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Tuberculosis surveillance in Singapore, 2013

The National Tuberculosis (TB) Control Programme was established in the late 1950s with the setting up of the TB Control Unit and a National TB registry. The programme was enhanced with the launch of the Singapore Tuberculosis Elimination Programme (STEP) in 1997. The main aim of STEP is to eliminate TB in Singapore by detecting, diagnosing and treating all infectious TB cases; identifying and treating infected TB contacts; and preventing the emergence of multidrug-resistant TB.

TB among Singapore's total population [citizens, permanent residents (PRs), and long-staying foreigners]

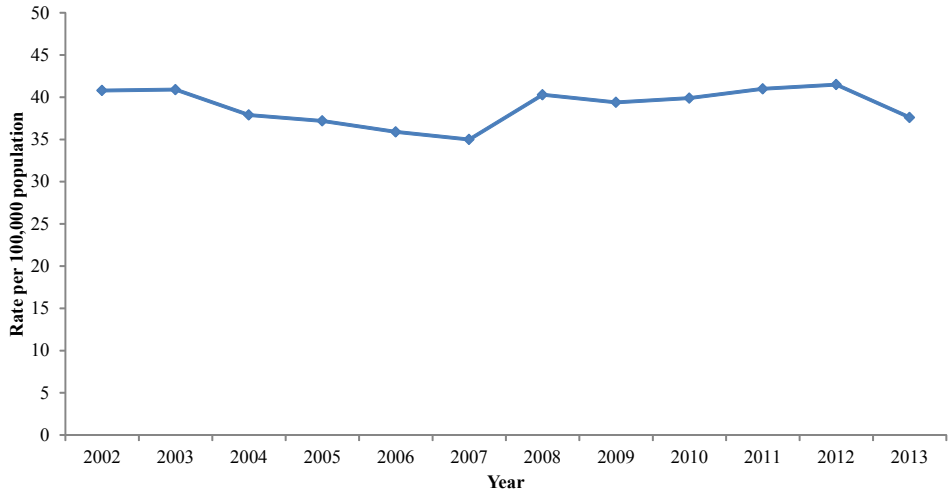
A total of 2,962 cases of TB were notified in 2013. This comprised 1,420 new and 119 relapsed cases among Singapore residents (citizens and PRs) and 1,381 new and 42 relapsed cases among non-residents (long-and short-term pass holders)

Of the reported new cases, 2,028 were Singapore residents (citizens and PRs) and long-staying foreigners, giving an incidence rate of 37.6 per 100,000 population (*Fig. 1*)

The majority (86.3%) of cases had pulmonary TB with or without extra-pulmonary involvement, while the remainder (13.7%) had exclusively extrapulmonary TB.

Of the 2,028 new cases notified in 2013, 885 (43.6%) were 50 years old and above, and 1,276 (62.9%) were males. Among the 1,750 new pulmonary TB cases in Singapore residents and long-staying foreigners, 1,669 (95.4%) had bacteriological tests done. The proportion found to have demonstrable bacillary disease was 64.9%.

Figure 1
Incidence rate of TB among Singapore residents and long-staying foreigners, 2002-2013



TB in Singapore residents (citizens and permanent residents)

Of the 1,420 new TB cases among Singapore residents notified in 2013, the majority (88.0%) had pulmonary TB with or without extra-pulmonary involvement, while 12.0% had exclusively extrapulmonary TB. The most common site of extrapulmonary TB was the lymphatic system (123 new cases) followed by the pleura (110 new cases). There was no case of TB meningitis reported among Singapore residents below 15 years of age. Of the 1,249 new pulmonary TB cases, 1,207 (96.6%) had bacteriological tests done. The proportion found to have demonstrable bacillary disease was 72.8%.

