ORIGINAL ARTICLE

Review of dengue fever cases in Hong Kong during 1998 to 2005

CME

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Objective To describe the epidemiology, clinical and laboratory findings, and outcomes of patients presenting locally with dengue.

Design Retrospective review of case records.

Setting Public hospitals, Hong Kong.

Patients Medical records of all laboratory-confirmed dengue patients admitted to public hospitals during 1998 to 2005 were reviewed retrospectively.

Results A total of 126 cases were identified, 123 (98%) being dengue fever and three (2%) dengue haemorrhagic fever. One patient who had blood transfusion–acquired dengue fever was highlighted. A total of 116 (92%) cases were 'imported', while 10 (8%) were local. Among the 56 dengue cases confirmed by reverse transcription–polymerase chain reaction, dengue virus type 1 was the most common accounting for 48% of them, followed by type 2, type 3, and type 4 responsible for 23%, 16%, and 13%, respectively. Only type 1 and type 2 were present in locally acquired infections. The median age of the patients was 38 years and the mean duration of hospitalisation was 6 days. There was no mortality, and nearly all patients (98%) presented with fever. Other symptoms at presentation included: myalgia (83%), headache (65%), fatigue (59%), and skin rash (60%). More than one third of patients had gastro-intestinal and upper respiratory complaints. Maculopapular skin rash was the most common physical finding. Thrombocytopenia, neutropenia, and lymphopenia were present in 86%, 78%, and 69% of the patients, respectively. In only 29% of the patients was dengue fever included in the initial differential diagnosis. The demographic, clinical, and laboratory findings as well as outcomes did not differ significantly among the four dengue serotypes, but the lowest lymphocyte counts of type 3 was lower than the other serotypes (P=0.004).

Conclusion When physicians encounter patients with a relevant travel history, presenting with fever and skin rash, and having compatible haematological findings, dengue fever should be included in the differential diagnosis.

Key words
Dengue; Dengue hemorrhagic fever; Serotyping

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Introduction

Dengue is the most common and widespread arthropod-borne viral infection in the world today. It is recognised in over 100 countries throughout the tropics and subtropical areas and threatens the health of approximately 40% of the world's population, of nearly 2.5 billion people.[1] The highest burden of disease occurs in South-East Asia and the Western Pacific, where it is one of the 10 leading causes of hospitalisation and childhood mortality.[2]

In Hong Kong, dengue fever was made notifiable since March 1994 and all infections reported to the Department of Health (DH) are investigated to establish their source. The number of cases reported is showing an increasing trend in recent years; the vast majority being imported from other countries. Hong Kong experienced its first local dengue case in September 2002.[3] Thereafter, several others were encountered in Ma Wan and local cases were subsequently identified sporadically in 2002 and 2003.

The epidemiology, clinical manifestations, and laboratory findings of dengue fever infections and its complications have been extensively described in the medical literature,[4,5] but comprehensive review is lacking for our local patients.

回顧1998至2005年間香港的登革熱病症

目的 對本地登革熱病症的流行病學情況、臨床發現、化驗結果和治療結果作出描述。

設計 病例個案回顧。

安排 香港的公立醫院。

患者 1998至2005年間，入住公立醫院並由化驗確診為登革熱病人的醫療紀錄作回顧。

結果 126宗病例中，123人(98%)患上登革熱，3人(2%)患上出血性登革熱，1人因輸血而染病。116宗(92%)病例是在外地感染回港後發病，10宗(8%)病例在本港感染。由反聚合酶連鎖反應確定的56宗病例中，以「登革病毒一型」最常見，佔同類病症的48%，其次為二型(23%)、三型(16%)和四型(13%)。本地感染個案中只發現一型和二型病毒。病人的年齡中位數為38歲，平均住院期為6日。沒有病人因感染登革熱而死亡。幾乎所有病人(98%)都出現發燒病徵，其他病徵包括肌肉痛(83%)、頭痛(65%)、疲倦(59%)和皮膚出疹(60%)。超過三分一病人出現腸胃和上呼吸道不適。皮膚出疹是最常見在肢體上的病徵。血小板減少、白血球減少和淋巴細胞減少的出現比率分別為86%、78%和69%。只有29名病人在初步診斷時有將登革熱考慮在內。四種登革血清在人口分佈、臨床狀況、化驗發現和治療結果上都沒有明顯分別，但「登革病毒三型」的最低淋巴球數目較其他類型少(P=0.004)。

結論 醫療人員如發現病人有相關旅行歷史，有發燒和皮膚出疹，和出現相似的血液學結果，便應把登革熱作為鑒別診斷。

The objective of this review was to describe the epidemiology and explore the clinical characteristics and laboratory findings of dengue fever and dengue haemorrhagic fever (DHF) cases admitted to Hong Kong public hospitals during the period 1998 to 2005. We also compared the clinical and laboratory features of the four dengue serotypes identified by the polymerase chain reaction (PCR) technique.

