31st year of publication

Epidemiological News Bulletin

QUARTERLY

JANUARY - MARCH 2005 VOL. 31 NO. 1 A PUBLICATION OF THE MINISTRY OF HEALTH, SINGAPORE

CONTENTS

Suggested citation:
Ministry of Health, Singapore. [Article title]. Epidemiol News Bull [Year]; [Vol]:[inclusive page numbers]

MOH Weekly Infectious Diseases Bulletin
http://www.moh.gov.sg/corp/publications/idbulletin

ISSN 0218-0103

http://www.moh.gov.sg/corp/publications/enb

Dengue surveillance in Singapore, 2004

A total of 9,459 laboratory confirmed cases of dengue [comprising 9291 cases of dengue fever (DF) and 168 cases of dengue haemorrhagic fever (DHF)] were reported in 2004, an increase of 97.6% from the 4,788 dengue cases reported in 2003. Of these, 9,358 were local residents, comprising 61 imported and 9,297 indigenous cases. The other 101 cases were foreigners not residing in Singapore and who acquired the infection overseas, including 91 who came to Singapore for medical treatment. Majority of the indigenous cases (83%) received inpatient treatment. There were nine reported dengue deaths, including a foreigner from overseas who sought medical treatment in Singapore (Preliminary figure from the Registry of Births and Deaths).

The incidence rate among the indigenous cases was highest in the 15-24 year age group with a male to female ratio of 1.6:1 (*Table 1*). Among the three major ethnic groups, Chinese had the highest incidence rate, followed by Malays and Indians. Foreigners comprised 23.9% of the indigenous cases *(Table 2*).

Most of the cases were concentrated in the central (30.8%) and south-eastern (29.7%) parts of Singapore [according to the boundary demarcated by the Community Development Council / National Environment Agency (NEA) Regional Office]. About three-quarters of the cases occurred singly and sporadically. The number of localities with dengue transmission increased by more than three-fold compared to the previous year. Residents in Housing & Development Board (HDB) flats, compound houses and condominiums constituted 75.2%, 17.1% and 7.5% of the cases, respectively. However, the incidence rate of residents of compound houses (681 per 100,000) was almost four times higher than that of HDB residents (175 per 100,000).

Table 1
Age-gender distribution and age-specific incidence rates of indigenous DF/DHF cases, 2004

Age-group	Male	Female	Total (%)	Incidence rates per 100,000*
0 - 4	62	43	105 (1.1)	49.9
5 - 14	597	403	1000 (10.8)	189.1
15 - 24	1307	740	2047 (22.0)	322.6
25 - 34	1601	800	2401 (25.8)	279.8
35 - 44	1157	706	1863 (20.0)	241.7
45 - 54	577	450	1027 (11.0)	171.5
55+	419	435	854 (9.2)	133.7
Total	5720	3577	9297 (100.0)	219.3

*Rates are based on 2004-estimated mid-year population
(Source: Department of Statistics, Singapore)

Table 2

Ethnic-gender distribution and ethnic-specific incidence rates of indigenous DF/DHF cases, 2004

Ethnic group	Male	Female	Total (%)	Incidence rates per 100,000*
Chinese	3289	2438	5727 (61.6)	216.1
Malays	487	321	808 (8.7)	168.6
Indians	211	147	358 (3.9)	122.1
Others	119	65	184 (2.0)	286.2
Foreigners	1614	606	2220 (23.9)	294.7
Total	5720	3577	9297 (100.0)	219.3

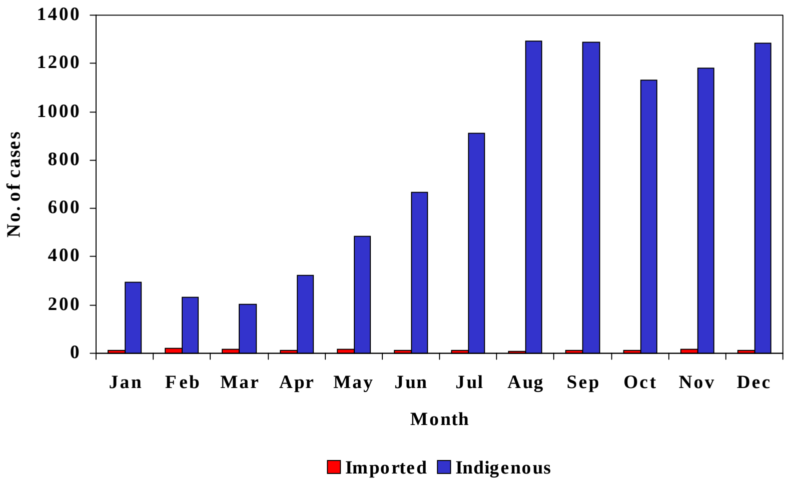
*Rates are based on 2004-estimated mid-year population
(Source: Department of Statistics, Singapore)

The incidence increased sharply from April to August and remained high for the rest of the year (*Fig. 1*).

Laboratory surveillance

A total of 560 blood samples obtained from both inpatients and outpatients were tested for dengue virus by polymerase chain reactions (PCR) at the Department of Pathology, Singapore General Hospital, KK Women's and Children's Hospital's laboratory and Environmental Health Institute, NEA. Of these, 215 (38.4%) were positive. All four dengue serotypes were detected, comprising DEN-1 (136 cases), DEN-2 (56 cases), DEN-3 (5 cases), and DEN-4 (6 cases) (*Table 3*). DEN-1 had emerged as the predominant circulat-

Figure 1
Monthly distribution of DF/DHF cases in Singapore, 2004



ing serotype in the second half of 2004 whereas in previous years (2001-2003) DEN-2 was the predominant serotype (*Fig 2*).

Aedes surveillance

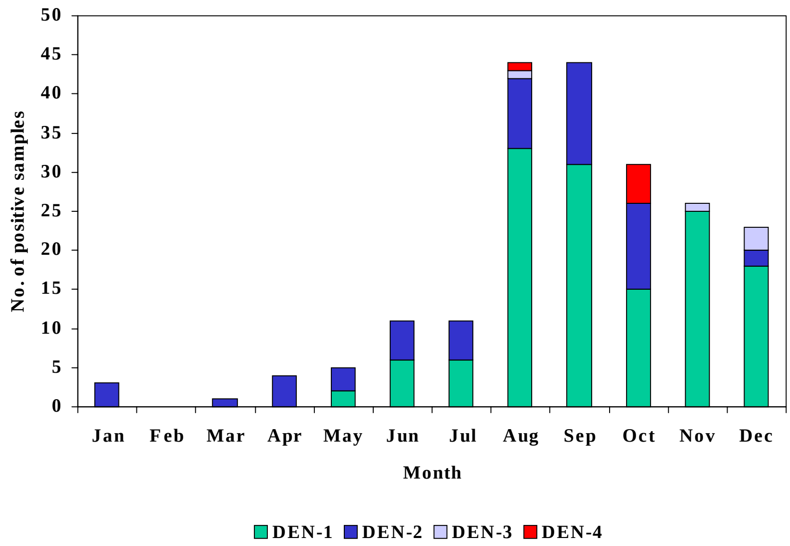
Aedes surveillance and source reduction are routinely carried out daily by NEA officers. The focus is primarily on areas which has historically high dengue cases. Every month, a total of 40,000 residential premises and 900 non-residential premises are inspected. A geographical information system is used for clustering and analysis of mosquito breeding sites and dengue cases. In addition, 2,000 ovitraps are placed around Singapore for *Aedes* surveillance (*Fig. 3*). The distribution of dengue cases was more closely associated with *Aedes aegypti* than *Aedes albopictus* (*Fig 4*). (Note: *Aedes aegypti* and *Aedes albopictus* are now known as *Stegomyia aegypti* and *Stegomyia albopicta*, respectively.)