Of the new cases, 1,171 (82.5%) were Singapore-born and 248 (17.5%) were foreign-born. There were 119 relapsed cases (94 males and 25 females) which accounted for 7.7% of all reported cases (new & relapse). Among the relapsed cases, 108 (90.8%) were Singapore-born and 11 (9.2%) were foreign-born. A prior diagnosis of human immunodeficiency virus (HIV) infection was reported in 44 (3.1%) of the new cases, quite similar to that in the previous year (2.7%). Of the relapsed cases, 6.7% had been previously diagnosed with HIV, compared with 3.7% in 2012. Most of these TB-HIV infections were observed in older age groups, males and Chinese.

Distribution by age and gender

As in previous years, TB in Singapore residents (citizens and PRs) continues to be a disease of older males (*Table 1*). Of the 1420 new cases notified in 2013, 854 (60.1%) were 50 years old and above, and 986 (69.4%) were males.

Ethnic distribution

As in previous years, Malays had the highest TB incidence among the three main ethnic groups. The incidence rate in Malays decreased from 66.1 per 100,000 in 2012 to 57.3 per 100,000 population in 2013. Over the same period, the incidence rate

Table 1

Age-gender distribution and incidence rates of reported TB among Singapore residents, 2013

Age (yrs)	Male	Female	Total (%)	Incidence rate per 100,000 population*		
				Male	Female	Total
0 – 4	1	0	1 (0.1)	1.1	0.0	0.5
5 – 9	1	1	2 (0.2)	1.0	1.0	1.0
10 – 14	3	1	4 (0.3)	2.6	0.9	1.8
15 – 19	17	19	36 (2.5)	13.1	15.2	14.1
20 – 29	57	64	121(8.5)	22.1	24.2	23.2
30 – 39	87	78	165 (11.6)	30.1	24.9	27.4
40 – 49	169	68	237 (16.7)	54.3	21.4	37.7
50 – 59	247	56	303 (21.3)	82.7	19.0	51.0
60 – 69	178	58	236 (16.6)	98.5	31.0	64.1
70 – 79	149	44	193 (13.6)	186.7	45.6	109.4
80 +	77	45	122 (8.6)	252.5	86.9	148.3
Total	986	434	1,420 (100)	52.1	22.2	36.9

* Rates are based on 2013 mid-year population.
(Source: Singapore Department of Statistics)

in the Chinese population decreased from 37.6 per 100,000 population to 34.3 per 100,000 population, while that of the Indians was stable at 26.4 per 100,000 population (*Table 2*)

Tuberculosis in non-residents

In 2013, there were 1,381 new TB cases notified among non-residents in Singapore, comprising 501 cases of pulmonary TB and 107 cases of extrapulmonary cases among long-term pass holders, and 678 cases of pulmonary TB and 95 cases of extrapulmonary TB for short-tern pass holders. As in previous years, the number of new TB cases notified among short-term pass holders outnumbered long-term pass holders. However in 2013, work permit holders formed the largest group (434 cases), in contrast to the preceding two years when work permit applicants formed the largest group (*Table 3*). As a proportion, long-term pass holders and short-term pass holders contributed 21.7% and 27.6% of notified new cases in 2013, respectively.

TB drug resistance

TB drug resistance for Singapore residents are presented separately amongst those who are Singapore-born and foreign-born. Cases with unknown place of births were excluded from the analysis. The data presented is based on the drug susceptibility testing result of mycobacterial cultures taken at baseline (from three months before to two weeks after

Table 2

Ethnic-gender distribution and ethnic-specific incidence rates of reported TB among Singapore residents, 2013

Ethnic group	Male	Female	Total (%)	Incidence rate per 100,000 population*
Chinese	688	292	980 (69.0)	34.3
Malay	210	84	294 (20.7)	57.3
Indian	66	27	93 (6.6)	26.4
Others	22	31	53 (3.7)	41.9
Total	986	434	1,420 (100)	36.9

* Rates are based on 2013 mid-year population.
(Source: Singapore Department of Statistics)

Table 3

Distribution of new TB cases among non-residents by pass category/status, 2009 – 2013