Methods

We included patients admitted to public hospitals during 1998 to 2005 by using selective criteria "any diagnosis ICD9CM code" starting with "061 dengue" through the Clinical Data Analysis and Reporting System. A patient list was retrieved and matched with the laboratory-confirmed dengue cases notified to the DH. A case was defined as confirmed by detection of viral genomic sequences in autopsy tissue, serum or cerebrospinal fluid samples by PCR; a four-fold or more rise in immunoglobulin G (IgG) or IgM antibody titres to one or more dengue virus antigens in paired serum samples; or a positive IgM antibody titre in late acute or convalescent phase serum specimens (obtained between September 2003 and July 2004). The epidemiological data and virological results were provided by the Surveillance and Epidemiology Branch, Centre for Health Protection, DH. The clinical presentations, laboratory findings, and outcomes of all the confirmed cases were retrospectively reviewed through medical records.

The dengue cases were categorised into dengue fever, DHF, and dengue shock syndrome. In this paper, the definition of DHF was based on the World Health Organization's criteria and defined as: fever lasting 2 to 7 days, haemorrhagic tendencies (a positive tourniquet test; petechiae, ecchymoses or purpura; bleeding from the mucosa, gastro-intestinal tract, injection sites or other locations; haematemesis or melaena), thrombocytopenia (with platelet counts ≤100 x 10^9 /L) and evidence of plasma leakage due to increased vascular permeability (a rise in haematocrit ≥20% above average for age, sex in the population, a drop in the haematocrit following volume-replacement treatment of ≥20% from baseline, and features consistent with plasma leakage such as pleural effusion, ascites, and hypoproteinaemia). Dengue shock syndrome was defined as DHF together with direct evidence of circulatory failure or indirect evidence manifested as a rapid and weak pulse, narrow pulse pressure (20 mm Hg or hypotension for age) or cold, clammy skin and altered mental status.

Statistical analysis was carried out to compare the epidemiological, clinical, and laboratory findings among the four dengue serotypes. The categorical variables were compared by the Chi squared and Fisher's exact tests. Normally distributed data were compared by analysis of variance and data with skewed distributions by the Kruskal-Wallis test.

Results

Disease trend

In all, 126 patients with laboratory-confirmed dengue fever were admitted to public hospitals from 1998 to 2005. Only three (2%) patients suffered from DHF, while the remaining 123 (98%) had dengue fever; no dengue shock syndrome was reported. The number of patients encountered showed an upward trend from 1998 (2 cases) to 2003 (35 cases), and subsequently remained more or less constant in 2004 (20 cases) and 2005 (24 cases). A total of 116 (92%) were imported, while in 10 (8%) the infection was locally acquired (Fig 1).

No locally acquired disease was reported until in 2002, when nine patients were identified. Among them, six cases were confirmed to be epidemiologically related to the Ma Wan outbreak. Another patient acquired the infection through blood transfusion from one of the Ma Wan cases. The remaining two locally acquired cases in 2002 and one

