough. Among the changes made were (with the earlier penalty in parenthesis):

- First offence – fine not exceeding RM 10,000 or imprisonment for a term not exceeding 2 years, or both (previously RM 1,000 fine and 3 months’ imprisonment);
- Second or subsequent offence – a fine not exceeding RM 50,000 or imprisonment for a term not exceeding 5 years (previously RM 2,000 fine and 1 year imprisonment);
- Continuing offence – further fine not exceeding RM 500 for every day that the offence is continued (previously RM 50).

Community participation and intersectoral collaboration - national cleanliness and anti-mosquito campaigns

In 1999, the Government reaffirmed its commitment towards the control of mosquito-borne diseases such as dengue by the launching of a multi-ministerial National Cleanliness and Anti-Mosquito Campaign that is still ongoing. The aim of the campaign is to create awareness amongst the community on the dangers of mosquitoes and to inculcate good practices to rid of mosquito-breeding sites in and around their places of stay, work and play.

The campaign will be further strengthened with a nationwide “Promotion of a Healthy Environment” campaign, to be launched in 2002. The aim is to promote community participation in ensuring the environment is free from mosquitoes and pests.

Changing insecticide fogging formulation and mass Abating

Traditionally, malathion was the chemical of choice for dengue control. Observations and feedback by the fogging teams indicated that the people did not accept fogging inside their houses since malathion was smelly and diesel-solvent which left oily residues on the floors and walls of houses.

The use of malathion was stopped in 1996 and replaced with water-based pyrethroid fogging formulations such as Resigen and Aqua-resigen. The use of Abate larvicide on a large scale in high-risk areas was also initiated in 1998 to reduce Aedes larval density.

Reducing disease burden - DHF case fatality

The DHF case fatality was still high at 9.9% in 2000, against the target of not more than 1%. While one of the reasons for the high rate was due to the under-reporting of DHF cases (DHF cases being initially notified as
DF and remained so, even after revision of diagnosis, thus affecting the denominator for DHF cases), strengthening of patient management in hospitals is certainly one strategy to reduce deaths.

In this respect, the Ministry of Health, together with the Academy of Medicine, Malaysia, developed a Clinical Practice Guideline on the management of dengue infection in 2000\(^5\). Further, under the revised indicators for the national Quality Assurance (QA) programme for patient care that is being implemented this year, dengue case fatality has been included as a national indicator to improve the quality of care for DFH patients (one of the 53 indicators on patient care). Under this QA programme, DHF deaths are considered sentinel events that need to be audited immediately. Appropriate remedial actions are to be taken to rectify any weaknesses identified in the audit. The QA on DHF deaths would certainly create greater awareness about the proper management of DHF and bring about reduction in such deaths.

**Conclusion**

Control of dengue and dengue haemorrhagic fever is a multi-sectoral effort which requires strong community participation.

The Ministry of Health in Malaysia will continue to provide the leadership in getting all parties to work together while enhancing its own capacity and technical capability to face the many challenges in the control of dengue in the country. Several initiatives have been taken to strengthen dengue control in the country but certainly, more could be done. With proper focus, new initiatives and continual effort, we hope to achieve or even surpass the targets set for the programme.

**References**

Dengue Outbreak 2000 in Bangladesh: From Speculation to Reality and Exercises

by
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Abstract
An outbreak of DF/DHF occurred in three major cities and 17 other towns of Bangladesh in June 2000. The total number of cases recorded was 5551: DF 4385 (98.9%) and DHF 1166 (21.1%), with 93 deaths (1.6%). In 1996-97, a well-designed hospital-based descriptive study revealed evidence of dengue infection in a significant proportion of febrile cases (13.7%) with three serotypes of the dengue virus (DEN-1, DEN-2 and DEN-3) where the secondary infection pattern outnumbered the primary type. These findings confirmed the continuation of transmission and the potential for future outbreaks. An entomological survey in the same city revealed the presence of the vector *Aedes aegypti* with a Breteau index of 18.2% during this period. When the outbreak became a reality, initially the people, the medical profession and the control programme implementers were in a state of confusion due to the lack of knowledge, skill and attitude necessary for its containment. Soon the National Control Programme developed appropriate plans of action and instruments of operation in collaboration with WHO to tackle the situation in all spheres with successful operationalization. The outcome was the development of national guidelines for the clinical management of dengue syndrome, training of doctors, reorientation of specialists, entomological mapping, documentation of cases, operational studies for testing case definitions and collection of sero-evidences as well as empowering the community to ensure their appropriate participation for prevention and control. Besides successes there were failures too.

Keywords: Dengue outbreak, case management, entomological assessment, lessons learnt.

Introduction
Dengue is a common communicable infectious disease of which the frequency is next only to malaria globally. The new pattern of dengue, dengue haemorrhagic fever (DHF), appeared in Thailand in the 1950s and almost invaded all the countries in the South-East Asian Region. It has now become a public health problem of great concern. Outbreaks of DF and DHF have now become a regular cyclical phenomenon

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Dengue Outbreak 2000 in Bangladesh: From Speculation to Reality and Exercises

with increasing incidence, morbidity and mortality in almost all the countries surrounding Bangladesh which have similar socio-economic, climatic and geographical features.

Bangladesh was thought to be free from dengue except some sporadic reports of incidence since 1965\(^2\). As a result the people, the medical profession and the disease control programme were not acquainted with and aware about dengue in any of its different aspects like diagnosis, management, prevention and control. The dengue outbreak of 2000 changed the notion and other attributes related to dengue. The evidence of dengue infection was confirmed earlier by a well-designed descriptive study done in 1996-97 that was sponsored by the Integrated Control of Vector-Borne Diseases (ICOVED) Project of the Directorate-General of Health Services in collaboration with WHO\(^3\). Besides confirming the presence of dengue, the study also unveiled some evidence of the future outbreak potential.

In 2000 a major outbreak occurred in Bangladesh, mostly in three large cities with reports also coming in from 17 other towns. During this outbreak many clinical and public health exercises were performed, documentation was recorded and measures were taken to prepare for the future along with developing some scientific activities.

The endeavours of ICOVED

The 1995 endeavours of ICOVED included a sero-epidemiological study for dengue and dengue haemorrhagic fever, undertaken at the Chittagong Medical College Hospital (CMCH) over a period of about one year during 1996-97 among febrile patients of the paediatric age group with haemagglutination inhibition test (HIT) of paired sera one week apart. Out of the 255 paired samples 35(13.7\%) were found to be positive with evidence of more than one serotype of dengue virus, where secondary infection outnumbered the primary. An entomological survey vis-a-vis serological documentation revealed the presence of the vector Aedes aegypti with a Breteau index of 18.2 (Table 1).

<table>
<thead>
<tr>
<th>Table 1. ICOVED endeavours: Sero-survey and Entomological survey</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A. Sero-survey in Chittagong Medical College Hospital(^3)</strong></td>
</tr>
<tr>
<td>Total</td>
</tr>
<tr>
<td>Age Mean: 7.1 (± 0.2.8) Years</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Positive HIT</td>
</tr>
<tr>
<td>Primary</td>
</tr>
<tr>
<td>Secondary</td>
</tr>
<tr>
<td>Primary/Secondary</td>
</tr>
<tr>
<td>DEN-1 Serotype</td>
</tr>
<tr>
<td>DEN-2 Serotype</td>
</tr>
<tr>
<td>DEN-3 Serotype</td>
</tr>
<tr>
<td>DEN-4 Serotype</td>
</tr>
<tr>
<td>DEN-2+DEN-3 Serotypes</td>
</tr>
<tr>
<td>DEN-2+DEN-4 Serotypes</td>
</tr>
<tr>
<td>DEN-3+DEN-4 Serotypes</td>
</tr>
<tr>
<td><strong>B. Entomological survey in Chittagong city(^4)</strong></td>
</tr>
<tr>
<td>Vector</td>
</tr>
<tr>
<td>House index</td>
</tr>
<tr>
<td>Container index</td>
</tr>
<tr>
<td>Breteau index</td>
</tr>
</tbody>
</table>
The aforementioned ICOVED endeavours confirmed the presence of dengue cases, the vector and a possible continuation of the disease transmission. From these results at that time it was speculated that possibly a big outbreak was likely to occur within a few years.

The 2000 Outbreak

From June 2000 onwards, the spell and the toll of the dengue outbreak began to occur with cases of haemorrhagic fever filling the city hospitals and clinics mostly in Dhaka, Chittagong and Khulna. Cases were reported from 17 other cities as well. The outbreak lasted till December 2000. The total number of cases recorded were 5551: DF 4385 (78.9%), DHF 1166 (21.1%) with 93 (1.6%) deaths (Table 2). The proportion of DHF was less in Dhaka city, and the mortality was found to be less in Dhaka and Chittagong. The reason for this was the later is possibly that better case management facilities were available here than in other cities. The presence of more DF cases in Dhaka was a harbinger of more DHF cases there later.

Table 2. Reported cases of DF/DHF from July-December 2000

<table>
<thead>
<tr>
<th>Cities</th>
<th>Total</th>
<th>DF (%)</th>
<th>DHF (%)</th>
<th>Deaths (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dhaka</td>
<td>3964</td>
<td>3383 (85.3)</td>
<td>0581 (14.7)</td>
<td>51 (01.3)</td>
</tr>
<tr>
<td>Chittagong</td>
<td>0771</td>
<td>0473 (61.3)</td>
<td>0298 (38.7)</td>
<td>15 (01.9)</td>
</tr>
<tr>
<td>Khulna</td>
<td>0428</td>
<td>0259 (60.5)</td>
<td>0169 (39.5)</td>
<td>14 (03.3)</td>
</tr>
<tr>
<td>Others: 17 cities</td>
<td>0388</td>
<td>0270 (66.7)</td>
<td>0118 (33.3)</td>
<td>13 (03.3)</td>
</tr>
<tr>
<td>Total</td>
<td>5551</td>
<td>4385 (78.9)</td>
<td>1166 (21.1)</td>
<td>93 (01.6)</td>
</tr>
</tbody>
</table>

Clinical pattern of dengue cases

During the early part of the outbreak, members of the Malaria Research Group documented the clinical and epidemiological features of haemorrhagic fever cases admitted in the Medical and Paediatrics units of the CMCH during the month of August 2000. A total of 112 (83%) cases in adult Medical and 23 (17%) cases in Paediatrics units were recorded. The categorization of cases as per WHO case definition DF, DHF-I, DHF-II, DHF-III and DHF-IV were 24(21%), 80(71%), 5(5%), 1(1%) and 2(2%) respectively. Seventy-three percent of these were males and the over all case fatality was 2.7%. The mean age (years), duration of illness (days), duration of fever (days), duration of rash (days), rash appearance day (day), afebrile period (days) were 25.4, 8.1, 6, 3.3, 5.5 and 2.0 respectively. The most frequent features were: high fever (100%), severe headache (80%), external bleeding (79%), severe bodyache (64%), red eye (56%), eyeache (34%), altered bowel (33%), cough (30%), and abdominal pain (26%). Tourniquet test was done in 46 cases with positive result in 60%. The frequency of cutaneous bleeding were 64%, haemorrhage 79%, mean platelet count 96900 mm$^3$, PCV 49.1%, total leucocyte 6900mm$^3$ and haemoglobin 12 g/dl. Rapid dengue test was done in 43 cases with overall positivity 74.4%. This documentation revealed that there were more adult than pediatric patients.

Exercises for management of cases

Within the first week of the report of the dengue outbreak the Disease Control
Directorate initially arranged the collection of WHO guidelines for case management and test-kits for dengue serology and established reporting portals and a set-up for the documentation of cases. This effort was followed by training of doctors and orientation of specialists on dengue case management, formulation of National Guidelines for Clinical Management of Dengue Syndrome by customization of WHO guidelines and attaining a general consensus, entomological survey, plus initiation of clinical and virological documentations. Around 300 doctors were trained, 150 specialists were reoriented and a general national consensus on a uniform system of case definition and management was attained. The help of leading experts on dengue for its clinical and other aspects was ensured as well. All these efforts were collaborated by WHO.

**Entomological survey during 2000 outbreak**

During the 2000 outbreak a comprehensive entomological survey was conducted in major cities of Bangladesh to document the disease pattern and as a requirement for future preparedness.

<table>
<thead>
<tr>
<th>Cities</th>
<th>House Index (%)</th>
<th>Container Index (%)</th>
<th>Breteau Index</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dhaka</td>
<td>46</td>
<td>37</td>
<td>50</td>
</tr>
<tr>
<td>Chittagong</td>
<td>22</td>
<td>13</td>
<td>18</td>
</tr>
<tr>
<td>Khulna</td>
<td>40</td>
<td>31</td>
<td>42</td>
</tr>
<tr>
<td>Others: 17 cities</td>
<td>1.6, 14.5, 20.3</td>
<td>23, 19.9, 19.9</td>
<td>1.6, 18.7, 23.8</td>
</tr>
</tbody>
</table>

In all major cities entomological indices were present in a significant way (Table 3). But proper assessments and implications could not be inferred because of lack of earlier data and absence of critical threshold values.

**Continuing activities**

The National Control Programme has now adopted some activities on a continuing basis. These are: prospective serological survey in hospitals of two major cities plus a study for collecting febrile phase sera of eligible cases for viral isolation and PCR. In both the studies entries of national case definition will be tested in terms of specificity, sensitivity and predictive values in an attempt to choose the early markers for use in national control programme operations besides clinical use. In addition, entomological data collection, training and reorientation of doctors and health-care providers plus community empowering activities are also being continued.

**Discussion**

Dengue was not a matter of clinical concern or a public health issue till the outbreak of 2000. But there was evidence that dengue was present with outbreak potential. When the outbreak became a reality it changed many attitudes: clinicians’ views and activities; the perception and operational plans of national control programmes; attitudes of civil society and community empowerment; and capacity development. The pattern of the disease emergence in Bangladesh was not different from that in the neighbouring countries as well as the clinical...
issues involved except the patients’ age. Though dengue is mostly a paediatric disease, but in this outbreak most cases were adults. This fact was observed earlier also\(^9\). This is possibly because of the absence of cumulative acquired immunity.

The dengue outbreak might be considered a blessing in disguise. The most encouraging aspect was the general community’s response to it. Though initially there was panic, accusation and confusion, but for the first time in this country the community gave a tremendous response which is unmatched for any other infectious disease. People from all sections of the society, media, and other professions responded in a very pragmatic way to create and take preventive actions to combat dengue. The role of the public agencies was also relatively prompt and effective. For the first time in the country health agencies were able to disseminate the knowledge, skills and resources to effectively contain the problem. Moreover, health agencies were also able to develop a consensual National Guideline for Clinical Management of Dengue Syndrome in an effort to make the clinical management uniform, effective, user-friendly and cost-effective, which was devoid of any confusions and controversies. In other words, an appropriate tool for the early diagnosis and prompt treatment of dengue was made available which was the only effective tool for prevention and control\(^9\). The control programme’s terminology ‘dengue syndrome’ as adopted in the National Guideline to avoid confusion of the overlapping nature of the various manifestations of dengue provided appropriate emphasis on the nature and course of the disease and the measures to be taken. This received due endorsement from all concerned. It was due to these efforts that despite the large number of cases the mortality was kept low.

But there were failures too. One needs to understand the failures in order to avoid making similar mistakes in the future. As medical professionals we should accept the fact that we failed to respond properly at an appropriate time when the evidences were available a few years back. With the emergence and reporting of the disease we could have easily collected the relevant information, knowledge and skill through the information super highway and other linkages. Our general and specialized bodies could then have developed and disseminated guidelines for disease management as well as documentation tools, templates and linkages promptly. By this we could have easily avoided the management controversies and could have had a strong grip over the situation, not to speak of the trust of the people. Through this basic approach we could also guide the people and government agencies as well to choose and employ the most appropriate measures. In reality the reverse happened. We missed a golden opportunity to clinically document an outbreak afresh in our land.

This outbreak gave rise to certain issues which need to be resolved. The first and foremost is to find out the critical threshold of the entomological indices of the vector. The second is: what are the most appropriate measures for control and prevention. For this purpose there is a need to establish appropriate clinical markers and their correlation in terms of specificity, sensitivity and predictive values for early
diagnosis and prompt treatment like those developed in Thailand\(^\text{[10]}\). The next issue is appropriate community empowerment and participation. The track record of dengue reveals that it enters a country not to leave. In countries where dengue has emerged as a public health problem, it has remained so, proving thereby that it is not merely a clinical issue. The toll taken by dengue is enormous in all respects and its characteristics are unique in many ways\(^\text{[11]}\).

So, from the dengue outbreak in 2000 we need to learn evidence-based lessons\(^\text{[10]}\), consolidate them in proper ways and analyse them in a scientific format to prepare appropriate plans and programmes for effective implementation to combat the infection in the future. Moreover, this should prompt us to be more proactive.

In short, the public and the medical profession should be oriented to ‘learn to live with dengue’ and this orientation process should be coordinated by the National Control Programme through creating awareness and taking action, the first target to be to reduce mortality and the next to reduce morbidity.

References


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DF/DHF and Its Control in Fiji

by

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Abstract

Dengue haemorrhagic fever (DHF) first appeared in Fiji in 1975, with subsequent outbreaks in 1979-80, 1989-90 and 1997-98. The 1997-98 outbreak of DF/DHF was explosive with 24,000 cases and 13 deaths when the disease also spread to rural areas. The epidemiology of DF in Fiji is unique, as urban and rural transmissions occur through different sets of species. Aedes aegypti, Aedes albopictus, Aedes polynesiensis and Aedes pseudoscudellaris are abundant in urban, peri-urban and rural habitats, whereas Aedes horrescens and Aedes rotumae have a more patchy distribution. Therefore, Fiji’s dengue control efforts cannot be focused just on urban Aedes aegypti as elsewhere in the world. In Fiji, integrated methods of vector control placing particular emphasis on source reduction through strategically developed health promotion campaigns and community participation backed up by law enforcement are in place. Chemical control is not used as a routine measure in Fiji except during DF/DHF outbreaks.

An active surveillance system for early warning and detection of potential DF/DHF outbreak has been established following the 1997-98 epidemic (clinical, laboratory-based surveillance and entomological). For the first time these surveillance systems have coordinated well to address dengue control in Fiji and to activate appropriate public health response from communities.

Keywords: DF/DHF, Aedes spp., integrated control, surveillance systems, law enforcement, Fiji.

Introduction

Fiji, comprising about 300 islands, located in the southwest of the Pacific Ocean, lies between 15° and 22° south of the Equator. One-third of the islands are inhabited, and 70% of the population lives on the largest island, Viti Levu. Suva is the largest city, the main port and the Capital. Vanua Levu and Taveuni, the second and third largest islands, lie in the northeast of Viti Levu. Travel between these three islands is frequent,
rapid, easy and inexpensive, which facilitates the movement of human hosts and mosquitoes infected with dengue viruses.

**History of dengue**

DHF was first recognized in 1954 in the Philippines but was not seen in Fiji until 1975\(^1\). Subsequent DHF outbreaks in Fiji occurred in 1979-80, 1989-90 and 1997-98. During the last explosive outbreak of DF/DHF in 1997-98 there were more than 24,000 reported cases with 13 deaths due to DHF or DSS. Table 1 depicts the morbidity and mortality recorded between 1885-1989/1999\(^1,2\).

**Table 1. Dengue epidemics in Fiji from 1885-1998/1999**

<table>
<thead>
<tr>
<th>Year</th>
<th>Serotype</th>
<th>Number of cases</th>
<th>DHF-DSS</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>1885</td>
<td>Not known</td>
<td>Thousands</td>
<td>Not known</td>
<td>Not reported</td>
</tr>
<tr>
<td>1930</td>
<td>Not known</td>
<td>Thousands</td>
<td>Not known</td>
<td>Not reported</td>
</tr>
<tr>
<td>1943-44</td>
<td>Not known</td>
<td>Thousands</td>
<td>Not known</td>
<td>None</td>
</tr>
<tr>
<td>1971-72</td>
<td>DEN-2</td>
<td>4,000</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>1974-75</td>
<td>DEN-1</td>
<td>20,000</td>
<td>Yes</td>
<td>12</td>
</tr>
<tr>
<td>1980</td>
<td>Not known</td>
<td>127</td>
<td>Not known</td>
<td>Not reported</td>
</tr>
<tr>
<td>1981</td>
<td>DEN-4</td>
<td>Hundreds</td>
<td>Yes</td>
<td>1</td>
</tr>
<tr>
<td>1982</td>
<td>DEN-2</td>
<td>546+</td>
<td>Not known</td>
<td>Not reported</td>
</tr>
<tr>
<td>1983</td>
<td>Not known</td>
<td>237+</td>
<td>Not known</td>
<td>None</td>
</tr>
<tr>
<td>1989-90</td>
<td>DEN-1</td>
<td>3,686</td>
<td>Yes</td>
<td>30</td>
</tr>
<tr>
<td>1997-98</td>
<td>DEN-2</td>
<td>24,000</td>
<td>Yes</td>
<td>13</td>
</tr>
<tr>
<td>1998-99</td>
<td>Not known</td>
<td>300+</td>
<td>Not known</td>
<td>None</td>
</tr>
</tbody>
</table>

**Serotypes identified in Fiji**

Table 1 also highlights the circulation of different serotypes in different years. DEN-2 has been in circulation since the 1971-72 outbreak. DEN-1 was detected during the 1974-75 epidemic. This was followed by DEN-4 during 1981. In subsequent epidemics DEN-1 and DEN-2 were prevalent. DEN-3 has not been isolated so far.

**Vectors of dengue and DHF**

In Fiji there are 26 known species of mosquitoes. The epidemiology of dengue in Fiji is unique because it is the only country in the world where four to six species of mosquitoes may transmit the viruses. The most effective vector is *Aedes aegypti* because of its close association with man. Other known vectors are *Aedes albopictus, Aedes polynesiensis, Aedes pseudoscutellaris,* and *Aedes rotumae* (in Rotuma only). *Aedes horrescens* may also transmit the virus\(^2\). The breeding habitats of these vectors are given in Table 2.

**Table 2. Vectors and their breeding habitats in Fiji**

| (1) | *Aedes aegypti* (primary vector) - used tyres, water storage containers, tins, pot plants, flower vases and man-made containers |
| (2) | *Aedes albopictus* - same as above including natural breeding habitats like tree holes and plant leaf axils |
| (3) | *Aedes pseudoscutellaris* - miscellaneous and artificial containers |
| (4) | *Aedes polynesiensis* - crab holes, coconut and sea shells, tree holes, tins along coastal areas |
| (5) | *Aedes rotumae* (in Rotuma only) - tree holes, coconut shells and tins |
| (6) | *Aedes horrescens* - tree holes |
Although Aedes aegypti is known to be the major vector of dengue, the Breteau index of Aedes aegypti during epidemics on Suva island ranged from 35.7 (1977) to 109.8 (1979) as indicated in Table 3. Aedes albopictus and Aedes pseudoscotellaris have also been recognized as dengue vectors in Fiji (Vector-Borne Disease Working Committee 1997:3-4). Aedes albopictus was first recognized in Fiji in 1988 and appears to be replacing Aedes aegypti in some places and displacing Aedes pseudoscotellaris in most areas. It was evident that by 1988, Aedes albopictus already was well established and distributed in all the three major islands of the country.

Table 3. Breteau index of Aedes aegypti during the years of dengue epidemics (in Suva)

<table>
<thead>
<tr>
<th>Year</th>
<th>Breteau Index</th>
</tr>
</thead>
<tbody>
<tr>
<td>1972</td>
<td>51.0</td>
</tr>
<tr>
<td>1974</td>
<td>78.0</td>
</tr>
<tr>
<td>1975</td>
<td>48.2</td>
</tr>
<tr>
<td>1976</td>
<td>48.5</td>
</tr>
<tr>
<td>1977</td>
<td>35.7</td>
</tr>
<tr>
<td>1979</td>
<td>109.8</td>
</tr>
<tr>
<td>1989</td>
<td>79.0</td>
</tr>
</tbody>
</table>

Key containers

The entomological studies undertaken in Suva between 1978-1979 revealed that Aedes aegypti and Aedes pseudoscotellaris bred in flower vases, drums, plant containers and tyres, but preferentially in miscellaneous containers such as tin cans, plastic food-containers and, to a lesser degree, in coconut shells, old motor parts and, least of all, in ground pools. However, these measurements take no account of the relative productivity of each larval habitat. Drums and tyres can produce far more adult mosquitoes than other containers and thus attention should be focused initially on these ‘key containers’ (3). Recent research in Fiji has shown that tyres and drums comprising 10-20% of the total containers found positive for Aedes larvae are responsible for 83-99% of the adult Aedes produced.

National dengue control plans

Sentinel vector surveillance system

Three sentinel sites (Suva, Lautoka and Labasa) have been selected as they are regarded as high-risk areas of dengue transmission. The National Vector Control Unit and the area health staff survey these sites at quarterly intervals. The Unit is responsible for identification, data processing and feedback. The Centre is also responsible for the overall coordination of public health responses to curb any potential outbreaks of DF/DHF. In 1998 the Pacific Regional Vector-Borne Disease Project (PRVBDP) of The Secretariat of the Pacific Community (SPC) facilitated the Ministry of Health with professional skills and resources in training the health inspectorate staff which led to the establishment of mini vector identification laboratories at divisional stations. All vector identification work in Fiji has been decentralized since September 1998.

(1) Monthly Aedes larvae surveillance:
A countrywide monthly Aedes larvae monitoring programme is carried out by the health inspectorate staff of all the urban
and rural local authorities on a monthly basis. This survey includes inspection of at least 100 premises per month, covering residential, commercial and industrial zones. In Fiji, the sample size comprises 10 larvae (including pupae) per container from all water-holding containers in a premises. In Fiji the Breteau Index is classified as follows:

(a) < 5 – No risk of transmission
(b) 5–35 – significant risk of transmission
(c) >35 should be considered as high risk of transmission.

(2) **Adult mosquito surveillance**: The surveillance of Aedes adults as for most other mosquitoes currently involve the collection of adults (mainly females) at bait, nets and traps. Mosquito nets and suction tubes are used for the collection of Aedes aegypti adults resting indoors and other Aedes species resting in vegetation or biting man outdoors. Ovitraps to trap eggs are used to reflect adult densities as a useful tool for surveillance of Aedes vectors. Presently, human baits are not used because of the potential risk of infection. In Fiji the Aedes landing/biting rate of more than 2 per man-hour should be considered as high risk of transmission.

**Integrated vector control measures**

The Central Board of Health is the regulatory body that oversees the urban and rural local authorities, which implement public health legislation. The Health Inspectorate personnel of all local authorities carry out monthly mosquito surveillance and control activities.

(A) **Control strategies**

(1) **Source reduction** (elimination of breeding sources).

(2) **Chemical spraying**. Malathion ULV for focal spraying during epidemics only to reduce adult density. Aqua Resigen for peri-focal sprays of case locations and area within 400 metres of case location.

(3) **Chemical larviciding**. Temephos (Abate) for ground pools and water storage receptacles.

(4) **Health promotion**. Dengue control demands household-level interventions and behavioural modifications that require high levels of community participation and support to remove refuse or carefully protect essential water containers and other household items that can provide ideal breeding sites for Aedes aegypti. During dengue outbreaks, control programmes must convince people of the need to reduce their own, and particularly their children's, chances of being bitten by day-biting mosquitoes. Inter-island and inter-country travel also needs to be reduced during outbreaks.

