INTRODUCTION

The Expert Panel comprising local and international experts was formed on 14 Sep 2005 to undertake an independent review of the present dengue situation and to advise the government of Singapore on additional prevention and control measures. The panel has looked into the epidemiological features of the current outbreak, conducted field trips to observe dengue control operations and reviewed the national framework for dengue control. This report examines the dengue control programme in the light of the recent recrudescence of the disease, and presents a summary of key findings and recommendations to remedy the present problem. The objective of the review is to facilitate a quantum leap improvement in the disease situation.

Scope of the report

Chapter 1   Background on the disease  
Chapter 2   Epidemiology of dengue in Singapore  
Chapter 3   Dengue control operations in Singapore  
Chapter 4   Critique of present situation and strategies in dengue control  
Chapter 5   Conclusions and recommendations  
Appendix   Terms of reference and composition of the Expert Panel  

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Chapter 1

BACKGROUND ON THE DISEASE

1 AETIOLOGY OF DENGUE

1.1 Dengue fever/dengue haemorrhagic fever is a mosquito-borne viral disease. The causative agent is the dengue virus, of which there are four circulating serotypes identified as DEN-1, 2, 3 and 4. Because of this, a person can be infected more than once. Molecular evidence shows that there are strain differences within each serotype that may confer some viruses with greater epidemic potential than others.

1.2 The virus is transmitted through the bite of an infected female *Aedes* mosquito. The primary role of *Aedes aegypti* in dengue transmission is well established, together with the secondary role of *Aedes albopictus*. The female mosquito becomes infected when it feeds on an infective blood meal from a viraemic human. The virus then undergoes a period of 8-10 days development when it multiplies in the mosquito salivary gland. Thereafter, the mosquito becomes infective and continues to harbour the virus for the rest of its life.

1.3 The *Aedes* mosquito is highly adaptable and can exploit hard-to-find habitats in the urban environment so well that it forms an excellent vector, or transport system, for the virus to infect humans. This black and white striped urban mosquito is a day-time biter with two peaks of biting activities, one about two hours after sunrise and the other a few hours before sunset.

2 CLINICAL FEATURES

2.1 The incubation period of dengue is commonly 4-7 days but ranges from 3-14 days. A primary infection occurs in a person who has never been infected with any of the dengue viruses, and a secondary infection, in a person who has been previously infected with one or more serotypes of dengue.

2.2 Not all people who are infected will have symptoms. In those who do, dengue fever is the commonest form which typically presents as a mild flu-like illness, with fever and a rash which gives a flushed appearance to the skin. In more severe cases with dengue haemorrhagic fever, there is an increased tendency to bleed and this can occur as tiny points under the skin, mucous membrane of the mouth, or the conjunctiva. Massive bleeding could occur suddenly, and lead to shock and even death. Another cause of shock and death is the leakage of a blood component known as plasma into the lungs and other organs.

2.3 The presenting symptom is usually a fever which corresponds with blood-borne dissemination of the virus (viraemia) and lasts 3-5 days. It is during this time that isolation of the virus from the infected person is most successful. Viral antigen can be detected during the same period. If complications arise, they usually occur as the fever subsides, and it is about this time that antibodies begin to appear (in a primary infection) or rise (in a secondary infection).
2.4 Tests for blood antibody levels can give the clinician confirmation of dengue virus infection. IgM antibodies appear around the fifth day of the illness, rise for 1-3 weeks and last for 60-90 days. IgG antibodies appear by the 14th day in primary infections and the second day in secondary dengue and can usually be detected for life. Therefore, serological diagnosis for a primary dengue infection is possible only after the fifth day of illness by IgM antibody detection, but is possible after the second day of illness for secondary infections because of the rapid rise in IgG antibody.

3 A RE-EMERGING DISEASE GLOBALLY

3.1 While dengue fever has been around since the 18th century, dengue haemorrhagic fever emerged only after World War 2. Scientists believe that it was the devastation of war, political upheaval, and mass migration of refugees which caused Southeast Asia to become endemic with all four dengue viruses. This paved the way for recurrent infections which were more severe.

3.2 The global prevalence of dengue has grown dramatically in recent decades. Before 1970, only nine countries had experienced dengue haemorrhagic fever epidemics, a number that increased more than four-fold by 1995. The disease is now endemic in more than 100 countries in Africa, the Americas, the Eastern Mediterranean, Southeast Asia and the Western Pacific regions. Southeast Asian and Western Pacific countries are among the most seriously affected.