Table 3
Surveillance of dengue serotypes in Singapore, 2004

Serotype	No.	%
DEN-1	136	63.3%
DEN-2	56	26.0%
DEN-3	5	2.3%
DEN-4	6	2.8%
Untyped	12	5.6%
Total	215	100.0%

The overall *Aedes* premises index was around 2%, with the highest percentage detected in compound houses (*Fig 5*). The top five breeding habitats for *Ae. aegypti* were ornamental containers (47%), domestic containers (34%), bamboo pole holders (6%), roof gutters (5%), and other habitats (8%) (*Fig. 6*). In the case of *Ae. albopictus*, the most common breeding habitats were ornamental containers (39%), domestic containers (31%), discarded receptacles (8%), canvas/plastic sheets (7%), and other habitats (15%) (*Fig. 7*).

Figure 2
Dengue virus serotypes detected in 2004



(Source: Dept. of Pathology SGH, Environmental Health Institute and KKH Laboratory)

Figure 3
Locations of 2,000 ovitraps used for *Aedes* surveillance

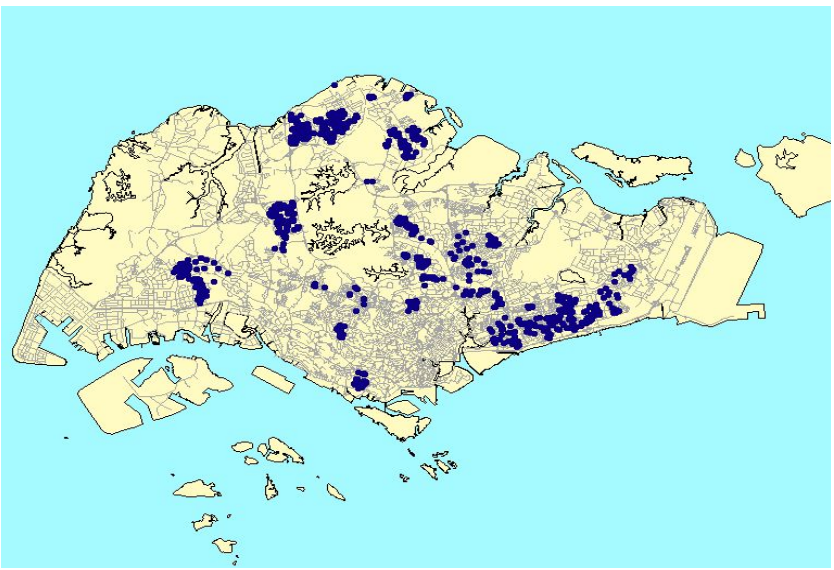


Figure 4
Geographical distribution of *Ae. albopictus*, *Ae. aegypti* and dengue cases, 2004

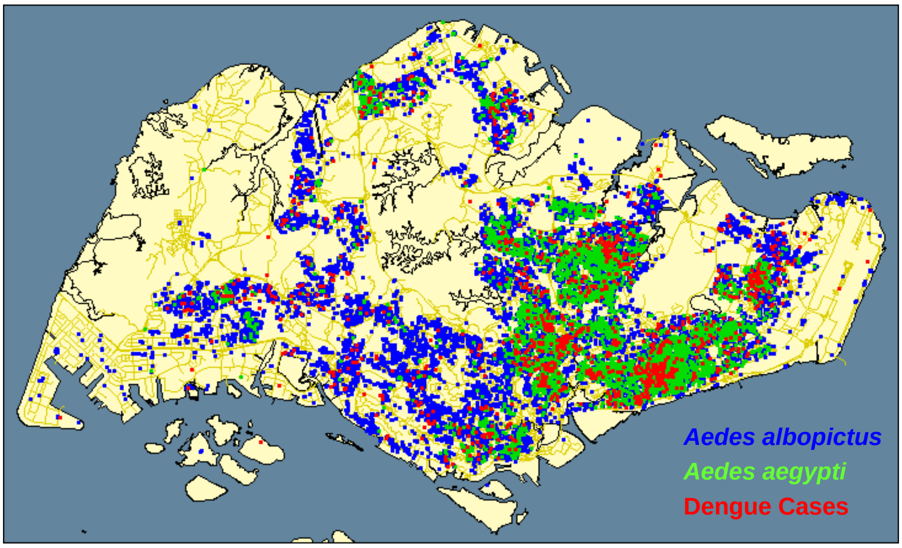


Figure 5
Percentage of premises breeding *Aedes* mosquitoes, 1998-2004

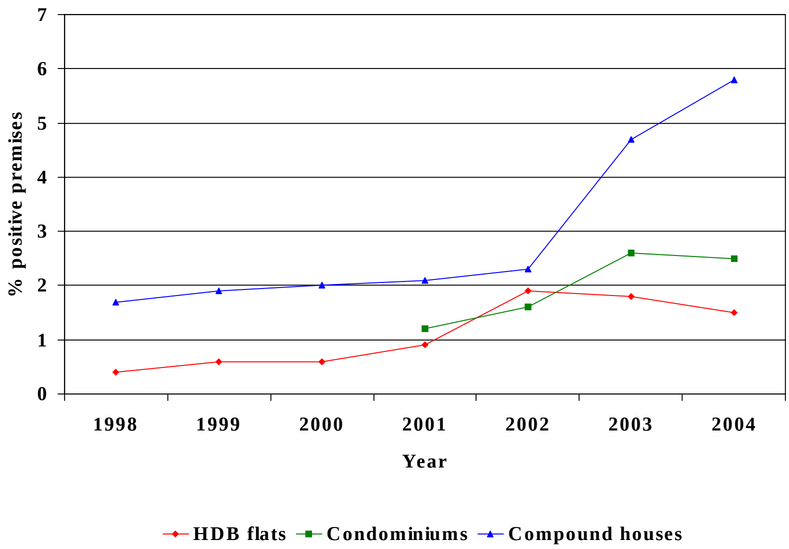


Figure 6
Distribution of *Ae. aegpyti* by top 5 breeding habitats, 2004

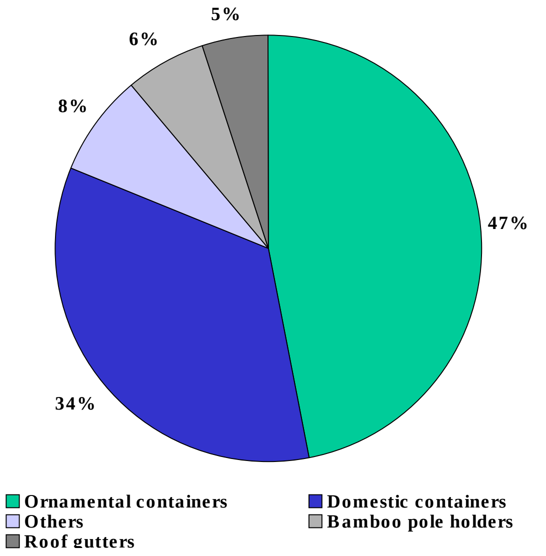
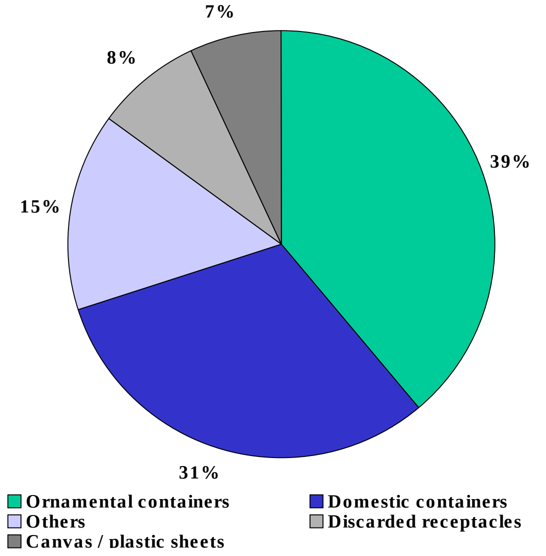