Dengue education messages are generally based on biomedical explanations of the disease and scientific observations of dengue.
mosquitoes, but these are often too abstract for people to be able to relate them to their own knowledge and immediate surroundings. Continued anti-dengue campaigns with community participation and involvement are essential to prevent outbreaks.

(5) **Law enforcement (backing for effective implementation of the programme).**

The penalty for offences related to mosquito breeding is very minimal. The Public Health Act of Fiji is under review to address this issue.

(6) **Biological control.**

(a) Fish Poecelia reticulata (Guppy) Tilapia - Control in pools, drains rice fields, etc.

(b) Toxorhynchites amboinensis (A predatory mosquito) - Control in tree holes, tyres, drums, etc.

(c) Bacillus thuringiensis var. Israelensis (Bacterium) - Control in ground pools with brackish water - coastal areas.

(d) Tolypocladium cylindrosporum (Fungus) lab trials and field trials - Nukui, Rewa.

(7) **Strategies for sustainability.**

The goal of the strategy for anti-dengue vector preventive and control work in Fiji is to prevent the recurrence of dengue epidemic as a public health problem. It has nine components as key areas of concentration:

- Develop diagnostic procedures to enable confirmatory tests of dengue fever cases.

- Develop clinical management of dengue cases both for use by the general public in rudimentary early case management and importantly at clinics, hospitals, and for outpatients and also for inpatients.

- Vector surveillance and control: This includes consistent mosquito surveillance and anti-mosquito work focusing first in cities, towns, neighbouring settlements and villages. It also includes designs and management of control programme that are practical and economical.

- Mobilization of communities for source reduction from church groups, women and youth groups, scouts and girl guides, schools, villages and similar types of groups. To be effective in source reduction, any attempts to address mosquito-breeding sites must include a strong and effective mobilization programme.

- Development and wide distribution of effective health promotion IEC materials to the general public and government and non-government institutions. Evaluation of these IEC materials must be an ongoing exercise to be responsive to public attitudes and behavioural patterns.

- Capacity-building and training in the entomological, surveillance and vector control aspects of the programme of divisional, district and area health inspectors, including those who are employed in city and town councils.
• Periodical exercises to alert key workers of the importance of emergency preparedness and coordination in vector mosquito surveillance and control work.

• Information and management training of key environmental health officers and other cadres of key health workers who are involved in surveillance and control work, source reduction, resource management and health promotion.

• Develop an improved anti-mosquito surveillance and control programme in each of the major cities, towns and each rural local authority. The plan will include zoning of each area to facilitate proper coverage and consistence in mosquito surveillance and control work.

Preparedness against outbreaks of arboviral diseases

(1) Main objective
The programme’s main objective is to strengthen active and quick response for the control of epidemics of arboviral diseases in Fiji.

(2) Immediate objectives
In order to develop preparedness against arboviral diseases, the following objectives are to be attained:

(1) To discover and report outbreaks of arboviral diseases as early as possible. Surveillance activities shall be conducted by means of monitoring the requests for serological tests of suspected patients and mosquito inoculation studies as well as by the results of vector surveillance.

(2) To train medical and paramedical staff on early diagnosis and treatment, and prevention and control measures of arboviral diseases. They shall also be trained in the use and maintenance of insecticide-spraying machines.

(3) To keep vehicle-mounted spraying machines in the main urban centres and portable spraying machines in other centres.

(4) To keep sufficient reserve of insecticides and spare parts for spraying machines in other centres.

(3) Outputs
The outputs of this programme will consist of the following:

(1) Stocking of insecticides and spraying equipment at national Vector Control Unit and at all other centres so that these are available immediately for emergency use during outbreak of arboviral disease.

(2) Long-range programme to control the larval population of vectors of arboviral diseases will be undertaken by the health inspectorate staff of each district.
(3) Establishment within each district of a group of trained personnel capable of carrying out both emergency and long-range programmes of arboviral disease control.

(4) The Wellcome Virus Laboratory to carry out regular serological tests of blood samples from all districts.

(5) The national Vector Control Unit, divisional vector control units, Suva and Lautoka City Council vector control units to carry out the identification of mosquito larval and adult specimens from all districts.

Conclusion

The main strategy for controlling dengue and other mosquito-borne diseases in Fiji is through reduction of the vector population. Most methods of attack are aimed at the breeding habitats, which can be divided into two basic areas: artificial and natural.

To control mosquitoes in artificial containers, environmental sanitation in conjunction with education of the public and constant surveillance by health authorities appears to be the key factor in lowering the population of dengue vectors. Natural habitats such as tree holes, crab holes, ground pools, leaf axils and hoof prints occur mainly in the rural and coastal areas. Because the range of habitats are so diverse, the application of insecticides would not only be very difficult but economically impracticable and ecologically unsafe. Environmental management or source reduction would also not be economical or logical as many of these natural breeding habitats are extensively used by the people of the region. The use of bio-control agents like pathogens, parasites and predators, which already exist in nature, are best suited to control mosquitoes in these natural habitats. Biological control in the South Pacific has been actively pursued and Fiji, in particular, has had outstanding success as against various agricultural pests. Fiji, in general, is well suited for bio-control programmes because of its isolation and small size.

References


Epidemiological Analysis of Deaths Associated with Dengue Haemorrhagic Fever in Southern Viet Nam in 1999-2000

by

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Abstract

A retrospective epidemiological study of deaths due to dengue haemorrhagic fever (DHF) in 19 provinces of southern Viet Nam in 1999 and 2000 was undertaken. Most deaths occurred among those less than 15 years old (92.7%), especially those aged 5-9 years; 81.6% of them were in the south-west provinces (Mekong delta region). Almost all the cases were hospitalized too late (3-4 days after the onset of the disease). One-half of the deaths occurred during the first 24 hours and one-third of the remaining deaths between the third and the sixth day of hospitalization. Most of the deaths occurred in provincial hospitals rather than in district hospitals.

Keywords: Dengue deaths, retrospective study, Viet Nam.

Introduction

Dengue haemorrhagic fever (DHF) is still the leading cause of mortality among the reported infectious diseases in southern Viet Nam(1), although morbidity decreased in 2000 (69.9/105) as compared to the average during the previous 5 years (1994-1998) (250.7/105). Mortality and the case-fatality rate followed the same pattern: 2000: 0.18/105 and 0.26%; 1994-1998: 0.71/105 and 0.29%, respectively(2,3). The dengue shock syndrome (DSS) (grade III, IV) occurrence rate was: 2000: 1.5%; 1999: 2.1%. Southern Viet Nam still accounted for 90% of total deaths due to DHF in the country(2,4).

It was considered necessary to explain the epidemiological characteristics of all DHF deaths in 19 provinces of southern Viet Nam in order to gather information for improving the control strategy and management to reduce the case-fatality rates in Viet Nam as per the objectives of the DHF control programme.

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Study method

The retrospective study was based on the data entered into the DHF death surveillance proforma of the National Target DHF Control Programme in southern Viet Nam for 1999 and 2000[5,6].

Sample size: It included 53 deaths out of 65 in 1999 and 43 deaths out of 49 in 2000 with full information on the DHF death form in 19 provinces of southern Viet Nam (the rest was not included because of incomplete information).

Results and discussions

(1) Distribution of deaths by age

In both years (1999-2000), those mainly affected were below 15 years of age (92.7%) (89/96 deaths); only 7.3% of them were aged above 15 years. Most deaths occurred among 5-9-year-olds (50%) (Figure 1), who also had the highest DHF morbidity[3,4]. It could have been that southern Viet Nam was an epidemic region and, thus, almost all DHF patients were infected at a younger age.

(2) Distribution of deaths by sex

In 1999-2000, the proportion of deaths among males and females was not equal (Figure 2): deaths among males were 44.8%, while among females these were 55.2%.

(3) Distribution of deaths by province

In 2000, 81.6% (40/49) of the deaths were reported from 9/12 provinces in the south-west region (Mekong delta region). These included: An Giang, Cantho, Dong thap, Kiengiang, Travinh, Camau, Tiengiang, Soc trang and Longan. The rest (18.4%) were in 6/7 provinces of the south-east region, i.e. Ho Chi Minh City, Binh duong, Dongnai, Bariavung tau, Tayninh and Binh phuoc. Bentre, Baclieu, Lamdong and Vinh long provinces did not record any deaths. A similar status was observed in 1999 (Figure 3).

The south-west region is a DHF endemic region and recorded high morbidity and mortality in southern Viet Nam[3,4]. In 2000, the DHF case-fatality rate in this region was 0.3% while this rate was 0.2% in the south-east. The south-west region is affected by many climatic and geographical factors such as a wet climate,
long stretch of rainy season, and having many rivers and canals. The main water source is surface water, so, the inhabitants are used to storing water in many types of containers which are suitable for larval development of Aedes mosquito. In addition, poor road infrastructure results in late hospital admissions. On the contrary, in the south-east region, the inhabitants get water from wells. The larval density there is lower because of low number of water containers. Road transport is more comfortable. Thus, the morbidity, mortality and case-fatality rates of DHF are lower there than in the south-west region.

(4) Distribution of deaths by urban and rural regions

During 1999-2000, most of the DHF deaths occurred in the rural region (Figure 4).

Rural inhabitants are economically poor. They spend almost all their time working to earn their living and therefore have little time for health care\(^1\). The difficulty in transport and lack of health communication make the patients stay for long at home before being transferred to a hospital. Patients so hospitalized are usually in a serious condition and easily go into shock with a higher risk of death.
(5) Time from onset of disease to hospitalization

Almost all the deaths were due to late hospitalization on the third or fourth day of the disease and even on the fifth or sixth day. As a result, late hospitalization is one of the important causes of increased death risk (8) (Figure 5).

(6) Time gap between hospitalization and death

In 2000, half of the deaths occurred during the first 24 hours of hospitalization and one-third of the remaining deaths occurred on the second or third day. The proportion of deaths after the fifth day of admission was very low (Figure 6).

(7) Time gap between onset of disease and death

Almost 83.7% of the deaths occurred between the third and the sixth day of the onset of the disease in the year 2000, 15% on the seventh day and only 2.3% on the second day. The same trend was observed in 1999.

If the patients were diagnosed early and treated effectively on the first day of the onset of the disease, the mortality would have been lower (Figure 7).

(8) Death locations

Over half of the deaths were reported from provincial hospitals, followed by district hospitals. In 2000, deaths at the central paediatric hospitals (Paediatric Hospital No.1

All these patients were admitted with severe status. This means that health communication in the past was not effective. It is necessary to improve the health communication system in order to help the population discover early signs and symptoms of DHF and transfer the patients to health facilities as soon as possible. In addition, training in DHF case management for all health staff is very important.
and Paediatric Hospital No.2 in Ho Chi Minh City) and at home had decreased (Figure 8).

![Figure 8. Location of deaths](image)

### Conclusion

The main age group where most DHF deaths occurred was those under 15 years of age, especially children aged 5-9 years. The proportion was the same for males and females. Almost all deaths were in the south-west (Mekong delta) region (81.6%). The case-fatality rate was 0.3%, higher than in the south-east. Most of the deaths occurred in rural areas. Most deaths were among those patients who were hospitalized on the third or fourth day of the onset of the disease. Half of the deaths occurred during the first 24 hours of hospitalization, perhaps due to late hospital admission with severe status. Deaths between the third and the sixth day of the disease amounted to 83.7%. There were more deaths in provincial hospitals than in district hospitals.

### References

Dengue and Dengue Haemorrhagic Fever in Children During the 2000 Outbreak in Chittagong, Bangladesh

by
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Abstract
An outbreak of dengue/dengue haemorrhagic fever occurred during 2000 in Chittagong, Bangladesh. A total of 72 children admitted to the Paediatrics ward of the Chittagong Medical College Hospital were evaluated. Sixty-four (89.0%) children came from the Chittagong metropolitan area and the rest 8 (11.0%) from the rural area. The clinical diagnosis of dengue fever (DF) was made in 26 children (36.0%), dengue haemorrhagic fever (DHF) in 36 (50.0%), and dengue shock syndrome (DSS) in 10 children (14.0%) according to WHO case definition. The mean age was 8.4 ± 3.0 years. The distinct features of the present study were: rural occurrence of the disease, which affected malnourished children and more of the students; a higher prevalence of haemorrhagic manifestations and hepatomegaly; jaundice, cough, splenomegaly and encephalopathy; and high PCV in a half and low platelet in one-fourth of the DF patients. The recorded case fatality was 5 (7.0%). It was found that respiratory difficulty, pleural effusion, splenomegaly, tachycardia, low blood pressure, narrow pulse pressure, prolonged capillary reflit time, shock, convulsion, coma and platelet count of 100,000/cmm or less were significantly associated with a 5-25 times higher risk of death. Country-specific control measures, case definition, and case management are desirable.

Keywords: DF/DHF, paediatric group, Chittagong, Bangladesh.

Introduction
Globally, more than 2.5 billion people are at risk for dengue/dengue haemorrhagic fever, with 500,000 DHF cases which require hospitalization each year. Of these, 90% are children less than 15 years of age, with the mortality average of 5% of DHF cases(1).

There has been a growing proportion of DHF cases and the occurrence of outbreaks has become a regular feature in the WHO South-East Asia Region(2).

Dengue was first reported in Bangladesh in 1964 when it was known as “Dacca Fever”(3); since then, it has remained...
Dengue and Dengue Haemorrhagic fever in Children during the 2000 Outbreak in Chittagong, Bangladesh

endemic. The seroprevalence was found to be 13% and DEN-2, DEN-3, and DEN-4 virus serotypes were documented in 1997[4]. In 2000, a large number of haemorrhagic fever cases were admitted to the Paediatrics and Medicine departments of the Chittagong Medical College Hospital (CMCH), Chittagong, with a similar situation prevailing in Dhaka. It was then declared as an outbreak of dengue at the national level. This outbreak was the first of its kind when 5,551 cases were reported with 93 deaths up to December 2000.

There were 72 children with dengue/dengue haemorrhagic fever admitted to the Paediatrics ward of the CMCH during the outbreak. The current analysis was carried out in order to document the clinical manifestations, and the morbidity and mortality of dengue/dengue haemorrhagic fever in Bangladesh.

Materials and methods

All children (n=72) diagnosed as having dengue fever (DF)/dengue haemorrhagic fever (DHF)/dengue shock syndrome (DSS) and aged up to 12 years, admitted in the Paediatrics ward of the CMCH, during August-November 2000 were studied. The clinical details were recorded on admission and followed prospectively till discharge. The diagnosis of DF, DHF and DSS were made according to the WHO guidelines for the treatment of dengue/DHF in small hospitals[5].

For all the patients, the total count of white blood cells (TWBC), haemoglobin, PCV by microcentrifuge technique, and absolute platelet counts on a cell counter were done. Serology for dengue antibody was done in all cases using PANBIO INDX Dip-Stick test for dengue fever (ELISA DOT technique) to detect IgM and IgG. Other investigations such as malarial parasite in blood, serum bilirubin, AST, ALT, prothrombin time, creatinine, electrolytes, serum protein, CSF profile, chest-radiograph, ultrasound of chest and abdomen were done whenever it was indicated by the condition of the patient.

The data were computer-processed using SPSS Windows. Univariate and bivariate analyses were done. Relative risk with 95% confidence interval was calculated for predictors of outcome.

Results

Among the admitted children, 64 (89%) came from the urban metropolitan area of Chittagong and the rest 8 (11%) from rural areas. The diagnosis of DF was made in 26 (36%) children, DHF in 36 (50%) children and DSS in 10 (14%) children. The age range of patients admitted was 2.5-12 years. The under-5 children constituted 14%, 5-9-years age group 42% and 10-12-years group 44%. The estimated mean age for DF was 9.0±2.8 years; DHF 8.5±3.1 years and DSS 6.6±2.6 years. There were 42 (58%) male and 30 (42%) female children. Forty-eight (67%) children were students, 10 (14%) were pre-school age and the rest were involved in commercial work. Eighty-three per cent of the children were suffering from different grades of malnutrition and 13% belonged to the severe malnutrition status, i.e. less than 60% of the NCHS# standard, but no association between the nutritional status and disease severity was observed.
Table 1. Clinical manifestations of DF, DHF and DSS patients

<table>
<thead>
<tr>
<th>Clinical features</th>
<th>DF-26(%)</th>
<th>DHF-36(%)</th>
<th>DSS-10 (%)</th>
<th>Total-72(%)</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration: Fever on admission (days)</td>
<td>4.8 ± 1.8</td>
<td>5.0 ± 2.2</td>
<td>4.1 ± 2.7</td>
<td>4.8 ± 2.1</td>
<td>NS</td>
</tr>
<tr>
<td>Total duration: Fever(days)</td>
<td>8.0 ± 2.5</td>
<td>9.5 ± 4.5</td>
<td>6.5 ± 4.9</td>
<td>8.2 ± 3.5</td>
<td>NS</td>
</tr>
<tr>
<td>Headache</td>
<td>22 (85.0)</td>
<td>27 (75.0)</td>
<td>7 (70.0)</td>
<td>56 (78.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Arthralgia/myalgia</td>
<td>19 (73.0)</td>
<td>28 (78.0)</td>
<td>8 (80.0)</td>
<td>55 (76.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Bleeding (any type)</td>
<td>16 (61.5)</td>
<td>36 (100.0)</td>
<td>10 (100.0)</td>
<td>62 (86.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Retro-orbital pain</td>
<td>7 (27.0)</td>
<td>8 (22.0)</td>
<td>2 (20.0)</td>
<td>17 (24.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Skin rash</td>
<td>3 (12.0)</td>
<td>18 (50.0)</td>
<td>6 (60.0)</td>
<td>27 (38.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Sub-conjunctival Haemorrhage</td>
<td>1 (4.0)</td>
<td>3 (8.0)</td>
<td>1 (10)</td>
<td>5 (5.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Jaundice</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>1 (10)</td>
<td>1 (1.5)</td>
<td>NS</td>
</tr>
<tr>
<td>Cough</td>
<td>2 (8.0)</td>
<td>1 (3.0)</td>
<td>0 (0)</td>
<td>3 (4.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Respiratory difficulty</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>4 (40.0)</td>
<td>4 (6.0)</td>
<td>&lt;0.00</td>
</tr>
<tr>
<td>Pleural effusion</td>
<td>0 (0)</td>
<td>1 (3.0)</td>
<td>1 (10)</td>
<td>2 (3.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>6 (23.0)</td>
<td>5 (14.0)</td>
<td>3 (30.0)</td>
<td>14 (19.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Vomiting</td>
<td>4 (15.0)</td>
<td>4 (11.0)</td>
<td>1 (10)</td>
<td>9 (13.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Abdominal distention</td>
<td>0 (0)</td>
<td>1 (3.0)</td>
<td>1 (10)</td>
<td>2 (3.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Ascites</td>
<td>0 (0)</td>
<td>1 (3.0)</td>
<td>0(0)</td>
<td>1 (1.5)</td>
<td>NS</td>
</tr>
<tr>
<td>Hepatomegaly</td>
<td>0 (0)</td>
<td>26 (72.3)</td>
<td>10 (100.0)</td>
<td>36 (50.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Splenomegaly</td>
<td>0 (0)</td>
<td>4 (11.0)</td>
<td>1 (10)</td>
<td>5 (7.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Epistaxis</td>
<td>3 (12.0)</td>
<td>10 (28.0)</td>
<td>2 (20.0)</td>
<td>15 (21.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Gum bleeding</td>
<td>4 (16.0)</td>
<td>6 (17.0)</td>
<td>1 (10)</td>
<td>10 (16.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Skin bleeding</td>
<td>8 (31.0)</td>
<td>23 (64.0)</td>
<td>8 (80.0)</td>
<td>39 (54.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Malena</td>
<td>2 (8.0)</td>
<td>19 (53.0)</td>
<td>10 (100.0)</td>
<td>31 (43.0)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Hematemesis</td>
<td>5 (19.0)</td>
<td>12 (33.0)</td>
<td>7 (70.0)</td>
<td>24 (33.0)</td>
<td>&lt;0.04</td>
</tr>
<tr>
<td>PV Bleeding</td>
<td>0 (0)</td>
<td>2 (6.0)</td>
<td>1 (10.0)</td>
<td>3 (4.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Hematuria</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>1 (10.0)</td>
<td>1 (1.5)</td>
<td>NS</td>
</tr>
<tr>
<td>Bleeding Injection site</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>1 (10.0)</td>
<td>1 (1.5)</td>
<td>NS</td>
</tr>
<tr>
<td>Cold clammy skin</td>
<td>2 (8.0)</td>
<td>8 (22.0)</td>
<td>8 (80.0)</td>
<td>18 (25.0)</td>
<td>&lt;0.00</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>1 (4.0)</td>
<td>7 (19.0)</td>
<td>8 (80.0)</td>
<td>16 (22.0)</td>
<td>&lt;0.00</td>
</tr>
</tbody>
</table>
Dengue and Dengue Haemorrhagic Fever in Children during the 2000 Outbreak in Chittagong, Bangladesh

Clinical features  DF-26(%) DHF-36(%) DSS-10 (%) Total-72(%) P*

Low blood pressure  1 (4.0)  6 (17.0)  4 (40.0)  11 (15.0) NS
Narrow pulse pressure  0 (0)  0 (0)  8 (80.0)  8 (11.0) <0.00
Prolonged Capillary refill time  0 (0)  0 (0)  9 (90.0)  9 (13.0) <0.00
Shock  0 (0)  0 (0)  4 (40)  4 (6.0) <0.00
Convulsion  2 (8.0)  3 (8.0)  3 (30.0)  8 (11.0) NS
Coma  0 (0)  2 (6.0)  7 (70.0)  9 (13.0) <0.00
Tourniquet test  10 (38.0)  32 (89.0)  5 (50.0)  47 (65.0) <0.00
PCV(High)  15 (58.0)  27 (75.0)  7 (70.0)  49 (68.0) NS
Platelet: < 100000/cmm  2 (8.0)  18 (50.0)  7 (70.0)  27 (38.0) NS
Total WBC count: Low-High  5 (19.0)  4 (11.0)  0 (0)  9 (13.0) NS
IgG  16 (62.0)  26 (72.0)  7 (70.0)  49 (68.0)
IgM  15 (58.0)  23 (64.0)  7 (70.0)  45 (63.0)

*P values for DHF/DSS  NS: Not significant

The clinical features are shown in Table 1. All cases of DF, DHF and DSS had fever of a mean duration of 4.4+1.8 days, 5.0+2.2 days and 4.1+2.7 days respectively. The total days required to become afebrile was 8.0+2.5 days in DF, 9.5+4.5 days in DHF and 6.5+4.9 days in DSS. Headache and arthralgia/myalgia were complained by about 80% of the DF, DHF and DSS cases. Sixty-two (86%) of the patients had different forms of bleeding manifestations.

The other predominant features of DF were skin bleeding in the form of petechie and purpura (32%), retro-orbital pain (27%), diarrhoea (23.0%), vomiting (15%) and skin rash (12%). Thirty-eight per cent of the DF cases had positive tourniquet test.

There was skin rash in about 60% of the DHF and DSS cases. The hepatomegaly and bleeding from skin were found in 72% and 64% of the DHF and 100% and 80% of the DSS cases respectively. There were significant differences between the DSS and DHF patients in the manifestations of respiratory difficulty (40% vs. 0%), malena (100% vs. 53%), haematemesis (70% vs. 33%), cold clammy skin (80% vs. 22%), tachycardia (80% vs. 19%), narrow pulse pressure (80% vs. 0%), prolonged capillary refill time (90% vs. 0%), shock (40% vs. 0%), coma (70% vs. 6%), and tourniquet test (50% vs. 89%). Out of the 8 (11%) convulsive patients, three had febrile convulsion, three had dengue encephalopathy, one had hepatic encephalopathy and one had dyselectrolytemia.
A minor proportion of the cases had jaundice (1.5%), cough (4%), pleural effusion (3%), abdominal distention (3%), ascites (1.5%), and splenomegaly (7%). Only 19% of the DF patients had leucopenia, but 15 (58%) and 2 (8%) children suffering from DF had high PCV and thrombocytopenia of 100,000/cmm or less respectively. In contrast about 30% of the children suffering from DHF and DSS had normal PCV; and 50% of DHF and 30% of DSS children had a platelet count of more than 100,000/cmm. The IgM for dengue was positive in 45 (63%) of the children.

There were five deaths giving an overall mortality of 7%. The mortality in DHF was two (5.5%) and that of DSS three (30%) and the difference is very significant (P<0.001). The data were analysed to identify the predictors of outcome and are shown in Table 2 with calculated relative risk and 95% confidence interval. It is evident that respiratory difficulty, pleural effusion, splenomegaly, tachycardia, low blood pressure, narrow pulse pressure, prolonged capillary refill time, shock, convulsion, coma and platelet count of 100,000/cmm or less were significantly associated with a 5-25 times higher risk of death.

Table 2. Predictors of outcome

<table>
<thead>
<tr>
<th>Predictors</th>
<th>Dead (5)</th>
<th>Alive (67)</th>
<th>RR*</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory difficulty</td>
<td>2 (40.0)</td>
<td>2 (3.0)</td>
<td>11.33</td>
<td>2.59 - 49.69</td>
<td>&lt;0.00</td>
</tr>
<tr>
<td>Pleural effusion</td>
<td>1 (20.0)</td>
<td>1 (1.5)</td>
<td>8.75</td>
<td>1.63 - 47.00</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Splenomegaly</td>
<td>2 (40.0)</td>
<td>3 (4.5)</td>
<td>8.93</td>
<td>1.91 - 41.73</td>
<td>&lt;0.00</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>4 (80.0)</td>
<td>12 (18.0)</td>
<td>14.00</td>
<td>1.68 - 116.61</td>
<td>&lt;0.00</td>
</tr>
<tr>
<td>Low blood pressure</td>
<td>4 (80.0)</td>
<td>7 (10.5)</td>
<td>22.18</td>
<td>2.73 - 180.27</td>
<td>&lt;0.00</td>
</tr>
<tr>
<td>Narrow pulse pressure</td>
<td>3 (60.0)</td>
<td>5 (7.5)</td>
<td>12.63</td>
<td>2.35 - 61.33</td>
<td>&lt;0.00</td>
</tr>
<tr>
<td>Prolonged capillary refill time</td>
<td>3 (60.0)</td>
<td>6 (9.0)</td>
<td>10.50</td>
<td>2.02 - 52.52</td>
<td>&lt;0.00</td>
</tr>
<tr>
<td>Shock</td>
<td>3 (60.0)</td>
<td>1 (1.5)</td>
<td>25.13</td>
<td>5.83 - 110.12</td>
<td>&lt;0.00</td>
</tr>
<tr>
<td>Convulsion</td>
<td>2 (40.0)</td>
<td>6 (9.0)</td>
<td>5.33</td>
<td>1.04 - 27.26</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Coma</td>
<td>3 (60.0)</td>
<td>6 (9.0)</td>
<td>10.50</td>
<td>2.02 - 54.52</td>
<td>&lt;0.00</td>
</tr>
<tr>
<td>Platelet &lt;100,000/cmm</td>
<td>4 (80.0)</td>
<td>23 (34.0)</td>
<td>6.67</td>
<td>1.04 - 56.59</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

*RR: Relative risk

Discussion

This was the first documented epidemic of dengue in Bangladesh and both urban and rural populations were affected. According to the present study, the predominant age group that was affected was 9-12 years which was found to be 5-9 years in the sero-prevalence survey of 1997(4), suggesting that
the age of infection is progressively increasing in Bangladesh like that in Singapore\(^6\) and Malaysia\(^7\) where dengue has been endemic for several years. In our series most of the children were students, thereby indicating the importance of school environment while mounting control measures\(^8\). Girls were not affected severely like elsewhere\(^9\) and a sizeable proportion of our children were malnourished. This is contrary to the earlier belief that DSS is rarely seen in clinically-malnourished children\(^10\).