3.3 Some 2.5 billion people - two fifths of the world’s population - are now at risk from dengue. Based on estimates by the World Health Organization, there are 50-100 million cases of dengue infection worldwide every year. About 500,000 cases of dengue haemorrhagic fever require hospitalization, of whom a very large proportion are children. At least 2.5% of cases die, although case fatality could be twice as high. Without proper treatment, dengue case fatality rates can exceed 20%. With modern intensive supportive therapy, such rates can be reduced to less than 1%.

3.4 According to the US Centers for Disease Control and Prevention, the reasons for the dramatic global emergence of dengue as a major public health problem are complex but four important factors can be identified.

3.5 Firstly, major global demographic changes have occurred, the most important of which have been uncontrolled urbanization and concurrent population growth. These demographic changes have resulted in substandard housing and inadequate water, sewer, and waste management systems, all of which increase Aedes aegypti population densities and facilitate transmission of Aedes aegypti-borne disease.

3.6 Secondly, the public health infrastructure has deteriorated in many countries. Limited financial and human resources and competing priorities have resulted in a "crisis mentality" with emphasis on implementing so-called emergency control methods in response to epidemics rather than on developing programmes to prevent epidemic transmission. This approach has been particularly detrimental to dengue control because, in many countries, surveillance is passive; the system to detect increased transmission normally relies on reports by local physicians who often do not consider dengue in their differential diagnoses. As a result, an epidemic has often reached or passed its peak before it is recognized.
3.7  Thirdly, increased travel by airplane provides the ideal mechanism for infected human transport of dengue viruses between urban centres of the tropics, resulting in a frequent exchange of dengue viruses and other pathogens.

3.8  Lastly, effective mosquito control is virtually nonexistent in many dengue-endemic countries. Considerable emphasis in the past had been placed on ultra-low-volume insecticide space sprays for *Aedes aegypti* adult mosquito control, a relatively ineffective approach for interrupting epidemic dengue transmission.
Chapter 2

EPIDEMIOLOGY OF DENGUE IN SINGAPORE

1 CHANGING EPIDEMIOLOGY

1.1 In Singapore, dengue is endemic with year-round transmission. The disease was first recognized as a public health problem in the 1960s when our nationwide Aedes control programme was implemented. The programme basically integrated larval source reduction with public health education, and backed this by law enforcement. The soundness of such a comprehensive strategy is still considered by many experts as a model for the rest of the world. This programme resulted in a marked decline in dengue incidence which coincided with a drop of the overall Aedes house index (percentage of houses positive for Aedes breeding) from over 25% to the present 1-2%. Despite the low Aedes house index, however, outbreaks recurred from 1989 with a discernible seasonal increase in the second half of each year.

1.2 The incidence of dengue has increased from a baseline of 9.3 cases per 100,000 population in 1988 to 108.5 cases per 100,000 population fifteen years later in 2003. Unlike the epidemic in 1973 when children aged 5-14 years were the highest risk group, 65-68% of the cases today are in young adults aged 15-44 years. This trend is also seen among the reported death cases. Compared to 1973 when virtually all the fatal cases were below 10 years of age, majority of the serologically confirmed deaths today involve adults.

1.3 The previous patterns of dengue have been replaced by almost annual epidemics of progressively larger order of magnitude. The surge in cases since the late 1980s could be seen to peak every six years in 1992, 1998 and 2004 followed by short periods of respite. All four dengue serotypes have been detected from the blood samples of infected persons, with DEN-3 predominating in 1992, DEN-2 in 1998 and DEN-1 in 2004. Outbreaks in the 1960s and 1970s had occurred in the urban slums and resettlement areas whereas the more recent outbreaks were traced to landed areas and construction sites.

2 SEROLOGICAL EVIDENCE OF CHANGE

2.1 Dengue outbreaks occur when there is a highly susceptible population living in an area where the dengue virus is circulating, usually preceded by a gradual localized build-up of Aedes mosquito density. To assess the impact of the Aedes control programme on the prevalence of dengue infection in the general population, sero-epidemiological surveys were conducted in 1982-84, 1990-91, 1993 and 1998. These surveys showed that the overall immunity level of the population continued to decline from 46% in 1982-84 to 39% in 1993 to 29.4% in 1998. The prevalence of antibody was lowest among children and young adults, and this corresponded to the age groups with higher risk in the current outbreak.

2.2 Based on the sero-epidemiological evidence, it would appear that the effective Aedes control programme implemented in Singapore during the last three decades has brought about a paradoxical situation in that outbreaks tend to occur more
frequently and with greater intensity because of the low herd immunity of the human population against dengue virus infection.