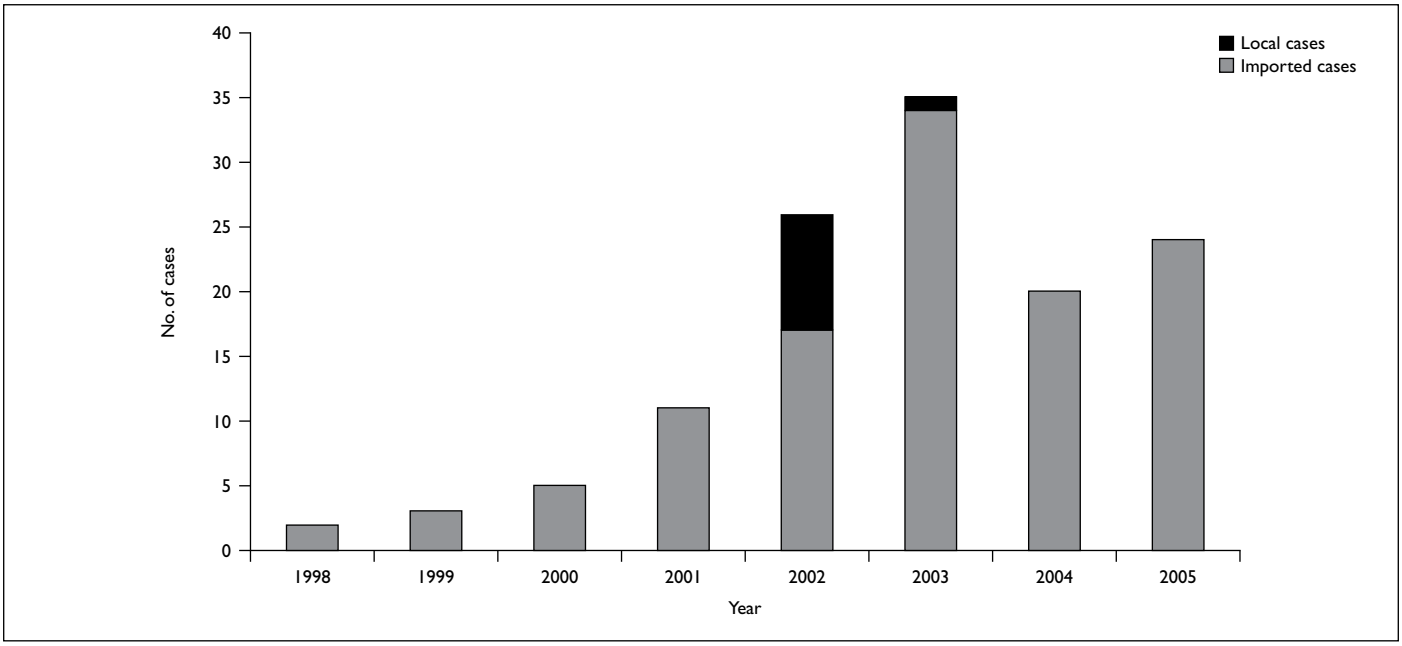

FIG 1. Numbers of dengue fever cases admitted to public hospitals in Hong Kong, 1998-2005