The distinct features of the present study were the rural occurrence of the disease which affected malnourished and more of the students; a higher prevalence of haemorrhagic manifestations and hepatomegaly; no echymoses, jaundice, cough, splenomegaly or encephalopathy; and high PCV in half and low platelet in one-fourth of the DF patients. This highlights the need to study region-specific and even country-specific clinical features in dengue infection.

Splenomegaly was found in 11% of the DHF/DSS children which needs to be interpreted with caution in a malaria-endemic area like Chittagong. In severe falciparum malaria there may be bleeding manifestations and thrombocytopenia\(^11\). The differentiating features may be high-grade fever along with pallor disproportionate to blood loss. Jaundice was found in one DSS patient who had convulsion, the other cause being excluded, was diagnosed as hepatic encephalopathy. A significantly higher elevation of aspartate aminotransferase (AST) than alanine aminotransferase (ALT) suggests DHF rather than hepatitis A, B, or C virus infection. Hepatitis is usually caused by DEN-3 virus\(^12\). In an epidemic in Malaysia, eight cases of hepatic encephalopathy were observed\(^13\). Dengue encephalitis/encephalopathy is an increasingly recognized entity and dengue virus has been isolated in the brain section\(^14\) and in the cerebrospinal fluid\(^15\). Besides dengue encephalopathy, central nervous system manifestations may be due to intracranial haemorrhage, electrolyte imbalance or hypoxic ischaemic encephalopathy due to profound circulatory failure\(^16\). In an endemic area, dengue virus should be considered as a possible aetiological agent in children presenting with encephalitis/encephalopathy.

The overall mortality recorded in the present study was five (7%), which was two (5.5%) for DHF and three (30%) for DSS. It was found to be low in comparison with the mortality of the first epidemic in Bangkok back in 1958\(^17\). Possibly, the reduced death rate was due to the awareness about the illness and timely and better management. Our case-fatality rate was still higher and one of the reasons could be that our hospital being a tertiary-level health facility, more serious cases were received. It was also found that the presence of factors like respiratory difficulty, pleural effusion, splenomegaly, tachycardia, low blood pressure, narrow pulse pressure, prolonged capillary refill time, shock, convulsion, coma and platelet count of 100,000/cmm or less was found to be significantly associated with a 5-25 times higher risk of death.

DHF/DSS is believed to occur due to the antibody-dependent enhancement of
the secondary infection\textsuperscript{(18)}. It is apprehended that the future epidemics in Bangladesh may be more devastating if control measures and case-management protocols are not developed in a country-specific way, based on the experience of the 2000 epidemic in Chittagong, Bangladesh.

References

Changing Pattern of Dengue Transmission in Singapore

by Eng Eong Ooi*

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Abstract

Dengue is a re-emerging disease of concern in many parts of the world. In Singapore, an integrated vector control programme, incorporating source reduction, law enforcement and public education, has been in place since 1970. This programme resulted in a period of very low incidence of dengue in Singapore between 1974 and 1985. From 1986, however, there has been a resurgence of the disease where the trend of the annual incidences is similar to that of other countries in the region. This occurred despite the vector control programme. Two epidemiological features were observed during this period. Firstly, the resurgence affected mainly adults with very few cases among children. Secondly, there were about 1.6 times more male than female cases. A recent seroepidemiological study carried out to investigate the low incidence of dengue in children found a very low seroconversion rate. More interestingly, the results suggested that the transmission of dengue in Singapore was occurring in non-residential areas. This study examined the preponderance of male dengue cases in the Singapore population between the years 1998 and 2000.

Keywords: DF/DHF, morbidity male/female, transmission, residential/non-residential areas, Singapore

Introduction

Dengue fever (DF) and dengue haemorrhagic fever (DHF) are caused by dengue viruses, of which there are four antigenically related but distinct serotypes. They belong to the genus Flavivirus. Dengue is an important mosquito-borne viral disease that is re-emerging in many parts of the world[1]. The viruses are transmitted by the Aedes mosquitoes, principally Aedes aegypti.

In the absence of an effective dengue vaccine and antiviral drug, reduction of the Aedes aegypti population is the method of choice for controlling dengue.

In Singapore, a well-established mosquito-control programme, incorporating source reduction, public-health education and law enforcement, has been in place.

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since the 1970s. This resulted in a period of very low dengue incidence between 1974 and 1985\(^2\). There was, however, a resurgence of dengue from 1986 onwards despite the control measures where the national Aedes spp House index (HI), which is a measure of the percentage of houses positive for Aedes breeding, remained below 2%. Most of the reported cases were in the young adult population with a very low incidence rate in young children. Over 70% of the cases in the year 2000 were aged 25 years and above. This was in contrast to the late 1970s where only approximately 30% of the cases were aged 25 years and above.

To explain this epidemiological observation, Goh suggested that the successful mosquito control measures resulted in a population of young adults with low herd immunity to dengue viruses\(^3\). That, however, does not explain why children, who are most susceptible to infection, are not presenting with the disease. A recent serological study\(^4\) showed that this low dengue incidence rate in young children was not due to asymptomatic infection but that children were not being infected. Furthermore, there was a significant rise in the seroconversion rate in children aged 6 years and older and this coincided with the start of formal schooling. This result suggests that there may be a change in the location where dengue is acquired whereby those that spend more time away from home are at greater risk of dengue infection\(^4\).

Besides affecting mainly adults, it has also been observed that there are more male than female dengue cases reported in Singapore where the male to female morbidity ratio for dengue was 1.6:1 in this period of resurgence\(^5\). Until now, there has been no study conducted to explain this epidemiological observation. Since the pathogenesis of the dengue disease could be due to the immune response to the viral infection, it is possible that the difference in the incidence rates of dengue in males and females in Singapore is due to the physiological differences between males and females. However, based on the findings of the serological study\(^4\), we hypothesize that the transmission of dengue viruses is occurring in places away from residences and that the preponderance of male cases is a consequence of the social structure of the society.

**Methods**

Dengue was made a legally notifiable disease since 1967. Since 1998, however, the details of the reported cases are captured in an electronic database maintained by the Quarantine and Epidemiology Department, Ministry of the Environment. In this study, all cases of dengue among local residents from 1998 to 2000 were included. The cases were categorized according to age groups and gender.

A nationwide population census was conducted in 2000. The census reported details of the structure of the Singapore population, including the population demographics of our workforce. Advance release of the data collected during this census is available at the Department of Statistics' website.
Results
The total number of cases included in this study was 5,310, of which 3,297 were males and 2,013 females. The overall male to female ratio was 1.6:1. However, in the age groups 0 to 4 years and 55 years and above, the ratios were 0.7:1 and 1.1:1, respectively (Figure). These populations consist of young children and largely retirees who are likely to spend more of their time at home. In contrast, the age groups between 15 and 54 years showed a large male preponderance (Figure) with an overall male to female ratio of cases of 1.7:1 (Table).

Data from the population census conducted by the Singapore Department of Statistics in 2000 showed that there are almost equal numbers of males and females in Singapore. In total, there are 1,630,293 males and 1,632,916 females (male to female ratio = 0.99:1). This indicates that the difference in the proportion of male to female cases was not due to the difference in the proportion of males and females in the total Singapore population. The census also reported more males than females in the working population. The number of working males was 876,050 as compared to 569,550 working females. This population had an age range from 15 years onwards, with the majority between 25 and 54 years.

Table. Analysis of the dengue cases in the working age group

<table>
<thead>
<tr>
<th>Morbidity features</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cases among 15 to 54-year-olds</td>
<td>2813</td>
<td>1628</td>
</tr>
<tr>
<td>Ratio of male cases to female cases</td>
<td>1.73</td>
<td>1</td>
</tr>
<tr>
<td>Total working population</td>
<td>876,050</td>
<td>569,550</td>
</tr>
<tr>
<td>Ratio of total cases among working males to total cases among working females</td>
<td>1.1</td>
<td>1</td>
</tr>
</tbody>
</table>

The data were then analyzed using the gender-specific working population numbers as the denominators instead of the total male/female population. The calculated dengue morbidity rates for those aged between 15 to 54 years and the male to female ratio of dengue rates was nearly equal (1.1:1) (Table). This indicated that the difference in the male to female morbidity ratio for dengue was due largely to the difference in the proportion of males and females in the workforce.

Discussion
Singapore is a city-state where the majority of the population in the working age group is employed. Most of the population lives in high-rise apartments. The workday commonly starts at around 8.30 am and ends in the early evening. This implies that
during the peak biting periods of the Aedes mosquitoes, which is in mid-morning and early afternoon, most of the adult population would either be on the way to work or at work. Our findings in this study, as well as those in the earlier serological study, indicated that the likelihood of dengue infection increased with more time being spent away from home.

The reason for the change in the places where the transmission of dengue occurs could be due to our vector control programme. Extensive studies done by Chan and colleagues[6] showed that most of the Aedes breeding occurred in residences as indicated by the HI data collected in 1966-68: slum houses, 27.2%; shop houses, 16.4%; and apartments, 5.0%. In contrast, the HI data published in 1997[7] showed that most of the breeding was in non-residential areas such as construction sites, 8.3%; factories, 7.8%; and vacant premises, 14.6%. The residential properties had very low HI: landed residences, 2.1%; apartments, 0.6%. It may thus be possible that the vector control programme has successfully reduced the Aedes mosquito density in residences. In response, however, the mosquitoes have adapted to the vector control programme and now breed and hence feed in places other than residences.

Some authors have reported a slight excess of adult females cases as compared to males in dengue outbreaks[8,9], while others have found varying male to female morbidity ratios[10,11]. Excess of cases in females and pre-school children have been attributed to the dengue transmission occurring at home, while other findings have not been fully explored. This is the first report studying the predominance of male cases in Singapore.

The resurgence of dengue in Singapore from 1986 affected mainly adults and spared the children. Together with our previous study[4], the results from this study strongly indicated that dengue transmission in Singapore may occur largely away from home.

In conclusion, the difference in the male to female morbidity rates was associated with the difference in the proportion of working males and females, indicating thereby that the risk of dengue increased with the increasing time spent away from home.

Acknowledgements

I would like to thank Dr Goh Kee Tai for his encouragement and my colleagues, Mohan and Chua Lian Tee, for their help in retrieving the data for analysis.

References


A Guide to DHF/DSS Management - The Singapore Experience

by
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Abstract
A guide to the medical management of dengue for reducing its case-fatality rate as experienced in Singapore is furnished. The mortality from dengue in Singapore is low and most cases recover uneventfully. However, complacency and under-estimation of the disease does occur. It is important to recognize the symptoms of severity and understand the pathophysiology that leads to dengue shock syndrome (DSS). A protocol giving indications of platelet transfusion will guide appropriate usage. Patients should be informed prior to platelet transfusion as to its possible dangers. In our experience, with good initial appropriate support in a stable patient, platelet transfusion is seldom needed till the platelets fall below 10,000/mm$^3$. DSS is reversible if appropriately treated with fluids and plasma infusion to reverse the osmotic permeability gradient due to hypoalbuminaemia. Severe pulmonary oedema causes adult respiratory distress syndrome (ARDS). The lung effusions and hypotension must be differentiated from other causes of shock and pulmonary oedema. Correction of acid-base balance and internal bleeding if present, recognition and appropriate treatment of septicaemia and pneumonia, and avoiding fluid overload usually result in recovery. Nosocomial and mycoplasma pneumonias, not uncommonly, complicate severe ARDS. Fatalities are often from these unrecognized infections.

Keywords: DHF, DSS, management, guidelines, Singapore.

Introduction
In recent years dengue has been a major international health problem with high levels of dengue fever/dengue haemorrhagic fever (DF/DHF) in the WHO Western Pacific Region. Malaysia had 19,544 cases (1997), Philippines 12,811 cases (1997), Viet Nam 108,000 cases (1997), Australia 165 cases (Dec.’97–May ’98), Fiji 24,780 cases (Dec.’97–May ’98) and Singapore 5,285 cases with 153 being imported in 1998$^{(1)}$ and in 1999, 1355 dengue cases with 217 imported$^{(2)}$. There has been a resurgence in 1998 and in 2001. Fatality varied from 1%-4% in this Region.

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Around sixty million cases occur annually with 30,000 fatalities worldwide\(^3\). The changing climate pattern due to the El Nino weather phenomenon is thought to be the cause\(^4\). Tourists travelling in the region often visit Singapore and fall ill, while others from neighbouring countries seek medical treatment in Singapore. The critically ill are transported there by international air emergency services.

The fact that there are no antibiotics or antiviral drugs for dengue and most patients recover has, in my opinion, led to complacency and under-estimation of the disease. Not recognizing the symptoms of its severity and ignorance of the pathophysiology of dengue that leads to DSS, further contribute to complacency in its treatment.

**Diagnostic criteria**

**DF/DHF**

- Abrupt onset of high fever, continuous and lasting 2-7 days, headache, myalgia and arthralgia.
- Haemorrhagic manifestations including any of the following:
  - Positive tourniquet test
  - Petechiae, purpura, ecchymosis
  - Epistaxis, gum bleeding
  - Haematemesis and/or melaena
- Enlargement of liver
- Thrombocytopenia (100,000/mm\(^3\) or less)
- Haemoconcentration (haematocrit increased by 20% or more)

The presence of the first two clinical criteria plus thrombocytopenia and haemoconcentration are sufficient to establish the clinical diagnosis of DHF.

**Dengue shock syndrome (DSS)**

- All the above criteria, plus
- Shock as manifested by rapid and weak pulse with narrowing of pulse pressure (< 20mmHg regardless of pressure levels) or hypotension with cold, clammy skin and restlessness.

(Based on “Dengue Haemorrhagic Fever: Diagnosis, Treatment, Prevention and Control”, WHO, 1997)

**Pathophysiology**

In DHF/DSS the severity is due to the increase in vascular permeability leading to plasma loss from the vascular compartment. This vascular permeability may show as pleural effusion and ascites on clinical examination and can be confirmed by radiology and ultrasound.

Hypoalbuminaemia contributes to the problem. The face and legs may also be oedematous. In severe cases there is a reduction in the plasma volume of > 20%. Disseminated intravascular coagulation (DIVC) occurs and causes thrombocytopenia, prolonged prothrombin and partial thromboplastin times (PT/PTT), decreased fibrinogen levels and increased
fibrinogen degradation products. Thrombocyte
pyopenia is also due to bone marrow depression.

Clinical manifestations

Early clinical signs and symptoms that suggest possible progression to DHF/DSS are high fever, severe muscle ache, arthralgia, anorexia, vomiting, epigastric pain, abdominal distension, diarrhoea, headache, eyeball discomfort, dyspnoea, tachycardia, a rapid fall in platelet count of 25% – 50% or more per day and a falling blood pressure.

During the early stage, a chest X-ray may show evidence of pleural effusion mainly on the right side, but could be bilateral with pulmonary oedema. An ultrasound of the abdomen may show an oedematous gall bladder or ascites.

Low platelet is manifested by easy bruising or bleeding. In severe cases hypotension leads to DSS generally after the third day of the illness with the patient having cold extremities, rising haematocrit, restlessness, oliguria, tachycardia, abdominal pain and narrowing of pulse pressure (<20 mm Hg) as warning signs. If the shock is not corrected it becomes refractory and the patient may die from a gastro-intestinal haemorrhage within 24 hours, and often may be mentally alert till just before death.

Essentials of management

- Do not underestimate the illness. Take a good history.
- Monitor the patient regularly for changes in clinical condition, i.e. blood counts, PT/PTT, haematocrit, electrolytes, acid base balance, liver function tests, pulse, temperature and blood pressure. Rapidly-dropping blood counts may need monitoring 3-4 times daily and blood pressure should be taken every 2 hours.
- Exclude other causes of febrile illness, e.g. malaria, typhoid, typhus, liver abscess, leptospirosis, meliodosis, drug allergy, HIV, lymphoma, septicemia, etc. A blood culture must be done.
- A serological test, if done early, may be negative, but if suggestive symptoms are present, dengue should still be suspected. A PCR (polymerase chain reaction), if available, detects the infection earlier.
- Hospitalization should be considered if the patient shows symptoms of severe dengue, especially nausea, vomiting and diarrhoea, a falling platelet count below 100,000 mm$^3$ or less, bleeding from gastro-intestinal or uro-genital tract or a persisting high haematocrit despite fluid replacement.

Principles of management

Prognosis depends on early recognition and prompt treatment of shock with rapid replacement of plasma loss with fluids,
electrolyte solutions, plasma or plasma expanders. Adjust intravenous fluids administration according to vital signs, haematocrit and urine output. With early correction of electrolytes, metabolic disturbance and acidosis with sodium bicarbonate, DSS and intravascular coagulation is prevented.

Do not mistake DSS for other causes of shock, e.g. myocarditis; ECG and echo-cardiogram will assist in the diagnosis.

**Indications for platelet transfusion**

(a) Stable patients with platelet counts <10,000/mm$^3$.

(b) Patients with platelet counts <20,000/ mm$^3$ with minor bleeding.

(c) Patients with platelet counts 50 000/ mm$^3$ with significant bleeding.

(Information regarding potential risks and benefits should be given to the patient before administration of platelets and other blood products.)

DF/DHF usually responds to symptomatic treatment. Antipyretics can be given for fever >39°C, together with cooling procedures, e.g. ice-packs on the head and neck. Avoid salicylates, it can cause gastritis, gastric bleeding, acidosis or Reyes syndrome (fatty liver and encephalopathy) in children. Paracetamol can be given, or if the patient is vomiting Voltaren suppositories. Antacids are prescribed for epigastric pain and antiemetics for vomiting. Rehydration may be needed. If there is significant bleeding, blood transfusion can be given and Vitamin K1 added. Platelets may be needed if thrombocytopenia is severe.

DSS patients are best monitored in the intensive care unit, given oxygen, a central venous pressure line (CVP) inserted if possible, and a urinary catheter for urine output to guide fluid replacement. A strict intake and output chart should be observed. Blood gases, ECG, chest X-ray, electrolytes, serum albumen and blood counts should be monitored.

Respiratory failure commonly supervenes due to pulmonary oedema and patient may develop respiratory failure needing respirator assistance. Correct hypotension with intravenous fluids, e.g. dextro-saline, dextran, haemacell, etc., as well as a vasopressor, e.g. dopamine. If unsuccessful and hypoalbumenaemia is severe, give sufficient plasma or plasmanate to correct the low serum albumen. This will reverse the osmotic gradient to prevent further fluid extravasation and correct hypotension. Nosocomial respiratory tract and mycoplasma pneumoniae infections are not uncommon in hospitalized patients with pulmonary oedema. They should be given appropriate antibiotics. Septicaemias, if present, must be treated. Diuretics may need to be used to promote urine flow and excrete excess fluid. Recovery from DSS usually occurs with these emergency procedures if done urgently, but should hypotension persist despite a falling haematocrit, internal bleeding should be considered.

Intravenous fluids should be discontinued when haematocrit drops to 40% with vital signs being stable, urine output
satisfactory and patient feels better. With recovery at this stage reabsorption of extravasated plasma occurs. Pulmonary oedema and cerebral oedema can occur if more fluid is given.

Patients can be discharged if afebrile, have normal blood pressure for 48 hours, are able to eat, are not breathless, have good urine output and platelet count more than 50,000 mm$^3$ with stable blood counts and haematocrit.

**Conclusion**

Dengue is a multisystem disease, but with good medical care and public health control, deaths can be further reduced. Fatalities are increased due to the unfamiliarity of DSS shock treatment, unrecognized pneumonia and septicaemia. A guide to its management should be available in hospitals.

**References**

Abstract

The treatment of dengue shock syndrome (DSS) is a medical emergency. Prompt and vigorous volume replacement therapy is required, with extreme care to avoid fluid overload. Recognition of the importance of increased vascular permeability in the pathophysiology of DSS and of the critical need for parenteral fluids in resuscitation has had a dramatic effect on mortality from the disease over the last 40 years. However, until recently there has been little research to determine the optimal fluid regimen, and the choice of fluid has remained largely empirical. Colloid and crystalloid fluids have different physicochemical properties which influence the patterns of distribution and elimination, as well as the secondary osmotic effects. In two recent double-blind randomized trials in Viet Nam, initial resuscitation with colloid fluids (dextran 70 or 3% gelatin) restored cardiac index and pulse pressure and normalized haematocrit more quickly than either of the crystalloid fluids (physiological saline or Ringer’s lactate). There was no difference, however, in the overall recovery time or the subsequent requirement for fluids. From the larger study it was apparent that the major determinant of clinical response was the width of the pulse pressure at presentation with shock, the small number of children with pulse pressures of < 10 mm Hg requiring significantly more resuscitation than those with higher pulse pressures. Within this more compromised group there was a trend to earlier, sustained recovery among those who received one of the colloids. It appears that the majority of children with DSS recover with timely infusion of crystalloid fluids alone, but that an important minority may benefit from initial resuscitation with a colloid. Large trials will be necessary to confirm this effect and to clearly characterize the subgroup of children who might benefit from initial colloid therapy. Given the huge burden of dengue disease in South-East Asia, if a true benefit is established in a subgroup of patients, this may have a significant influence on mortality in the region.

Keywords: Dengue shock syndrome, medical emergency, volume replacement, resuscitation.

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**Introduction**

Infection with dengue virus is one of the leading causes of illness and hospital admission of children in South-East Asia\(^1\,2\). Infection may be asymptomatic, or may result in a variety of clinical syndromes ranging from dengue fever (DF), a non-specific febrile illness, to dengue haemorrhagic fever (DHF) and dengue shock syndrome (DSS). The pathognomonic feature differentiating DHF from DF is an increase in vascular permeability resulting in the leakage of plasma from the intravascular compartment to the extravascular space\(^3\,4\). In severe DHF the loss of plasma is critical, the patient becomes hypovolaemic, exhibits signs of circulatory compromise, and may progress to profound shock.

The management of established DSS involves immediate resuscitation with parenteral fluids, with the intention of restoring and maintaining adequate circulation during the period of increased vascular permeability. Particular care is required to try to avoid fluid overload with all its complications, especially in settings without access to sophisticated intensive care facilities. If appropriate fluid resuscitation is started at an early stage, shock is usually reversible, and once the capillary leak has been resolved, most patients recover rapidly. The current recommendation from the World Health Organization (WHO)\(^5\) is for initial volume replacement with crystalloid solutions, followed by plasma or colloid solutions for those patients with profound or refractory shock.

**Normal fluid balance and the crystalloid/colloid debate**

For many years there has been a controversy regarding the use of crystalloid or colloid solutions for the emergency management of hypovolaemic shock, irrespective of the underlying disease process\(^6\,7\,8\). Total body water is distributed between three main fluid compartments in the body. Intracellular fluid makes up approximately two-thirds of the whole, with the remaining one-third, the extracellular fluid, being distributed between the intravascular (25%) and interstitial compartments (75%) [Figure 1].

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**Figure 1. Physiology of normal fluid balance**

- Membrane permeable to almost all solutes except proteins
- Membrane highly permeable to water but not most solutes

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\(^1\) Reference
\(^2\) Reference
\(^3\) Reference
\(^4\) Reference
\(^5\) Reference
\(^6\) Reference
\(^7\) Reference
\(^8\) Reference
Thus, only 25% of the one-third of the total body fluid (8%) contributes to the normal circulating blood volume. The intracellular fluid is separated from the extracellular fluid by a selective cell membrane that is highly permeable to water, but not to most of the electrolytes or proteins in the body. Within the extracellular compartment however, the intravascular and interstitial fluids communicate continuously through the pores of the endothelial membrane, which are highly permeable to almost all solutes except proteins. Parenterally-administered fluids distribute rapidly throughout the three fluid compartments - intravascular, interstitial and intracellular, according to specific physicochemical properties of the individual solutions. The proportion of the fluid remaining within the intravascular space is one of the major determinants of the effectiveness of a given fluid for volume resuscitation.

Broadly speaking, isotonic crystalloid solutions distribute equally between the intravascular and interstitial compartments, but do not enter the intracellular compartment. In contrast, a proportion of all hypotonic crystalloid solutions, determined largely by the content of the major extracellular ion, sodium, passes quickly into the intracellular compartment, and the volume left within the intravascular compartment may be minimal. Thus, one litre of physiological saline administered parenterally to a healthy person will distribute throughout the extracellular fluid space to maintain normal osmolality, with 25% (250 ml) remaining within the intravascular space and 75% passing to the interstitial space within a few minutes. In contrast, one litre of 5% dextrose, which contains no sodium and can thus be regarded effectively as free water, will distribute equally throughout all the three fluid compartments to maintain normal osmolality, but in this case only 25% of the one-third of the total volume, that is approximately 80 ml of fluid, will remain within the intravascular compartment. For this reason hypotonic crystalloid solutions should never be used in situations where the restoration of the circulating blood volume is a priority.

Theoretically, colloid solutions offer advantages over crystalloid solutions for emergency resuscitation. Firstly, the immediate distribution is primarily within the intravascular compartment limited by the permeability of the endothelial barrier. Secondly, the colloid molecules increase plasma oncotic pressure thereby altering the balance of fluid flux across the endothelium and drawing fluid back into the intravascular compartment from the interstitial space. Thus, in contrast to crystalloid solutions, a bolus of a colloid solution provides volume expansion over and above the actual volume of fluid infused. All synthetic colloids are polydisperse, with a range of molecules of different molecular weights in one solution. The magnitude of the effect on plasma oncotic pressure is determined by the average molecular weight of the colloid molecules; small molecules exert a relatively greater osmotic effect than larger molecules at the same concentration. However, large molecules remain within circulation longer than small molecules, which are rapidly excreted by the kidneys or may be lost from circulation by leakage across the endothelium. Thus, for example, 6% dextran
Volume Replacement in Dengue Shock Syndrome

70 (average molecular weight 70,000 Daltons) and 6% hydroxyethyl starch (average molecular weight 200,000 Daltons) provide volume expansion for at least 6-8 hours, whilst 4% gelatin solutions, consisting of molecules of considerably smaller average molecular weight (35,000 Daltons), remain effective for only 2-3 hours\(^9\). There is, however, a concern particular to patients with increased vascular permeability, that colloid molecules may themselves leak into the interstitium and exert a reverse osmotic effect, thereby drawing out intravascular fluid and worsening the situation\(^10\).

Another significant determinant of the effect of a colloid infusion is the concentration of the solution. Hyperoncotic solutions, such as 10% Dextran 40, have considerably greater ability to draw fluid back into the intravascular compartment than isoncotic preparations of the same molecule. However, there are major concerns about the safety of hyperoncotic solutions, especially in hypovolaemic patients, in whom there is a real risk of developing acute renal failure\(^11,12\). Other concerns relating to the use of colloid solutions include the potential for allergic reactions and the established adverse effects on blood coagulation\(^9\). Crystalloid solutions are generally safe, reaction free, and have only dilutional effects on coagulation.