3 THE CURRENT EPIDEMIC

3.1 As at 24 Sep 2005, a total of 10,951 dengue cases have been reported this year, exceeding all previous records for annual disease incidence. In the first half of the year, we saw an average of 204 dengue cases per week. An uptrend in disease incidence was first noted during the month of May and this reached 546 cases in the last week of Aug.

3.2 In terms of circulating virus strain, DEN-1 remains as the predominant strain even though DEN-3 has become more prevalent in recent months. The predominant circulating dengue virus serotype had shifted from DEN-2 in 2001-2003 to DEN-1 in 2004-2005.

3.3 Among cases, the male-to-female ratio was 1.4:1 with adults aged 15–44 years representing 65% of all reported cases. The highest age-specific incidence was in the 15-24 years age group while the lowest was in those under 5 years. As a proportion of the reported cases, the 5-14 years age group registered significant increase from 9% in 2003 to 13% in 2005.

3.4 Majority (99%) of the infections were acquired locally. There has been an expansion in the geographical distribution of dengue outbreaks recently, from traditional landed areas in the eastern and south-eastern sectors of the island to new areas in the western and northern sectors where public housing estates are located. Whereas Housing and Development Board (HDB) flat dwellers represented 46-65% of reported dengue cases annually in the past, this proportion has increased to 75% in 2004 and 2005.

3.5 We observed two significant epidemiological findings in this epidemic. The first is a marked increase in dengue cases among HDB flat dwellers which shot up threefold from 2003 to 2004, with no corresponding change noted for residents of landed property and private flats. Compared to previous epidemics in 1992 and 1998, these were increases of 275% and 100%, respectively. We assessed the contribution caused by a greater influx of susceptible persons into more dengue prone HDB estates but this could not account for the sizable increase in recent years. The second feature is a shift in the distribution of dengue to involve more active young adults aged 15-24 years as well as school children aged 5-14 years. The shift was more marked for males than females. This shift towards the younger age groups bucks the historical pattern that occurred from 1980-2000. Taken together, the two features suggest an increase in infections acquired outside the homes in our public housing estates.

4 HEALTH IMPACT OF THE EPIDEMIC

4.1 To date, there have been 12 reported dengue deaths this year, giving a case fatality of 1.1 per 1,000 cases. Case fatality rate has declined over the past 5 years. In 2004, the case fatality rate was less than 1 per 1,000 cases.
The proportion of dengue haemorrhagic fever in total dengue notifications has remained low at 0.6-6% over the past 20 months from Jan 2004-Aug 2005. Dengue haemorrhagic fever contributed to 3.2% and 2.1% of all reported cases in Jul and Aug this year, respectively. Data from the Centre for Transfusion Medicine show that platelet transfusions for dengue accounted for more than 10% of all such transfusions in Jun 2005 (423 out of 4,017 units transfused). The number of platelet transfusions for dengue increased 48% from 286 units in Jan 2005 to 423 units in Jun 2005.

4.2 The number of dengue hospitalizations was relatively low from late-2004 until May 2005 when a sharp increase was observed, corresponding with the increase in reported cases. On average, 88% of monthly admissions were to public-sector hospitals and almost 80% of the public-sector hospital admissions were to Tan Tock Seng Hospital (37%), Changi General Hospital (24%) and Singapore General Hospital (19%). As at mid-Sep, the average bed utilization (ie, total beds occupied by ‘dengue’ and ‘suspect dengue’ patients as a percentage of total beds in service) has ranged between 2% (KK Women and Children’s Hospital, average of 18 patients per day) and 8% (Alexandra Hospital, average of 29 patients per day). TTSH recorded the highest absolute number of beds occupied at 87 per day. Average bed occupancy in public sector acute hospitals increased from 82% in Dec 2004 to 84% in Jun 2005. In June 2005, Changi General Hospital recorded the highest average bed occupancy rate of 92%, followed by Tan Tock Seng Hospital (89%), Alexandra Hospital (87%), Singapore General Hospital (86%) and National University Hospital (84%).
1 MODELLING EPIDEMIC CONTROL

1.1 Mathematical modelling can provide the theoretical basis to formulate the best approach for dengue prevention and control. Transmission dynamics is a function of the basic reproduction number, defined as the number of secondary infections produced by a single infected person in an entirely susceptible population during the infectious period. If an infection is unable to produce at least one secondary infection, the disease will die out. This is the aim of every control programme.

1.2 In order to estimate the impact of alternative control strategies, we looked at sensitivity analysis of the reproduction number to the following parameters: biting rate, herd immunity, egg carrying capacity and mosquito mortality rate. A paucity of entomological and climatological data limited the conclusions because the model outcome is a logical corollary of its assumptions.