Pass category / status	No. of new TB cases notified				
	2009	**2010**	**2011**	**2012**	**2013**
Long-term immigration pass holders residing in Singapore					
Work permit holders	403	403	442	458	434
Employment pass holder	32	41	47	53	52
Other pass holders *	89	106	104	132	122
Sub-total	524	550	593	643	608
Short stay foreigners					
Work permit applicants	218	329	462	528	389
Visitors **	220	253	237	238	216
Others ***	113	181	207	151	168
Sub-total	551	763	906	917	773
Total	**1,075**	**1,313**	**1,499**	**1,560**	**1,381**

* Professional pass holder, dependent pass holder, long-term social visit pass holder and student pass holder and S pass holder

** Short term social visitor

*** Professional visit pass applicant, dependent pass applicant, long-term social visit pass applicant, student pass applicant, employment pass applicant, S pass applicant and illegal immigrant

the date of notification or date of starting treatment, whichever earlier).

Singapore-born residents

The overall incidence of drug resistance among 713 new pulmonary TB cases in whom drug-susceptibility testing was performed was 6.6%: with 5.3% (38 cases) resistant to one drug and 1.3% (9 cases) resistant to more than one drug (*Table 4*). Multi-drug-resistant TB (MDR-TB), i.e. resistance to both rifampicin and isoniazid, was detected in 2 cases (0.3%), while resistance to isoniazid but not rifampicin was detected in 21 cases (2.9 %).

The overall incidence of drug resistance among 61 relapsed pulmonary TB cases with drug susceptibility testing performed was 6.6%: 5.0% (3 cases) were resistant to one drug and 1.6% (1 case) was resistant to more than one drug. There was one MDR-TB case (1.6%) and one case (1.6%) resistant to isoniazid but not rifampicin. No Singapore-born resident with initially pan-sensitive or isoniazid mono-resistant TB developed MDR-TB during treatment in 2013.

Table 4

***Mycobacterium tuberculosis* drug susceptibility in Singapore-born residents with pulmonary tuberculosis, 2010 – 2013**

Sensitivity result of sputum examination*	2010		2011		2012		2013	
	No.	%	No.	%	No.	%	No.	%
New cases								
**Sensitive to:								
Streptomycin, isoniazid, rifampicin	738	95.0	762	94.7	784	92.7	666	93.4
Resistant to:								
Single drug	33	4.2	32	4.0	52	6.1	38	5.3
More than 1 drug	6	0.8	11	1.3	10	1.2	9	1.3
Total examined	**777**	**100**	**805**	**100**	**846**	**100**	**713**	**100**
***Resistant to isoniazid	**12**	**1.5**	**16**	**2.0**	**28**	**3.3**	**21**	**2.9**
Resistant to rifampicin & isoniazid	**1**	**0.1**	**3**	**0.4**	**6**	**0.7**	**2**	**0.3**
Relapsed cases								
Sensitive to:								
Streptomycin, isoniazid, rifampicin	58	85.3	78	88.6	70	92.1	57	93.4
Resistant to:								
Single drug	8	11.8	9	10.2	5	6.6	3	5.0
More than 1 drug	2	2.9	1	1.1	1	1.3	1	1.6
Total examined	**68**	**100**	**88**	**100**	**76**	**100**	**61**	**100**
Resistant to isoniazid	**3**	**4.4**	**6**	**6.8**	**3**	**3.9**	**1**	**1.6**
Resistant to rifampicin & isoniazid	**1**	**1.5**	**0**	**0**	**0**	**0**	**¥ 1**	**1.6**

* In the case of dual lesions, the sensitivity result recorded is that of organisms cultured from sputum.