Figure 7
Distribution of *Ae. albopictus* by top 5 breeding habitats, 2004



[Reported by Kita Y, Communicable Diseases Division (Surveillance), Ministry of Health and Tang CS, Environmental Health Institute, National Environment Agency]

Editorial comments

Singapore is known for its well-established public health infrastructures, sound environmental management, close inter-agency collaboration and organised concerted health educational efforts in dengue prevention and control. Despite its successful implementation of the nationwide integrated *Aedes* mosquito control programme with the overall *Aedes* house index maintained at between 1 and 2 since the 1980s, dengue has re-emerged as an important vector-borne disease. Epidemics occurred in a 6-year cycle in 1992 (incidence rate of 102 per 100,000), 1998 (166 per 100,000) and 2004 (219 per 100,000). Factors which could have contributed to the resurgence include declining herd immunity of the population with only 6.4% of children and young adults below 25 years of age possessing haemagglutination-inhibition antibody to dengue 2[1], localised build-up of *Aedes* population, change in *Aedes* bionomics resulting in a higher risk of children acquiring dengue infection outside the home[2], and periodic emergence of a predominant dengue serotype. Unlike most other dengue endemic countries in the region, dengue fever comprised more than 98 % of the reported cases and the median age was 25 years with males outnumbering females by 1.6 times.

In the current vector control programme implemented by NEA, Ministry of the Environment, source reduction is the main strategy. There is a systematic surveillance programme and an effective control strategy to quickly curtail disease transmission. A geographic information system is used for tracking vector distribution and population for the surveillance and control of disease outbreaks. Law enforcement and public education are also integral parts of the control strategy.

To support the operations, a multi-disciplinary research team conducts studies on the human host, the mosquito vectors and the dengue virus. The studies include development of molecular tools for diagnosis and epidemiological studies; phylogenetic relations among the viruses; testing of insecticide efficacy**;** monitoring of resistance among local mosquitoes; and development of new vector control tools, such as Gravitrap.

While the public have a high level of knowledge on dengue and the *Aedes* mosquito, there has been no substantial change in their attitude and behaviours in taking proactive measures in the prevention of *Aedes* breeding in their premises. More innovative community-based integrated *Aedes* control measures have been implemented and the results are being assessed.

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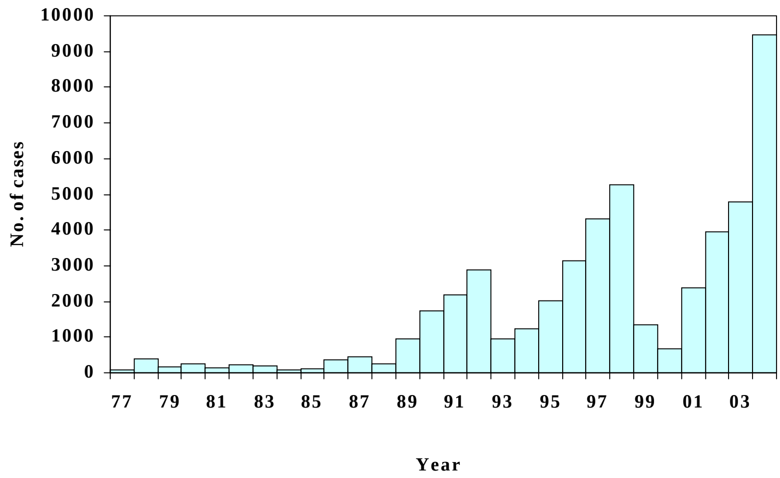
Identification of foci of dengue transmission based on movement history using the computerized link analysis system

Introduction

Dengue fever is a mosquito-borne viral disease endemic in Southeast Asia. It is a re-emerging disease of concern in Singapore[1]. Although Singapore has a well-established *Aedes* mosquito control programme, the number of notified dengue cases has seen an increasing trend in the past 15 years with 6-year cyclical epidemics in 1992, 1998 and 2004 (*Fig 8*). In 2004, 9459 cases were notified, almost double the number reported in the previous year.

For vector control operations, foci of dengue transmission are identified based on the home and workplace/school addresses of notified cases. A focus of dengue transmission or dengue cluster is traditionally defined as a locality with 2 or more cases having onset of illness within the 14-day incubation period and living or working/studying within a 150 m radius. However, as dengue is spread by day-biting *Aedes* mosquitoes[2] and the disease incidence is highest in the highly mobile young adults [3], the sources of infection could be from non-residential/

Figure 8
Yearly notified number of dengue cases in Singapore, 1977 – 2004



work /school localities. This paper describes an alternative method to identify clusters of dengue cases based on the movement history other than places of residence, workplace or school.

Methodology

All clinically diagnosed and laboratory confirmed dengue cases notified to the Ministry of Health (MOH) between 2 Aug and 3 Dec and living within the boundary of a pre-determined residential area in eastern Singapore were interviewed to ascertain their movement history during the 14-day period prior to their onset of illness. Information was obtained in a standard questionnaires form on transport-related (e.g. bus-stop and taxi-stand), food-related (e.g. supermarket and hawker centre) and recreation-related (e.g. swimming pool and park) locations and any other places where the cases had visited.

Xanalys Watson is a software programme that analyses interconnected data and presents the results in a pictorial manner. It has applications in several fields including criminal investigation. It was first applied for contact tracing purposes in MOH during the SARS outbreak in 2003. Templates were created using the Watson software to produce the dengue Link Analysis System (LAS) which was employed to cluster cases who had travelled to a common destination and with dates of onset within 14 days of one another.

Results

A total of 208 cases were investigated and 34 clusters were identified through LAS. The most common type of cluster identified was bus stops while the largest clusters were detected at shopping malls (*Table 4*).

During the same period, clustering based on residential, workplace and school addresses continued. This method resulted in the identification of 14 clusters, fewer than the 34 clusters detected by LAS, but the average size of the clusters was larger (*Table 5*). Both methods were comparable in the ability to cluster cases.

Table 4
Dengue clusters identified through Link Analysis System

Location	No of clusters	Total no of cases*	Average size of cluster
Bus stop	13	30	2.3
Swimming pool/park	6	15	2.5
Home	6	13	2.2
School	4	15	3.8
Market	3	11	3.7
Shopping mall	2	13	6.5
Total	34	-	-

* Cases can belong to more than 1 cluster

Table 5
Comparison of dengue clusters identified based on movement pattern and residence, workplace/school

Type of cluster	No of clusters	Average size of cluster	% of cases clustered
Based on movement pattern	34	2.85	30%
Based on residence and workplace/school	14	3.85	27%

Comments

Clustering dengue cases based on the 14-day movement pattern was a more labour-intensive method than that using residential, workplace and school addresses as it required lengthy interviews and data entry of a larger amount of information. The finding was also subject to recall bias and patients' willingness to truthfully share their movement history. Nonetheless, preliminary results from this study are promising.