1.3 Nonetheless, in terms of epidemiological model parameters, the force of infection (ie, periodicity of dengue epidemics) can be seen as a product of: (1) number of *Aedes* vector mosquitoes per person, (2) their biting rate, (3) vector competency, and (4) prevalence of infected female mosquitoes. Search and destroy operations of larval breeding habitats reduce (1) and adulticidal fogging reduce (4), while (2) and (3) are difficult to alter because they represent biological properties of the mosquito. Patients are viraemic during the febrile stage of disease and can serve as reservoirs of infection that transmit dengue through the mosquito vector. Precautionary measures taken by these patients to prevent mosquito bites (eg, use of insect repellents as a form of chemical quarantine) would help reduce (4).

2 THE *Aedes* CONTROL PROGRAMME

2.1 The *Aedes* control programme in Singapore consists of three key elements – active surveillance, public education and community involvement, and enforcement.

2.2 Active surveillance. The National Environment Agency (NEA) conducts active surveillance in areas prone to dengue and/or high density of mosquitoes (e.g. construction sites, schools, compounds of landed properties). On the average, some 40,000 residential premises and 900 non-residential premises and grounds (construction sites, schools, etc.) are inspected every month. Areas that are prone to dengue constitute about 10% of Singapore’s land area, and are surveyed once in every six months. Surveillance operations are coordinated through the Situation Room located at NEA HQ, using a Geographical Information System (GIS), to monitor and analyze the distribution of *Aedes* mosquitoes and dengue cases.
2.3 **Public education and community involvement.** NEA carries out public education on dengue through posters at bus shelters and MRT Stations, panels in MRT and LRT trains, advertisements in newspapers, and dengue messaging on radio. For private and public organizations (e.g. schools, construction sites), NEA works with them to put in place dengue control programmes, for example, the Environmental Control Officers programme for construction sites. In Apr 2004, the ‘Mozzie Attack’ programme was launched with the aim to encourage residents to get rid of stagnant water that can potentially breed mosquitoes in their homes. The programme has successfully rolled out in all 84 constituencies in Singapore. NEA also keeps the grassroots and other agencies updated regularly, and actively engages the members of the public as well as other key strategic partners such as the Community Development Councils\(^1\) in the common fight against the *Aedes* mosquito. NEA has also assisted in the formation of Dengue Prevention Volunteer Groups to further bring the dengue prevention message to the grassroots.

2.4 **Enforcement.** The Control of Vectors and Pesticides Act is the main legislation dealing with propagation of conditions conducive for mosquito breeding. NEA typically enforces the law against recalcitrant persons who continually breed mosquitoes or do not remove potential mosquito breeding habitats in their premises despite having being told to do so. Owners of residential premises found with mosquito breeding are fined $100 for the first offence and $200 for repeat offences. For non-domestic premises (e.g. commercial buildings and temples) found with mosquito breeding, the owner of the premises will be fined $200. The corresponding penalties for construction sites are heavier (starting at $2,000), given the greater propensity for breeding to be found in these premises.

3 **NEA’S KEY OPERATIONAL STRATEGIES IN DENGUE CONTROL**

3.1 Currently, Ministry of Health (MOH) notifies NEA of suspected/confirmed dengue cases. When dengue cases are reported in an area, the NEA will carry out search and destroy and fogging operations at the affected locality and the immediate neighbourhood quickly, to break the disease transmission by preventing more mosquitoes from breeding through removal of all breeding sources as well as killing the adult mosquitoes present which could be carrying the dengue virus. When a dengue cluster (i.e. 2 or more dengue fever cases within 150 metres of their respective residential/workplace addresses and within 14 days of their respective onset dates) is reported, the NEA will send in an outbreak control team to thoroughly comb the area and carry out fogging and checks until the cluster is closed. NEA will also alert the residents and rope in the grassroots organizations to help in an immediate outreach programme to get the residents in the affected area to remove the breeding habitats in their homes. About 88% of the clusters are closed within 14 days from the onset date of the last reported case. However, clusters accounted for only about a third of the reported cases.

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\(^1\) A Community Development Council is a committee that is appointed in each of the five Districts in Singapore (each District comprising one or more electoral constituencies). Chaired by a Mayor, it functions as a local administration of its District, initiating, planning and managing community programmes to promote community bonding and social cohesion.
4 CURRENT RESEARCH IN SINGAPORE

4.1 An Environmental Health Institute (EHI) was established in Apr 2003 and undertakes research on vector-borne diseases. Staffed with 6 post-graduate degree (PhD and Masters) holders that specialize in entomology, microbiology and immunology, and 20 bachelor graduates and diploma holders, EHI works on 4 programmes: Vector Control, Epidemiology, Surveillance and Diagnostics.