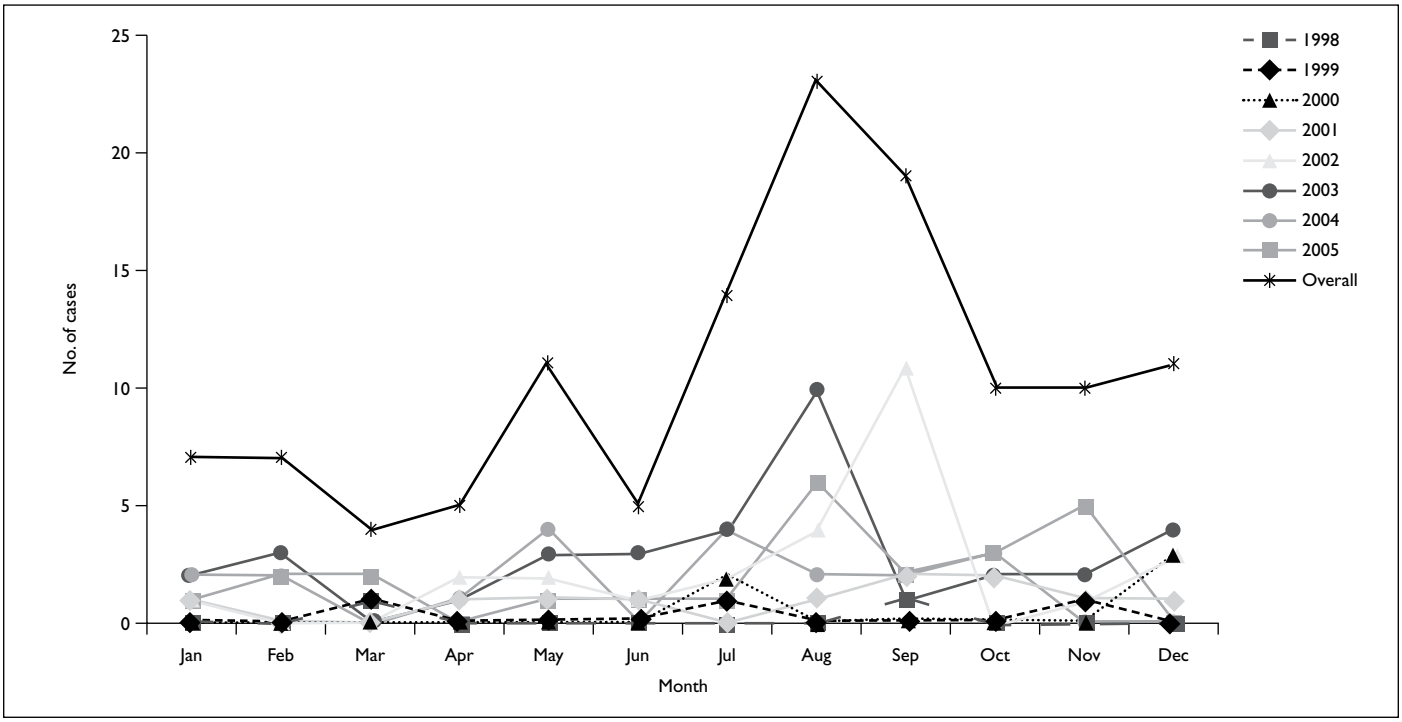

FIG 2. Seasonal variation of dengue fever cases admitted to public hospitals in Hong Kong

in 2003 were sporadic.

Seasonality

In Hong Kong, dengue cases were reported all year round. Figure 2 demonstrates the seasonal variation of cases, with a peak from July to September.

Country of origin for infection

Among the 116 imported cases, 106 (91%) were acquired in South-East Asian countries (Indonesia, Thailand, the Philippines, Vietnam, Singapore, Malaysia, Cambodia, Macau, and the Pacific Islands), eight (7%) originated from South Asia (India, Pakistan, Bangladesh, Sri-Lanka, and Nepal), and one (1%)

from Pitcairn island. Data for one case could not be determined as the patient had recently travelled to more than one country where the infection was endemic.

Patient demographics

The median age of the patients was 38 (range, 5-72) years and the female-to-male ratio was 1:1.2; five (4%) were paediatric patients (aged under 16 years); 114 (90%) were Hong Kong residents. A small proportion of the patients were migrant workers or tourists (4% and 5%, respectively). Among the Hong Kong residents, 86 (75%) were Chinese, 11 (10%) were from other Asian nations (Indonesia, the Philippines, Myanmar, Thailand), three (3%) were White and two (2%) belonged to the Pakistani/Nepalese group. Data on the origin of the remaining 12 patients were missing.

Serotype prevalence

Laboratory data on reverse-transcription PCR serotyping were available since 2002 and the serotypes of the corresponding 56 cases are shown in Figure 3.

All four serotypes, DEN-1, DEN-2, DEN-3 and DEN-4 were present among imported cases; while only DEN-1 (n=6) and DEN-2 (n=1) were present in local cases. Overall, DEN-1 was the most prevalent dengue serotype, responsible for nearly half (48%, 27/56) of all cases, followed by DEN-2 which accounted for about one quarter (23%, 13/56).

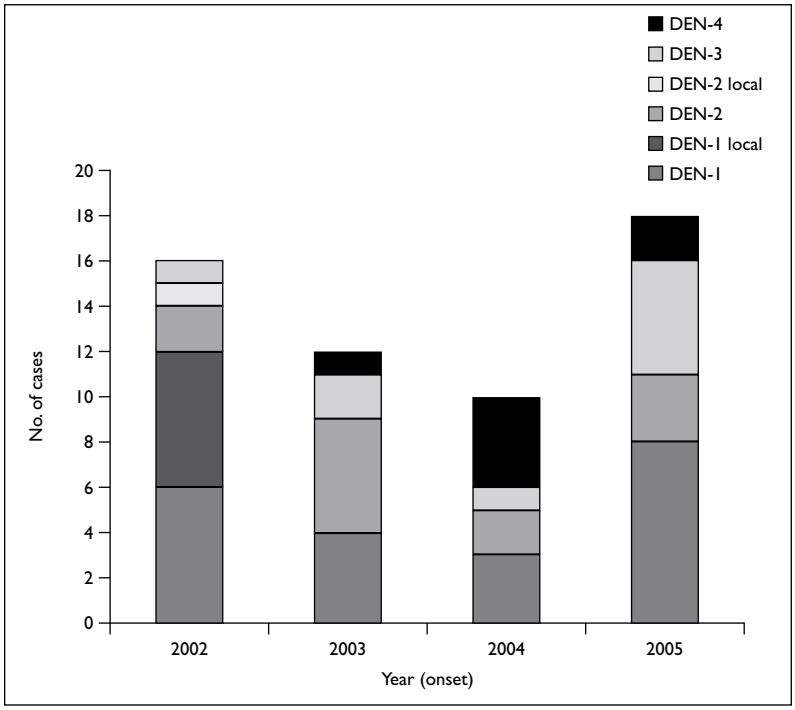

FIG 3. Distribution of serotypes among the dengue fever cases identified from 2002 to 2005