** Sensitive to isoniazid, rifampicin,streptomycin and ethambutol

***Any of isoniazid resistance, exclusive of MDR

¥ MDR case was notified as both pulmonary and extra-pulmonary TB, but MDR result was from an extra-pulmonary specimen only

There was no case of extensively-drug-resistant TB (XDR-TB), i.e. MDRTB with resistance to any fluoroquinolone and second-line injectable agent, among Singapore-born TB cases in 2013

Foreign-born residents

In 2013, the overall incidence of drug resistance among 143 new pulmonary TB cases in whom drug-susceptibility testing was performed was 11.9%, with 8.4% (12 cases) resistant to one drug and 3.5% (5 cases) resistant to more than one drug (*Table 5*). There were no MDR-TB cases. Resistance to isoniazid was 6.9% (10 cases). No drug resistance was detected among the 6 relapsed pulmonary TB cases in foreign-born residents with drug susceptibility testing performed.

Non-residents

In 2013, the overall incidence of drug resistance in new pulmonary TB cases among 392 non-residents with drug-susceptibility testing performed was 13.0%, with 8.2% (32 cases) being resistant to one drug and 4.8% (19 cases) resistant to more than one drug (*Table 6*). MDR-TB was detected in 12 cases (3.1%), and resistance to isoniazid but not rifampicin was detected in 27 cases (6.9%). Among the 20 relapsed pulmonary

Table 5

***Mycobacterium tuberculosis* drug susceptibility in foreign-born residents with pulmonary tuberculosis, 2010 – 2013**

Sensitivity result of sputum examination *	2010		2011		2012		2013	
	No.	%	No.	%	No.	%	No.	%
New cases								
**Sensitive to:								
Streptomycin, isoniazid, rifampicin	133	92.4	135	91.8	101	89.4	126	88.1
Resistant to:								
Single drug	7	4.9	5	3.4	7	6.2	12	8.4
More than 1 drug	4	2.8	7	4.8	5	4.4	5	3.5
Total examined	**144**	**100**	**147**	**100**	**113**	**100**	**143**	**100**
***Resistant to isoniazid	**7**	**4.9**	**5**	**3.4**	**7**	**6.2**	**10**	**7.0**
Resistant to rifampicin & isoniazid	**1**	**0.7**	**3**	**2.0**	**2**	**1.8**	**0**	**0**
Relapsed cases								
Sensitive to:								
Streptomycin, isoniazid, rifampicin	7	77.8	13	86.7	9	90.0	6	100
Resistant to:								
Single drug	2	22.2	1	6.6	0	0	0	0
More than 1 drug	0	0.0	1	6.6	1	10.0	0	0
Total examined	**9**	**100**	**15**	**100**	**10**	**100**	**6**	**100**
Resistant to isoniazid	**1**	**11.1**	**1**	**6.6**	**0**	**0.0**	**0**	**0**
Resistant to rifampicin & isoniazid	**0**	**0**	**0**	**0**	**1**	**10.0**	**0**	**0**

* In the case of dual lesions, the sensitivity result recorded is that of organisms cultured from sputum.
** Sensitive to isoniazid, rifampicin, streptomycin and ethambutol
***Any of isoniazid resistance, exclusive of MDR

TB cases with drug susceptibility testing performed, 5.0% (1 case) was resistant to one drug and 20.0% (4 cases) to more than one drug. Four cases (20.0%) were MDR-TB, and 1 case (5.0%) was resistant to isoniazid but not rifampicin.

Tuberculosis mortality

In 2013, there were 46 deaths from tuberculosis among Singapore residents giving a mortality rate of 1.2 cases per 100,000 population (*Table 7*). The majority were males (76.1%) and aged 60 years and above (84.8%).

Comments

The incidence rate of TB per 100,000 population declined from 307 in 1960 to 56.3 in 1987. From 1987 to 1997, the incidence rate of new TB cases among Singapore citizens and permanent residents stagnated around 50-55 per 100,000 population. Following enhanced TB control measures implemented