4.2 **Vector Control.** The vector control programme seeks to understand the behaviour of mosquitoes, and develop and evaluate vector control tools and measures. Following are some examples of the findings.

- **Flight range.** Research has shown that *Aedes* mosquitoes in Singapore have a flight range of at least 560m in urban setting, and 740m in rural areas. This is in contrast to traditional belief that they do not fly more than 100m. In addition, it was also found that the *Aedes* mosquitoes could disperse through all 21 floors of an apartment block after their release from the 12th floor. Their competence in long-range flight for oviposition (laying eggs) may suggest that the successful minimization of potential breeding sites in Singapore has forced them to go further for oviposition.

- **Aedes adaptation.** A study has demonstrated the ability of *Aedes* mosquitoes to adapt. Mosquitoes bred from clean water had preference for clean water for oviposition. However, when bred in water with repellent, the new generation of *Aedes* showed no preference between clean water and water with repellent.

- **New vector control tools and strategies.** Besides introducing environmentally friendly and effective biological agents (Bti) for control, a gravitrap (lethal ovitrap) for trapping both larvae and adults of *Aedes* mosquitoes has been developed. Feasibility test on such a mosquito control method will be conducted after mass production of the traps in 3 months’ time. Meanwhile, a pilot study will be conducted, using conventional ovitraps for monitoring *Aedes* population, and possibly for controlled breeding. Community participation will be considered for this pilot.

- **Effectiveness of insecticides.** Efficacy and resistance testing are regularly done to ensure that the 2 major mosquitoes (adults and larvae) in Singapore, *Culex* and *Aedes*, are susceptible to the chemicals used.

- **Transgenic mosquitoes for vector control.** As a long-term project, EHI is working with OxiTech (UK) and Oxford University, to explore the use of dominant lethal male *Aedes* to control mosquito population to a lower level.

4.3 **Epidemiological Research.** The research programme aims to understand the transmission dynamics of dengue in Singapore. Dengue occurs in cycle within the year, usually peaking in the hottest months of June to August, like in other countries in the region. However, last year, we were hit by an unusual cycle, which lasted till Feb 2005. As a result, at the lowest point in Apr 05, the number of human
cases remains as high as the peaks of 2002 and 2003. Data from the previous years is currently under analysis to gain a better understanding of the situation.

- **Cluster analysis on transmission and proportion of un-notified dengue cases.** Transmission dynamic within a cluster is analyzed to support operations.

- **Sero-prevalence.** Antibody tests are performed on volunteers to determine the level of immunity to dengue, within a population. The project also seeks to determine the proportion of asymptomatic and undiagnosed cases.

- **Virus analyses.** Singapore sees regular importation of dengue cases. Nucleotide sequencing of part of the viruses has been performed on isolates of DEN-1, 2 and 3 from recent years, to understand the impact of importation. Phylogenetic analysis shows that majority of each serotype clusters tightly in a group, suggesting local transmissions. More sequencing will be performed to determine when the virus was introduced. In addition, aided by experiments in human cell line and mosquitoes, we seek to determine the epidemic potential of the viruses.

4.4 **Surveillance.** Surveillance seeks to monitor the re-emergence of new serotypes and emergence of new strains of dengue virus.

- **Spatial and temporal distribution of the four serotypes of dengue.** A PCR serotyping technique, which has increased the throughput of serotype surveillance, has been developed. Ongoing surveillance and research projects have shown a non-uniform distribution of serotypes in Singapore. As a result, a collaborative project has been initiated among MOH, NEA and Tan Tock Seng Hospital to understand the distribution of the 4 serotypes, and possibly understand the impact of the emergence of new serotype in a region.

- **Sequencing of viruses.** Working with the Dengue Consortium which comprises the Genome Institute of Singapore and other institutions, EHI commenced on whole genome sequencing to detect emergence of a new strain, and mutations that may have altered the properties of the virus.

- **Survey of Aedes larvae for dengue virus.** Besides viruses from humans, a project on isolation of dengue virus from Aedes larvae has been initiated. Adult female Aedes is known to be able to transmit dengue virus to its eggs, which subsequently develops into infected larvae. Though the rate of transmission is reportedly less than 3%, EHI will test the feasibility of using its in-house developed PCR for such purpose.