DEN-1 denotes dengue virus type 1, DEN-2 dengue virus type 2, DEN-3 dengue virus type 3, and DEN-4 dengue virus type 4

Clinical presentations and outcome

Approximately 98% (122/124) of patients presented with fever; the mean value for the highest temperature being 38.2°C (standard deviation, 1.0°C) [Table 1]. The second commonest presenting symptom was myalgia, 83% (75/90). Two thirds of patients had headache, fatigue, and skin rashes. One third of the patients (24/71) complained of retro-orbital pain. The chief presenting complaints in more than one third of the patients were gastro-intestinal (nausea, vomiting and/or diarrhoea) or upper respiratory tract (dry cough and/or sore throat) or both. Over one quarter of patients (28/108, 26%) complained of abdominal pain, and one complained of blurred vision. Except for petechiae which were present in 45% (47/105) of the patients, other spontaneous bleeding was uncommon. Maculopapular skin rash was the commonest physical finding; in 70% of those with a rash it occurred predominately on the trunk. Lymphadenopathy was uncommon, which was only elicited in 16% of the patients. No patient demonstrated biphasic fever. Only one patient had clinical and radiological features of plasma leakage (pleural effusion), and was confirmed to be due to DHF as the final diagnosis. The mean duration of hospitalisation for these patients was 6 days, and there was no mortality.

Laboratory findings

Thrombocytopenia was the most common haematological finding, which affected 107 (86%) of the 124 patients with available platelet counts (Table 1). The mean value of the lowest platelet counts was 64 x 10^9 /L. Among those with available results, neutropenia, atypical lymphocytes, and lymphopenia were present in 78%, 75%, and 69% of the patients respectively; half had prolonged activated partial thromboplastin time values. Corresponding proportions with deranged liver function tests and hypoalbuminaemia are also shown in Table 1. Mean values for aspartate aminotransferase and alanine aminotransferase were 212 IU/L and 169 IU/L, respectively.

Clinical differential diagnosis

Dengue infection was included as an initial clinical differential diagnosis in only 29% of the patients. Other differential diagnoses included: viral infection, upper respiratory tract infection, gastroenteritis, typhoid fever, chest infection, malaria, scarlet fever, scrub typhus, influenza, and fever for investigation.

TABLE 1. Recorded clinical symptoms, physical and laboratory findings of dengue cases

Symptoms/findings	No. of patients (%)	Remarks (reference range for laboratory tests)
Clinical symptoms		
Fever	122/124 (98)	
Myalgia	75/90 (83)	
Headache	68/105 (65)	
Skin rash	72/121 (60)	
Fatigue	50/85 (59)	
Dizziness	20/44 (45)	
Retro-orbital pain	24/71 (34)	
Gastro-intestinal tract (nausea, vomiting, and/or diarrhoea)	39/112 (35)	
Upper respiratory tract (non-productive cough, sore throat)	32/112 (29)	
Bleeding manifestations		
Epistaxis	7/67 (10)	
Gum bleeding	8/66 (12)	
Haematemesis	1/65 (2)	Dengue haemorrhagic fever
Tarry stool	1/69 (1)	Dengue haemorrhagic fever
Petechiae	47/105 (45)	
Clinical signs		
Skin rash	86/124 (69)	
Lymphadenopathy	19/116 (16)	
Laboratory findings		
Thrombocytopenia	107/124 (86)	Platelets: 145-370 x 10^9/L
Lymphopenia	79/114 (69)	Lymphocytes: 1.0-3.1 x 10^9/L
Neutropenia	89/114 (78)	Neutrophils: 1.7-5.8 x 10^9/L
Atypical lymphocytes	92/123 (75)	
Prolonged activated partial thromboplastin time	49/97 (51)	Activated partial thromboplastin time: 27.5-40.5 sec
Elevated aspartate aminotransferase	29/32 (91)	Aspartate aminotransferase: <38 IU/L
Elevated alanine aminotransferase	98/123 (80)	Alanine aminotransferase: 3-36 IU/L
Hypoalbuminaemia	34/123 (28)	Albumin: 35-52 g/L

Comparison of epidemiological, clinical, and laboratory findings among the four dengue virus serotypes

There were no statistically significant differences in terms of disease severity between the four virus types, patient gender, age and duration of hospitalisation, headache, myalgia, arthralgia, retro-orbital pain, skin rash, fatigue, gastro-intestinal and respiratory symptoms (Table 2). The percentages of patients with bleeding tendencies were 50%, 67%, 63%, and 33% for DEN-1, DEN-2, DEN-3, and DEN-4 virus type infections, respectively. Further analysis of the haemorrhagic manifestations was conducted by categorisation into epistaxis, gum bleeding, haematuria, and petechiae; 75% of these patients exhibited petechiae only, with no statistically significant difference between virus types (P=0.58). Nor was there any statistically significant difference between patients having different virus subtype infections for laboratory variables, except that the lowest lymphocyte counts of patients infected by serotype 3 was lower than the other serotypes (P=0.004).