Table 6

***Mycobacterium tuberculosis* drug susceptibility in non-residents with pulmonary tuberculosis, 2010 – 2013**

Sensitivity result of sputum examination *	2010		2011		2012		2013	
	No.	%	No.	%	No.	%	No.	%
New cases								
**Sensitive to:								
Streptomycin, isoniazid, rifampicin	363	84.6	435	84.5	346	83.2	341	87.0
Resistant to:								
Single drug	28	6.5	44	8.5	35	8.4	32	8.2
More than 1 drug	38	8.9	36	6.9	35	8.4	19	4.8
Total examined	**429**	**100**	**515**	**100**	**416**	**100**	**392**	**100**
***Resistant to isoniazid**	**42**	**9.8**	**40**	**7.8**	**35**	**8.4**	**27**	**6.9**
Resistant to rifampicin & isoniazid	**13**	**3.0**	**13**	**2.5**	**20**	**4.8**	**¥ 12**	**3.1**
Relapsed cases								
Sensitive to:								
Streptomycin, isoniazid, rifampicin	8	53.3	19	65.5	15	78.9	15	75.0
Resistant to:								
Single drug	0	0.0	3	10.3	1	5.3	1	5.0
More than 1 drug	7	46.7	7	24.1	3	15.8	4	20.0
Total examined	**15**	**100**	**29**	**100**	**19**	**100**	**20**	**100**
Resistant to isoniazid	**1**	**6.7**	**3**	**10.3**	**1**	**5.3**	**1**	**5.0**
Resistant to rifampicin & isoniazid	**6**	**40.0**	**6**	**20.7**	**3**	**15.8**	**4**	**20.0**

* In the case of dual lesions, the sensitivity result recorded is that of organisms cultured from sputum.

** Sensitive to isoniazid, rifampicin,streptomycin and ethambutol

***Any of isoniazid resistance, exclusive of MDR

¥ One MDR case was notified as both pulmonary and extra-pulmonary TB, but MDR result was from an extra-pulmonary specimen only

by STEP[1], the incidence rate declined from 56.9 per 100,000 population in 1998 to a historical low of 35.1 per 100,000 population in 2007. However, in 2008, the incidence rate increased for the first time over the last decade to 39.8 per 100,000 population. During the period 2009-2012, the incidence rate stagnated at between 38.6 and 40.9 per 100,000 population, before decreasing to 36.9 per 100,000 in 2013 (*Fig. 2*).

Non-residents constituted a large proportion of the new cases notified. For short-term pass holders, it increased from 14.3 % in 2002 to 27.6% in 2013; and for long-term pass holders, it increased from 13.9 % to 21.7% in the same period.

The frequency of TB drug resistance remained low. Among Singapore residents, MDR-TB was