4.5 **Diagnostics.** Laboratory diagnosis of dengue fever serves a number of functions: management of patients; outbreak control; and epidemiological surveillance. Working very closely with various hospitals like Tan Tock Seng Hospital, National University Hospital and KK Women and Children’s Hospital, EHI has developed diagnostic tools to target the various stages of the disease.
4.6 In addition, there are various research projects conducted at Tan Tock Seng Hospital, which seek to understand the disease, eg, to determine any predictors of dengue haemorrhagic fever, and the pathogenicity of ocular manifestation among some dengue patients.
1 OBSERVATIONS

1.1 The salient findings of the panel on the present dengue situation are as follows:

- The current epidemic of dengue in Singapore is unprecedented and coincides with the regional increase in incidence of the disease.

- Because dengue is a resurgent problem in the region, the introduction of dengue viruses to Singapore can be expected to occur on a regular basis. If *Aedes aegypti*, the principal vector mosquito, is present in the city, outbreaks are likely to occur.

- The highly successful dengue control programme in Singapore is one of the best in the world and has resulted in sustained suppression of the *Aedes aegypti* vector. In spite of this, the incidence of dengue has been increasing in recent years.

- Transmission persists in Singapore because the principal vector mosquito, *Aedes aegypti*, exists in the presence of a high human population density. The role of other factors such as the importation of exotic strains of virus and the low herd immunity is unclear.

- In the urban environment, the *Aedes aegypti* vector is highly adaptable and exploits hard-to-find habitats. This problem requires focused research on the biology and behaviour of the vector mosquito and enhanced efforts to identify and destroy new habitats.

- It is a common perception that most dengue transmission occurs at home. However, recent epidemiological evidence indicates that significant transmission also occurs at sites away from the home.

- Current emphasis on active clusters may be an oversimplification of transmission dynamics. This limits the effectiveness of vector control measures, because 60-70% of all notifications occur outside of known clusters and in some instances transmission is not reported.

- Infected people can infect mosquitoes with dengue viruses 24-48 hours prior to onset of symptoms. In addition, asymptomatic people may also infect mosquitoes. The high mobility of the Singapore population and the local dispersal of mosquitoes mean that the virus may be widespread in the community before it is reported; an additional reason why control efforts should not be focused solely on clusters.
The success of the Singapore programme has reduced *Aedes aegypti* populations to such a low level that conventional methods of assessing populations such as the house index are no longer sufficient. New and innovative means of detecting the presence of the mosquito are required.

An increase in *Aedes aegypti* populations is not always a pre-requisite for increased dengue transmission.

Efforts to reduce mosquito populations during inter-epidemic periods may be highly effective in preventing epidemic transmission.

Community participation has been, and will continue to be an important component of effective *Aedes aegypti* control in Singapore.

Recent evaluation of fogging to kill adult *Aedes aegypti* mosquitoes, as practised by many dengue-endemic countries, has revealed that it is ineffective in stopping epidemic transmission.

2 WHAT ARE THE GAPS IN DENGUE SURVEILLANCE AND CONTROL?

2.1 There is worldwide recognition that the Singapore dengue control programme is one of the best in the world. Nevertheless, the recent recrudescence of epidemic dengue suggests that the programme is faltering. New approaches and enhanced efforts are required.

2.2 The Singapore dengue control programme should be reconstituted as a focused vector control and research unit. This programme should be directed by a single individual responsible for vector control operations and research, and empowered to access national surveillance data. This programme should be adequately staffed by dedicated vector control personnel.

2.3 Epidemiologists and operational staff within the vector control unit should be empowered under the relevant sections of the Infectious Diseases Act to conduct investigations of dengue cases to facilitate targeted control operations on the ground. In our opinion:

- The biggest gap is definitive leadership within the programme
- The programme should be strengthened by a greater emphasis on creative research
- All strategies should be tailored to fit the unique Singapore environment

2.4 Above all, there is an urgent need for effective coordination, communication and data sharing between epidemiologists, surveillance and operational control officers.