Dengue haemorrhagic fever

Of the 126 patients under study, three (2%) were classified as DHF; all were imported from South-East Asian countries, and none could recall a previous history of dengue infection. Their demographic, clinical, and laboratory findings are shown in Table 3. They all received intravenous fluid replacement and platelet transfusions, recovered uneventfully without progression to dengue shock syndrome, and were discharged on day 6 or day 7 after hospital admission. Although these three patients did not recall prior infection, in one it was likely, as evidenced by respective acute and convalescence antibody titres.

Discussion

This is a comprehensive review of dengue fever patients admitted to Hong Kong public hospitals over the past 8 years. Epidemiological data showed that more than 70% of the patients were local Chinese residents with a travel history to neighbouring South-East Asian countries, where dengue fever is more endemic.[6] The most prevalent serotype was DEN-1, followed by DEN-2, DEN-3, and DEN-4, which was consistent with the serotype patterns in the countries from which such infections were imported.[7,8] The outbreak in Ma Wan was the first local one in Hong Kong; only DEN-1 and DEN-2 virus subtypes were encountered in local patients during 2002 and 2003.

Seasonal variations in dengue infections should be interpreted with cautions. Dengue fever is a travel-related arthropod-borne viral disease in Hong Kong; disease activity is closely related to and depends on the seasonal and weather conditions of countries from which the virus is imported. It is difficult to determine the seasonal patterns of dengue fever acquired locally based on the few reported cases. Monthly ovitrap surveillance in Hong Kong showed that the density of *Aedes albopictus* increases from April and peaks in June.[9] It is important to alert the public to keep vigilance against this mosquito-borne viral disease during this peak period.

We report here the first blood transfusion–transmitted dengue in the literature. The patient was a 76-year-old woman, with a history of hypertension and bronchiectasis. She was admitted in 2002 because of progressive malaise. Blood tests revealed

TABLE 2. Comparison of demographic, clinical, and laboratory findings in patients infected with the four dengue serotypes*

	PCR† type 1 (n=27)	PCR type 2 (n=13)	PCR type 3 (n=9)	PCR type 4 (n=7)	Overall (n=56)	P value
Gender (M:F)	13:14	6:7	5:4	3:4	27:29	1.0000
Age, median (IQR)	36.0 (24.0-52.0)	54.0 (33.0-66.0)	28.0 (23.5-61.0)	35.0 (21.0-63.0)	36.0 (26.3-57.8)	0.3559
Duration of hospitalisation, median (IQR) [days]	5.0 (4.0-7.0)	6.0 (3.0-7.5)	7.0 (4.5-8.5)	5.0 (4.0-6.0)	5.0 (4.0-7.0)	0.4589
Retro-orbital pain	9/18 (50)	3/10 (30)	0/4 (0)	1/6 (17)	13/38 (34)	0.2297
Rash—symptom	15/25 (60)	8/13 (62)	2/9 (22)	2/7 (29)	27/54 (50)	0.1332
Rash—sign	17/26 (65)	10/13 (77)	6/9 (67)	1/7 (14)	34/55 (62)	0.0509
Abdominal pain	3/25 (12)	2/12 (17)	1/8 (13)	1/7 (14)	7/52 (13)	1.0000
Diarrhoea	11/25 (44)	5/12 (42)	2/8 (25)	1/6 (17)	19/51 (37)	0.5956
Bleeding manifestation (epistaxis, gum bleeding, petechiae, haematuria)	13/26 (50)	8/12 (67)	5/8 (63)	2/6 (33)	28/52 (54)	0.5775
Hepatomegaly	2/26 (8)	2/13 (15)	0/9 (0)	1/7 (14)	5/55 (9)	0.5883
Leukopenia	25/26 (96)	10/13 (77)	9/9 (100)	5/7 (71)	49/55 (89)	0.0529
Lymphopenia	20/22 (91)	9/13 (69)	8/9 (89)	4/6 (67)	41/50 (82)	0.2550
Atypical lymphocyte	18/26 (69)	10/13 (77)	7/9 (78)	6/7 (86)	41/55 (75)	0.8848
Thrombocytopenia	26/26 (100)	11/13 (85)	8/9 (89)	6/7 (86)	51/55 (93)	0.0931
Elevated aspartate aminotransferase	8/9 (89)	3/4 (75)	4/4 (100)	2/2 (100)	17/19 (89)	1.0000
Elevated alanine aminotransferase	23/26 (88)	11/13 (85)	7/9 (78)	6/7 (86)	47/55 (85)	0.8954
Hypoalbuminaemia	10/26 (38)	5/13 (38)	5/9 (56)	4/7 (57)	24/55 (44)	0.6658
Highest temperature, mean (SD)	38.6 (1.0)	38.2 (1.1)	38.6 (1.3)	38.7 (0.6)	38.5 (1.0)	0.6893
Transfusion	4/23 (17)	2/12 (17)	1/8 (13)	2/6 (33)	9/49 (18)	0.8548