In some of the clusters identified by the traditional approach, targeted vector control operations did not seem to be effective in breaking the chain of transmission. This could be due to the infection being acquired in localities other than places of residence, workplace and school. Using movement patterns to cluster dengue cases resulted in a list of common community areas that are frequently visited by residents and these should be earmarked for routine vector control operations.

The ability to accurately identify the actual foci of dengue transmission would be invaluable in reducing dengue incidence, as it would aid in focusing vector control efforts in the right locations. Advancement in dengue clustering continues to be an important aspect of controlling the disease in Singapore.

(Reported by Lalitha K, Lim J, Tan TK , Lim S, Ooi PL, Disease Control Branch, Ministry of Health)

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Socioeconomic determinants of dengue incidence in Singapore

Introduction

Dengue fever remains a major health problem in many areas of the world, especially in Southeast Asia [1-3]. Much efforts have been focused on the prevention and control of dengue infection. The most effective strategy to control a dengue outbreak is to eliminate *Aedes* mosquitoes and larval breeding habitats [4].

In Singapore, dengue haemorrhagic fever was first recognized as a public health problem during the early 1960's and a nationwide *Aedes* control programme which incorporated source reduction, public education and law enforcement was implemented in 1969. The *Aedes* house index (% of premises positive for *Aedes* breeding) was markedly reduced from more than 25% before 1970 to 1-2% for the entire country since 1982. The significant decline of dengue incidence (about 60 per 100,000 population in 1973 to below 10 per 100,000 in 1982) was the result of an effective *Aedes* surveillance and control programme [5]. Although the *Aedes* mosquito population has been successfully reduced to a relatively low level as indicated by the overall house index, there was a progressive resurgence of dengue with a periodicity of about 5 to 6 years from 1986 onwards [6, 7].

In the last two decades, several studies have investigated risk factors for dengue fever in affected communities, including those with poor living conditions, social inequalities, and illiteracy [3]. Identified dengue risk factors vary greatly depending on the location, population density, previous exposure to specific serotypes and availability of ovipoistion sites. Discernible seasonal distribution in dengue incidence is well-documented. Studies have shown the relationship between dengue incidence, elevated temperature, *Aedes aegypti* and rainfall [8]. However, not much is known about what other risk factors i.e. socio-economic/demographic variables could influence the occurrence of dengue. Geographical correlation analysis may help to answer this question.

The aim of this study was to examine whether or not there was any correlation between socio-economic/demographic variables and dengue incidence by geographical areas using the Development Guide Plan zones in Singapore.

Materials and methods

Units of analysis

The analyses were based on the geographic units, namely Development Guide Plan (DGP) zones. There are 55 DGP zones for the physical development of Singapore according to their different regions and subsidiary areas. Each DGP covers a planning area with a population of around 150,000 served by a town centre. In order to obtain stability of disease incidence, 4 DGP zones with less 10,000 persons have been merged with the adjacent zones. Besides, there were small numbers of dengue cases that occurred in 23 non-sampled DGP zones located in the rural areas with a small population size. Hence, only 28 of the DGP groups with enumerated population denominators were included in the final analyses.

Population census

The socio-economic/demographic (SED) variables were extracted from the Singapore Population Census 2000 reports [9]. The proportions with individual SED characteristics computed for each DGP group were used as SED variables for the analysis.

Data analyses

The residential address of each notified case of dengue fever/dengue haemorrhagic fever was first geo-coded into 28 DGP groups using ArcView version 9 software. Crude DGP-specific incidence of dengue was calculated based on the total number of cases reported from 1998 to 2002 inclusive, with the person-years denominator being the sum of the annual population estimates for each of the years. The population estimates were obtained by interpolating or extrapolating linear trend of each DGP zone from the Population Census 1990 to the Population Census 2000 to account for population changes over the study period. The possible geographical correlation between crude incidence of dengue (on log scale) and each SED variable was assessed by using the Spearman's rank correlation coefficient.

Potential SED variables identified by the correlation analysis were summarized into factor scores using the maximum likelihood estimation with varimax (orthogonal) rotation method [10]. The factor scores were then included in the weighted linear regression model to examine the relative contribution of each variable on DGP group-specific dengue incidence with log-transformation and weighted by the DGP group's population size. The average densities of the two *Aedes* mosquitoes were defined as the total number of *Aedes aeqypti* and *Aedes albopictus* larvae, respectively, observed divided by the number of habitats where larval breeding was found.

All analyses were performed with S-Plus version 6.0 and Stata version 8.0 software.

Results

Geographic variations in dengue incidence

During the study period (1998-2002), there were 16.4 million person-years of observation with 11,888 reported cases of dengue fever (after excluding 210 cases that occurred in the non-sampled DGP zones). *Fig. 9* shows the incidence of dengue in each of the 28 DGP groups studied in Singapore. The overall incidence of dengue fever was 72.7 per 100,000 person-years. The incidence of dengue fever ranged from 18.8 to 271.2 per 100,000 and all the incidence rates were significantly different ($p<0.01$) from the DGP average, except for two DGP groups (DGP groups 16 and 17) (*Fig. 9*).

Association with socio-economic/demographic factors

From the pair-wise ecological correlation analyses (*Table 6*), the following variables were most significantly associated ($p<0.01$) (only those variables with $r>0.5$ were extracted) with incidence of dengue: landed properties and others ($r=0.65$); services production industries (0.59); and 'other' ethnic group (0.56); aged 65+ (0.56); and non-owner tenancy (0.53).

In the factor analysis, two factors were extracted based on 18 SED variables which could explain 80% of the total variations (*Table 7*). Factor 1 with the first six greatest in absolute value of factor loadings

Figure 9
Incidence rates per 100,000 person-years of dengue fever by Development Guide Plan (DGP) group in Singapore, 1998-2002

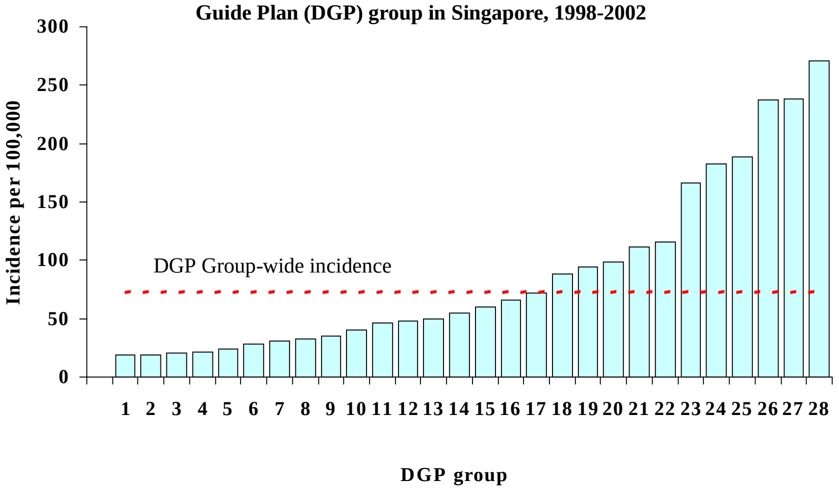

Table 6

Spearman's rank correlation coefficient (r) between dengue incidence and proportions with individual socio-economic/ demographic characteristics, and average densities of *Aedes aegypti* and *Aedes albopictus* [based on 28 Development Guide Plan (DGP) groups in Singapore, 1998-2002]