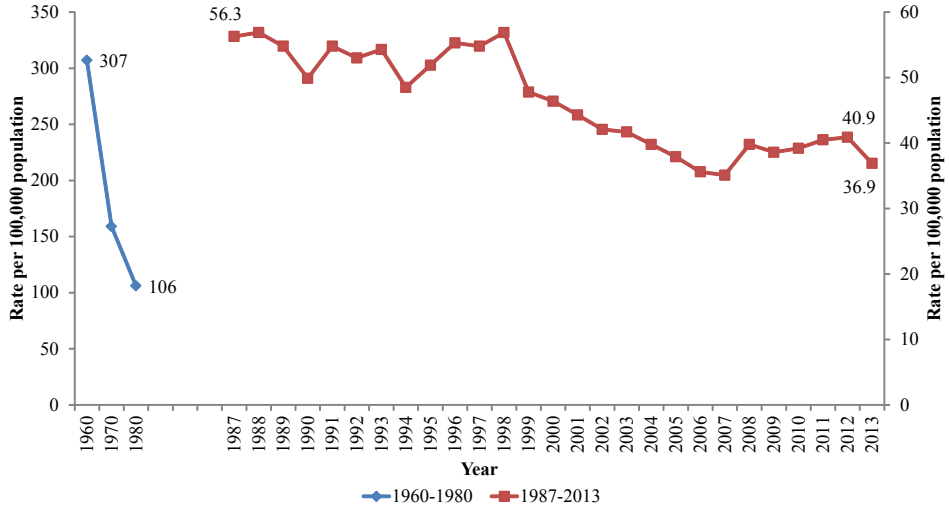
Table 7

Age-gender distribution and age-specific mortality rates of tuberculosis, 2013

Age (years)	Male	Female	Total (%)	Mortality rate per 100,000 population*
10 – 19	0	0	0	0
20 - 29	0	0	0	0
30 – 39	0	1	1 (2.2)	0.2
40 – 49	3	0	3 (6.5)	0.5
50 – 59	3	0	3 (6.5)	0.5
60 – 69	5	2	7 (15.2)	1.9
70 +	24	8	32 (69.6)	12.4
Total	**35**	**11**	**46 (100)**	**1.2**

* Rates are based on 2013 estimated mid-year population.
(Source: Singapore Department of Statistics, Registry of Births & Deaths)

Figure 2
Incidence rate of TB among Singapore residents, 1960 – 1980 and 1987-2013



detected in 0.3% of the new cases and 1.6% of relapsed cases in 2013. The corresponding frequency of MDR-TB in non-residents was higher at 3.1% and 20%, respectively. No case of XDR-TB among Singapore-born TB cases was identified in 2013. A high degree of vigilance is being maintained[2].

Among Singapore residents, relapsed cases have declined from 158 in 2011 to 119 in 2013. While TB remains a disease of the older population, there is an increasing trend among adults aged 20-59 years over the last decade[3].

Delay in seeking treatment and diagnosis of symptomatic cases[4,5], and difficulties in enforcement of recalcitrant TB treatment defaulters remained a problem[6], While directly-observed therapy (DOT) has been increasing from 10% before 1997 to over 55% currently, more efforts are being taken to promote this mode of treatment. Ageing population and an increasing prevalence of diabetes will pose further challenges in the elimination of TB in Singapore. Infection with HIV is also known to increase a person's susceptibility to TB.

Following a review in 2012, measures to strengthen case detection and treatment have been rolled out progressively to enhance STEP, which addressed two key challenges for TB control: delay diagnosis of infectious TB cases and non-compliance with complete treatment regimen until a complete cure.

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Epidemiology of hepatitis B virus infection in Singapore

Introduction

The disease burden of hepatitis B virus (HBV) infection constitutes a major public health concern, as HBV infection is an important cause of severe illness and death due to chronic active hepatitis, liver cirrhosis and primary liver cancer.[1] HBV is transmitted through exposure to infected bodily fluids. While HBV infection often occurs during childbirth or early childhood, it can be prevented through vaccination

at birth followed by at least two additional doses during infancy.

Hepatitis B carriers and those with chronic hepatitis and cirrhosis due to HBV infection are at a much higher risk of developing liver cancer. The global burden of disease due to acute hepatitis B and C and to cancer and cirrhosis of the liver is forecast to be ranked higher as a cause of death over the next two decades.[2] It was estimated that more than 240 million people have chronic liver infections, with 78,000 deaths annually from the acute or chronic consequences of hepatitis B.[3]

In May 2014, the 67th World Health Assembly (WHA), the governing body of the World Health Organization (WHO), recognising viral hepatitis as a global public health problem, called on governments and populations to take immediate action to prevent, diagnose and treat the disease.[4] The WHA also urged Member States to support or enable an integrated and cost-effective approach to the prevention, control and management of viral hepatitis. In Singapore, the total annual cost of chronic HBV infection and its associated complications was estimated to be about US$279 million, with total direct cost amounting to 12% of the national healthcare expenditure in 2003.[5]

Acute viral hepatitis was made a notifiable disease in Singapore under the Infectious Diseases Act in 1976.[6] Between 1977 and 1981, a total of 677 cases of hepatitis B were reported, with a mean annual morbidity rate of 5.6 per 100,000 population.[7] The case fatality rate was 2.1% and the mean morbidity rate was 0.12 per 100,000 population. Based on epidemiological surveillance, HBV accounted for 24% to 54% of the reported acute viral hepatitis cases in Singapore from 1982 to 1996.[8]