**Fluid trials in dengue shock syndrome**

Thus, it is apparent that the choice of fluid for resuscitation of hypovolaemic shock is not straightforward. However, despite the importance of the question there have been only two randomized and blinded clinical trials, published in international literature, that have attempted to investigate the impact of different fluid regimens in the initial resuscitation of DSS\(^{13,14}\). The first study\(^{13}\), a pilot involving 50 children with DSS, was not designed to answer definitively the question of colloid versus crystalloid. However, the trial did demonstrate that there were important differences in the immediate clinical response to different fluid regimens, with significantly greater improvements in surrogate markers of recovery such as cardiac index, hematocrit and pulse pressure among children who received a colloid rather than a crystalloid at first presentation. All the children recovered fully with fluid management alone, and there were no differences in overall time to recovery or total fluid requirements.

The second study, conducted over a one-year period in a single hospital, recruited 230 children with DSS who received one of four different fluids, two crystalloids and two colloids, for initial resuscitation\(^{14}\). The most significant factor predicting the clinical response to resuscitation was the width of the pulse pressure at presentation. Children with a pulse pressure of \(<10\) mm Hg on admission were both more likely to suffer prolonged shock and to experience subsequent episodes of shock than those presenting with higher pulse pressures. Although few clear differences in outcome were demonstrable between the recipients of the four different fluids, it was apparent that the subgroup with the lowest pulse pressures at presentation improved significantly more quickly if they received one of the colloids, whereas in the children presenting with
higher pulse pressures there was no difference in the outcome between the groups. This suggests that most children with DSS can be effectively managed with crystalloid fluids alone, but that early treatment with colloids may improve the outcome in the important minority with very severe shock.

**Conclusion**

At present the WHO guidelines still include hypotonic crystalloid solutions among those recommended for the initial resuscitation of children with shock\(^5\). This is not appropriate, and solutions such as half-strength physiological saline or 5% dextrose diluted in physiological saline should not be recommended. If a crystalloid is used it should be isotonic (e.g. physiological saline or lactated Ringer's/Hartmann's solutions). Accepting this, perhaps the most important question that needs to be addressed is whether a colloid is better than a crystalloid for primary resuscitation, and if so, in what particular circumstances. If a true benefit from colloid resuscitation is demonstrable, particularly if agreement can be reached among clinicians and researchers of the international dengue community as to which particular surrogates are most meaningful. As the global burden of dengue disease increases, if a true benefit from a particular fluid regimen is established even in a subgroup of patients, this may have a significant influence on overall mortality.

**Acknowledgement**

Grateful thanks are offered to Dr Jeremy Farrar and all the staff of the Wellcome Trust Clinical Research Unit and the Centre for Tropical Diseases, Ho Chi Minh City.

**References**


Volume Replacement in Dengue Shock Syndrome


Efficacy of Clinical Diagnosis of Dengue Fever in Paediatric Age Groups as Determined by WHO Case Definition 1997 in Thailand

by
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Abstract
A descriptive cross-sectional study was undertaken at the Paediatrics department of the Sawanpracharak Medical Centre, Bangkok, from September 1998 to September 1999. Patients admitted with a tentative diagnosis of dengue infection were followed throughout their hospital stay. Daily records were kept of the patients' symptoms, their physical examination findings and laboratory data. Clinical diagnosis of DF/DHF/DSS or other febrile illness was made by paediatricians at the time of discharge based on the WHO 1997 case definition. During the study, 176 patients, aged 1-13 years, were recruited based on initial admission diagnosis. At the end of hospitalization, 71 patients (40%) were diagnosed as having DF by their paediatricians. Based on ELISA and/or PCR, only 45 were confirmed to have DF. In the study of our population, the sensitivity, specificity, PPV and NPV according to the WHO 1997 DF case definition were 100%, 21.21%, 63.38% and 100% respectively. The four leading clinical manifestations in the sample of 45 confirmed cases included: fever 100%, positive tourniquet test 86.67%, headache 80.48% and leukopenia 62.22%. By using fever with two other clinical manifestations, only fever with positive tourniquet test and leukopenia differentiated DF from other febrile illness (p=0.042) and had the highest predictive value (PPV=72.72%). It was also found that fever with positive tourniquet test, or fever with leukopenia with one other clinical manifestation, had a higher chance of more PPV than fever combined with just any two clinical manifestations.

The study brought out the fact that WHO case definition for DF has very high sensitivity but runs the risk of over-diagnosis to the extent of 36.62% (PPV=63.38%). To reduce this risk, the study found that the combination of fever with positive tourniquet and leukopenia was the best (PPV=72.72%). The combination of fever with positive tourniquet or leukopenia and one other clinical manifestation (PPV=72.72%-61.53%) was better than fever with any two clinical manifestations (PPV=64.2%-40.00%).

Keywords: DF/DHF/DSS, WHO case definition, over-diagnosis, paediatric age group, Thailand.

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Background

In most tropical countries of Asia where the dengue virus is endemic, all the three spectrums of the dengue infection, i.e. dengue fever (DF), dengue haemorrhagic fever (DHF) and dengue shock syndrome (DSS), are a common occurrence. DHF/DSS have a typical and stereotypical manifestation characterized by abnormal haemostasis and plasma leakage\(^1\). These make the clinical diagnosis of DHF/DSS more reliable and accurate\(^2\). DF, on the other hand, has a great variability of clinical features which depends on many factors such as the person, the place and the time\(^3\). It may be confused clinically with other infections, viz. influenza, measles, typhoid, leptospirosis, or any non-specific viral syndrome\(^4\). Given these variabilities, WHO proposed the clinical diagnosis of DF to “probable DF” and “confirmed DF”. Probable DF is defined by using clinical criteria with presumptive support serology, single specimen positive for HI or ELISA and/or with the occurrence at the same location and time as other confirmed cases of DF. Confirmed DF needs more specific dengue laboratory support such as viral isolation, four-fold rising of antibody, and viral antigen demonstration\(^5\). The diagnosis of DF therefore becomes difficult as compared to DHF/DSS which are more reliable in terms of clinical manifestations and simple laboratory techniques. DF cases precede and accompany DHF epidemics and both have the viremia stage which permits transmission by mosquito\(^6\). In our situation where the laboratory facilities are either limited or non-existent, “probable DF” is practically diagnosed by clinical criteria, supported by the occurrence in the epidemic period instead of presumptive supportive serology. A retrospective study was therefore designed to:

1. evaluate the validity of the WHO 1997 case definition of DF Dx in the paediatric age group, and
2. determine more sensitive clinical manifestations or combinations in case definition which have more predictive value for DF Dx.

The study was carried out at the Paediatrics Department, Sawanpracharak Medical Centre, Bangkok, Thailand, between September 1998 and September 1999 as a descriptive cross-sectional study.

Methodology

Patients admitted with a provisional diagnosis of dengue infection or suspected dengue infection (Flow chart) were followed throughout their hospital stay. Parents or guardians of all patients had to sign an informed consent before participating in this study. A detailed history-taking and clinical examination was performed. Blood specimens were collected for CBC, liver function and dengue confirmation test on the day of admission. The dengue confirmation test included ELISA serology and PCR performed at AFRIMS (Armed Forces Research Institute of Medical Sciences). The tests were repeated on the second specimen collected 10-14 days later. Daily physical examination findings, tourniquet tests and CBC were followed by attending paediatricians. Clinical diagnosis was based on the WHO 1997 case definition for DF/DHF/DSS. The diagnosis of
Efficacy of Clinical Diagnosis of DF in Paediatric Age Groups as Determined by WHO Case Definition 1997 in Thailand

non-dengue acute febrile illness cases (other febrile illness = OFI-1) was based on the symptom of self-limited acute febrile illness without defined sources of other infection and absence of clinical criteria of dengue case definition. The final diagnosis of DF was linked to confirmatory tests, either from ELISA and/or PCR. Non-dengue febrile illness (other febrile illness = OFI-2) was based on negative confirmatory test.

**Results**

**Clinical diagnosis at end of admission**

There were 176 patients between the age groups ranging from 1 to 13 years. At the end of the admission, the clinical diagnosis of DF, DHF/DSS and OFI-1 were 71, 98 and 7 respectively (Table 1). But when based on ELISA and/or PCR, the final diagnosis of DF, DHF/DSS and OFI-2 were 45, 93 and 38 respectively.

### Table 1. Comparative clinical Dx and final Dx in DF/DHF/DSS/OFI at the end of admission

<table>
<thead>
<tr>
<th>Clinical Dx</th>
<th>DF</th>
<th>DHF/DSS</th>
<th>OFI-2</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>DF</td>
<td>45</td>
<td>0</td>
<td>26</td>
<td>71</td>
</tr>
<tr>
<td>DHF/DSS</td>
<td>0</td>
<td>93</td>
<td>5</td>
<td>98</td>
</tr>
<tr>
<td>OFI-1</td>
<td>0</td>
<td>0</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>Total</td>
<td>45</td>
<td>93</td>
<td>38</td>
<td>176</td>
</tr>
</tbody>
</table>

**Profile of dengue study test**

In the 45 confirmed DF cases, 36 patients were supported by positive ELISA or ELISA and PCR and 9 patients were confirmed by only PCR. Among the 36 cases with ELISA support we found that acute primary infection was 22.22% in 8/36 cases and acute secondary infection was 77.77% in 28/36 cases. Nineteen out of the 45 confirmed DF cases had positive PCR for DEN-1(5), DEN-2(2) and DEN-3(12). No activity of DEN-4 was detected.

**Patients’ profile in DF and OFI-2 group**

<table>
<thead>
<tr>
<th>Features</th>
<th>DF (n=45)</th>
<th>OFI-2 (n=38)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male: female</td>
<td>1.4:1</td>
<td>1.7:1</td>
</tr>
<tr>
<td>Age (mean ± SD, yr)</td>
<td>8.3±3.56</td>
<td>7.07±2.49</td>
</tr>
<tr>
<td>Maximum-minimum age</td>
<td>13-1 yr.</td>
<td>13-1 yr.</td>
</tr>
<tr>
<td>Days with fever before admission (mean ± SD, days)</td>
<td>3.71±1.72</td>
<td>3.73±1.81</td>
</tr>
<tr>
<td>Mean admission duration (mean ± SD, days)</td>
<td>3.37±1.51</td>
<td>3.52±1.75</td>
</tr>
</tbody>
</table>
1. Validity and yield of DF Dx

Table 2 includes the validity and yield of DF Dx. In our population, the sensitivity, specificity, PPV and NPV of the WHO 1997 case definition to diagnose DF were 100%, 21.21%, 63.38% and 100% respectively.

<table>
<thead>
<tr>
<th>Clinical manifestations</th>
<th>DF 71 cases</th>
<th>OFI 7 cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Final Dx</td>
<td>DF 45 cases</td>
<td>OFI 38 cases</td>
</tr>
<tr>
<td></td>
<td>Sensitivity (45/45) = 100%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Specificity (7/33) = 21.21%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Positive predictive value (45/71) = 63.38%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Negative predictive value (7/7) = 100%</td>
<td></td>
</tr>
</tbody>
</table>

Table 3. Proportion of clinical manifestations according to WHO case definition 1997 in confirmed DF & OFI cases

<table>
<thead>
<tr>
<th>Clinical manifestations</th>
<th>Percentage</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>100 (45/45)</td>
<td>100 (38/38)</td>
</tr>
<tr>
<td>Haemorrhagic manifestation</td>
<td>86.66 (39/45)</td>
<td>63.15 (24/38)</td>
</tr>
<tr>
<td>as positive TT</td>
<td>15.55 (7/45)</td>
<td>5.26 (2/38)</td>
</tr>
<tr>
<td>as spontaneous skin bleeding</td>
<td>88.89 (40/45)</td>
<td>65.79 (25/38)</td>
</tr>
<tr>
<td>Headache</td>
<td>80.48 (33/41)*</td>
<td>76.32 (29/38)</td>
</tr>
<tr>
<td>Leukopenia (WBC&lt;5,000/cumm)</td>
<td>62.22 (28/45)</td>
<td>65.79 (25/38)</td>
</tr>
<tr>
<td>Myalgia</td>
<td>41.46 (17/41)*</td>
<td>28.95 (11/38)</td>
</tr>
<tr>
<td>Retro-orbital pain</td>
<td>29.26 (12/41)*</td>
<td>23.68 (9/38)</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>25.00 (11/41)*</td>
<td>18.42 (7/38)</td>
</tr>
<tr>
<td>Rash</td>
<td>20.00 (9/45)</td>
<td>21.03 (8/38)</td>
</tr>
</tbody>
</table>

* Children < 4 years were omitted because they were unable to express these symptoms

2. Clinical manifestations are more predictive of DF Dx

Table 3 includes the proportion of clinical manifestations as per WHO case definition in confirmed DF and OFI cases. We found that the four leading clinical manifestations, according to the case definition, as presented in our 45 confirmed cases, comprised of fever (100%), positive tourniquet test (86.67%), headache (80.48%) and leukopenia (62.22%).

3. Clinical manifestation combinations more predictive of DF Dx

Positive predictive value of bi-clinical features as per WHO case definition of DF Dx in included in Table 4. By using fever with two clinical features, we found that fever with a positive tourniquet test and leukopenia (WBC < 5000 cell) was the only combination which distinguished DF significantly from other febrile illness (p=0.042) and had the highest predictive value (PPV= 72.72%).
Table 4. Positive predictive value of bi-clinical features in WHO 1997 case definition of DF Dx

<table>
<thead>
<tr>
<th>Clinical features</th>
<th>Positive predictive value %</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive TT + leukopenia</td>
<td>72.72</td>
<td>0.042</td>
</tr>
<tr>
<td>Leukopenia + myalgia</td>
<td>70.70</td>
<td>0.285</td>
</tr>
<tr>
<td>Positive TT + arthralgia</td>
<td>68.75</td>
<td>0.194</td>
</tr>
<tr>
<td>Positive TT + myalgia</td>
<td>68.18</td>
<td>0.125</td>
</tr>
<tr>
<td>Leukopenia + rash</td>
<td>66.67</td>
<td>0.525</td>
</tr>
<tr>
<td>Positive TT + retro-orbital pain</td>
<td>64.70</td>
<td>0.330</td>
</tr>
<tr>
<td>Myalgia + retro-orbital pain</td>
<td>64.28</td>
<td>0.407</td>
</tr>
<tr>
<td>Positive TT + headache</td>
<td>62.50</td>
<td>0.076</td>
</tr>
<tr>
<td>Leukopenia + headache</td>
<td>62.50</td>
<td>0.334</td>
</tr>
<tr>
<td>Myalgia + arthralgia</td>
<td>62.50</td>
<td>0.459</td>
</tr>
<tr>
<td>Positive TT + rash</td>
<td>61.53</td>
<td>0.564</td>
</tr>
</tbody>
</table>

Table 5. Comparative PPV between the group of fever with positive TT or leukopenia and one clinical feature and the group of fever with any two clinical features

<table>
<thead>
<tr>
<th>Group 1 Fever with positive TT or leukopenia and one other clinical feature</th>
<th>Group 2 Fever with any two clinical features</th>
</tr>
</thead>
<tbody>
<tr>
<td>PPV</td>
<td>P-value</td>
</tr>
<tr>
<td>1. TTW</td>
<td>72.72</td>
</tr>
<tr>
<td>2. WM</td>
<td>70.00</td>
</tr>
<tr>
<td>3. TTA</td>
<td>68.75</td>
</tr>
<tr>
<td>4. TTM</td>
<td>68.18</td>
</tr>
<tr>
<td>5. WR</td>
<td>66.6</td>
</tr>
<tr>
<td>6. TTE</td>
<td>64.70</td>
</tr>
<tr>
<td>7. TTH</td>
<td>62.05</td>
</tr>
<tr>
<td>8. WH</td>
<td>62.50</td>
</tr>
<tr>
<td>9. WE</td>
<td>62.50</td>
</tr>
<tr>
<td>10. TTR</td>
<td>61.53</td>
</tr>
</tbody>
</table>

TT = positive tourniquet test, W = leukopenia, M = myalgia, A = arthralgia, E = retro-orbital pain, R = rash, H = headache
4. Comparative PPV between the group of fever with positive TT or leukopenia and one clinical feature and the group of fever with any two clinical features

We found that the first group (Table 5) was more predictive of DF than the second group.

Discussion

From this study, it was evident that DF had no gender predilection and the majority of the cases were still in school-age children. There was no difference between DF and other febrile illnesses in mean fever days before admission and the number of hospital days. As previously reported, DF can be from both primary and secondary dengue infection. Kalyanarooj et al. found that 69.36% of DF patients had secondary dengue infection\(^{(9)}\). Our study showed it as 77.77% and this confirms that DF occurred more by secondary dengue infection.

We found that the WHO 1997 DF case definition has very high sensitivity but moderate PPV and low specificity. This might be due to two reasons: firstly, the concept of case definition is to help in early diagnosis of the case so that clinical features which are just more characteristic of the disease are included\(^{(4)}\); secondly, clinical manifestations in DF are non-specific as noted earlier. Four in seven clinical manifestations, i.e. myalgia, arthralgia, retro-orbital pain and headache, are non-specific which might be manifested by other acute febrile illnesses.

Clinical manifestations in case definition which are more predictive of DF Dx

Four leading clinical manifestations in DF are fever, haemorrhagic manifestation (mostly positive TT), headache and leukopenia (Table 3). Only positive TT differentiates DF significantly from other febrile illness group. We looked out for spontaneous skin bleeding and found only 15.55% of DF cases. TT reflects capillary fragility and was found to be often positive in dengue viral infection. The percentage of positive TT in DF patients at the end of admission reported by Kalyanarooj et al. was 87.50%, whereas our study put it at 86.66%. There are no separate data on the day-positive TT for DF patients but on dengue infection patients (DF and DHF patients) and were reported to be positive as 45.55%, 55.56%, 67.72%, and 77.82% of cases on day 4, 3, 2, and 1 before defervescence, respectively\(^{(7)}\). So TT should be considered as a simple clinical tool in assisting the diagnosis of DF and other dengue infections.

Appropriateness of applying the case definition to diagnose DF in paediatric age group

We think that it is not appropriate to apply WHO case definition to the paediatric age group verbatim. Most of the clinical features have been drawn on the basis of adult symptoms. The clinical course of classic dengue fever has been well-described by Siler (1926)\(^{(8)}\) and Sabin (1959)\(^{(9)}\) who observed adults with experimentally-induced and naturally-acquired infections. The classic
symptoms are: abrupt onset of fever along with headache with severe retro-orbital pain (pain associated with eye movement), severe myalgia and arthralgia in the back and loin. Approximately 60-100% of adult patients have classic DF symptoms\(^\text{(10)}\). These symptoms are seldom reported in children\(^\text{(11)}\) and children, particularly those under 4 years, could not verbalize these symptoms. Thus, these clinical features might not be appropriate to apply to children.

**Suggested modifications in the application of WHO case definition to paediatric age group**

As all the cases included in this study occurred during the dengue epidemic period, we shall use this situation to support the clinical lead to diagnose “probable DF”. We find that if we apply the case definition directly, we run the risk of over-diagnosis of DF to the extent of 36.67% (100-PPV) (Table 3). But if we use fever with positive TT and leukopenia, the PPV goes up to 72.72% (Table 5) decreasing over-diagnosis to 27.28%. And fever with positive TT and leukopenia is the only clinical feature combination which has the highest PPV and differentiates DF significantly from other febrile illness group (Table 4). So we suggest using fever with positive tourniquet plus leukopenia as a priority criteria for a “probable DF” diagnosis. Kalayanaroj et al. reported that using positive TT and leukopenia to diagnose dengue infection gives PPV of 83.19%\(^\text{(12)}\). This figure is higher than ours because their data was based on dengue infection group rather than only on DF group. We also think that it might be useful even in a non-epidemic period situation, otherwise areas with limited laboratory support will not be able to diagnose DF.

In cases that do not have both positive TT and leukopenia in the same person, we found that the group of fever with positive TT or leukopenia and one other clinical feature had a higher PPV range than the group of fever with any two clinical features which numbered 72.72%-61.53% as compared to 64.28%-40.00% (Table 5). In our opinion, in an epidemic period the combination of the first group would be, any way, useful to diagnose DF. But in non-epidemic period it is probably not useful because the PPV is a bit too low.

In non-epidemic period, we suggest that the diagnosis of probable DF should be made in the patient who has undifferentiated febrile illness and has fever with positive tourniquet or other signs of bleeding and leukopenia only.

**Need to encourage reporting of DF**

In our country situation, we encourage the diagnosis of even “probable DF” because it benefits in the implementation of the disease control programme and also in the quality of disease statistics\(^\text{(13)}\). WHO suggests that each country should report DF and DHF/DSS separately and propose the case fatality of DHF/DSS should be less than 1%\(^\text{(14)}\). The Thai Ministry of Public Health had set the target for the dengue case-fatality rate in the year 1999-2000 to be less than 0.2% and it actually occurred at 0.24%\(^\text{(15)}\). This data generally included the DF and DHF/DSS cases as the denominator which might make for such a low case-fatality rate. If we could
diagnose DF separately from the DHF group, we will have a more accurate data on the case fatality of DHF/DSS which will show the real situation with regard to our treatment capacity.

**Advantage of applying DF diagnosis to the control programme**

From this study it is apparent that if the outbreak control is based on applying the WHO case definition directly, the control action will unnecessarily exceed by around 36.67% (100-PPV). It can be considered in two ways, appropriate or not appropriate (too costly). In our opinion if the country has no budget constraints it is worthwhile to do so. Because one DF case may mean considerable numbers of asymptomatic dengue infection and mild DF cases in the community which is difficult to assess. One documented data showed that “it has been estimated that during the outbreaks between 150-200 cases of dengue infection occur for each patient with DSS seen in the hospital”[16].

**Conclusion**

By using the WHO case definition in the paediatric age group for DF Dx at the end of admission, the chances of over DF Dx is 36.67%. Four leading clinical features in case definition are: fever, positive TT, headache and leukopenia. Only fever combined with positive TT and leukopenia differentiate DF from other febrile illness significantly and has the highest PPV. The objective signs have higher PPV than subjective symptoms. Among the various combinations of clinical features, the group of fever with TT+ or leukopenia and one other clinical feature has a higher PPV than fever with two subjective clinical features.

In our considered opinion, in a country where laboratory confirmation of dengue is not practically available, to identify DF cases as “probable DF” should be accepted to improve the statistics of dengue morbidity/mortality reports and the control programme. We suggest applying the WHO 1997 clinical case definition to diagnose “probable DF” in the paediatric age group as follows: in non-epidemic period: fever with positive TT and leukopenia; in epidemic period: fever with positive TT and leukopenia or fever with positive TT or leukopenia and any other clinical feature rather than fever with any two other clinical features in the definition.

**Acknowledgement**

We would like to express our gratitude to Dr Suchitra Nimmanitya for her outstanding suggestions and advice. We also wish to thank the entire paediatrics and laboratory staff at the Sawanpracharak Medical Centre for their tireless efforts in conducting the study. Finally, a big ‘thank you’ to AFRIMS for the support of serology and virology confirmation tests.

**References**


Interleukin (IL-2) Levels in Past Dengue Infection

by
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Abstract

Several reports relate the role of different cytokines in the pathogenesis of dengue. Here, we report the production, after trigger with dengue virus, of IL-2 by peripheral blood mononuclear cells of individuals with history of dengue infection 20 years ago.

Key words: Dengue, cytokines, dengue virus, Havana, Cuba

Introduction

Dengue haemorrhagic fever (DHF) is the extreme and severe manifestation of the dengue infection entailing a rapid clinical deterioration, circulatory collapses and shock. The severe disease mostly depends on the intrinsic immune response of the host, which is responsible for additional damages that are qualitatively different to those provoked by the virus itself[1].

Interleukin-2 (IL-2) is the major autocrine growth factor for T lymphocytes. This cytokine stimulates the activation, differentiation and proliferation of T, B, NK cells and monocytes. Levels of IL-2 and soluble CD4+ and CD8+ molecules in plasma from DHF patients are significantly higher than those from dengue fever patients (DF)[2,3]. IL-2 is capable of stimulating either human T cell (HT-2) or murine (CTLL-2) cell lines to grow. Quantification of CTLL-2 proliferation is a standardized assay to indirectly measure IL-2 concentration[4].

The memory T cell response to dengue virus is not very well understood. Based on these facts, the present research was designed to study a long-lasting memory T cell response through the detection and quantification of IL-2 in supernatants of dengue-stimulated human lymphocyte
cultures from dengue 1 or 2 Cuban immune individuals that suffered their primary infection 21 years (DEN-1) and 17 years (DEN-2) ago.

The unique Cuban epidemiological situation on dengue allows us to perform this study\(^5\). In 1977, Cuba suffered a DEN-1 epidemic that affected the whole country with more than 400,000 reports. This epidemic was followed by a DHF outbreak in 1981 caused by the serotype 2\(^6\). More than 344,000 reports, 10,000 DHF and 158 fatal cases were reported. After more than 14 years without dengue circulation, in 1997, a small DEN-2 outbreak was observed in Santiago de Cuba municipality, where 3012 cases were confirmed with 205 DHF and 12 fatal cases, all in adults\(^7\). Taking into account these antecedents, all dengue-immune Cuban individuals have been infected in either the 1977 epidemic (DEN-1), and/or during the DEN-2 epidemics (1981 and 1997).

Considering the probable role of IL-2, both in protection and/or in the pathogenesis of DHF\(^8\), we decided to quantify its production in dengue-stimulated PBMC from DEN-1 or DEN-2 immune individuals.

**Methodology**

In 1998, 20 healthy adult volunteers from Havana city were bled. These individuals could have been infected during the 1977 (DEN-1) and/or 1981 (DEN-2) epidemics. Serum samples were tested for quantifying the presence of total anti-dengue virus antibodies using an inhibition immunoenzymatic assay\(^9\). Neutralizing antibodies were determined in those positive sera by plaque reduction neutralization assay on BHK21 clone 15 cells according to Morens et al.\(^{10}\) with minor modifications. DEN-1 (Hawaii strain) and DEN-2 (A15 Cuban strain) viruses were employed\(^{11}\). Those DEN-1 or DEN-2 immune individuals were enrolled in the study.

Peripheral blood mononuclear cells (PBMC) (3x10\(^6\)/well), isolated by the Boyum method\(^{12}\), were incubated at 37°C in 5% CO\(_2\) atmosphere with DEN-1 (Hawaii strain) and DEN-2 (NGC strain) antigens at a concentration of 184.5µg/ml / 2.1x10\(^3\) pfu and 260 µg/ml/4.5x10\(^3\) pfu, respectively. The supernatants were collected for IL-2 quantification after 48h incubation. Cell cultures with media were used as negative control.

The IL-2 assay consisted in culturing the IL-2-dependent cytotoxic T lymphocyte cell line CTLL2 (CTLL-2 ATCC TIB 214, 302 catalog Cell Lines & Hybridomas; 7th edition, 1992, edited by ATCC Maryland) in the presence of either non-stimulated or antigen-stimulated culture supernatants. CTLL-2 proliferation was detected by a non-radioactive cell proliferation assay (Cell Titer 96\(^{TM}\) AQ\(\text{ueous}\) Non-Radioactive Cell Proliferation Assay, Promega).

**Results and discussions**

Total dengue antibodies were detected in 5/20 (25%) individuals. Table 1 shows the neutralizing antibody titer to DEN-1 or DEN-2 viruses in those dengue-immune individuals.