Socio-economic/demographic variable (denominator)	r	p value
Landed properties and others (resident population)	0.645	0.001
Services production industries (working residents aged 15 years and over)	0.592	0.002
'Other' ethnic group (resident population)	0.560	0.004
Aged 65 years and above (resident population)	0.559	0.004
Non-owner (resident private households)	0.533	0.007
Financial & business services industries (working residents aged 15 years and over)	0.500	0.010
Widowed female (resident population aged 15 years and over)	0.475	0.014
Economically inactive (resident population aged 15 years and over)	0.464	0.016
Attending upper secondary education (resident students aged 5 years and over)	0.453	0.019
Monthly gross income from work below $1000 (resident private households)	0.430	0.026
Female Chinese (resident population)	0.429	0.026
No family nucleus (resident private households)	0.427	0.027
Female living alone (resident population aged 15 years and over)	0.403	0.037
Average density of *Aedes aegypti*	0.395	0.040
Household size: 8 or above (resident private households)	0.394	0.041
Household size: 1 (resident private households)	0.394	0.041
Attending university education (resident students aged 5 years and over)	0.365	0.058
Average density of *Aedes albopictus*	0.273	0.156
Indian (resident population)	0.260	0.177
Workers :agriculture & fishery, craftsmen etc (working residents aged 15 years and over)	- 0.450	0.019

Table 7

Results of factor analysis: rotated factors and factor loadings [based on 28 Development Guide Plan (DGP) groups in Singapore, 1998-2002]

Socio-economic/demographic variable (denominator)	Factor 1	Factor 2
Landed properties and others (resident population)		0.826
Services production industries (working residents aged 15 years and over)		0.724
‘Other’ ethnic group (resident population)		0.938
Aged 65 years and above (resident population)	0.962	
Non-owner (resident private households)	0.906	
Financial & business services industries (working residents aged 15 years and over)		0.956
Widowed female (resident population aged 15 years and over)	0.945	
Economically inactive (resident population aged 15 years and over)	0.904	
Attending upper secondary education (resident students aged 5 years and over)		0.747
Monthly gross income from work below $1000 (resident private households)	0.995	
Female Chinese (resident population)		0.622
No family nucleus (resident private households)	0.963	
Female living alone (resident population aged 15 years and over)	0.784	
Average density of *Aedes aegypti*		0.877
Household size: 8 or above (resident private households)	0.938	
Household size: 1 (resident private households)	0.709	
Attending university education (resident students aged 5 years and over)		
Average density of *Aedes albopictus*		-0.957
Percentage total variance	46.3%	34.1%
Percentage cumulative variance	46.3%	80.4%

Data are factor loadings, the correlation between the individual variable and each factor.
Only variables with loadings > ±0.60 are shown.

were considered “dominant”: low gross monthly income from work (<$1,000), no family nucleus, aged 65+, living alone, female widowed and economically inactive. Likewise, for Factor 2, these were non-worker, business industries, ‘other’ ethnic group, household size 8 or above, landed property, and attending upper secondary school.

These 2 factors scores and the two indices for average density of *Aedes* mosquitoes were then included in the weighted linear regression analysis. Four variables together could explain 32% of the variations (R^2=0.32) in the regression model. However, only Factor 1 was significantly positively associated (p=0.022) with the incidence rates with higher factor scores reflecting low gross monthly income from work, no family nucleus, aged 65+, living alone, female widowed and economically inactive.

Discussion

Singapore is a modern tropical island city state with one of the highest urban population densities in the world (6,004 residents per square kilometre). In this study, substantial geographical variations in the incidence of dengue have been demonstrated, and these variations have been shown to be associated with differences in the socio-economic/demographic characteristics of the population.

Our study has several methodological limitations. First, the actual extent of dengue infection based on the notified cases was probably under-estimated as more than 90% of the infections are in fact asymptomatic or sub-clinical [11]. However, if this discount factor randomly occurred across all geographical areas, the magnitude of ecological correlation analyses based on relative geographical variations would only tend to bias toward the null [12]. In addition, regarding the size and choice of a geographical unit, a recent study showed that for a given time point and deprivation score, the deprivation gap in crude survival was some 25 times smaller when estimated with larger geographical units than with small ones. This implies our estimates to be conservative [13].

Second, like other dengue-endemic countries, the disease incidence has been shown to be significantly associated with rainfall, temperature and other environmental factors in Singapore. However, a local study showed that these meteorological conditions only preceded dengue incidence by 8-20 weeks [14]. In our study, as the dengue incidence was aggregated over a 5-year period, the short- and medium-term fluctuations of meteorological conditions are less likely to have an impact on the disease occurrence.

Third, the association between socio-economic/demographic factors and dengue incidence was assessed based on ecological data. Therefore, as with any ecological analysis, interpretation must be cautious. Specifically, our findings do not necessarily infer that these factors alter a person's risk of contracting dengue. Further individual-based studies are needed to validate the hypothesis generated from these findings [15].

In a study conducted in Thailand, the socio-demographic characteristics that influenced decision making of the patient's caretaker to take treatment alternatives included the level of education, occupation, residential areas and lay symptom assessment. For the economic factors, the capability to reimburse the cost of treatment, the family income and the financial resources were also important [16]. In our study, the dengue incidence was ecologically associated with some socio-economic/demographic characteristics of the population, such those without or with lower income (economically inactive; Spearman's r=0.46 or monthly gross income from work below $1,000; 0.43), living alone (household size 1; 0.39), gender (female living alone; 0.40 or widowed female; 0.48), and less attention paid to environmental hygiene (aged 65+; 0.56, no family nucleus; 0.43, household size 1; 0.39, and widowed female; 0.48). In such a population group, *Aedes* larval breeding sites in the premises could be increased due poor hygienic conditions [17], failure to check for breeding and reluctance to have their homes fogged with insecticide [18]. In addition, non-owner tenancy householders (r=0.53) could be less responsible in cleaning up their premises. Living in landed properties was also associated with a higher dengue incidence (r=0.65) as it has been consistently observed that there are more breeding habitats in these premises [5].

We found that areas with a high proportion of socio-economically disadvantaged residents (i.e. the Factor 1's score) have significantly higher incidence rates of dengue. This association was independent of the average densities of the two *Aedes* mosquitoes in the area. Because this finding is based on ecological data, we cannot conclude that persons from poor families have a higher risk of dengue fever. However, it is consistent with the hypothesis that susceptibility to infection is associated with low socio-economic status [19].The higher dengue incidence in the socio-economically disadvantaged residents could also be due to socio-behavioral barriers in seeking healthcare [20, 21] or some other behavioural or environmental processes operating at household or individual levels that supported breeding of *Aedes* mosquitoes and/or transmission of dengue viruses [22].

Until a safe and effective vaccine is available, controlling *Aedes* mosquitoes, enhanced entomological and virological surveillance [23], and improved case management are the principal options available for reducing the burden of dengue in Singapore. More cost-effective integrated control measures such as public health educational campaign targeting at 'hot-spot' areas, in which both dengue incidence and factor scores are high, could be a logical approach to minimize the impact of the disease [22 - 25]. [The 'high-high' areas defined as the first one-third of the DGP groups with high dengue incidence accounted for 28.3% of the total annual cases, but only 10.4% of the total population size, and the first one-third of the factor scores (data not shown).]