The cornerstone of Singapore's HBV prevention and control strategies is universal vaccination against hepatitis B as part of the national childhood immunisation programme (NCIP). Other components include surveillance, routine antenatal screening and screening of voluntary blood donors for HBV carriers, adoption of universal precautions and public education.[9] Singapore was among the first countries in the world to implement a national childhood HBV immunisation programme. Hepatitis B vaccination for infants born to carrier mothers was incorporated into the NCIP on 1 October 1985, and it was extended to all newborns since 1 September 1987. The immunisation schedule consists of three doses, with the first dose administered at birth, the second dose at 4–6 weeks and the third dose at 5 months. One dose of hepatitis B immunoglobulin is also concurrently administered at birth to babies born to hepatitis B e antigen-carrier mothers. A catch-up hepatitis B vaccination programme targeted at students in secondary schools, junior colleges, centralised institutes, institutes of technical education, polytechnics and universities who were born before 1987 and who were likely to have missed the national HBV childhood immunisation programme was implemented over a four-year period from 2001 to 2004.[10] To complement the school immunisation programme, a mass media education programme was also launched in February 2001 to educate the public on the risks of hepatitis B infection and encourage members of the public who have not been vaccinated to be screened and immunised against HBV infection.

The objective of this study was to determine the epidemiology of hepatitis B in Singapore. We examined the trends based on notifications of acute hepatitis B, vaccination coverage against hepatitis B and prevalence of HBV serological markers.

Materials and methods

Case surveillance

Acute hepatitis B is a legally notifiable infectious disease in Singapore, and all medical practitioners and medical laboratories are required to notify acute viral hepatitis to the Ministry of Health (MOH) within 72 hours from time of diagnosis.

Cases of acute hepatitis B are serologically confirmed with the presence of hepatitis B surface antigen (HBsAg) and IgM antibody against hepatitis B core antigen (IgM anti-HBc), which are both associated with acute clinical presentation.

The epidemiological data of all laboratory-confirmed cases of acute hepatitis B notified to the Communicable Diseases Division, MOH, under the Infectious Diseases Act from 2003 to 2013 were analysed.

Vaccination coverage

The National Immunisation Registry (NIR) of the Health Promotion Board (HPB) monitors and tracks the vaccination coverage in the NCIP among children who are Singapore residents (Singapore citizens and permanent residents). The annual coverage rate for each cohort of Singapore residents who completed the full course of vaccination by two years of age was obtained from NIR.

Serological surveys in adult population

National seroprevalence studies were conducted by MOH in 1999, 2005 and 2012 to determine the HBV prevalence in the adult Singapore resident population using residual sera obtained during the National Health Surveys (NHS) in 1998[11], 2004[12] and 2010[13], respectively. The NHS was a population-based cross-sectional survey conducted by MOH to determine the prevalence of chronic diseases and lifestyle-related risk factors in Singapore adult residents aged 18 years and older. Ethical approval was given by the Institutional Review Board Ethics Committee of HPB. Residual sera from NHS participants who had consented to the use of their residual sera for further research were tested. Personal identifiers of participants were permanently removed, and new study numbers were tagged to the residual sera to ensure strict anonymity of the NHS participants. The numbers of residual sera tested for HBV markers were 4,698 from NHS 1998, 4,153 from NHS 2004 and 3,293 from NHS 2010.

A national paediatric seroprevalence survey (NPSS) was conducted between August 2008 and July 2010 to estimate the immunity level against hepatitis B. Residual sera from children and adolescents aged 1-17 years, who had been hospitalised or attended day surgery in KK Women's and Children's Hospital (KKH) and National University Hospital, were collected prospectively following the completion of routine biochemical investigations. Sera of patients known to be immunocompromised, on immunosuppressive therapy, or who had been diagnosed with infectious diseases such as hepatitis B, measles, mumps, rubella, chickenpox, diphtheria, pertussis, poliomyelitis, dengue or hand, foot, and mouth disease were excluded. A total of 1,200 samples were collected, which comprised 400 in each of the three age groups of 1-6, 7-12, and 13-17 years.