Levels of IL-2 (7.27-78.23 UI/ml) were detected in the supernatant of stimulated PBMC from dengue-immune individuals (Table and Figure). A serotype-specific stimulation in all cases and a slight cross-reactivity in some of them were detected.
Table. Case distribution according to ELISA antibody titers serotype specificity and IL-2 concentration

<table>
<thead>
<tr>
<th>Individuals</th>
<th>Antibody Titer</th>
<th>Type of infection</th>
<th>IL-2 concentration (UI/ml)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>DEN-1</td>
<td>DEN-2</td>
</tr>
<tr>
<td>#1</td>
<td>1/160</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>#2</td>
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<tr>
<td>#5</td>
<td>1/80</td>
<td>+</td>
<td>-</td>
</tr>
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</table>

The presence of IL-2 in the supernatants of dengue-stimulated PBMC from immune individuals is in line with the results previously published by Kurane et al.\(^2\) who detected IL-2 in the sera of children with dengue. Our results are also in agreement with the previous results found by Pérez et al.\(^3\) who detected memory lymphocytes to dengue after long periods of the primary infection. These results could explain at least in part the recent epidemiological observation done in 1997 in Santiago de Cuba municipality\(^4\) where after more than 20 years of the DEN-1 primary infection, a DHF outbreak caused by DEN-2 virus was reported. It seems that there is no time-limit for the sensitization after a primary dengue infection.
The study of other cytokines in dengue-stimulated PBMC from immune individuals could clarify the immunological cascade disruption and their role in the pathogenesis of this disease.

Acknowledgments

We thank Dr Virginia Capó, Dr Luis Fonte and Ariel Quintana from the Tropical Medicine Institute, and Dr Irene Bosh, from the Center for Infectious and Vaccine Research University of Massachusetts Medical School, USA, for critically reading the manuscript and offering helpful advice.

References


Legislation for Control of Dengue in Singapore

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Abstract
In Singapore, three pieces of legislation, namely, the Infectious Diseases Act (IDA), the Control of Vectors and Pesticides Act (CVPA) and the Environmental Public Health Act (EPHA) provide very wide powers to prevent and control dengue. They prescribe hefty penalties against offenders for failure to comply with the laws. Despite that, the experience showed that it was inadequate to rely only on legislation to control dengue. It is more effective to make the community understand, through communication, the importance of preventing mosquito-breeding within their premises and assist them to have a proper system to do so. Through working with various agencies, much better long-term cooperation and results can be achieved than through enforcement of law. Legislation can be used in emergency situations like disease outbreak or when dealing with recalcitrant offenders.

Keywords: Dengue, legislation, control, community participation, Singapore.

Introduction
In Singapore, three pieces of legislation are enforced for the prevention and control of dengue; these are: the Infectious Diseases Act (IDA)\(^1\); the Control of Vectors and Pesticides Act (CVPA)\(^2\); and the Environmental Public Health Act (EPHA)\(^3\).

Each of these laws deals with different aspects of dengue control. The IDA deals with notification, investigation and treatment of dengue; the CVPA deals with vector control; and the EPHA deals with environmental sanitation and other environmental public health issues.

The Infectious Diseases Act (IDA)
Dengue fever and dengue haemorrhagic fever are notifiable as infectious diseases under the IDA. The Act requires any doctor, laboratory or anyone who has reason to
believe or suspect a DF/DHF case to notify the Ministry of Health (MOH) and the Ministry of the Environment (ENV) within 24 hours. Such notifications are required to be sent by fax or email. The Act also requires anyone who is possibly infected to undergo medical examination, and anyone infected to be quarantined and treated.

Other powers authorized by the Act to deal with infectious diseases (dengue and others) include epidemiological surveillance, investigation, post-mortem examination and disposal of corpses, disinfection of vessels and premises, destruction of infected animals, food and water, prevention of overcrowding, prohibition to carry on business and closure of food establishment.

**The Control of Vectors and Pesticides Act (CVPA)**

The CVPA prohibits anyone from creating a condition favourable to the propagation of vectors. It also prohibits anyone from breeding, keeping, importing and exporting vectors without permission. It gives public health officers the following powers to prevent the propagation of vectors:

- To enter and inspect premises, vessels or aircraft with the owner/occupier’s consent, or after giving at least 12 hours’ notice;
- To serve an order on owner/occupier of premises to take measures within a stipulated time;
- To require the owner/occupier to carry out fogging or spraying at his own expense;
- To carry out any measure if the owner/occupier fails to do so, and to recover the costs incurred.

In practice, we do not enforce these regulations, based on mere presence of favourable conditions. Enforcement action is taken only when actual vector mosquito breeding is established. For premises with existing or foreseeable conditions for mosquito breeding, an order is served to the owner/occupier to remove or rectify the conditions. For example, orders are served to construction sites at the start of the project to ensure good housekeeping, to prevent vector breeding, and to engage pest control operators to carry out regular control; to vacant premises owners to maintain the unoccupied premises mosquito-free; and to householders to remove, maintain or repair their gutters. In an outbreak caused at a construction site, the officers can carry out emergency vector control measures within the site, and all costs incurred (manpower, chemicals, contractor’s cost) are charged to the construction site.

Currently, the fines for all types of premises (except construction sites) found breeding mosquitoes is S$200. In the case of construction sites, they are fined S$1,000 for mosquito breeding found the first time at their sites, and S$2,000 for the second time. For subsequent offences, they will go to the court, where they can be fined up to S$10,000 and/or 6 months’ jail. If anyone served with an order fails to comply with it, he will be fined S$2,000 for the first offence, S$4,000 for the second, and S$5,000 for the third offence. He goes to the
court for subsequent offences and can be fined up to $50,000 and/or 6 months' jail.

The Environmental Public Health Act (EPHA)

The EPHA deals with many aspects of environmental public health. The parts relevant to dengue prevention pertain to: (i) public cleansing; (ii) public nuisances, and (iii) insanitary premises.

Is legislation the solution?

The purpose of legislation is to ensure compliance with advices/messages to speed up behavioural changes. However, it alone is not the solution. The message should be internalized and people motivated to act in the desired way by themselves, instead of through the fear of enforcement. To illustrate this point, we use the case of the IDA, which requires doctors to notify ENV on any DF/DHF case. To comply strictly with the law, the doctor would need to take blood sample from any febrile patient and send it for diagnosis in a laboratory to confirm if the patient is infected with DF/DHF. However, doctors are not prepared to take blood samples from patients because of the cost that will be passed on to the patients, until the symptoms are quite obviously DF/DHF. By this time much precious time has already been lost for control measures to be taken to prevent the transmission of the disease.

On the other hand, if doctors understand the public health importance of controlling the vectors quickly to stop transmission, they would be more motivated to take blood samples once the patients indicate that they had fever for five or more days. The ENV has arranged with a selected group of doctors to send blood samples for diagnosis without charge. This clears the obstacles and encourages doctors to do what is necessary, not because they are required by law to do so. Similarly, householders, management of estates and management of construction sites, once motivated, could greatly contribute to the control of the disease rather than be compelled by legislation to act. When they are convinced that maintaining their premises free from mosquito breeding is beneficial to them and to the people they have a duty to protect, legislation is of secondary importance.

Nevertheless, legislation has its place in dengue control for the recalcitrant or those who pay lip service only, especially after repeated reminders and efforts to educate them. It is always useful to have a “stick” which can be used when the situation warrants it.

Community participation

Although Singapore is known for its use of legislation in dengue control, we rather play the role of facilitator and educator to work with and help various target groups to implement a system or re-design structures to prevent mosquito-breeding. Given below are some examples:

- Schools used to be a major source of mosquito-breeding and as much as 25% of cases were among schoolchildren and teenagers. We started to work with the Ministry of Education (MOE) to identify the common breeding habitats in
Legislation for Control of Dengue in Singapore

schools, held talks with all principals, school operations managers and senior officers from MOE on the problem and control measures, and finally convinced them of the need to carry out routine mosquito control in schools. We also advised MOE on contract specifications for mosquito control measures, and educated students and teachers on where to look for the habitats. There is now a system of regular mosquito control in all government and government-aided schools, and ENV audits the situation. The situation in schools is much improved now.

• The Housing and Development Board (HDB) changed the design of bamboo pole-holders for new flats after we highlighted to them that these holders bred mosquitoes and posed a big problem as their numbers were very large in public housing estates. The new designs in new housing estates are mosquito-proof.

• Vacant flats were also a problematic breeding source as the water closets, cisterns and gully traps and other potential habitats were not removed after the flats were vacated. We have worked out a Standard Operating Procedure (SOP) with HDB to make sure such potential habitats are treated, drained or removed when a flat becomes vacant.

• Bus shelters were provided with roof gutters. Over time, the gutters were choked and bred mosquitoes. With our persuasion, despite the hefty cost involved, the Land Transport Authority (LTA) changed the design of bus shelters to do away with gutters. The remaining shelters with gutters are maintained regularly, and will be replaced by the new gutter-less type in phases.

• Similarly, we had worked with the Singapore Institute of Architects to convince them to design structures and houses without gutters and other structures that might become potential habitats for mosquitoes.

• ENV has also encouraged the formation of dengue prevention volunteer groups (DPVGs) amongst residents of estates. The volunteers are educated on the types of mosquito habitats in a household, and they visit houses on weekends to educate residents in turn. There are now 35 such volunteer groups.

Health education

We have always attempted to reach out to the public with messages on mosquito prevention through talks, the mass media, exhibitions, campaigns, etc. Whether the approach is one of mass outreach but low impact, or small target group but intensive, we have not been successful in sustaining the results. Most people did not remember what they had seen or heard once it was over.

There is a need to involve sociologists and behavioural scientists to understand what will make people act and continue to
act. In our public communications, there is also a need for expertise in mass communications to convey the right message across to achieve the desired perceptions or results.

**Conclusion**

In conclusion, it can be said that legislation is useful for dealing with recalcitrant offenders and in emergency situations to bring an outbreak under control. But it is not the solution to overcome mosquito-breeding problems. It is more effective to make the community understand the importance of mosquito prevention, and to help them put in place a proper system for mosquito control. Side by side with legislation, there must be good, sustained public education and communications plans. Legislation should therefore be used as a tool with discretion. Blanket legislation does not work for all target groups.

**References**

1. The Infectious Disease Act (Chapter 137), 1 August 1977, Government of Singapore.
3. The Environmental Public Health Act (Chapter 95) 1 July 1987, Government of Singapore.
Modeling Dengue Cluster Size as a Function of Aedes aegypti Population and Climate in Singapore

By
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Abstract
In Singapore, a dengue cluster is defined as at least two cases located within 200 metres of each other, and whose dates of the onset of symptoms are within three weeks of each other. In 2000-2001, there were a total of 102 clusters with cluster size ranging from 2 to 29 cases. A nonlinear regression model of cluster size during this two-year period was developed using various entomological and climatic independent variables. The resultant model ($R^2 = 0.66882$) was a combination of quadratic functions of the detected number of habitats positive for Ae. aegypti, the number of detected habitats positive for Ae. albopictus, and the average amount of rainfall one week before the cluster period. The model may be useful for assessing the risk of a large-sized cluster occurring in an area.

Key words: Dengue cluster, nonlinear, regression model, climate, risk, Singapore

Introduction
Unlike most other countries where dengue is endemic, Singapore is a small and extremely urbanized nation. Here, dengue outbreaks or epidemics are identified and controlled in the scale of "clusters". A dengue cluster or focus of transmission is defined as at least two confirmed cases, with no recent travel history, that are located within 200 m (taken as the flight range of Aedes aegypti or Aedes albopictus) of each other and whose dates of the onset of symptoms are within three weeks of each other. Typically, the Quarantine and Epidemiological Department identifies these clusters while the Vector Control and Research Department controls the clusters by conducting thorough, extensive source reduction and adulticiding operations in the cluster area. Since some of these clusters can be quite large (> 20 cases) and consequently difficult to control, it is critical to have a good understanding of the factors contributing to cluster size.

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Previous studies have shown that data with as much as 1-5 months lag of Ae. aegypti parous rate\(^1\), elevated temperature, Ae. aegypti adult density, and Ae. aegypti House Index\(^2\) were important predictors of weekly dengue incidence in Singapore on a nation-wide scale. This present study seeks to discover the nature of the relationship between dengue and Aedes population as well as climatic factors by analysing dengue incidence at the much smaller cluster scale. Given that some components of this relationship may be nonlinear in nature, such as a possibly exponential relationship between dengue incidence and temperature\(^3\), a linear relationship was not assumed and a nonlinear regression analysis was therefore applied. The ultimate aim is to develop a model of dengue cluster size that will be beneficial for preventing the occurrence of large clusters.

**Materials and methods**

Data of confirmed cases of dengue clusters over a two-year period (2000-2001) were reviewed. The vast majority of the cases were confirmed by hospitals serodiagnostically although some were by virus isolation. Cluster size is defined as the total number of confirmed cases in a cluster. Data used in the modelling of cluster size include entomological data gathered by environmental health officers. During each cluster control operation, these officers would thoroughly search every premise plus all outdoor areas (e.g. litter, drains, subterranean pits, etc.) for any habitat that is breeding mosquitoes. The resultant data were used as independent variables - the total number of habitats positive for Ae. aegypti detected (Ae. aegypti hab), the total estimated count of Ae. aegypti immatures (Ae. aegypti count), the total number of habitats positive for Ae. albopictus detected (Ae. albopictus hab), and the total estimated count of Ae. albopictus immatures (Ae. albopictus count). Climatic data obtained from the Meteorological Services, Singapore, were also included in the model-building process. Data of weekly rainfall, temperature and relative humidity one week before the cluster period were averaged and used as independent variables. The cluster period was taken as the date between and inclusive of the onset date of the first case and the onset date of the last case in the cluster.

A nonlinear regression model was used to model dengue cluster size. First, linear, quadratic, cubic and exponential regression models were estimated between the cluster size and each independent variable. The best-fit curve for each independent variable was then selected to be included into a nonlinear regression model, and their regression coefficients used as the initial values in the iterative procedure to search for the best model. All computations were performed using the SPSS software\(^4\).

**Results and discussion**

A total of 102 dengue clusters were identified in years 2000 (9 clusters) and 2001 (93 clusters). The cluster size ranged from 2 cases to 29 cases. The frequency distribution of the cluster size was normal (Kolmogorov-Smirnov statistic = 0.254, df = 101, p < 0.001) with a right skew. The mean, median and mode cluster sizes were 6 cases, 3 cases and 3 cases respectively, with a standard deviation of 5.84 cases.
Table. Results of various univariate models of dengue cluster size and Ae. aegypti hab, Ae. aegypti count, Ae. albopictus hab, Ae. albopictus count, rainfall, temperature, and humidity

<table>
<thead>
<tr>
<th></th>
<th>$R^2$</th>
<th>Df</th>
<th>F</th>
<th>P</th>
</tr>
</thead>
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<tr>
<td><strong>Ae. aegypti hab</strong></td>
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<td>99</td>
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<td>101</td>
<td>42.38</td>
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<td></td>
<td></td>
</tr>
<tr>
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<td>0.244</td>
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$R^2$ = Determinant coefficient  
$df$ = Degrees of freedom  
$F$ = Statistics to determine significance  
$P$ = value to determine the confidence
Results for the curve estimations of cluster size with each independent variable are summarized in the Table. Regression coefficients were most significant for the cubic models of cluster size versus Ae. aegypti hab, Ae. aegypti count, Ae. albopictus hab, and Ae. albopictus count. In the curve fit of cluster size versus the climatic variables, regression coefficients were significant only for the cubic model ($R^2 = 0.102$, df = 99, $F = 3.65$, $p < 0.05$) of cluster size versus rainfall. The temperature and relative humidity were not found to have any significant relationship with cluster size in any of the tested models.

Modelling of cluster size versus all the significant independent variables in a linear combination of cubic models resulted in the following nonlinear regression model ($R^2 = 0.669$):

\[
\text{Cluster size} = \sum_{i=1}^{12} a_i \cdot (\text{variable}_i)^{\text{power}_i} + r_1 \cdot (\text{Rainfall})^3 + r_2 \cdot (\text{Rainfall})^2 + r_3 \cdot (\text{Rainfall})
\]

Based on the significant regression coefficients of the best curve estimates, the following values for the coefficients were used as the initial values to fit into the nonlinear regression model: $a_1 = 3.3229$, $a_2 = 0.1653$, $a_3 = 0.0027$, $a_4 = 3.3729$, $a_5 = 0.0042$, $a_6 = 2.0670$, $a_7 = 0.7983$, $a_8 = -0.0204$, $a_9 = 3.5664$, $a_{10} = 0.0109$, $r_1 = 2.1717$, $r_2 = 0.288$, $r_3 = -0.0044$. After six iterations using the Levenberg-Marquardt algorithm, the resultant nonlinear model was ($R^2 = 0.66882$, RSS = 1102.481638):

\[
\text{Cluster size} =
\]

1. $0.0079 \cdot (\text{Ae. aegypti hab})^2$
2. $-0.0605 \cdot (\text{Ae. aegypti hab})$
3. $-0.0112 \cdot (\text{Ae. albopictus hab})^2$
4. $+0.4357 \cdot (\text{Ae. albopictus hab})$
5. $-0.0328 \cdot (\text{Rainfall})^2$
6. $+0.1978 \cdot (\text{Rainfall})$

Through the use of a nonlinear regression model, a significant relationship was found between dengue cluster size and number of habitats positive for Ae. aegypti, number of habitats positive for Ae. albopictus, and rainfall. In addition, the best model for cluster size appears to be a linear combination of quadratic functions of these factors. The final relationship was independent of estimated immature counts of Ae. aegypti or Ae. albopictus, temperature and relative humidity.

In this investigation, the temperature was unrelated to dengue cluster size. This was surprising in the light of the documented associations between the temperature and dengue transmission dynamics. Among other effects, temperature is known to increase the biting frequency of the Ae. aegypti\cite{5,6} and decrease the extrinsic incubation period of the virus\cite{3}, thus...
increasing the transmission potential of dengue. In a previous unpublished study, annual temperature was significantly and strongly positively correlated with the number of dengue clusters in a year (R = 0.806, P < 0.001). The present study covers a period between 2000, a post-La Nina/neutral year, and 2001, a neutral/pre-El Nino year. Although the difference in the total number of clusters in these two years was clearly apparent, the temperature variation during this period may not be large enough to have a significant effect on the cluster size.

A point to consider when extrapolating from statistical models fitted to the epidemiological data is the possibility of error in measuring the variables. However, the model could be improved if it included other independent variables such as human population living in various housing types, herd immunity and the interaction of the four dengue serotypes. And it would undoubtedly be better if it was based on the transmission threshold theory and if Aedes aegypti (and Ae. albopictus) pupae per person were used instead of estimated immature count(7).

Nevertheless, the model suggests an application of potential public health interest. The moderate predictive power of the model accounting for about two-thirds of the dengue cluster-size variations in 2000-2001 may prove useful for dengue control operational purposes. It may have operational usefulness for assessing, and more importantly, responding to the risk of a large dengue cluster in a localized area based on current entomological surveillance data and rainfall data of the previous week.

**Acknowledgements**

We would like to thank Mr S. Mohan from the Quarantine and Epidemiology Department for his much appreciated help in providing data on the dengue clusters. We also appreciate the efforts of the Aedes control section of the Vector Control and Research Department in the cluster control operations.

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Susceptibility of Two Cambodian Populations of Aedes aegypti Mosquito Larvae to Temephos During 2001

by
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Abstract

Two populations of Aedes aegypti, i.e. Phnom Penh (temephos-treated area) and Kampong Cham (area untreated with temephos) were evaluated for their susceptibility to temephos. Larval bioassays were carried out in accordance with WHO standard methods.

Results showed that, when compared with the WHO diagnostic dosage of 0.02mg/l, the Phnom Penh population was resistant (LC95: 0.034mg/l) whereas that of Kampong Cham was susceptible (LC95: 0.015mg/l). 95% confidence intervals of 0.0298 – 0.0382 and 0.0115 – 0.0193, respectively, did not overlap, indicating that the difference in susceptibility between the two populations was significant.

Resistance of Ae. aegypti to temephos appears to be incipient in Cambodia. More studies are required with wider representations of localities.

Keywords: Aedes aegypti, temephos, susceptibility, Cambodia.

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Introduction

The most widely used larvicide for Ae. aegypti control, in potable water, is temephos (Abate®) 1% sand granules which, when applied at a dosage of 1ppm, has been proven to be effective for 8-12 weeks\(^2\). Although temephos is used in many national dengue vector control programmes, insecticide resistance has been documented in Ae. aegypti in some countries in the Americas\(^2,3\) and in Malaysia\(^4\).

The largest DHF epidemic recorded in Cambodia occurred in 1998\(^5\). Based on the 3-4 year cyclical pattern\(^6\), a major outbreak was anticipated for the year 2001. As part of a short-term, pre-emptive approach, pre-packaged 1% temephos sand granules were distributed for application in water storage jars, as a larvicide campaign, between April and August 2001, prior to and during the main transmission season in the capital city, Phnom Penh, and in other high human population density/transmission risk areas.

Recent field bioassay studies indicated the operational effectiveness of temephos against Ae. aegypti in Phnom Penh (Yeang Chang and Michael Nathan, unpublished data). The larval susceptibility studies herein described were undertaken at the National Centre for Parasitology, Entomology and Malaria Control, Cambodia, to further assess the susceptibility status of two geographically-distinct populations of Ae. aegypti.

Materials and methods

Two areas were selected for comparison based on their history of temephos use - Phnom Penh (temephos-treated area) and Kampong Cham (temephos-untreated area).

Ae. aegypti eggs were collected from both study areas using ovitraps as per the technique described by Polson et al\(^7\). A total of 1,709 eggs were obtained from the two collection sites. Eggs were allowed to dry for three days and then flooded in batches to induce hatching.

Insecticide-susceptibility tests were carried out on late 3\(^{rd}\) to early 4\(^{th}\) stage larvae of the F1 generation, in accordance with WHO instructions for determining the susceptibility of mosquito larvae to temephos\(^8\).

Larvae were initially screened at 0.02mg/l concentration (WHO diagnostic dosage) to determine whether to adjust tests to higher or lower dosages. Each test consisted of three replicates and one control, each with 20 larvae in plastic cups containing 250 ml. of distilled water with the required insecticide concentration. Mortality counts were made after 24 hours. Tests were done until repeatable results were obtained.

Data were analysed by the Probit analysis programme in SPSS version 9.0 to obtain LC50 and LC95 values. The obtained LC95 for both populations were compared with those of the WHO tentative diagnostic dosage of 0.02mg/l of temephos for larvae of Ae. aegypti in order to determine whether the populations tested were susceptible or resistant. [A population is considered to be susceptible to temephos if, when exposed to a concentration of 0.02mg/l, the per cent mortality is equal to or greater than 95%. A resistant population is one in which there is
less than 95% mortality when such a population is exposed to a concentration of 0.02mg/l of temephos.

**Results**

The overall mortalities from five replicates of both populations tested are shown in Table 1. The pooled data from Phnom Penh and Kampong Cham showed significant heterogeneity about log dose/probit mortality regression lines \((X^2 = 14.10; \text{df} = 4; p = 0.007\) and \((X^2 = 6.34; \text{df} = 3; 0.05 < p < 0.1, \text{respectively})\). Therefore, confidence limits based on the pooled data were of doubtful validity. Instead, data collected on each of the five days on LC50 and LC95 were compared with SPSS 9.0. Standard errors and confidence limits were then calculated from the replicates and are shown in Table 2.

This data showed that when compared with the WHO recommended diagnostic dosage of temephos of 0.02mg/litre, the mean LC95 of the Phnom Penh Aedes aegypti population was 1.7 times higher, whereas the mean LC95 of Kampong Cham was markedly less than the WHO discriminating dose.

These results obtained showed that the 95% confidence intervals of the LC50 and LC95 in the Phnom Penh population did not overlap with those of the Kampong Cham population. An unpaired t-test on the pooled standard deviation of the samples further demonstrated significant difference in the susceptibility of the two populations to temephos \((t = 9.02; \text{df} = 8; p < 0.001)\).

### Table 1. Concentration of temephos and overall resulting mortalities in Aedes aegypti populations from all replicates

<table>
<thead>
<tr>
<th>Population</th>
<th>Phnom Penh</th>
<th>Kampong Cham</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. dead</td>
<td>No. tested</td>
</tr>
<tr>
<td>Concentration of temephos (mg/l)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.004</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>0.005</td>
<td>10</td>
<td>198</td>
</tr>
<tr>
<td>0.01</td>
<td>37</td>
<td>200</td>
</tr>
<tr>
<td>0.02</td>
<td>111</td>
<td>197</td>
</tr>
<tr>
<td>0.03</td>
<td>173</td>
<td>199</td>
</tr>
<tr>
<td>0.04</td>
<td>192</td>
<td>200</td>
</tr>
</tbody>
</table>
Table 2. Susceptibility status of Aedes aegypti larvae to temephos

<table>
<thead>
<tr>
<th>Population</th>
<th>Phnom Penh</th>
<th>Kampong Cham</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of tests</td>
<td>LC50 (mg/l)</td>
<td>LC 95 (mg/l)</td>
</tr>
<tr>
<td>1</td>
<td>0.0131</td>
<td>0.030</td>
</tr>
<tr>
<td>2</td>
<td>0.0178</td>
<td>0.033</td>
</tr>
<tr>
<td>3</td>
<td>0.020</td>
<td>0.032</td>
</tr>
<tr>
<td>4</td>
<td>0.023</td>
<td>0.037</td>
</tr>
<tr>
<td>5</td>
<td>0.024</td>
<td>0.038</td>
</tr>
<tr>
<td>Mean</td>
<td>0.0196</td>
<td>0.034</td>
</tr>
<tr>
<td>Standard deviation</td>
<td>0.0044</td>
<td>0.0034</td>
</tr>
<tr>
<td>95% confidence intervals</td>
<td>0.0141 - 0.025</td>
<td>0.0298 - 0.0382</td>
</tr>
</tbody>
</table>

Discussion

This study, the first in Cambodia on the susceptibility of Ae. aegypti to temephos, revealed a significant difference in the two Ae. aegypti larval populations. The Phnom Penh population exhibited some degree of resistance to temephos while the Kampong Cham population was susceptible. Exposure of the Phnom Penh population to temephos, since 1995 and later the increased frequency due to the extended transmission during the dry season as well, appears to have resulted in the development of resistance in that population. On the other hand, the absence of insecticidal pressure for at least the past 2-3 years may account for the continued susceptibility of the Kampong Cham population.

The emergence of resistance to temephos is important, as temephos is in widespread use in dengue prevention and control programmes and is one of only four larvicides approved by WHO for application to potable water. The recommended field dosage of 1.0mg/l far exceeds the calculated LC95 of 0.035mg/l of the larvae from Phnom Penh, so if properly applied it should remain very effective. Curtis et al. found that in Tanzania where Culex quinquefasciatus is known to be resistant to chlorpyrifos, resistance did not prevent fresh insecticide applications killing larvae, but it did reduce the time before re-application was needed.

If resistant populations such as that of Phnom Penh are frequently exposed to temephos, higher levels of resistance appear inevitable, as is now the case in some countries in the Caribbean where 1mg/litre of temephos is ineffective against some strains of Ae. aegypti.
Acknowledgements

We would like to express our sincere gratitude to the London School of Hygiene and Tropical Medicine, UK, for financial support; to Dr Mike Nathan, WHO, Geneva, for assistance in the formulation of the project and review of the manuscript; the National Centre for Parasitology, Entomology and Malaria Control, for the invitation to conduct research in Cambodia, and for assistance in the execution of the study; the staff of the United States Navy Medical Research Unit - 2 (NAMRU-2) for use of laboratory space and their invaluable assistance in the conduct of field work; and the chiefs and residents of both the study areas for giving access to their homes for the collection of field material.