The results of the present study suggest that dengue control in Singapore could benefit with the participation of low socio-economic households in eliminating larval breeding. Further efforts should be directed at addressing the barriers to behaviour change, correcting misconception on the spread of dengue by social and close contact, and educating them and the illiterate on measures to prevent dengue [18].

(Reported by Ma S, Epidemiology and Disease Control Division, MOH, Ooi EE, Defence Science Organisation, DMERI; Kurupatham L and Ooi PL, Disease Control Branch, MOH, and Chew SK, Epidemiology and Disease Control Division/ Communicable Disease Division, MOH)

(Acknowledgements: We are grateful to Goh KT for his useful comments and suggestions and we would also like to thank Wong J KY, Loh E, Heng CT and Soh PY of the National Environmental Agency for helping out with the geo-coding of data to the DGP zones)

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Economic burden of dengue: comparison with SARS, HIV/AIDS and traffic accidents

Introduction

The reported incidence of dengue has increased sharply in Singapore in recent years. Since the late 1980s, the incidence rates have been cyclical and in 2004 the incidence reached an all time high. The high number of reported cases and hospitalizations has been a matter of concern. This paper analyzes the economic impact of dengue if the current cyclical trend continues until 2011.

In a number of developing countries, the economic cost of dengue is high. Evidence from Indonesia indicates that the economic burden of dengue is very high partly due to inadequate infrastructure[1]. Studies in Latin America have shown similar results [2-6]. Similar studies in other Asian countries such as Thailand also indicate high economic costs[7]. It should be noted that unlike Singapore, most of these countries have poorer physical infrastructure to deal with environmental health issues. Singapore is probably the only country along the equator whose infrastructure to deal with environmental health problems is equivalent to that of developed countries. In this paper, it is argued that the economic burden of dengue is miniscule compared to diseases such as SARS as well as traffic accidents as the case fatality rate is very small. Furthermore, there is no disability due to dengue unlike traffic accidents.

Materials and methods

The data on reported dengue cases and bill sizes for dengue hospitalizations were obtained from the Ministry of Health (MOH). Comparative data on SARS were obtained from MOH as well as from the Asian Development Bank study on SARS. Data on HIV/AIDS were obtained from MOH and UNAIDS, while data on the economic burden of traffic accidents were obtained from a study undertaken by the National University of Singapore[8].

In 2004, a total of 9459 dengue cases were reported.These cases were broken down into hospitalized and non-hospitalized cases. There were eight deaths due to dengue in 2004. The total bill sizes for the hospitals where the patients were admitted were obtained for the period ending July 2004, and this amount was divided by the number of cases admitted to arrive at an average bill size per patient The proportion not hospitalized was multiplied by $40 for outpatient services. The expenditures of National Environment Agency (NEA) which is responsible for vector surveillance and control were not considered to be an economic burden and hence these were not included in the economic costs. The NEA expenditures are essentially preventive in nature. Due to these expenditures, higher number of dengue cases are avoided, and hence the economic burden is likely to be much lower than otherwise would be the case.

An annual economic growth rate of 4% for Singapore was assumed. The average per capita income was calculated and this was divided by the number of working days in a year. A five-day medical leave period was assumed for those not hospitalized and a 10-day medical leave was assumed for those hospitalized. Economic loss due to hospitalization is the per capita income per day multiplied by 10 days and the numbers hospitalized, plus costs of hospitalization and consultation. Economic loss due to getting dengue without hospitalization is the per capita income multiplied by 5 days and the dengue cases not hospitalized plus their consultation costs. Economic cost due to death is the number of deaths times the income lost in the future based on a 4% growth rate. The costs due to hospitalization, deaths and consultation as well as medical costs are aggregated to arrive at the total economic costs. The same proportion of hospitalization is assumed for all years based on the 2004 numbers.

Results

Trends in Singapore

Dengue control expenditures by NEA rose from $13.8 million to $18.3 million during the ten years ending 2004. Despite these increases, the number of cases reported has been increasing and falling sharply in well defined cycles since the late 1980s (*Fig. 10*) and each time a higher peak is reached. The trend is similar regarding incidence rates (*Fig. 11*). This trend coincides with rapid economic development. In the past, sharp increases in dengue incidence have not resulted in a slowdown of economic activity. Furthermore, although the reported cases reached an all time high of 9,459 in 2004, economic growth rate was reported at 8.4%, the highest since 2000. In contrast, SARS outbreak in March 2003 resulted in a sharp contraction of GDP in the second quarter of that year.

For 2004, until the end of June, the cumulative reported cases of dengue were lower than in 2003 (2,353 for 2004 compared to 2,780 for 2003). However, this began to change in July and the number of cases reported since August 2004 showed a marked acceleration compared to the same period for 2003. Of the 3,213 reported cases by the end of July 2004, 2,638 cases were hospitalized. However, for all of 2003, six deaths were reported, whereas until July

Figure 10
No. of of dengue cases in Singapore, 1977-2004

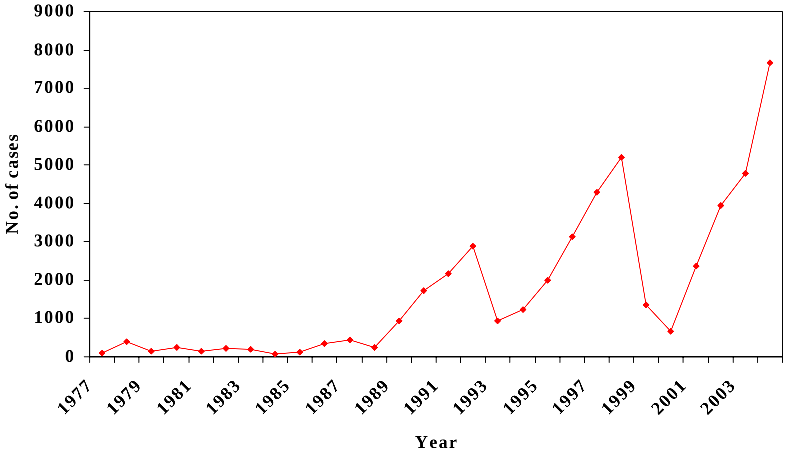
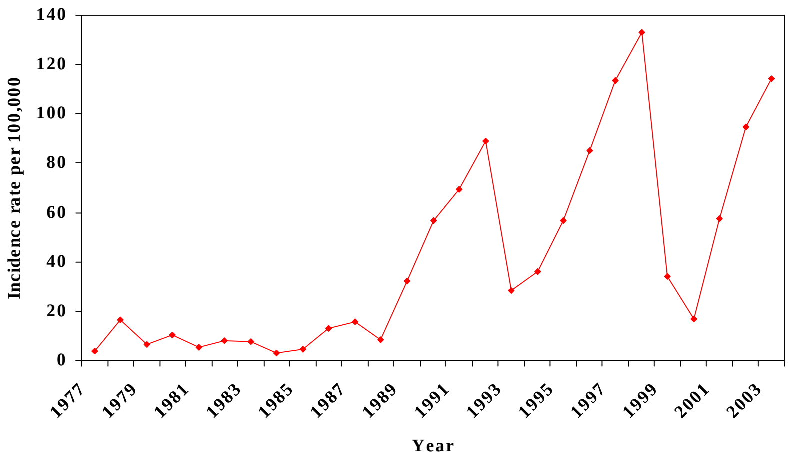


Figure 11
Incidence rates of dengue in Singapore, 1977 - 2003



2004 three deaths were reported. Most of the deaths were over the age of 40 years and the disease did not seem to have taken its toll on the younger generation during the past two years.