* Data are shown in No. (%), except otherwise stated
† PCR denotes polymerase chain reaction

TABLE 3. Demographic, clinical, and laboratory findings in patients with dengue haemorrhagic fever

Sex/age (years)	Ethnicity	Fever	Haemorrhagic manifestations	Lowest platelet count (x 10^9/L)	Plasma leakage	Laboratory findings	
						Serotype	Serology titer
M/38	Thai	37.2°C	Petechiae, bloody diarrhoea	9	Pleural effusion	Not done	Immunoglobulin M +ve
M/46	Chinese	38.4°C	Petechiae, bruises	9	Ascites	DEN 2	Immunoglobulin M +ve
F/49	Thai	38°C	Coffee ground vomitus, petechiae	8	Hypoalbuminaemia, haemoconcentration	DEN 1	4-fold increase*

* 1st titre: 640 (DEN-1), 5120 (DEN-2), 1280 (DEN-3), 1280 (DEN-4); 2nd titre: 5120 (DEN-1), 10 240 (DEN-2), 10 240 (DEN-3), 10 240 (DEN-4)

macrocytic anaemia and pancytopenia. She was diagnosed to have vitamin B12 deficiency anaemia, which was treated by vitamin B12 replacement and received a blood transfusion on 24 August 2002. On day 2 post-transfusion, she developed low-grade fever, but no skin rash, headache, myalgia, arthralgia, or retro-orbital pain. The patient was treated with antibiotics as for a urinary tract infection, based on the microbiological findings. The fever subsided 3 days later and the patient recovered uneventfully. The blood product she received was donated by a 17-year-old asymptomatic patient living in Ma Wan, during his viremic phase on 17 July 2002. On 24 July 2002, he developed generalised skin rash and attended the Accident and Emergency Department of Yan Chai Hospital. In October, he was subsequently picked up as one of the dengue cases based on serology results during the active case finding exercise in Ma Wan. Molecular testing performed on the donated blood product was positive for dengue virus type 1. The woman who had received the blood transfusion was recalled for blood testing on 7 October 2002, and was found to be positive for corresponding IgM antibodies and had a haemagglutination-inhibition titre of 1:2560. This incident was the first documented cases of such transmission in the literature, and since October

2002, the Hong Kong Red Cross Blood Transfusion Service (BTS) has intensified its donor deferral systems to counter this possibility. Specifically, it now asks about symptoms of dengue fever in the Blood Donor Registration Form (Supplement) by reminding all prospective donors to inform the BTS staff of all instances for flu, fever, headache, eye pain, muscle/joint pain, vomiting, and skin rash experienced 2 weeks before or after blood donation.

In our study, dengue fever was far more common than DHF and dengue shock syndrome, which were rare events. Our patients only manifested mild bleeding with good clinical outcomes and no fatalities. The clinical presentations of dengue fever, such as fever, myalgia, headache, and arthralgia, were comparable to findings reported in other studies.[10-12] Our patients (35%) presented with fewer gastroenteritis symptoms compared to those of others (50-98%).[11,12] Lymphadenopathy was documented in only 16% of our patients, which is much lower than the figure of 50% reported elsewhere.[13] This difference may be accounted for by less-than-adequate physical examination. Gum bleeding and epistaxis were reported in 12% and 10% of our patients respectively, which was also much lower than that reported previously.[11,12] Such differences could be due to the populations studied; patients recruited in endemic countries were mainly encountered during outbreaks in which both dengue fever and DHF were common. Previous studies showed dengue disease severity correlated with high viremia titres, secondary infection, and DEN-2 serotype infection.[14,15] Our findings showed that the haemorrhagic tendencies and duration of hospitalisation were not related to specific serotypes. Although some of our patients did receive platelet transfusions, the efficacy of such treatment in speeding recovery remains controversial. According to Thai experts, platelets are almost immediately destroyed by immune lysis after administration.[16]