References


Susceptibility Status of Immature and Adult Stages of Aedes aegypti Against Conventional Insecticides in Delhi, India

by

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Abstract

Insecticide-susceptibility tests were carried out using WHO standard test kits against various organophosphates, organochlorines, carbamates and synthetic pyrethroid compounds under ambient room temperature of 27 ± 1 °C and relative humidity of 75-80%. The results revealed that adult Aedes aegypti was resistant to DDT and dieldrin, tolerant to propoxur and fenitrothion, but was susceptible to malathion, deltamethrin, permethrin and lambdacyhalothrin. However, the larvae were found to be susceptible to all the three larvicides tested, viz. temephos, fenthion and malathion.

Keywords: Aedes aegypti, susceptibility, resistance, Delhi.

Introduction

India is endemic for DF/DHF. During September 1996 a major outbreak of dengue/DHF occurred in Delhi, the Capital city of India, when 10,252 cases and 423 deaths were recorded(1). Since insecticides are being used for controlling malaria and other vectors of public health importance in Delhi, it was considered essential to know the current susceptibility status of Aedes aegypti against insecticides commonly used in the public health programmes in Delhi. The studies were undertaken during 1999-2000.

Materials and methods

Insecticide-susceptibility tests were carried out using the WHO standard test kits against various organophosphates, organochlorines, carbamates and synthetic pyrethroid compounds under ambient room temperature of 27+1°C and relative humidity of 75-80%. The procedures adopted for adult and larval assays were as follows:

Adult Bioassay: One-to-two-day-old mosquitoes emerging from the field-collected larvae and pupae under laboratory conditions were allowed to feed on 10% glucose solution soaked in cotton pads and
were exposed against the discriminating dosages of adulticides for 1 hour to DDT – 4%, dieldrin – 0.4%, malathion – 5%, deltamethrin – 0.025%, permethrin – 0.25% and lambdacyhalothrin – 0.1% and for 2 hours to fenitrothion – 1.0% and propoxur – 0.1%, as per standard WHO technique (WHO, 1981)(2a, 2b). For each adulticide, four replicates were run concurrently, each containing 25 female mosquitoes. After the requisite exposure period, the mosquitoes were transferred to the recovery chambers and cotton pads soaked in 10% glucose solution were given as food during the recovery period. Mortality counts were made after 24 hours of the recovery period.

Larval Bioassay: For larval bioassay, the late-third or early-fourth instar larvae collected from the field were separated. The selected larvae were washed in tap water to remove debris and kept under observation for a period of 24 hours to detect and remove unhealthy or dead larvae. The larvae were tested against the discriminating dosages of larvicides, viz. temephos (Abate) – 0.02 mgm/litre, fenthion (Baytex) – 0.05 mgm/litre and malathion – 1.0 mgm/litre. Four replicates and a control, each containing 50 larvae, were run for each experiment. Brewer’s yeast was given as food during the treatment period. The adult and larval tests showing more than 20% control mortality were discarded and repeated. In case control mortality ranged from 5% to 20%; the corrected mortality was calculated using Abbot’s Formula.

Results and discussions

Adult Bioassay: The results of the adult susceptibility test revealed that this species was resistant to DDT and dieldrin as only 74% and 46% mortality, respectively, could be obtained (Table 1). This might be due to the extensive use of these insecticides for the control of malaria and other vector species. Discriminating dosages of propoxur and fenitrothion, however, caused 85% and 91% mortality, indicating tolerance of the species to these insecticides. Exposure of adults to the discriminating dosages of malathion, deltamethrin, permethrin and lambdacyhalothrin induced 100% mortality indicating that the species was susceptible to these insecticides.

Azeez (1967)[3] was the first to record DDT resistance in the adult Aedes aegypti in Jharia, Bihar, India. Raghavan et al. (1967)[4], Madhukar and Pillai (1968)[5], Kaul (1976)[6] and Mahadev et al. (1993)[7] also reported the resistance of the species to DDT in different part of the country but found it susceptible to malathion and deltamethrin.

Larval Bioassay: The results of the larval susceptibility tests revealed that all the three larvicides, viz. temephos, fenthion and malathion, induced 99%, 99.5% and 100% mortality within 24 hours of the treatment, indicating the susceptible status of these larvae (Table 2). The present observations are in conformity with the research work of Bhatnagar et al. (1969)[8], Biswas et al. (1988)[9] and Mourya et al. (1993)[10]. Das and Rajagopalan (1979)[11] reported 100% mortality of these larvae at much lower dosages of temephos – 0.0078 mgm/litre, fenthion – 0.008 mgm/litre and malathion – 0.48 mgm/litre.
Table 1. Results of susceptibility tests carried out against the adults of Aedes aegypti mosquito using various insecticides

<table>
<thead>
<tr>
<th>Insecticide</th>
<th>Discriminating dosages used (%)</th>
<th>Exposure period in hours</th>
<th>No. of mosquitoes exposed</th>
<th>No. of mosquitoes died</th>
<th>Percent mortality obtained</th>
<th>Susceptibility status</th>
</tr>
</thead>
<tbody>
<tr>
<td>DDT</td>
<td>4.0</td>
<td>1</td>
<td>100</td>
<td>74</td>
<td>74</td>
<td>Resistant</td>
</tr>
<tr>
<td>Dieldrin</td>
<td>0.4</td>
<td>1</td>
<td>100</td>
<td>6</td>
<td>46</td>
<td>Resistant</td>
</tr>
<tr>
<td>Fenitrothion</td>
<td>1.0</td>
<td>2</td>
<td>100</td>
<td>91</td>
<td>91</td>
<td>Tolerant*</td>
</tr>
<tr>
<td>Propoxur</td>
<td>0.1</td>
<td>2</td>
<td>100</td>
<td>85</td>
<td>85</td>
<td>Tolerant*</td>
</tr>
<tr>
<td>Malathion</td>
<td>5.0</td>
<td>1</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Deltamethrin</td>
<td>0.025</td>
<td>1</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Permethrin</td>
<td>0.25</td>
<td>1</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Lambdacyhalothrin</td>
<td>0.1</td>
<td>1</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>Susceptible</td>
</tr>
</tbody>
</table>

* So far there is no report of tolerance or resistance in Aedes aegypti from any part of the world. Present study does not indicate number of populated tested. More tests based upon different populations and sample size are required for validation and confirmation of results - Editor

Table 2. Results of susceptibility tests carried out against the larvae of Aedes aegypti mosquito against various larvicides

<table>
<thead>
<tr>
<th>Insecticide</th>
<th>Discriminating dosages used (mg/l)</th>
<th>Exposure period in hours</th>
<th>No. of larvae exposed</th>
<th>No. of larvae died</th>
<th>Percent mortality obtained</th>
<th>Susceptibility status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temephos</td>
<td>0.02</td>
<td>24</td>
<td>200</td>
<td>198</td>
<td>99</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Fenthion</td>
<td>0.05</td>
<td>24</td>
<td>200</td>
<td>199</td>
<td>99.5</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Malathion</td>
<td>1.0</td>
<td>24</td>
<td>200</td>
<td>200</td>
<td>100</td>
<td>Susceptible</td>
</tr>
</tbody>
</table>

The present findings thus revealed that for the control of Aedes larvae, temephos (Abate), and for the adult Aedes aegypti, malathion, could be used for effective control of dengue/DHF as per the WHO recommended dosages in a cost-effective manner.
Acknowledgements

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Geographical Spread of Anopheles stephensi, Vector of Urban Malaria, and Aedes aegypti, Vector of Dengue/DHF, in the Arabian Sea Islands of Lakshadweep, India

by

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Abstract

The Indian islands of Lakshadweep in the Arabian sea are known to be endemic for bancroftian filariasis. However, malaria endemicity was reported to be associated with the invasion of vector species Anopheles tessellatus from Maldives. Indigenous transmission of malaria was recorded during 1972. Thereafter the National Anti-Malaria Programme (NAMP) brought these islands under DDT spray. Since 1981, only imported cases of malaria are being reported from these islands. During March 2000, a brief survey of two islands, viz. Agatti and Kavaratti, revealed the presence of Anopheles stephensi, a known vector of urban malaria in the country. Earlier on the mainland, the southward peninsular spread of An. stephensi, including in Kerala, a non-malarious state, was recorded and the species was reported to be involved in two major outbreaks of malaria. It appears that over the years An. stephensi has invaded the Lakshadweep islands and gained a permanent foothold on these islands due to the availability of a large number of community and rain-harvesting cement storage tanks. These developments also threaten the northern islands of Maldives which are about 90 km south of Lakshadweep, where water storage practices are identical. Aedes aegypti which was earlier detected in the neighbouring group of Minicoy islands during 1974, has now spread widely in all the islands and poses an imminent threat of DF/DHF epidemics.

Keywords: Geographical spread, dengue, malaria vectors Aedes aegypti, Anopheles stephensi.

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**Introduction**

Lakshadweep, the smallest Union Territory (UT) of India, is a group of 36 islands, of which 10 are inhabited. These are: Androth, Agatti, Bitra, Chetlet, Kadamath, Kalpeni, Kavaratti, Kiltan and Minicoy. These islands are a narrow strip of land, 3-4 metres above the mean sea level, and lie in the Arabian Sea about 220-440 km away from the Kerala coast of India at between 8° and 12° North latitude and 71° and 74° East latitude. The total land area of these islands is about 32 sq km, out of which about 26.32 sq km is in use. As per the 1991 census, the total population of the Lakshadweep islands was 51,681. The main occupations of the islanders include coconut cultivation, production of coir, fishing, etc.

The Lakshadweep islands are endemic for bancroftian filariasis and malaria. Filariasis is endemic practically in all the islands, primarily as a socioeconomic problem related to the coir industry, as coir soakage pits heavily breed Culex quinquefasciatus mosquito, the vector of Wuchereria bancrofti. Malaria in these islands is unstable and sporadic, depending upon the presence of the vector species. However, an analysis of the epidemiological data revealed that filariasis and malaria infections were showing declining trends, the former due to the introduction of DEC-medicated salt therapy during 1976-79 and the large-scale introduction of mosquito larvivorous fishes, such as Gambusia affinis and Poecilia reticulata during 1980 and the latter due to the effective implementation of the National Anti-Malaria Programme (NAMP), ensuring early detection and prompt treatment of all malaria cases through active and passive surveillance. During 1997-99, only four imported cases of Plasmodium vivax were reported from these islands.

During March 2000, Agatti and Kavaratti islands were visited to ascertain the current status of malaria and filariasis and to collect information on the prevalence of the vectors of malaria, filariasis and DF/DHF. The findings of this brief survey are presented in this communication.

**Materials and methods**

Larval collections were made using a ladle, larval net, well net and a pipette. The larvae collected from Kavaratti were preserved in 70% alcohol, mounted in Bhatia’s medium and identified at the larval stage; however, larvae collected from Agatti were transported live in polythene bags containing water from the breeding sites to the laboratory at the National Institute of Communicable Diseases (NICD), Delhi. The mosquito larvae were kept for rearing in an insectory having an ambient temperature of 27±1°C. Brewer’s yeast was provided as food. The adults (emerged) were mounted, preserved and identified using standard identification keys.

**Results**

The analysis of the data collected revealed the presence of five mosquito species, viz. An. stephensi (type form), An. varuna, Cx. quinquefasciatus, Ae. aegypti and Ae.
albopictus. The breeding habitats of these species are shown in the table.

Table. Breeding habitats of various mosquito species observed in Agatti and Kavaratti islands of Lakshadweep

<table>
<thead>
<tr>
<th>Mosquito species</th>
<th>Breeding habitats</th>
</tr>
</thead>
<tbody>
<tr>
<td>An. stephensi</td>
<td>Small cement tanks containing clean/turbid water attached to mosques/community lavatories</td>
</tr>
<tr>
<td>An. varuna</td>
<td>Draw wells with clean water</td>
</tr>
<tr>
<td>Cx. quinquefasciatus</td>
<td>Coir soakage pits, rainwater harvesting tanks</td>
</tr>
<tr>
<td>Ae. aegypti</td>
<td>Small cement tanks, used tyres, solid waste material holding rain water</td>
</tr>
<tr>
<td>Ae. albopictus</td>
<td>Small pots holding drinking water for birds, metallic containers holding rainwater collection and tree holes</td>
</tr>
</tbody>
</table>

Discussion

Lakshadweep islands being flat coral islands just 2 to 3 metres above the mean sea level are devoid of any natural breeding sites like streams, swamps and marshes, restricting the diversity of mosquito fauna. Only those mosquito species have become endemic which can afford to breed in man-made breeding sites. This explains why only a few mosquito species could become endemic, in spite of invasion from the neighbouring coastal states of Kerala and Karnataka on the mainland and from Maldives which is just 90 km south of the neighbouring Minicoy island.

Amongst the anopheline species, An. varuna invaded from the Kerala coast and occupied draw-wells as their breeding sites. An. tesselatus was introduced from Maldives and spread to other islands and maintained low-grade transmission; however, these species failed to gain a foothold. The spontaneous disappearance of malaria from Minicoy island was attributed to this phenomenon. Similarly, An. varuna failed to initiate malaria transmission on these islands.

Earlier, it was observed that A. stephensi (type from), the vector of urban malaria, had shown a southward geographical spread on the Indian mainland due to rapid urbanization and water storage practices. During the 1970s, the species invaded Goa on the western coast and Kanyakumari on the tip of the southern coast in the 1980s. The species finally entered Kerala and contributed to the malaria outbreak during 1996 at Valiathura near Thiruvananthapuram airport, where over 100 cases of malaria were recorded. This was followed by another outbreak in Kasargod during 1998 when 405 cases and three deaths were reported. In both these outbreaks, An. stephensi was found to be involved in the disease transmission (Source: NAMP). Prior to this, Kerala state had never reported indigenous malaria cases for decades. On the basis of the observations made, it is felt that littoral countries to the south of India, such as Maldives and Sri Lanka, are also at great risk and are required to undertake stringent measures at their airports and seaports as per the International Health Regulations to prevent the entry of this species[8,9].

The invasion of Lakshadweep islands by An. stephensi is a very serious development. Being a container-breeding species, it fits
well with the social and cultural habits of the communities like water storage in small cement tanks, rainwater harvesting tanks, etc. Frequent outbreaks of malaria in different towns of Kerala and high trade traffic between Kerala and these islands will provide a fillip to the indigenous transmission of malaria.

The establishment of An. stephensi poses immediate threat not only to the Lakshadweep islands but also to the adjoining Maldives via the same route (country sailing vessels) as the Maldivian species (An. tesselatus and An. subpictus), once found their way to Lakshadweep.

The establishment of Ae. aegypti, the vector of DF/DHF, is yet another serious development; the presence of this species was originally recorded in Minicoy islands in 1974[3], which has now invaded the other islands of Lakshadweep, posing imminent threat of DF/DHF outbreaks.

Cx. quinquefasciatus is already an endemic species breeding in the coir soakage pits, an essential industry tied to the economy of these islands.

Acknowledgements
The authors are grateful to Dr K. K. Datta, Director, National Institute of Communicable Diseases, Delhi, and Dr Kuniseethi Koya, Director of Medical and Health Services, Kavaratti, Lakshadweep Islands, for providing the opportunity and extending valuable support during the study. Thanks are also due to Dr B. N. Nagpal, Malaria Research Centre, Delhi, for confirming An. stephensi (type form) on the basis of spiracular indices. Special thanks to Mr N. L. Kalra, former Entomologist, National Institute of Communicable Diseases, and WHO short-term consultant, for giving valuable suggestions in the writing of this manuscript.

References
Abstract

Prediction of dengue risk based on sociocultural factors and its possible spatial relationships was investigated in a dengue endemic area of Jalore in Rajasthan state, India. Data were collected through personal interviews, from 77 households, randomly selected from both dengue-affected samples (DAS) and unaffected samples (UAS). Findings indicated that out of sixty socioeconomic and sociocultural variables, only sixteen were co-related significantly at 0.5 and 0.1 level. These sixteen variables were used in the stepwise regression model; only eight variables, namely, frequency of days of cleaning of water storage containers, housing pattern, use of evaporation cooler, frequency of cleaning of evaporation cooler, protection of water storage containers, mosquito protection measures, frequency of water supply and frequency of waste disposal made a significant contribution to the incidences of DF/DHF/DSS with a $R^2$ of 0.958.

The geographical information system (GIS) has been used to link the spatial and significant sociocultural indicators with the disease data. Using factorial discriminant analysis and spatial modelling with these eight sociocultural indicators, five classes of risk categories ranging from “very low” to “very high” were identified. Validation of these risk categories on individual houses showed that 94.5% of the houses were correctly classified. The nearest neighbourhood method had been used to prepare a spatial extrapolated social risk area map. The paper highlights the statistical and spatial model development based on the analysis of sociocultural practices adopted by DAS and UAS and from the application of GIS.

Keywords: Aedes aegypti, DF, DHF, DSS, sociocultural practices, Pearson’s correlation, regression, geographical information system (GIS)
Introduction
Dengue fever (DF) associated with dengue haemorrhagic fever/dengue shock syndrome (DHF/DSS) has emerged as an important public health problem in the countries of the South-East Asia and Western Pacific regions. In India dengue fever has been known since the 19th century and epidemics have been reported from almost all part of the country. In Rajasthan, serological studies on outbreaks of dengue fever have been reported from Jaipur and Ajmer. However, in an arid region like Jalore, an epidemic occurred during 1985 and again in 1990. The 1990 outbreak of dengue in Jalore occurred in summer (April-May) in contrast to other parts of India, where such outbreaks are commonly reported after the rains between August and November. Until now, nearly all research efforts had focused on the biological, entomological and clinical aspects of DF/DHF/DSS separately. Location-specific studies demonstrating an integrated use of sociocultural practices were lacking. This called for an in-depth study of the interrelationship of sociocultural practices and identification of the most significant risk indicators under the influence of local conditions using statistical modelling as an analytical tool. This study, conducted during December 2000 and July 2001, looked into these issues to evaluate and model the relationships between sociocultural practices and the incidences of DF/DHF/DSS.

Methods
Description of study area
Jalore town is one of eleven desert districts in Rajasthan and is situated in the south-western zone of the state. It lies between 24° 37' and 25° 49' latitude and 71° 11' and 73° 05' east longitude. The town has a population of about 40,000 and the climate is characterized as dry with extremes of temperature rising as high as 48°C in summer months and going down to 10°C in winter months. The area has a sandy terrain and high wind velocity. It is situated at 736 metres above sea level. The average yearly rainfall is 421.6 mm, occurring mainly in July and August.

Primary and secondary data
Primary data were collected through a field survey. A structured questionnaire composed of sixty variables, all potentially influencing the occurrence of DF/DHF/DSS, were designed to obtain information through personal interviews and discussions with both dengue-affected samples (DAS) and unaffected samples (UAS). The questionnaire collected data about family details, human dwellings, occupational patterns, awareness and knowledge about dengue, mosquito protection practices, sanitation and waste disposal management, cultural practices regarding storage of water containers and health care. Each individual household in the study area was defined as a sampling unit. All available dengue patients were taken as sample and an equal number of randomly-selected unaffected samples in the study area were also interviewed.

Secondary data included demographic information about the town of Jalore; its climate; a list of DF/DHF patients and cases of deaths, along with their addresses as registered in Government Hospital, Jalore, during the 1990 outbreak; entomological data of dengue (adult house index, container
index); physical environment (land use, land cover), and topographical and administrative map. These data were acquired with the help of the census book, government/non-government agencies and from published reports.

**Statistical analysis of social data**

Correlation, regression and discriminant analysis were the major statistical tools used in this study for investigating and testing the statistical significance in the relationship between sociocultural parameters and dengue incidences.

**GIS modelling with social data**

After the risk categories of each household were identified from discriminant analysis, a database was created in the geographical information system (GIS), which was then linked with spatial point data of each house and surfaces were created from point samples. The inverse distance weighting (IDW) interpolation (nearest neighbour technique) was employed to produce the desired results. The IDW interpolator assumes that each input point has a local influence that diminishes with distance. It weighs the points closer to the processing cell as greater than those farther away. A specified number of points, or optionally all points within a specified radius, can be used to determine the output value for each location. IDW interpolation gives values to each cell in the output grid theme by weighing the value of each point by the distance that point is from the one being analysed and then averaging the values.

**Results and discussion**

**Statistical methodology**

All the sociocultural variables were studied through four steps:

(1) Based on literature review, an attempt was made to group the number of variables by combining related variables into one group. Data were therefore arranged into the following six groups: socioeconomic; human dwellings; environment management practices; mosquito protection practices; cultural practices of water storage; and technological adoptions;

(2) Detection and screening of data outliers to reduce misleading results. In the first screening of the sixty variables, forty-eight variables were selected;

(3) A second screening of variables was conducted based on a significance test of Pearson’s correlation coefficient;

(4) Development of a regressive-predictive model.

**Correlation of sociocultural practices with dengue incidences**

Pearson’s correlation coefficient was computed for the forty-eight variables from the six groups with the incidence of DF/DHF/DSS. This statistical technique could identify and isolate sixteen variables that had the strongest positive or negative correlations, tested at 1% and 5% of significance levels.
Regressive-predictive model

From the six groups, the sixteen variables that were significantly correlated to the dengue incidence were submitted to multiple regression analysis. The different characteristics of the sociocultural variables interact together to contribute a combined effect on the dengue incidence. The sixteen variables, which were found to correlate significantly to dengue incidence, were only used for multiple regression analysis. Stepwise regression technique was employed to explore and identify statistically significant sociocultural risk indicators and their relative contribution to the occurrence of dengue incidence by eliminating the insignificant variables. Results of stepwise regression analysis revealed that, out of sixteen, only eight independent variables contributed effectively to dengue incidences. The eight variables were used to derive the following regression equation:

\[ Y = -0.07516 + 0.928X1 - 0.819X2 + 0.757X3 + 0.006042X4 + 0.284X5 - 0.647X6 - 0.317X7 - 0.216X8 \]

where,

- \( Y \) = Incidence of dengue (dependent variable)
- \( X1 \) = Frequency of cleaning of water storage containers
- \( X2 \) = Housing pattern
- \( X3 \) = Use of water cooler
- \( X4 \) = Frequency of cleaning of the water cooler
- \( X5 \) = Protection/covering of water storage containers
- \( X6 \) = Mosquito protection measures used by the households
- \( X7 \) = Frequency of water supply
- \( X8 \) = Frequency of waste disposal at community level.

The results of the stepwise multiple regression analysis indicated that the multiple R and R² for the final model were 0.979 and 0.958 respectively. Adjusted R² was 0.938 explaining 93.8% of the total variation in the dengue incidence.

Discussion of significant variables

Frequency of cleaning of water storage containers: The model showed that the variable Frequency of cleaning of water storage containers made a positive contribution to dengue incidence. The Aedes aegypti mosquito is a domestic breeder and breeding can occur in water storage containers, which are not emptied and cleaned for sufficiently long periods. The Aedes aegypti eggs are normally laid on the damp walls of both artificial and natural containers and they could resist desiccation for several weeks to several months. The eggs hatch when submerged in water. Since water is essential during the first 8 days in the life of mosquitoes, therefore if the frequency of cleaning is more than 8 days, this could contribute to an increase in the abundance of adult mosquitoes and the risk of dengue virus transmission. Whereas, changing water and emptying water storage containers once or twice a week will greatly reduce the risk of dengue fever. It was observed in the study area that people cleaned containers daily, but only those...
which were used to store water for drinking purpose. However, those containers which were used to store water for other domestic purposes, i.e. washing, bathing, etc., were cleaned infrequently. These containers were normally cleaned after 10-15 days, or even after one month, thus providing ideal oviposition sites for mosquitoes and subsequent sticking of the eggs. The eggs would then hatch and develop into mosquitoes when inundated.

**Use of water evaporation coolers:** The use of water evaporation coolers generally starts with the onset of summer months. In Jalore, the use of coolers was observed to start in the middle of March or early April. Coolers were used until the end of July. Most coolers were found fitted in openings, initially used as windows, whereas some coolers were of the portable type. Coolers and other containers become excellent places for Aedes mosquito breeding and can lead to widespread transmission of dengue fever. The cooler plays an important role in the breeding of secondary foci. It was observed that once the cooler was fixed to windows, it remained there. With the onset of the monsoons, the breeding of Aedes aegypti larvae spreads from its mother foci to secondary foci, which are coolers. The model indicates the positive relationship of dengue incidence to the use of water coolers in Jalore. Studies by Katyal et al., 1996 indicate that coolers play an important role in mosquito breeding, which seems to support research results.

**Uncovered water storage containers:** Open water storage containers provide ideal breeding places for Aedes aegypti mosquitoes. During the survey it was observed that portable cement tanks, metallic/plastic drums and overhead/underground tanks were used to store clean water within premises. Most domestic water storage containers were kept uncovered except for underground tanks. Different studies indicate that uncovered water containers and pitchers were significantly associated with dengue infection.

The regression model indicates that the presence of uncovered water containers makes a positive contribution to dengue incidence. It is interesting to note that the epidemic occurred in the summer months (April-May) when there was scarcity of water. This scarcity could result in increased storage of water, thereby increasing the risk of dengue incidence and thus holding a positive correlation.

**Protection measures against mosquitoes:** Use of nets, screening of houses, creating smoke with neem leaves, spraying of insecticides and closing of doors and windows were the common protective measures used against mosquitoes. These measures either reduce the number of mosquitoes or provide protection against bites and thus reduce the risk of dengue infection. The model showed that the variable mosquito protection measures had negative association with the dengue incidence, i.e. the more protection measures were used, the less incidence there was of dengue.

**Housing pattern:** A review of the available literature indicated that in a crowded area, many people living within the short flight range of the vector from its breeding source could be exposed to transmission even if the house index was...
low. Therefore, higher population density and interconnection of houses could lead to more efficient transmission of the virus and thus increased exposure to infection. The transmission of the disease is normally limited by the flight distance of Aedes aegypti during its lifetime. The flight distance of Aedes aegypti could range from a few metres to more than 50 metres in a closed urban environment. In urban environment where interconnections are not very common, the independent nature of houses limits the flight range of Aedes aegypti and reduces the transmission of the disease. The prediction model indicated that the variable connectivity of houses (independent = 1, connected = 0) had a negative correlation with dengue incidence. This correlation is in line with the results from available studies.

**Cleaning of water evaporation coolers**: The model showed that the variable frequency of cleaning of water coolers had a negative impact on dengue incidence. Generally, the prolonged stay of water in a cooler permits damp space as well as litter formation, thus providing nutrition to larval habitats. This permits the growth and emergence of Aedes aegypti mosquitoes, thus increasing dengue risk. The negative correlation indicated that if the frequency of cleaning of coolers was high, there would be less chances of dengue infection. This could appear as evidence given the fact that cleaning prevents potential breeding of mosquitoes by removing litter.

**Frequency of water supply**: The model showed that the variable frequency of water supply was negatively correlated to incidences of dengue. Water supply in most houses, especially during summer (March to June), was inadequate and not reliable. Water scarcity, resulting in increased and prolonged storage of water for domestic use in various types of containers, subsequently becomes the cause of breeding of Aedes aegypti. Water storage practices in the area, due to irregular water supplies, were a possible cause for higher vector concentration in the sampled houses, thus increasing dengue transmission. It means more frequent the supply of water, more the practice of water storage and more the presence of vectors, thus increasing the growth, transmission and risk of dengue infection.