In comparison to other countries in the region, the case fatality ratio varies in South East Asia although they have been declining steadily in most countries according to the World Health Organization[9]. Indonesia recorded the sharpest fall in case fatality ratio from a high of 4.48% in 1989 to a low of 1.12 in 2004. India's case fatality ratio stood at 0.56 in 2004, while in Thailand the corresponding figure was 0.13. Overall in South East Asia, the ratio was 0.84 in 2004. However, in 2004, there was a surge in the number of deaths (38 reported deaths) due to dengue in Malaysia[10]. Meanwhile, dengue continues to have an impact on Latin American countries. In 2004, 3,400 people had been infected in El Salvador with eight fatalities, while the corresponding figure in Honduras was 6,500 reported cases and nine deaths[11]. Dengue fever is widespread in Africa and the case fatality ratio is high, although data are limited thus making comparisons difficult.

Globally, 500,000 cases require hospitalization each year, most of them children[9]. The year 2001 witnessed a high level of global dengue epidemic activity in the American hemisphere, the Pacific islands and continental Asia. During 2002, over 30 Latin American countries reported more than 1,000,000 dengue fever cases. This has been followed by extensive epidemics in several parts of India during 2003[12].

Economic burden of dengue

This section projects the economic burden of dengue in Singapore for a period of eight years based on past trends. An eight year period is chosen because it encompasses one complete cycle from the current peak to the next. The economic burden will include days of work lost, hospitalization and medical consultation. The burden due to death would be severe if the person is young as the future earning potential is high. Furthermore, it is assumed that in an economy with declining birth rates, the person cannot be replaced.

The results are presented in *Figs 12 and 13* assuming an average age at death of 52 and 42. The projection assumes that there would be neither vaccines nor treatment for dengue. The following are the results with average age of death both at 52 and 42. As of 31 December , 9,459 cases, including eight deaths, were reported in 2004 . The reported cases are projected to sharply decline until 2006, when it is expected to rise again. The next peak projected at 11,000 cases is reached in 2010 followed by a sharp drop in 2011 to 5,200 cases.

Fig. 13 also shows the losses each year as a result of dengue based on past trends. Initially, the peak is reached in 2004 with an economic cost of $24.9 million if the average age at death is 52 and $27.9 million if the average age at death is 42. Beginning 2005, the economic losses per year fall, until 2006, when they begin to increase again, peaking in 2010 at $31.5 million (average age at death 52) or $34.5 million (average age at death, 42) before falling sharply in 2011.

The cumulative economic cost of dengue is $135.2 million for the eight years ending 2011 with an average age at death of 52 and $159.4 million with an average age of 42, accounting for roughly 0.26% of GDP for the entire period or an annual rate of 0.027%. It is evident from this analysis that the economic burden due to dengue is very small.

As of April 2005, there have been 3,000 dengue cases which is much higher than that projected in this paper. At this rate, Singapore may have about the same number of cases in 2005 as in 2004. However, even if the cases continue to remain high at around the same numbers as 2004 for every year until 2011 the economic burden of dengue would not be catastrophic, around $180.8 million if the average age is 52 and $204.3 million if the average age is 42.

Figure 12
Trends and projections in reported cases of dengue in Singapore, 1977-2011

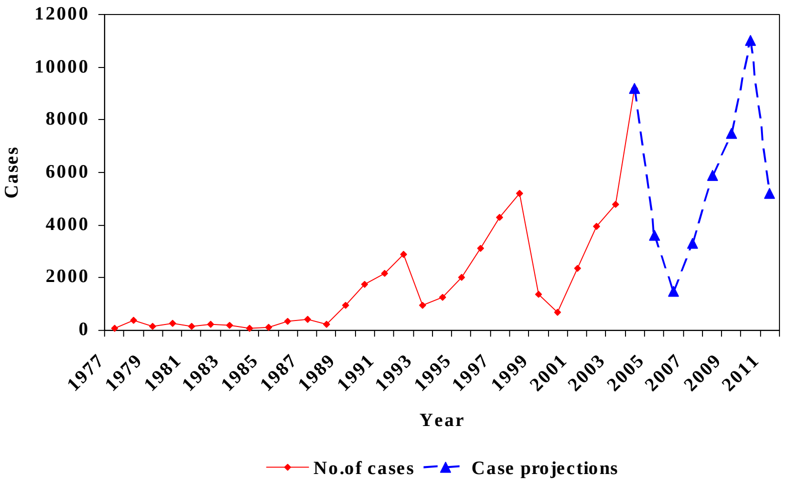


Figure 13
Projected economic burden and cases of dengue, 2004-2011

Discussion

To put these results in perspective, there is a need to compare them with the recent studies undertaken on the economic burden of SARS and traffic accidents as well as some preliminary calculations for HIV. For the period March to May 2003, SARS hit Singapore very hard. Tourist arrivals basically dried up and there was a sharp decline in economic activity. It was estimated that had SARS continued for the whole year, economic activity would have declined to the tune of 2%-4% according to the Asian Development Bank.

While SARS resulted in serious economic consequences for Singapore compared to dengue, traffic accidents, although not as devastating as SARS, cause a bigger drop in economic activity than dengue. In 2002 it was estimated that the economic cost from death and disability due to traffic accidents per year was 0.26%; ie, traffic accidents result in a decline of 0.26% in economic activity per year. This is exactly ten times more than the economic cost of dengue, which takes ten years at current trends to cause a reduction of 0.26% in economic activity.

Finally, HIV/AIDS also resulted in higher economic loss than dengue. UNAIDS estimated that there were 4,100 cases of HIV/AIDS in Singapore at the end of 2003[13]. It is estimated that this has resulted in a reduction of nearly 0.1% of GDP during 2004 compared to 0.026% for dengue. Thus, although Singapore has a relatively low prevalence of HIV, it causes far higher economic loss than does dengue.

There are several major reasons as to why even a low incidence of SARS, HIV and traffic accidents causes a higher economic damage than dengue. First, dengue is not spread through human contact unlike SARS. It is spread by the *Aedes* mosquitoes . Secondly, the case fatality ratio of 8 out of 9459 is far lower than that of SARS where the case fatality ratio was much higher at 33 out of 238. Since, SARS is spread through human contact, tourists stopped coming, hotel occupancy rates declined, foreign delegations failed to show up for business meetings and economic activity declined. This is clearly not the case with dengue. With traffic accidents, there is a higher chance of disability unlike dengue and the fatality rates are also relatively higher. Hence, the economic costs tend to be also relatively higher. Finally, with HIV/AIDS, the economic costs are much lower compared to SARS and traffic accidents but higher than dengue, as it is spread through intimate contact, exchange of needles and blood transfusion. It is not spread through simple human contact.

Conclusion and policy implications

Overall, it is very clear that the economic cost of dengue is extremely low compared to diseases such as SARS and to a lesser extent HIV/AIDS. Hence, the focus of health policy planners in Singapore should be on other diseases and behaviour pattern which cause much more serious damage than dengue. It is absolutely essential to try to prevent SARS from recurring again as the economic damage would be very high. Early detection and prevention of SARS is essential. In the case of SARS, prevention is indeed better than cure as case fatality ratios are far higher. Similarly with HIV/AIDS, health education should be the major goal as once a person gets the disease the chances of dying are considerably higher and the economic cost is also higher than that of dengue. Economic costs due to traffic accidents are also high due to the higher rates of disability. However, the prevention of traffic accidents is usually beyond the scope of the health planners as this is largely under the jurisdiction of transportation planners and law enforcement. Better traffic rules and stiffer penalties would alleviate the healthcare costs and economic burden due to traffic accidents.