Disease surveillance

2.5 The system lacks:

- The ability to detect and monitor the introduction of new strains of dengue virus that may have greater virulence or epidemic potential
• Standardized case detection and disease monitoring protocols (perhaps we are not aware of such a system?)
• Structured integration of the medical community and the surveillance system (again, we may not be aware of this)
• Continuing medical education of physicians and nurses on clinical diagnosis and management of severe dengue

Entomological surveillance and control

2.6 In our opinion, there is insufficient entomological expertise at the regional office level. Ideally, each regional office should have a PhD level entomologist directing research, control and evaluation activities. In addition:
• We question whether there are sufficient field inspectors in view of Singapore’s increasing human population
• We strongly recommend stricter supervision and evaluation of the field inspectors
• Larval habitats should be thoroughly mapped and followed using the Geographical Information System
• Entomological surveillance should be improved in order to detect low populations of mosquitoes
• There should be an enhanced capacity to pinpoint cryptic breeding sites and sites of infection
• There is an urgent need to monitor the adult mosquito population
• Evaluation of the efficacy of adult mosquito control operations must be a priority

Dengue cluster management

2.7 We see no value in using polymerase chain reaction tests to improve the effectiveness of cluster-focused dengue control. We suggest that case management based on suspected case reports and epidemiologic investigation would be a much more effective strategy.

Adulticidal fogging for control of epidemics

2.8 Fogging is unlikely to have any impact on the adult population except when applied indoors. However, practical restraints make it unlikely that such treatments could have major impact during an epidemic

Use of biological controls

2.9 Biological approaches to mosquito control (e.g., use of larvivorous fish, dragonflies, copepods) are effective under certain conditions. Unfortunately, in the urban Singapore environment, such methods are not applicable.

Use of chemical repellents

2.10 The public should always be encouraged to use personal protection measures such as chemical repellents on exposed skin and clothing. However, there are no good data to show that this has impact on dengue transmission, including use on symptomatic patients
Use of quarantine

2.11 Viraemic people can infect mosquitoes with dengue viruses 24-48 hours prior to onset of symptoms. In addition, asymptomatic people may also be infective. The high mobility of the Singapore population and local dispersal of mosquitoes mean that the virus may be widespread in the community before it is reported. For these reasons, quarantine of dengue patients would have little or no value.

3 EARLY WARNING SYSTEM FOR DENGUE

3.1 Effective early warning surveillance for epidemic dengue requires an active, laboratory-based disease surveillance system. We feel that Singapore needs a more structured dengue control programme that should include the following components:
   - A laboratory-based active disease surveillance system that can predict epidemic activity
   - An emergency response plan for epidemic activity
   - A continuing medical education programme to educate physicians and nurses on clinical diagnosis and management of severe dengue
   - An integrated, community-based mosquito control programme
   - New and more reliable methods for monitoring the adult mosquito population. These would be used to detect changes in the adult mosquito population and to direct targeted operational control
   - Conventional and lethal ovitraps to monitor mosquito populations, particularly when these are low (lethal ovitraps may also have potential as a mosquito control device)

3.2 Operational research should be guided by epidemiological and entomological research.

4 COMPARISON OF STRATEGIES

4.1 On the issue of how different Singapore’s strategies (and results) are when compared to other urban centres such as Hong Kong, we note that there is little resemblance between the programmes because dengue is not endemic in Hong Kong where most cases are imported and the virus is transmitted by *Aedes albopictus* (*Aedes aegypti* is absent). In Taiwan, where dengue is restricted to the southern part of the island, is transmitted by *Aedes aegypti* and is probably endemic, the situation is more similar. However, in Taiwan, there is very close working collaboration between their Ministry of the Environment and Ministry of Health. Moreover, Taiwan has a national public health laboratory that is responsible for laboratory-based disease surveillance. We recommend exchange visits between Singapore and Taiwan.
CONCLUSIONS AND RECOMMENDATIONS

1  PREAMBLE

1.1  There is global recognition that the Singapore dengue control programme is the best in the world and has resulted in sustained suppression of the *Aedes aegypti* vector for three decades.

1.2  Because dengue is a resurgent problem globally, the introduction of dengue viruses to Singapore can be expected to recur on a regular basis. If *Aedes aegypti*, the principal vector mosquito, is present in the city, epidemics are likely to occur.

1.3  The current epidemic of dengue in Singapore coincides with the regional increase in incidence of the disease. The causes of this epidemic may include the importation of new strains of dengue virus with greater epidemic potential into the densely populated city. In addition, the prior success of the Singapore dengue control programme has resulted in a highly susceptible human population. We stress however, that transmission cannot exist without the presence of the principal vector mosquito *Aedes aegypti*, which is highly adaptable and exploits hard-to-find habitats in the urban environment.

1.4  The solution to this problem requires increased focus on epidemiological and entomological research for even more effective targeted dengue control operations.

2  SHORT-TERM COST-EFFECTIVE STRATEGIES

2.1  Effective prevention and control of epidemic dengue requires an active laboratory-based disease surveillance programme to provide early warning for epidemic transmission. Laboratory methods should include the latest technology in both serological and virological diagnosis. Quality control for this programme should be provided by a national reference laboratory for infectious diseases.