**Frequency of solid waste removal**: Frequency of garbage removal was the eighth contributing factor, which influenced in a negative direction. The presence of solid wastes around the households, such as cans, car parts, bottles, old used tyres and other junk material found in several houses, created potential breeding sites. Dumping of solid waste for long periods of time such as 15-20 days supported the breeding of Aedes aegypti and increased the transmission of disease. If the frequency of collection and disposal of solid waste by local bodies increases, it would control the Aedes breeding and thus would reduce transmission.

**Development of spatial model**

Both spatial and sociocultural parameters could be important in determining disease emergence and transmission. GIS could create possible links between spatial data
and their related descriptive information, which could include socioeconomic and sociocultural parameters. The objective of spatial modelling was to determine the applicability of GIS as a tool to identify varying degrees of spatial social risks in Jalore related to dengue incidence and transmission.

**Weighting of sociocultural practices**

Method of “weights” was observed to be a suitable technique which would have a combined effect of various social risk factors contributing to the incidence of dengue. To develop a combined social risk category, the eight social risk indicators identified from stepwise regression analysis were selected. Based on a review of literature, weights were then assigned to their associated parameters indicating the degree of an individual risk indicator. In order to maintain uniformity among all social risk indicators, an equal weighing method was used. Weights of 1-3 were assigned to associated practices. For a given social risk indicator, a higher weight \(^{(3)}\) was given to the practices with a higher risk of dengue incidence, medium weight \(^{(2)}\) was assigned to the one contributing medium risk in the incidence of dengue, and a low score \(^{(1)}\) was given to the practice with low risk of dengue incidence. For example, in the case of the risk indicator - “Frequency of solid waste removal”, the lowest value of 1 was assigned to the practice of short duration (once in 1-4 days), 2 to medium duration (once in 5-15 days) and 3 to long duration (more than 15 days). The detailed weighting for all the eight risk indicators is presented in Table 1.

<table>
<thead>
<tr>
<th><strong>Social risk indicators</strong></th>
<th><strong>Risk scores</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Frequency of cleaning of water storage containers</strong></td>
<td></td>
</tr>
<tr>
<td>a. 1-4 days</td>
<td>1</td>
</tr>
<tr>
<td>b. 5-15 days</td>
<td>2</td>
</tr>
<tr>
<td>c. &gt;16 days</td>
<td>3</td>
</tr>
<tr>
<td><strong>Housing pattern</strong></td>
<td></td>
</tr>
<tr>
<td>a. Independent house</td>
<td>1</td>
</tr>
<tr>
<td>b. Mixed</td>
<td>2</td>
</tr>
<tr>
<td>c. Interconnections</td>
<td>3</td>
</tr>
<tr>
<td><strong>Use of water coolers</strong></td>
<td></td>
</tr>
<tr>
<td>a. 5 days/month</td>
<td>1</td>
</tr>
<tr>
<td>b. 6-10 days/month</td>
<td>2</td>
</tr>
<tr>
<td>c. &gt;15 days/month</td>
<td>3</td>
</tr>
<tr>
<td><strong>Frequency of cleaning of water cooler</strong></td>
<td></td>
</tr>
<tr>
<td>a. 1-4 days</td>
<td>1</td>
</tr>
<tr>
<td>b. 5-15 days</td>
<td>2</td>
</tr>
<tr>
<td>c. &gt;16 days</td>
<td>3</td>
</tr>
<tr>
<td><strong>Protection of water storage container</strong></td>
<td></td>
</tr>
<tr>
<td>a. Fully covered</td>
<td>1</td>
</tr>
<tr>
<td>b. Sometimes</td>
<td>2</td>
</tr>
<tr>
<td>c. Mostly uncovered</td>
<td>3</td>
</tr>
<tr>
<td><strong>Mosquito protection measures</strong></td>
<td></td>
</tr>
<tr>
<td>a. Screens</td>
<td>1</td>
</tr>
<tr>
<td>b. Insecticides</td>
<td>1</td>
</tr>
<tr>
<td>c. close windows</td>
<td>2</td>
</tr>
<tr>
<td>d. Smoke/burning herbs (neem)</td>
<td>1</td>
</tr>
<tr>
<td>e. Mosquito-net</td>
<td>2</td>
</tr>
<tr>
<td><strong>Frequency of water supply</strong></td>
<td></td>
</tr>
<tr>
<td>a. Everyday</td>
<td>1</td>
</tr>
<tr>
<td>b. Alternate</td>
<td>1</td>
</tr>
<tr>
<td>c. Every 3 days</td>
<td>2</td>
</tr>
<tr>
<td>d. 4-7 days</td>
<td>2</td>
</tr>
<tr>
<td><strong>Frequency of waste removal</strong></td>
<td></td>
</tr>
<tr>
<td>a. Everyday</td>
<td>1</td>
</tr>
<tr>
<td>b. Weekly</td>
<td>2</td>
</tr>
<tr>
<td>c. &gt;15 days</td>
<td>3</td>
</tr>
</tbody>
</table>
Since the sociocultural practices related to the eight social risk indicators varied from household to household, these scores were assigned separately for each of the 77 households belonging to DAS and UAS groups.

**Development of social risk levels**

The discriminant analysis approach was used to obtain household-wise social risk scores, and by using the histogram/box plot technique, social risk scores were translated into social risk levels. The histogram depicts the mean, minimum and maximum values and standard deviation of discriminant scores of the 77 households. To derive risk levels, percentiles technique was used. For example, if five possible risk levels are to be identified, discriminant scores at 20 percentile, 40 percentile, 60 percentile and 80 percentile could be used as the cut-off points as shown in Table 2 and Figure 1.

**Table 2. Percentile households and discriminant scores**

<table>
<thead>
<tr>
<th>Percentile</th>
<th>Discriminant score</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>-2.5360433</td>
</tr>
<tr>
<td>20</td>
<td>-2.0483010</td>
</tr>
<tr>
<td>25</td>
<td>-1.8912598</td>
</tr>
<tr>
<td>30</td>
<td>-1.6407418</td>
</tr>
<tr>
<td>40</td>
<td>-0.9233625</td>
</tr>
<tr>
<td>50</td>
<td>-0.1139570</td>
</tr>
<tr>
<td>60</td>
<td>0.4975759</td>
</tr>
<tr>
<td>70</td>
<td>1.4409430</td>
</tr>
<tr>
<td>75</td>
<td>1.7847998</td>
</tr>
<tr>
<td>80</td>
<td>2.3510595</td>
</tr>
<tr>
<td>90</td>
<td>2.9958430</td>
</tr>
<tr>
<td>100</td>
<td>3.6073759</td>
</tr>
</tbody>
</table>

These risk levels were termed as very low, low, medium, high and very high risk levels respectively with scores of 1, 2, 3, 4 and 5 for the assigned risk levels respectively. For each household, it is necessary to check the predicted risk levels from discriminant scores to their actual class. For this, estimates of the classification function coefficients were used. It was observed that the application resulted in 94.8% correct classification under the risk level categories, which was very positive from statistical considerations.

**Figure 1. Histogram of discriminant scores**

**Development of a spatial social risk model**

As the sample households were spatially distributed and social risk information with regard to these households was collected and analysed, it could provide spatially-distributed social risk levels. The spatial (point data) with their attributes were input into GIS and a spatial point-wise risk-level map was developed. This was achieved by digitizing spatial locations of houses of DAS (37 households) and UAS (40 households) samples located in the Jalore administrative map as shown in Figure 2. On the
administrative map of Jalore, locations of houses of DAS and UAS were overlayed. GIS databases were developed separately for DAS as well as UAS groups having information on social risk levels. Nearest neighbourhood technique of extrapolation was used to develop a social risk map of the area. This provided location-wise social risks of dengue incidence. Analysed results are presented in Figure 3.

**Figure 2. Spatial location of dengue affected and unaffected houses in Jalore**

**Figure 3. Dengue risk levels associated with social and cultural parameters in Jalore**
This figure (map) shows the spatial distribution of the five social risk levels, which were identified through discriminate analysis. The analysis indicated that a large percentage of the area (61.09%) had very low social risk, whereas 16.90% of the area had high risk, 12.35% had low risk, followed by 6.58% of the area with medium risk. Only a very small area, 3.09%, had very high risk. Overall, little more than 26% had medium to high social risk.

**Conclusion**

Prediction of dengue risk based on sociocultural factors was investigated in a dengue endemic area of Jalore. The data analysis and modelling revealed that the sociocultural factors such as the housing patterns, limited use of mosquito protection measures, irregular water supplies, poor management of waste disposal, storage of water on the premises due to inadequate water supplies in summer months, and prolonged storage of water for domestic and other purposes significantly affected the incidence of dengue. Storing of water in houses created conditions conducive to the breeding of *Aedes aegypti* mosquitoes and led to more pronounced vector presence. Stepwise regression analysis was found to be an appropriate technique for identifying significant social risk indicators which contributed to increased transmission of disease. It may, therefore, be concluded that any step taken to improve any of the above social and cultural practices would have favourable effects on reducing dengue cases. Such analysis provides valuable information for the planning of precautionary measures and for controlling the spread of DF/DHF/DSS. The objective of spatial modelling was to create a linkage between households, their sociocultural practices and dengue incidence. The spatial model is capable of identifying five different levels - very low, low, medium, high and very high-risk levels of dengue incidence for the study area. It would contribute significantly to the spatial prediction of social risk levels in Jalore. Furthermore, the approach could assist in focusing and implementing precautionary and preventive strategies to monitor and control the incidence of dengue more effectively.

**References**


Impact of Vertically-transmitted Dengue Virus on Viability of Eggs of Virus-Inoculated Aedes aegypti

by
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Abstract
Transovarial transmission (TOT) is known to occur in Aedes aegypti. This relationship carries tremendous epidemiological significance. The progeny of virus-inoculated Aedes aegypti were followed for seven generations to observe the impact of the virus on the viability of eggs and their rearing up to the adult stage. Dengue virus was found to exert an adverse effect on the viability of the eggs of the vertically-infected female mosquitoes and their larval and pupal stages up to adults when compared with the control population. While TOT ranged from 15.5% to 67.5% of the total mosquito populations in seven experimental generations, the corresponding adverse effect of the virus on eggs failing to hatch and grow into adults ranged from 30.0% to 68.1%.

Keywords: Transovarial transmission (TOT), dengue, Aedes aegypti.

Introduction
Dengue is endemic in South-East Asia where its more severe forms, dengue haemorrhagic fever (DHF) and dengue shock syndrome (DSS), are major public health concerns. Owing to its complex epidemiology, the prevention of dengue/dengue haemorrhagic fever needs a great deal of research inputs for a better comprehension of its transmission dynamics. Of the various components responsible for dengue transmission, viz. mosquito, virus, man and environment, interactions between susceptible vectors and the virus have a direct bearing on the introduction and subsequent maintenance of dengue infection in a particular community. It has been reported by a number of workers from India, Myanmar, and Nigeria that the transovarial transmission (TOT) of the dengue virus takes place across generations of Aedes aegypti. The virus, through this mechanism, has been recently demonstrated

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to persist in seven generations of the inoculated parent mosquitoes\textsuperscript{(7)}. While the quantitative studies to determine the multiplication of the infected mosquitoes through TOT will have a direct relevance to the particular quantum of the disease in inhabiting susceptible human population, the study of the impact of the virus on the viability of the eggs of virus-carrying mosquitoes will add newer dimensions to our understanding of the host-parasite interactions in its cycle. The present paper deals with the results of an experiment concerning these aspects.

**Materials and methods**

The mosquitoes used in the present study were taken from a virus-free colony of *Aedes aegypti* which was being maintained in laboratory. Sixteen female mosquitoes were inoculated introthoracically (ITI)\textsuperscript{(8)} with DEN-3 virus strain (633978) obtained from the National Institute of Virology, Pune, India. 0.2 µl of viral suspension was inoculated and the transovarial transmission of the virus was studied in the adult progeny quantitatively for seven consecutive generations of *Aedes aegypti* in relation to its possible impact on the viability of eggs. At each generation the eggs laid by the experimentally-infected mosquitoes were counted and immersed into water. The virus transmitted vertically to the progeny was seen using the indirect fluorescence antibody test (IFA)\textsuperscript{(9)}. In the experimental mosquito population the number of eggs, which failed to hatch and reach up to adult stages, were matched with the control group. Ambient temperature was maintained between 25-29°C and relative humidity between 80-85 percent.

**Results and discussion**

The table 1 shows the trend of the impact of the transovarially-transmitted virus on the viability of eggs and per cent reaching adult stages. The proportion of mosquitoes carrying the dengue virus, viewed in terms of its ability to lay viable eggs in the respective

### Table. Per cent viability of eggs of vertically-infected *Aedes aegypti* by DEN-3 virus in seven successive generations

<table>
<thead>
<tr>
<th>Generation</th>
<th>Virus inoculated</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TOT in adults</td>
<td>Eggs to adult rearing</td>
</tr>
<tr>
<td></td>
<td>Examined</td>
<td>Positive</td>
</tr>
<tr>
<td>F1</td>
<td>50</td>
<td>26</td>
</tr>
<tr>
<td>F2</td>
<td>142</td>
<td>79</td>
</tr>
<tr>
<td>F3</td>
<td>431</td>
<td>240</td>
</tr>
<tr>
<td>F4</td>
<td>37</td>
<td>24</td>
</tr>
<tr>
<td>F5</td>
<td>65</td>
<td>20</td>
</tr>
<tr>
<td>F6</td>
<td>26</td>
<td>6</td>
</tr>
<tr>
<td>F7</td>
<td>180</td>
<td>38</td>
</tr>
</tbody>
</table>

TOT = Transovarial transmission; ND = Not done
generations, showed a clear trend in F1 generation where 52.0% of TOT caused the failure of eggs reaching adult stage to the extent of 55.6%. In F1 controls, without the passage of virus led to an estimated failure to the extent of 4.3%. Similarly, in F2 when the proportion of the virus attained 55.6% TOT, the corresponding failure rate 30.0%, while in the F3 generation the failure rate (34.2%) was less than the proportion of TOT (55.6%). Again, in the F4 and F5 generations the adverse effect of the virus could be seen as almost in proportion with the percentage of adults carrying the vertically-transmitted virus. In the control group of mosquitoes failure rate of eggs reaching the adult stage was insignificant.

The transovarial transmission of dengue virus appears to support the fact that it is originally the virus of mosquitoes which has adapted to primates\(^4\). The TOT has also been seen in the present paper as a controlling factor over the reproductive potential of an invertebrate host undergoing this mechanism. The observations made while matching with the control group clearly indicated that the presence of the virus in the mosquito system had detrimental effects on the viability of the eggs laid.

The present observations indicate that through the transovarial passage the dengue virus persists in optimum number of individuals in the subsequent generations of the mosquito host. On the other hand, in this maintenance mechanism, TOT exerts a biological control over the population multiplication. Nevertheless, individuals sustaining the virus are the best-selected individuals by virtue of their genetic superiority. It is this population which is important in the transmission dynamics of the dengue virus. The retention of virus for its further sustenance in the community will depend on the host-parasite relationship taking place in this sustaining population under the prevailing environmental conditions. Furtherance of such studies with the inclusion of seasonal parameters with genetic and molecular-biological basis may lead to important details revealing basic research components.

**Acknowledgements**

The authors are grateful to Mr N. L. Kalra, Consultant Scientist, Malaria Research Centre, Delhi, for his valuable guidance and suggestions. The assistance rendered by Dr Manju Singhi, Technical Officer, and Dr Himmat Singh, Research Assistant, is thankfully acknowledged.

**References**


Impact of vertically-transmitted dengue virus on viability of eggs of virus-inoculated Aedes aegypti


Aedes aegypti Prevalence in Hospitals and Schools, the Priority Sites for DHF Transmission in Delhi, India

by
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An outbreak of dengue haemorrhagic fever (DHF) swept the National Capital Territory of Delhi in 1996. A total of 10,252 cases and 423 deaths due to DHF were recorded in various parts of Delhi(1). Delhi has been endemic for dengue since the past several years. The first DHF outbreak was reported in 1988 which resulted in 33% mortality among children admitted in hospitals(2). Krishnamurthy et al. (1964) and Katyal et al. (1996) carried out comprehensive surveys of the Aedes aegypti population in Delhi. The urbanization of Delhi has since then occurred at a very fast rate, creating in the process greater opportunities for the breeding of Aedes aegypti and also for the circulation of dengue virus due to increased migration. Two major outbreaks, in 1988 and 1996, affected children below 15 years of age. This highlighted the need for a special assessment of schools and hospitals where there is a large presence of vectors and a high potential for the transmission of dengue exists.

Searches were made for Aedes breeding in varied types of habitats in different schools and hospitals in areas covered by the Municipal Corporation of Delhi (MCD), the New Delhi Municipal Council (NDMC), the Railways and the Delhi Cantonment. Container index (CI) was used for measuring the larval populations as per WHO technique (WHO, 1999)(3).

The degrees of Aedes prevalence in different schools and hospitals are given in Tables 1 and 2.

Table 1. Prevalence of Aedes aegypti in different schools of Delhi – 1998

<table>
<thead>
<tr>
<th>Locality/School</th>
<th>CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. G. N. College, Netaji Nagar</td>
<td>25.0</td>
</tr>
<tr>
<td>Govt. Sr. Secondary School, Moti Bagh</td>
<td>6.7</td>
</tr>
<tr>
<td>Govt. Sr. Secondary School, Pandara Park.</td>
<td>10.0</td>
</tr>
<tr>
<td>Shri Guru Govind Singh College of Commerce, Uttari Pitampura</td>
<td>6.8</td>
</tr>
<tr>
<td>Rajiv Gandhi Camp Huts IX, Rohini</td>
<td>5.0</td>
</tr>
<tr>
<td>Primary School, Lampur Village</td>
<td>5.0</td>
</tr>
<tr>
<td>Primary School, Janakpuri</td>
<td>5.0</td>
</tr>
<tr>
<td>Primary School, Hastal Road</td>
<td>28.3</td>
</tr>
<tr>
<td>Sr. Secondary School, YMCA Nizamuddin</td>
<td>8.0</td>
</tr>
<tr>
<td>Vivekanand University, Vivek Vihar</td>
<td>2.5</td>
</tr>
<tr>
<td>Primary School MCD, Parladpur</td>
<td>3.3</td>
</tr>
<tr>
<td>Kalindi College, Prasad Nagar</td>
<td>18.2</td>
</tr>
</tbody>
</table>

CI-Container Index
Table 2. Prevalence of Aedes aegypti in different hospitals of Delhi – 1998

<table>
<thead>
<tr>
<th>Locality/Hospital</th>
<th>CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kalawati Saran Hospital</td>
<td>7.7</td>
</tr>
<tr>
<td>Charak Hospital, Moti Bagh</td>
<td>2.8</td>
</tr>
<tr>
<td>Safdarjung Hospital</td>
<td>5.4</td>
</tr>
<tr>
<td>ESI Hospital Basaidarapur</td>
<td>11.6</td>
</tr>
<tr>
<td>Hindu Rao Hospital</td>
<td>4.0</td>
</tr>
<tr>
<td>Mental Hospital, Shahdara</td>
<td>3.8</td>
</tr>
<tr>
<td>GTB Hospital</td>
<td>2.0</td>
</tr>
<tr>
<td>Jaipur Golden Hospital</td>
<td>11.6</td>
</tr>
<tr>
<td>LNJP Hospital</td>
<td>6.7</td>
</tr>
<tr>
<td>Chest Clinic MCD Health Centre</td>
<td>3.3</td>
</tr>
<tr>
<td>Escort Heart Institute Hospital</td>
<td>1.9</td>
</tr>
<tr>
<td>Ganga Ram Hospital</td>
<td>7.1</td>
</tr>
<tr>
<td>B. L. Kapoor Hospital</td>
<td>45.1</td>
</tr>
</tbody>
</table>

All the schools and hospitals surveyed (Tables 1 and 2) were found positive for Aedes aegypti. The highest Container index (28.3 %) was reported at the MCD Primary School, Hastal. Among the hospitals surveyed, the B. L. Kapoor Hospital showed a very high Container index (45.1%). Hospitals and schools, being the most vulnerable areas, need to be monitored regularly to check the Aedes aegypti population to reduce the threat of DHF. In India, all dengue/DHF outbreaks have been associated with Aedes aegypti having a Container index of more than 20%. Dengue has been declared a dangerous disease under section 2(9)(b) of the Delhi Municipal Act, which enjoins upon all medical practitioners and other persons to give information to the Municipal Health Officer and the National Anti-Malaria Programme which is the nodal agency for monitoring dengue at the national level. Legislative measures are in force and under these byelaws, no school and hospital shall keep or maintain any water collection site or flowing water in which mosquitoes breed or are likely to breed.

References
Legislation for Dengue Control in Malaysia

by

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In Malaysia, there are three laws and legislation to cover the prevention and control of vector-borne diseases. These are: (a) Destruction of Disease-Bearing Insects Act 1975 (Act 154); (b) Prevention and Control of Infectious Diseases Act 1988 (Act 342); and (c) Local Government Act 1976 (Act 171). The Destruction of Disease-Bearing Insects Act (DDBIA) 1975 was enforced throughout the country with effect from 23 August 1982. The Destruction of Disease-Bearing Insects Act (DDBIA) 2000 came into operation throughout the country with effect from 1 January 2001.

Application

The DDBIA is intended to provide for the destruction and control of disease-borne insects. It also empowers the relevant authority to conduct medical examination and treatment of persons suffering from insect-borne diseases. For the prevention and control of dengue, most of the provisions vested under the DDBIA 1975 are strictly enforced. Section 18(d) of the Prevention and Control of Infectious Diseases Act 1988, which has provision for the closure of premises found harbouring disease-bearing insects, is used to supplement the DDBIA.

Achievement in law enforcement of DDBIA for dengue control

During the 5-year period from 1996 to 2000, an average of 4,316,113 premises were inspected annually for Aedes breeding, of which an average of 33,959 premises were found to be breeding Aedes (Table 1). The Aedes Premise Index thus worked out to about 0.78%.

An average of 13,435 warning notices and 22,660 compounds were issued annually to the offenders who harboured Aedes larvae in their premises. Of those who refused to pay the compounds, an average of 550 offenders were taken to court. For the same period, an average of 92 premises were closed or stop-work order issued to them.

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* This paper was presented at the WHO Health Forum organized by the Ministry of the Environment, Singapore, October 2001
# For correspondence: cyberseng@hotmail.com
Table 1. Enforcement of Destruction of Disease-Bearing Insects Act, 1975 (Amended 2000) in Malaysia

<table>
<thead>
<tr>
<th>Year</th>
<th>No. of premises examined</th>
<th>No. of premises found breeding Aedes</th>
<th>Aedes Premise Index (%)</th>
<th>No. of warning notices issued</th>
<th>No. of compounds issued</th>
<th>No. of court cases</th>
<th>Law Enforcement Index (%)</th>
<th>No. of premises closed</th>
</tr>
</thead>
<tbody>
<tr>
<td>1996</td>
<td>4,397,754</td>
<td>41,612</td>
<td>0.9</td>
<td>17,972</td>
<td>18,408</td>
<td>517</td>
<td>88.7</td>
<td>0</td>
</tr>
<tr>
<td>1997</td>
<td>4,239,489</td>
<td>42,902</td>
<td>1.0</td>
<td>19,878</td>
<td>28,834</td>
<td>989</td>
<td>115.8</td>
<td>256</td>
</tr>
<tr>
<td>1998</td>
<td>5,071,478</td>
<td>36,203</td>
<td>0.7</td>
<td>11,233</td>
<td>30,696</td>
<td>298</td>
<td>116.6</td>
<td>115</td>
</tr>
<tr>
<td>1999</td>
<td>3,915,499</td>
<td>27,961</td>
<td>0.7</td>
<td>9,490</td>
<td>20,154</td>
<td>436</td>
<td>107.6</td>
<td>73</td>
</tr>
<tr>
<td>2000</td>
<td>3,956,344</td>
<td>21,117</td>
<td>0.5</td>
<td>8,601</td>
<td>15,209</td>
<td>506</td>
<td>115.1</td>
<td>16</td>
</tr>
<tr>
<td>2001</td>
<td>1,828,648</td>
<td>13,808</td>
<td>0.8</td>
<td>4,039</td>
<td>9,861</td>
<td>249</td>
<td>102.5</td>
<td>27</td>
</tr>
</tbody>
</table>

Source: Vector-borne Disease Branch, Ministry of Health, Malaysia

Table 2 shows the achievement of law enforcement by states for the year 2000. A total of 3,956,344 premises were examined, out of which 21,117 (0.53%) premises were found to be positive for Aedes breeding. A total of 8,601 warning notices, 15,209 compounds, 506 court prosecutions and 16 stop-work or closure orders were issued. In 2000, court prosecutions were prominent in the urbanized states of Perak, Selangor, Federal Territory of Kuala Lumpur and Negeri Sembilan. The issuance of compounds was more pronounced in the states of Perak, Selangor and Johore where more than 2,000 compounds were issued for each of the states. The issue of warning notices was more active in the states of Kedah, Selangor, Terengganu and Sarawak where more than 1,000 notices were issued for each state. A total of 16 closure of premises or stop-work orders were issued; 5 in Kedah, 9 in Selangor and 2 in Kelantan.

Impact of legislation on dengue control

In the enforcement of the Disease-Bearing Insects Act 1975, the main focus is on finding Aedes mosquito larvae in and around premises during routine Aedes survey. Once the larvae are confirmed to be disease-bearing insects, the owner/occupier is issued a warning notice or a compound is offered. The owner/occupier is expected to abide by the instructions in the warning notice or settle the compound within the stipulated time, otherwise court prosecutions are proceeded. Therefore, legislation serves as a strong deterrent to mosquito breeding by careless and indifferent householders.
The ultimate objective of imposing fines and enforcing the law is to get public support in dengue control activities and their participation in source-reduction measures. Table 3 shows the relationship between the number of dengue cases reported, the number of compounds issued, and the fines collected during 1999 and 2000.

### Table 2. Enforcement of Destruction of Disease-Bearing Insects Act, 1975 (amended 2000) by states in Malaysia during 2000

<table>
<thead>
<tr>
<th>State</th>
<th>No. of premises examined</th>
<th>No. of premises found breeding Aedes</th>
<th>No. of warning notices issued</th>
<th>No. of compounds issued</th>
<th>No. of court cases</th>
<th>No of premises closed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perlis</td>
<td>23 173</td>
<td>179</td>
<td>19</td>
<td>160</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Kedah</td>
<td>336 050</td>
<td>991</td>
<td>1393</td>
<td>819</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>P.Pinang</td>
<td>324 927</td>
<td>730</td>
<td>11</td>
<td>643</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Perak</td>
<td>715 302</td>
<td>3745</td>
<td>799</td>
<td>2624</td>
<td>207</td>
<td>0</td>
</tr>
<tr>
<td>Selangor</td>
<td>517 010</td>
<td>5700</td>
<td>1271</td>
<td>4041</td>
<td>168</td>
<td>9</td>
</tr>
<tr>
<td>Wpkl</td>
<td>51 913</td>
<td>1490</td>
<td>616</td>
<td>510</td>
<td>96</td>
<td>0</td>
</tr>
<tr>
<td>N.Sembilan</td>
<td>151 337</td>
<td>512</td>
<td>20</td>
<td>459</td>
<td>20</td>
<td>0</td>
</tr>
<tr>
<td>Melaka</td>
<td>189 788</td>
<td>610</td>
<td>340</td>
<td>254</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>Kjohor</td>
<td>454 418</td>
<td>2637</td>
<td>286</td>
<td>2350</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Pahang</td>
<td>208 559</td>
<td>881</td>
<td>77</td>
<td>779</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Terengganu</td>
<td>202 699</td>
<td>513</td>
<td>1780</td>
<td>505</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Kelantan</td>
<td>281 578</td>
<td>719</td>
<td>274</td>
<td>345</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Sabah</td>
<td>257 172</td>
<td>915</td>
<td>687</td>
<td>696</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Sarawak</td>
<td>242 412</td>
<td>1495</td>
<td>1028</td>
<td>1024</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>3 956</strong></td>
<td><strong>21 117</strong></td>
<td><strong>8 601</strong></td>
<td><strong>15 209</strong></td>
<td><strong>506</strong></td>
<td><strong>16</strong></td>
</tr>
</tbody>
</table>

Source: Vector-borne Disease Branch, Ministry of Health, Malaysia
Table 3. Number of dengue cases, compounds, collection in fines under the DDBIA 1975 (amended 2000) for 1999 and 2000.