Our study had several limitations. First, the target patients were limited to those with laboratory-confirmed dengue admitted to public hospitals. During 1998 to 2005, DH received notification of 203 dengue cases, including 77 who were admitted to private hospitals or consulted general practitioners only. The disease burden might also be underestimated, because some patients might have recovered, without seeking medical attention, while others might not have undergone serological testing. Second, statistical analysis could not be carried out to compare clinical and laboratory parameters in patients with dengue fever and DHF, as there were too few of the latter. Third, laboratory results before 2002 were not available in the Public Health Laboratory Information System. Fourth, not all clinical symptoms and signs listed in Table 2 could be retrieved from the medical records, as some may not have been specifically asked for or looked for.

In conclusion, dengue fever should be considered in the differential diagnosis of febrile patients with or without a travel history. Health care providers should therefore have an understanding of the infection, the spectrum of its clinical features, and methods of diagnosis and appropriate treatment. Until the *Aedes* mosquito can be effectively controlled or a cost-effective vaccine is developed, dengue fever will remain a public health concern, especially in South-East Asia. Control at source is one of the keys to combating dengue fever and requires active participation from all sectors of the community.

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References

1. Dengue/dengue haemorrhagic fever. Wkly Epidemiol Rec 2000;75:193-6.
2. General considerations. In: Dengue haemorrhagic fever: diagnosis, treatment, prevention and control. 2nd ed. Geneva: World Health Organization; 1997:1-11.
3. Auyeung TW, Que TL, Lam KS, Ng HL, Szeto ML. The first patient with locally acquired dengue fever in Hong Kong. Hong Kong Med J 2003;9:127-9.
4. Nimmannitya S. Clinical spectrum and management of dengue haemorrhagic fever. Southeast Asian J Trop Med Public Health 1987;18:392-7.
5. Nimmanitya S, Cardosa J. Dengue haemorrhagic fever. In: Weatherall DJ, Ledingham JGG, Warrell DA, editors. Oxford textbook of medicine. 3rd ed. Oxford, UK: Oxford Medical Publications; 1995.
6. Situation of dengue fever/dengue haemorrhagic fever in the South-East Asia Region. WHO Regional Office for South East Asia website: http://www.searo.who.int/EN/Section10/Section332_1100.htm. Accessed 23 Aug 2007.
7. Weekly Infectious Disease Bulletin [serial online] 2005;31(1). Singapore, Ministry of Health, Singapore: http://www.moh.gov.sg/mohcorp/statisticsweeklybulletins.aspx. Accessed 23 Aug 2007.
8. Limkittikul K, Yingsakmongkon S, Jittmittraphap A, et al. Clinical differences among PCR-proven dengue serotype infections. Southeast Asian J Trop Med Public Health

2005;36:1432-8.
9. Average Monthly Ovitrap Index, 2000-2006. HKSAR Food and Environmental Hygiene Department website: http://www.fehd.gov.hk/safefood/dengue_fever/index.html. Accessed 23 Aug 2007.
10. Kalayanarooj S, Vaughn DW, Nimmannitya S, et al. Early clinical and laboratory indicators of acute dengue illness. J Infect Dis 1997;176:313-21.
11. Singh NP, Jhamb R, Agarwal SK, et al. The 2003 outbreak of Dengue fever in Delhi, India. Southeast Asian J Trop Med Public Health 2005;36:1174-8.
12. Hussin N, Jaafar J, Naing NN, Mat HA, Muhamad AH, Mamat MN. A review of dengue fever incidence in Kota Bharu, Kelantan, Malaysia during the years 1998-2003. Southeast Asian J Trop Med Public Health 2005;36:1179-86.
13. Ryan ET, Wilson ME, Kain KC. Illness after international travel. N Engl J Med 2002;347:505-16.
14. Vaughn DW, Green S, Kalayanarooj S, et al. Dengue viremia titer, antibody response pattern, and virus serotype correlate with disease severity. J Infect Dis 2000;181:2-9.
15. Thein S, Aung MM, Shwe TN, et al. Risk factors in dengue shock syndrome. Am J Trop Med Hyg 1997;56:566-72.
16. Alex C, Djatnika S, Ridad A, et al. Thrombocytopenia and platelet transfusions in Dengue Haemorrhagic Fever and Dengue Shock Syndrome. Dengue Bulletin 2003;27:138-43.