2.2  A continuing medical education programme should be implemented to increase the knowledge of physicians on clinical diagnosis, management, prevention and control. They should be encouraged to help educate the population on their responsibilities in dengue control activities. Feedback of surveillance data to the medical community is important.

2.3  It is a common perception that most dengue transmission occurs at home. However, recent epidemiological evidence indicates that significant transmission also occurs at sites away from the home. Current emphasis on active clusters does not provide an adequate understanding of transmission dynamics. This limits the effectiveness of vector control measures, because in the present situation, it appears that 60-70% of all notifications occur outside of known clusters and in some instances transmission is not reported. Dengue control should be driven by entomological, epidemiological, operational and formative research, and should not rely solely on identification on response to active clusters. In addition, efforts to reduce mosquito
population during inter-epidemic periods may be highly effective in preventing epidemic transmission.

2.4 The success of the Singapore programme has reduced *Aedes aegypti* populations to such a low level that conventional methods of assessing populations such as the house index are no longer sufficient. Moreover, an increase in *Aedes aegypti* populations is not always a pre-requisite for increased dengue transmission. Emphasis should now be placed on new and innovative methods of entomological surveillance to assess the impact of control activities on *Aedes aegypti* populations. For example, ovitraps and/or lethal ovitraps developed by NEA and others will be used to detect and eliminate low-density *Aedes aegypti* populations in various settings.

2.5 Feedback to the community on mosquito populations should be explored as a mechanism to stimulate community participation in control activities.

2.6 Continued efforts to enhance dengue control by the private sector should be emphasized, including social mobilization and mosquito control. For example, the NEA programme to create community ownership of the control programme by town councils contracting to the private sector is strongly endorsed by the committee.

2.7 Indoor fogging may be very effective in killing adult *Aedes aegypti*. However, recent evaluation of this approach to stop epidemic transmission, as practiced by many dengue-endemic countries, has revealed that it has limited efficacy in stopping epidemic transmission. The effectiveness of ultra-low volume and thermal fogging to control adult *Aedes aegypti* must be evaluated. Mosquito control activities, including those by private pest control operators, must continue to be subjected to stringent and improved quality control measures using new techniques.

3 LONG-TERM COST-EFFECTIVE STRATEGIES

3.1 In the longer term, we recommend the following strategies:
- Maintain *Aedes aegypti* populations at a low level in Singapore that will prevent epidemic dengue transmission
- Use vaccines and antiviral drugs when they become available
- Use new validated technologies as they become available

4 WHAT THE PUBLIC CAN DO IN DENGUE PREVENTION AND CONTROL

4.1 Effective long-term control of dengue requires community ownership. Therefore community participation will continue to be an important component of effective *Aedes aegypti* control in Singapore. The inclusion of grassroots organizations in surveillance of adult mosquitoes, e.g. by lethal ovitraps, should be explored.

4.2 Regular indoor use of insecticide sprays may prevent dengue transmission in the home. Use of personal protection measures such as repellents and mosquito nets may also prevent dengue transmission in the home.
Appendix

TERMS OF REFERENCE AND COMPOSITION OF THE EXPERT PANEL

TERMS OF REFERENCE

1. Review the current dengue situation in Singapore and identify possible causes for the resurgence
2. Identify gaps in dengue surveillance and control
3. Recommend operational research to address the gaps identified
4. Recommend short-term and long-term cost-effective strategies in the prevention and control of dengue

COMPOSITION

Members of the Expert Panel are:

- Dr Chee Yam Cheng, Clinical Professor and Assistant Chief Executive Officer, National Healthcare Group - Chairman
- Dr Helen Oh, Senior Consultant in Communicable Diseases, Dept of Medicine, Changi Hospital
- Dr Duane Gubler, Professor of Tropical Diseases, Director of the Asia-Pacific Institute for Tropical Medicine and Infectious Diseases, and Chair of the Dept of Tropical Medicine and Medical Microbiology, University of Hawaii at Manoa, USA
- Dr Paul Reiter, Professor of Entomology, Insects and Infectious Diseases Unit, Pasteur Institute, France
- Dr Eduardo Massad, Professor of Medical Informatics, University of Sao Paulo School of Medicine, Brazil
- Dr Goh Kee Tai, Clinical Associate Professor and Senior Consultant in Communicable Diseases, Ministry of Health - Secretary
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- Dr Steven Ooi Peng Lim, Associate Professor and Deputy Director (Disease Control), Ministry of Health - Rapporteur
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