<table>
<thead>
<tr>
<th>State</th>
<th>1999</th>
<th>2000</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of dengue cases</td>
<td>No. of compounds</td>
</tr>
<tr>
<td>Perlis</td>
<td>46</td>
<td>33</td>
</tr>
<tr>
<td>Kedah</td>
<td>892</td>
<td>888</td>
</tr>
<tr>
<td>Penang</td>
<td>585</td>
<td>1 484</td>
</tr>
<tr>
<td>Perak</td>
<td>1 047</td>
<td>4 484</td>
</tr>
<tr>
<td>Selangor</td>
<td>1 956</td>
<td>3 598</td>
</tr>
<tr>
<td>Fed. Terr. K. Lumpur</td>
<td>1 329</td>
<td>1 298</td>
</tr>
<tr>
<td>N. Sembilan</td>
<td>427</td>
<td>959</td>
</tr>
<tr>
<td>Malacca</td>
<td>229</td>
<td>336</td>
</tr>
<tr>
<td>Johor</td>
<td>957</td>
<td>1 550</td>
</tr>
<tr>
<td>Pahang</td>
<td>782</td>
<td>1 156</td>
</tr>
<tr>
<td>Terengganu</td>
<td>433</td>
<td>687</td>
</tr>
<tr>
<td>Kelantan</td>
<td>444</td>
<td>243</td>
</tr>
<tr>
<td>Sabah</td>
<td>344</td>
<td>1 205</td>
</tr>
<tr>
<td>Sarawak</td>
<td>675</td>
<td>2 233</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>10146</strong></td>
<td><strong>20154</strong></td>
</tr>
</tbody>
</table>

Source: Vector-borne Disease Branch, Ministry of Health, Malaysia

It is very difficult to draw a good conclusion from the figures but judging from the reduction in dengue cases in 2000 (7,118 cases) as compared to 1999 (10,146 cases), enforcement via compounding does play a role. Although the number of compounds issued in 2000 (15,209) was less than that in 1999 (20,154), it shows that there were less breeding places detected (21,117) in 2000 as compared to 27,961 in 1999. The issuing of compounds has made a positive impact on the reduction of Aedes breeding premises.

References

by
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The incidence of dengue and its more severe form dengue haemorrhagic fever (DHF) is increasing in the Region of the Americas. After the first significant DHF epidemic in Cuba in 1981, and subsequently in the last decade, we have seen a steady increase in DHF (Figure 1). Unfortunately, the trend reflects that which occurred in Asia 30 years ago.

In view of this during the 43rd Directing Council of the Pan American Health Organization (PAHO), in September 2001, the Ministers of Health of all countries in the Americas, unanimously approved a Resolution to address dengue and dengue haemorrhagic fever. The Resolution highlights the need for a long-term change in health management, adopting strongly-integrated actions for dengue control and prevention at all levels. The Resolution also urges the incorporation of social communication and community participation in the national programmes, with a focus on both individual and collective behaviour change.

As a result, the Resolution encourages national programmes to move from the traditional vector control approach of actions (using insecticides) to focusing on community actions emphasizing “ownership” of dengue control and prevention. Social communication, health education, environmental management of water supply and disposal, as well as solid waste management, form the basis of the new generation of prevention and control programmes on dengue.

The CD43.R4 Resolution agreed to by the Directing Council essentially concentrates on urging the Region’s ministries of health to promote inter- and intrasectoral coordinated actions, and to adopt environmental measures in the areas of urban planning and services. Coordinated environmental actions and partnership with...
agencies and local government can provide sustainable activities to build proper systems for the disposal of solid waste (including discarded automobile tyres) and to increase regular water supply and refuse collection in order to reduce sources of Aedes aegypti. In addition, under the Resolution, health ministries are encouraged to strengthen the important component of social communication and community participation. Thus the Resolution aims to further promote the practice of good health behaviour, which will contribute to personal protection and reduce breeding sites in and around the home, the community, the workplace, and recreational sites.

PAHO is convinced that strengthening the social element of the programme while maintaining the other components will minimize the threat of an increase of dengue haemorrhagic fever and the reappearance of urban yellow fever in the Americas. PAHO is also conscious that the transition from vertical to horizontal programmes is a long-term process that will affect determinant and/or risk factors along the way, most likely in five to seven years.

Previous dengue control programmes have not proved successful or sustainable because they are expensive, vertically-structured, insecticide-based and include community participation or health education only in case of emergency (“epidemic windows”). Implementing the new generation of dengue prevention and control programmes\(^5\) will be an opportunity to change the similar trend that dengue in the Americas shares with the region of South-East Asia, where hundreds of thousands of cases of dengue haemorrhagic fever occur every year.
Other elements included in the Resolution are the delivery of appropriate care to the patients inside and outside the formal health sector, including the recognition of the disease, the diagnosis and adequate response (with special attention to initial care in the home and knowledge of basic measures of treatment).

The Resolution also encourages the standardization of case-reporting throughout the Region to facilitate a better exchange of information concerning dengue outbreaks. Emphasis is on reporting the nature of the circulating viruses, clinical cases (probable cases), laboratory-confirmed cases, cases of dengue hemorrhagic fever, and deaths due to dengue hemorrhagic fever/dengue shock syndrome. The Resolution further encourages the identification of serotypes and the implementation of preparatory emergency mechanisms to cope with outbreaks and epidemics.

To confront the challenges that dengue, dengue hemorrhagic fever and the possible reurbanization of yellow fever pose to the Region, it was resolved that PAHO continue to allocate resources within the Office, as well as in technical cooperation provided to the countries to promulgate work and staff training related to dengue prevention and control.

PAHO, which functions as the Regional Office of the World Health Organization (WHO) in the Americas, was established officially in 1902 and is the oldest health organization in the world, celebrating its 100th anniversary this year. PAHO works with all countries of the Americas to improve health and elevate standards of living.

References
Rising Trend of Aedes aegypti Indices at Various International Ports and Airports of India

by

KS Gill, SK Sharma, Rakesh Katyal and Kaushal Kumar
National Institute of Communicable Diseases, 22, Shamnath Marg, Delhi – 110 054

All international ports and airports in India are under entomological surveillance for the prevention of yellow fever as per the requirements of the International Health Regulations (IHR). A recent outbreak of dengue haemorrhagic fever (DHF) in Delhi during 1996\(^1\) recorded 10,252 cases with 423 deaths. These developments heightened the perception of the threat of yellow fever in all countries of the South-East Asia Region\(^2\). Recognizing the need for a stricter implementation of IHR at international ports and airports, the WHO Regional Office for South-East Asia organized a special case study on the implementation status of IHR in three countries of the Region\(^3\) and, later, held a Regional consultation on disease surveillance and control at ports and airports during October 1998\(^4\). Major recommendations enjoined upon Member countries to strictly implement IHR to keep ports/airports free of Aedes aegypti infestation, not only as a preventive action against yellow fever but also to arrest the spread of DHF.

As a sequel to these recommendations, the National Institute of Communicable Diseases, which is the monitoring agency for the control of Aedes aegypti at ports/airports in India, carried out a retrospective study of the data for all major ports and airports during 2001. Table 1 below lists the larval indices of Aedes aegypti at various international ports/airports for the periods for which records were available\(^5\).

**Larval indices at international airports**

A retrospective analysis revealed that at Kolkata airport, the larval indices ranged from 0.0% in 1963 to 26.9% in 2000, whereas, at Chennai airport, these ranged from 0.0% in 1948 to 38.8% in 1999. In Mumbai, it ranged from 0.0% in 1956 to 9.2% in 1995. In Delhi it ranged from 0.0% in 1965 to as high as 60.7% in 2000, while in Vishakhapatnam it ranged from 2.2% in 1997 to 14.7% in 2000. Airports recently declared as international also recorded very high indices: Cochin (66.6%), Kozikhode (5.1%), Bangalore (7.9%), Thiruvananthapuram (5.2%) and Goa (15.3%).
Table 1. Larval indices of Aedes aegypti at various international ports and airports in India

<table>
<thead>
<tr>
<th>Name of the city</th>
<th>Period</th>
<th>Aedes aegypti larval index</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Airport</td>
</tr>
<tr>
<td>Kolkata (Calcutta)</td>
<td>1948</td>
<td>1.0%</td>
</tr>
<tr>
<td></td>
<td>1963</td>
<td>0.0%</td>
</tr>
<tr>
<td></td>
<td>1965</td>
<td>0.0%</td>
</tr>
<tr>
<td></td>
<td>1978</td>
<td>0.0%</td>
</tr>
<tr>
<td></td>
<td>1997</td>
<td>3.61%</td>
</tr>
<tr>
<td></td>
<td>2000</td>
<td>26.9%</td>
</tr>
<tr>
<td>Chennai (Madras)</td>
<td>1948</td>
<td>0.0%</td>
</tr>
<tr>
<td></td>
<td>1964</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>1965</td>
<td>1.0%</td>
</tr>
<tr>
<td></td>
<td>1998</td>
<td>13.5%</td>
</tr>
<tr>
<td></td>
<td>1999</td>
<td>38.8%</td>
</tr>
<tr>
<td>Mumbai (Bombay)</td>
<td>1956</td>
<td>0.0%</td>
</tr>
<tr>
<td></td>
<td>1961</td>
<td>0.46%</td>
</tr>
<tr>
<td></td>
<td>1965</td>
<td>0.0%</td>
</tr>
<tr>
<td></td>
<td>1977</td>
<td>1.09%</td>
</tr>
<tr>
<td></td>
<td>1995</td>
<td>9.2%</td>
</tr>
<tr>
<td>Delhi</td>
<td>1965</td>
<td>0.0%</td>
</tr>
<tr>
<td></td>
<td>1977</td>
<td>0.0%</td>
</tr>
<tr>
<td></td>
<td>1997</td>
<td>0.0%</td>
</tr>
<tr>
<td></td>
<td>2000</td>
<td>60.7%</td>
</tr>
<tr>
<td>Vishakhapatnam</td>
<td>1948</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>1964</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>1997</td>
<td>2.2%</td>
</tr>
<tr>
<td></td>
<td>1998</td>
<td>0.0%</td>
</tr>
<tr>
<td></td>
<td>1999</td>
<td>0.0%</td>
</tr>
<tr>
<td></td>
<td>2001</td>
<td>14.0%</td>
</tr>
<tr>
<td>Cochin</td>
<td>1948</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>1978</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>1999</td>
<td>66.6%</td>
</tr>
<tr>
<td>Kozhikode (Calicut)</td>
<td>1998</td>
<td>1.48%</td>
</tr>
<tr>
<td></td>
<td>1999</td>
<td>5.1%</td>
</tr>
<tr>
<td>Bangalore</td>
<td>1998</td>
<td>0.25%</td>
</tr>
<tr>
<td></td>
<td>1999</td>
<td>7.9%</td>
</tr>
<tr>
<td>Thiruvananthapuram (Trivandrum)</td>
<td>1998</td>
<td>0.0%</td>
</tr>
<tr>
<td></td>
<td>1999</td>
<td>5.2%</td>
</tr>
<tr>
<td>Goa</td>
<td>1978</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>2000</td>
<td>15.3%</td>
</tr>
</tbody>
</table>

Larval indices of Aedes aegypti in ports

At Kolkata port, the larval indices increased to 29.6% during 2000 as against 0.0% in 1963; at Chennai, it increased to 22.8% in 1999 as against 0.0% in 1964. At Mumbai, it increased to 12.19% from 2% in 1956. At Vishakhapatnam, the indices increased from 0.0% in 1948 to 29.45% in 2001. At Cochin it increased to 5.8% in 1999 against 0.0% in 1948. In Goa, the indices increased to as high as 50.4% against 29.3% in 1978.

Increased incidence of larval indices at ports and airports

It is apparent from the above table that major airports in India have shown substantial increases in the Aedes aegypti populations during the last three years. These ranged from 5% (in Kozikhode and Thiruvananthapuram) to 66% (in Cochin). A similar trend was observed at ports, but when compared to airports, the increase was almost 30-fold, with the exception of Goa, which recorded 50.4%.

Constraints which hampered the implementation of IHR included:

- Lack of infrastructure for taking effective vector control measures and carrying out entomological surveillance;
- Expansion of ports/airports areas have led to the construction of new buildings, runways, hangers, workshops, tyre dumps, scrap yards, which have raised the breeding potential manifold;
- Multiple agencies without linkages with national disease control programme authority;
• Control strategies privately managed which do not conform to national/WHO guidelines;
• Increased use of consumable plastic containers with poor disposal arrangements; and
• Growth of slums within 400 metres of the peripheral areas of ports and airports.

From the foregoing it is apparent that vector control activities at ports/airports in India require streamlining, with proper linkages among different stakeholders operating there and with the national disease control programme authority, who can provide technical inputs by way of capacity-building and guidelines.

References
Adverse Events Following Yellow Fever Vaccination

Weekly Epidemiological Record+ 2001, 76(29): 217-218

There have been recent reports\(^1\) of 7 cases of serious adverse events including 6 deaths) following yellow fever vaccination. The cases described in these reports occurred from 1996 to 2001 in Australia (1 case), Brazil (2 cases) and the United States (4 cases) and have raised concerns about the safety of the yellow fever vaccine. WHO has been fully aware of the reported cases and has closely monitored their investigation by national authorities in the respective countries.

WHO endorses the call for a renewed discussion of the safety of the yellow fever vaccine and the indications for its use. In particular, WHO recommends that travelers should be carefully assessed regarding their need for the vaccine and their personal level of risk.

Although the exact frequency of serious adverse events following yellow fever vaccination is yet to be determined, information currently available suggests that they are extremely rare. An estimated 150 million doses of vaccine were administered worldwide over the past 4 years, of which 54 million in Brazil, where only 2 cases of serious adverse events were reported.

Yellow fever remains a serious public health problem in Africa and South America and is a re-emerging disease which kills an estimated 30,000 people every year. It is also a major risk for travelers to endemic countries. The risk to unimmunized individuals either living in or traveling to areas where there is known yellow fever transmission is far greater than the risk of having a vaccine-related adverse event. Therefore the current WHO policy\(^2\) on yellow fever vaccination remains unchanged. However, there is a need to improve monitoring to detect potential severe adverse events and to quantify the actual rate of such events.

\(^{*}\) http://www.who.int/wer

1. The Lancet, 14 July 2001

2. For information please consult:
   http://www.who.int/vaccines/intermediate/yellowfever.htm and
Dengue/Dengue Haemorrhagic Fever (DF/DHF) Prevention and Control

Report of the Intercountry Consultation of Programme Managers of DF/DHF, Batam Island, Indonesia, 10-13 July 2001

SEA/Haem.Fev./75

The Intercountry Consultation of Programme Managers of DF/DHF from endemic countries and scientists/experts from the South-East Asia and Western Pacific Regions, which met at Batam Island, Indonesia reviewed the latest developments with regard to case management, prevention and control of DF/DHF recommended “Revised Regional Strategies for Prevention and Control of DF/DHF – July 2001” and further made recommendations for implementation of different elements in a time bound frame. These are briefly discussed below:

There are six basic elements of the revised regional strategies:

1. Establishing an effective disease and vector surveillance system based on reliable laboratory and health information systems;

2. Ensuring early recognition and effective case management of DHF/DSS to prevent case mortality;

3. Undertaking disease prevention and control through integrated vector management with community and intersectoral participation;

4. Undertaking activities to achieve sustainable behavioural changes and partnerships;

5. Establishing emergency response capacity to control outbreaks with appropriate medical services, vector control, communications and logistics, and

6. Strengthening regional and national capacities to undertake prevention and control of dengue and research related to epidemiology, disease and vector management and behavioural changes.

Recommendations

For Countries

(1) Passive and active surveillance for both DF and DHF should be developed or strengthened using WHO standardized case definitions and standard laboratory diagnostic methods and vector surveillance.

(2) A network of laboratories should be developed and strengthened to support
DF and DHF surveillance, including a national central laboratory to provide reference and quality control.

(3) An early warning system should be developed to predict, and an emergency response plan to control an epidemic.

(4) National guidelines on case management based on existing WHO guidelines should be developed and widely distributed and a programme for training all levels of medical personnel, both in the public and private sector drawn up.

(5) A National Expert committee on Case Management and Centre of Excellence for Case Management should be established.

(6) A situational analysis as a first step towards identification of risk behaviours and developing behaviour change strategies should be conducted.

(7) Social mobilization and communication activities that empower communities and establish/build on partnerships to prevent and control dengue should be initiated.

(8) With the coordination of WHO, a networking system for timely exchange of surveillance data using state-of-the-art information technology should be developed and implemented.

For WHO

(1) Effective implementation of the regional strategies for prevention and control of DF/DHF should be facilitated.

(2) Implementation of effective surveillance in the Region should be facilitated by convening a group of experts to draft standardized protocols and recommendations, soliciting outside donor support to help countries implement their programmes, and by establishing and strengthening the network of WHO collaborating centres for reference and research.

(3) Guidelines for case management of DF/DHF/DSS for nurses/paramedics should be developed and training for healthcare personnel continued to be provided through the intercountry network.

(4) Research and implementation of sustainable behaviour change activities in the Region should be facilitated through provision of technical support and intercountry networks to initiate social mobilization and communication activities.

(5) Collaborative studies on cost-effectiveness of vector control interventions and the socioeconomic burden of the disease should be undertaken.
Guidelines for Assessing the Efficacy of Insecticidal Space Sprays for Control of the Dengue Vector Aedes Aegypti

by

P Reiter and M B Nathan

WHO/CDS/CPEPVC/2001.1 – English only


The document lays stress on “how to carry out entomological assessments” of the impact of insecticidal space sprays on the main dengue vector, Aedes aegypti, and to guide them in that process.

All mosquito-collection methods have practical limitations and introduce sampling bias. The two methods recommended in these guidelines, infusion-baited ovitraps and backpack aspirator collections, sample different portions of the adult mosquito population. The former selectively monitors the activity of gravid, egg-laying females, whereas the latter monitors indoor resting females in all stages of the gonotrophic cycle. Both methods were developed to enable public health authorities to assess the impact of space spray applications of insecticides by monitoring the Ae. aegypti population on a daily basis.

Infusion-enhanced ovitraps are cheap and simple to operate, use minimal manpower, and are less reliant on skills and diligence. Collections from resting sites by backpack aspirator to monitor the adult population in a more direct way and provide material suitable for parous rate determination. However, they are more labour intensive, require higher skills and dedication, and are more intrusive to local inhabitants. If resources are available, the simultaneous use of both methods will increase confidence in the results.

Insight into the movement of aerosols in the target area can be obtained by cage bioassays but these are not a substitute for monitoring the effects of space sprays on the vector population.

The ultimate aim of operational evaluations is to determine whether space sprays are effective under local conditions, and if so, how often treatments must be applied in order to have an impact on dengue transmission. Local authorities should conduct such evaluations to determine whether space sprays are a useful public health intervention.
Criteria Used in Compiling the Infected Area List

Weekly Epidemiological Record 2001, 76(47): 371

Based on the International Health Regulations the following criteria are used in compiling and maintaining the infected area list (only official governmental information is used):

(1) An area is entered in the list on receipt of information of:
(a) a declaration of infection under Article 3;
(b) the first case of plague, cholera or yellow fever that is neither an imported case nor a transferred case;
(c) plague infection among domestic or wild rodents;
(d) activity of yellow-fever virus in vertebrates other than man using one of the following criteria:
   • the discovery of the specific lesions of yellow fever in the liver of vertebrates indigenous to the area; or
   • the isolation of yellow fever virus from any indigenous vertebrates.

(2) An area is deleted from the list on receipt of information as follows:
(a) if the area was declared infected (Article 3), it is deleted from the list on receipt of a declaration under Article 7 that the area is free from infection. If information is available which indicates that the area has not been free from infection during the time intervals stated in Article 7, the Article declaration is not published, the area remains on the list and the health administration concerned is queried as to the true situation;
(b) if the area entered in the list for reasons other than a declaration under Article 3 (see 1, (ii) to (iv) above), it is deleted from the list on receipt of negative weekly reports of the time intervals stated in Article 7. In the absence of such reports, the area is deleted from the list on receipt of notification of freedom from infection (Article 7) when at least the time period given in Article 7 has elapsed since the last notified case.

Health administrations are reminded that under the provisions of Article 3 of the International Health Regulations they should notify the Organization within 24 hours of being informed that the first case of a disease subject to the Regulations has occurred in their territory. The infected area should be notified within the subsequent 24 hours if not already communicated.

* http://www.who.int/wer
Health Conditions for Travelers to Saudi Arabia - Pilgrimage to Mecca (Hajj)
Weekly Epidemiological Record* 2001, 76(7): 54-55

The Ministry of Health of Saudi Arabia has issued requirements for the forthcoming Hajj season, as follows.

I. Yellow fever
(1) The following countries/areas are endemic for yellow fever:

**Africa**

**Americas**
Bolivia, Brazil, Columbia, Ecuador, French Guiana, Guyana, Panama, Peru, Suriname, Trinidad and Tobago and Venezuela.

All travellers arriving from countries known to be infected with yellow fever (as shown in the WHO Weekly epidemiological record) must present a valid yellow fever vaccination certificate in accordance with the International Health Regulations. In the absence of such a certificate, the person will be vaccinated upon arrival and placed under strict surveillance for 6 days from the day of vaccination or the last date of potential exposure to infection - whichever is earlier. Health offices at entry points will be responsible for notifying the appropriate Director-General of Health Affairs, in the region or governorate, about the place of the residence of the visitor.

(2) Aeroplanes and other means of transportation arriving from areas infected with yellow fever are requested to submit a certificate indicating disinsection in line with International Health Regulations.

II. Meningococcal meningitis
(1) For all arrivals

Visitors from all over the world arriving for the purpose of “Umra” or pilgrimage or for seasonal work in the Hajj areas are requested to produce a certificate of vaccination against meningitis issued not more than 3 years and not less than 10

* http://www.who.int/wer
Health Conditions for Travellers to Saudi Arabia – Pilgrimage to Mecca (Hajj)

days before arrival in Saudi Arabia. The responsible authorities in the country from where the visitor comes must ensure that vaccination has been carried as follows:

- adults and children over the age of 2 years must be given 1 dose of the A/C vaccine;
- children between 3 months and 2 years of age must be given 2 doses of the A vaccine with a 3-month interval between the 2 doses.

(2) Arrivals from countries in the African meningitis belt, namely


- It must be ensured that all visitors from these countries have been vaccinated in their countries, not more than 3 years and not less than 10 days before arrival. This should be documented on the vaccination certificate.
- Visitors from these countries will be checked at entry points to ensure that they are vaccinated. Suspect cases shall be isolated and preventive measures will be taken in respect of their direct contacts.
- If the authenticity of the vaccination certificate is felt to be questionable, revaccination is to be carried out.
- Chemoprophylaxis will be administered to all visitors from these countries to lower the carrier rate among them.

III. Epidemiological surveillance

Tight control is exercised at entry points in respect of pilgrims and “Umra” visitors, and through surveillance shall be made in respect of visitors coming from countries infected with diseases subject to the International Health Regulations, in addition to isolation of suspect cases and surveillance of their contacts.

IV. Foods

Foods carried by visitors and pilgrims are banned and not allowed into the country. Foods imported for commercial purposes shall be subject to the provisions of circulars No. 246/6/21 of 27/3/1408 (Hj); No. 274/6/21 of 11/4/1408 (Hj); and No. 1183/19 of 15/7/1410 (Hj).

The above, as well as all circulars issued in this respect, shall be strictly adhered to during the pilgrimage and “Umra” seasons.

Editorial note. The publication in the WR is to inform visitors of the full requirements for entry into the country; it does not mean an endorsement by WHO of all measures stipulated. Saudi Arabia is enforcing these measures in accordance with the International Health Regulations (1969), Third annotated edition, Part VIII, article 84 which states: “Migrants, nomads, seasonal workers or persons taking part in periodic mass congregations, and any ship, in particular small boats for international coastal traffic, aircraft, train, road vehicle or other means of transport carrying them, may be subjected to additional health measures conforming with the laws and regulations of each State concerned, and with any agreement concluded between any States”.

Malaria Vector Control - Insecticides for Indoor Residual Spraying

by

J. A. Najera and M. Zaim


Weekly Epidemiological Record 2001, 76(18): 140

WHO has just published a guide to the many complex factors that need to be considered when planning to use indoor residual spraying as an intervention for malaria control. This book, Malaria vector control - Insecticides for indoor residual spraying, draws on over 3 decades of extensive WHO experience and aims to help health authorities and programme managers know when residual spraying is an effective control measure and then select the most appropriate insecticides. With this goal in mind, the book covers both the general principles of residual spraying as part of a coherent control programme, and the distinct characteristics of specific insecticides. Throughout, emphasis is placed on the need to make decisions in line with a full understanding of the behaviour of malaria and its vectors with the local epidemiological situation.

The first chapter describes recent trends that underlie current WHO recommendations concerning the use of indoor residual spraying in malaria control. Against this background, the second and most extensive chapter sets out detailed criteria for the selection of insecticides. Purchasing guidelines are provided in chapter 3, which explains how to choose a good-quality product. Types of assistance available from WHO are also briefly described. The final chapter presents information on 11 insecticides recommended by WHO for indoor residual spraying for malaria control.

* http://www.who.int/wer
Instructions for contributors

The Dengue Bulletin welcomes all original research papers which have a direct or indirect bearing on dengue fever/dengue haemorrhagic fever prevention and control, including case management. Papers should not contain any political statement or reference. In addition to full papers, the Bulletin publishes short notes, review articles and book reviews.

Manuscripts should be typewritten in English in triple space on one side of white A4 size paper, with a margin of at least 4 cm. on either side of the text and should not exceed 15 pages. The title should be as short as possible. The name of the author(s) should appear after the title, followed by his or her official position, name of institution and complete address.

References to published works should be listed on a separate page at the end of the paper. References to periodicals should include the following elements: name and initials of author(s); title of paper or book in its original language; complete name of the journal, publishing house, or institution concerned; volume and issue number, relevant pages and date of publication, and place of publication (city and country). References should appear in the text in the same numerical order (Arabic numbers in parenthesis) as at the end of the article. For example:


Figures and tables (Arabic numerals), with appropriate captions and titles, should be included on separate pages, numbered consecutively, and attached at the end of the text with instructions as to where they belong.

Articles should include an abstract of not more than 300 words conveying the content of the paper and its main conclusions; an introduction explaining clearly why the work described was carried out and what it is expected to contribute to scientific and technical knowledge; and conclusions and recommendations, if pertinent.
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One hard copy, original and clear figures/tables and a computer diskette indicating the name of the software, of the manuscript should be submitted to:

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