Compared to the developing countries, the economic cost of dengue is very small as the case fatality ratio in Singapore is extremely low. Within Singapore, compared to other diseases such as SARS, the economic burden is also low. Based on these results there is no urgency regarding dengue. However, there is still a need for medical intervention to prevent deaths. The best option is to continue the current interventions through environmental health programmes. In order to determine the reason for sharp increases in dengue incidence rates in recent years, entomological studies on *Aedes* mosquitoes would be a better use of resources.

(Reported by Chellaraj G., Planning and Development Division, MOH)

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First outbreak of vancomycin-resistant *Enterococcus faecium* in a tertiary-care hospital in Singapore

Introduction

Vancomycin-resistant *Enterococcus* (VRE) was first isolated in 1986. Since then, VRE has rapidly spread in Europe and USA where it has become a major clinical problem. So far, South-East Asia has been relatively spared. VRE has been sporadically isolated in clinical specimens in Thailand and Singapore[1, 2]. However, nosocomial outbreaks of VRE have not been reported in our region.

Enterococci are intrinsically resistant to multiple antimiocrobial agents. In addition, they have acquired new mechanisms of resistance by transferring resistance genes encoded on plasmids and transposons. A number of phenotypes of vancomycin-resistant strains have been discovered. Strains with VanA phenotype are resistant to both vancomycin and teicoplanin while strains with VanB phenotype show resistance to vancomycin but remain sensitive to teicoplanin. The incidence of vancomycin resistance is much more common among strains of *Enterococcus faecium* than *Enterococcus faecalis*.[3]

Certain coexisting conditions, e.g., malignancies, organ transplants, and chronic renal failure, as well as the duration of hospitalization were found to be associated with increased risk for VRE. Antimicrobial agents are believed to predispose to nosocomial VRE largely through effects on competing gastrointestinal microflora. Several classes of antibiotics have been implicated including vacomycin, cephalosporins, quinolones and metronidazole.[4]

Methods

The Singapore General Hospital (SGH) is a 1600-bed acute tertiary care hospital.

This investigation was performed after VRE was isolated within the same week from the blood of two hematology inpatients hospitalized in the same ward.

Immediately after receiving the report of a second case of VRE bacteremia, a special task force was formed in order to coordinate the management of the outbreak.

The affected ward was closed, and patients who remained in the affected ward had faecal or rectal VRE surveillance cultures performed every other day. Only transfers to intensive care units and discharges to patients' own home were allowed prior to the documentation of non-VRE carriage (3 negative surveillance cultures). Transfers to other hospitals or nursing homes were allowed only for patients cleared of VRE carriage. If any of the surveillance cultures was positive, then a further three negative faecal or rectal cultures (performed one week apart) were required before the patient was presumed to have cleared the VRE carriage.

Environmental cultures were performed in order to investigate the spread of VRE. All patients who had contact with the two patients above but who had been discharged prior to the closure of the affected ward were identified. A computerized alert was designed to caution healthcare workers whenever these patients returned to hospital for inpatient or outpatient treatment. If these patients required hospitalization, they were isolated until proof of non-VRE carriage was obtained.

All patients from the affected ward were gradually discharged and the affected ward was reopened 5 weeks later. The above-mentioned infection control measures were terminated six months later when no further new cases were detected.

Clinical VRE isolates were classified as being associated with active infection or colonization by using standard definitions of the Centers for Disease Control and Prevention[5].

The VRE isolates were investigated with pulsed-field gel electrophoresis (PFGE) and Multiplex PCR for *vanA* and *vanB* genes.

Results

The first patient was a 20-year-old woman with relapsed acute myeloid leukemia who was hospitalized on March 22, 2004 for the second course of her salvage chemotherapy. She developed prolonged febrile neutropenia and was treated with a variety of broad-spectrum antibiotics. A blood culture performed on April 18 yielded VRE. Her condition deteriorated quickly and she was transferred to the intensive care unit (ICU) but died six days later.

The second patient was a 75-year-old woman with advanced multiple myeloma who was admitted to the same ward on March 30 for palliative therapy. Her hospitalization was complicated by severe lower gastrointestinal bleeding and acute renal failure. A blood culture done on April 25 yielded VRE. She died two days later.

Contact tracing identified 136 patients (13 in ICU and 123 in hematology ward) who were hospitalized together with the two patients above. Four of these patients had faecal or rectal cultures positive for VRE.

Environmental cultures were performed and they were all negative. All six isolates were identified as *Enterococcus faecium* and multiplex PCR for *van* genes confirmed the VanB phenotype.

All isolates had almost identical PFGE patterns suggesting that the outbreak was caused by single clone of VRE.

Discussion

The prevalence of resistance to the antimicrobial agents in Singapore has been steadily increasing. A review of the records of the microbiology laboratory in our institution revealed that methicillin resistance rates had been consistently above 40% since 1988. The emergence of VRE in our hospital could have created conditions for spread of vancomycin resistance genes to other species such as methicillin-resistant *Staphylococcus aureus* (MRSA). Until now, three independent single cases of emergence of vancomycin-resistant *Staphylococcus aureus* (VRSA) were reported from the USA.[6, 7] In two of them, an association with *vanA*-containing *Enterococcus* spp. at the same site of the affected patients could be established. Prompt control of VRE outbreak was critical in order to avert clinical and financial impact of hospital-wide spread of VRE and to prevent potential emergence of VRSA in our institution.

In 2003, SGH was affected by the outbreak of severe acute respiratory syndrome (SARS). Within a short period, stringent infection control measures and major organizational changes were introduced.[8] Many wards were converted into isolation facilities and a surveillance system was modified to identify and track patients with atypical pneumonias and their contacts.

During the VRE outbreak, this system allowed us to create a list of contacts of patients with the VRE bacteremia very quickly. The size of the problem was therefore rapidly defined. The need to take harsh measures to try to stamp out the disease was understood rapidly by all involved. Doctors and nurses of the affected ward were familiar with infection control practices and applied it quickly and effectively. More than familiarity with infection control procedures, their experiences one year earlier made strict measures readily acceptable. All these factors contributed to the quick control and elimination of VRE from the hematology unit.

Sporadic cases of VRE in Singapore have been reported since 1994[9, 10] So far, two local epidemiological studies were completed in order to investigate the prevalence of VRE.

In the first study[2] performed in 1997 in the National University Hospital, 299 consecutive stool specimens were tested for VRE. This survey showed that 35 patients carried enterococci of reduced susceptibility to vancomycin (MIC > 4 mg/ml). However, only two VRE isolates demonstrated high level vancomycin resistance.

The second survey (unpublished data) was conducted in the SGH among hematology and renal inpatients between 1999 and 2001. 327 patients had stool cultures performed on admission and then weekly as long as they remained hospitalized. VRE had not been isolated.

These studies showed that the incidence of VRE in Singapore prior to this outbreak had been very low. However, VRE may potentially become an important clinical problem in Singapore and South-East Asia.

The outbreak reported here was quickly brought under control by aggressive infection control measures and excellent cooperation among various hospital services. However, additional interventions such as a structured antibiotic utilization programme may be necessary to prevent similar outbreaks in the near future.

(Reported by Chlebicki MP, Ling ML, Koh TeH, Hsu LY, Tan BH, How KB, Sng LH, Wang GCY, Kurup A, Kang ML and Low J, Singapore General Hospital, Singapore)

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