The laboratory methods used in the three national seroprevalence studies for adults[10,14,15] and NPSS 2008-2010[16] had been previously described. The residual sera from NPSS 2008-2010 and NHS

2010 were tested for hepatitis B surface antigen (HBsAg) and antibody to HBsAg (anti-HBs) by the chemiluminescence immunoassay (CMIA). Those with anti-HBs levels ≥10 mIU/ml were considered to have immunity to HBV. Residual sera from NHS 2010 were further tested for hepatitis B e antigen (HBeAg) and antibody to hepatitis B core antigen (anti-HBc) by CMIA.

Statistical analysis

For the calculation of annual age-specific incidence rates, the denominators used were the corresponding estimated mid-year populations compiled by the Department of Statistics, Singapore.

For comparison with the HBV prevalence in 1998 and 2004, the study sample in 2010 was confined to Singapore residents aged 18-69 years who were ethnic Chinese, Malay and Indian; subjects aged 75-79 years and other ethnic groups were omitted. Age-standardisation of seroprevalence was calculated by the direct method, using the 2010 census Singapore resident population as the standard.

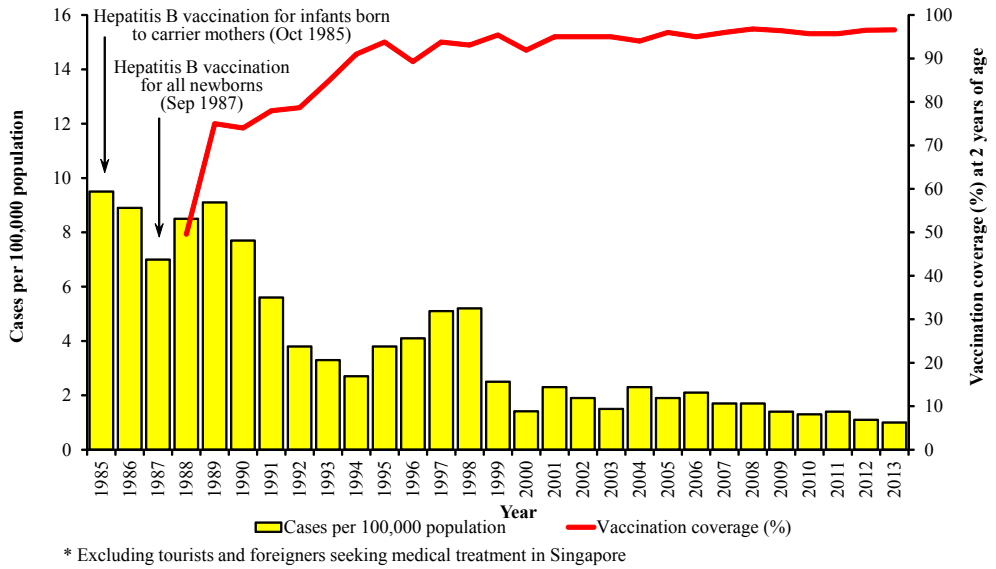
The Chi-square test or Fisher's exact test, where appropriate, was used to test for group differences. The Mantel-Haenszel chi-square test for trend was used to evaluate the difference in seronegative rates across age groups. Statistical analysis was performed using the statistical software package, SPSS Statistics software, version 19.0 (IBM, USA). Statistical significance was taken at $p < 0.05$.

Results

Incidence of acute hepatitis B

The annual incidence of acute hepatitis B per 100,000 population in Singapore, excluding tourists and foreigners seeking medical treatment in Singapore, declined from 9.5 in 1985 to 2.5 in 1999 and 1.0 in 2013 (*Fig. 3*).

Figure 3
Incidence of acute hepatitis B per 100,000 population and vaccination coverage among Singapore children at 2 years of age, 1985-2013*



* Excluding tourists and foreigners seeking medical treatment in Singapore

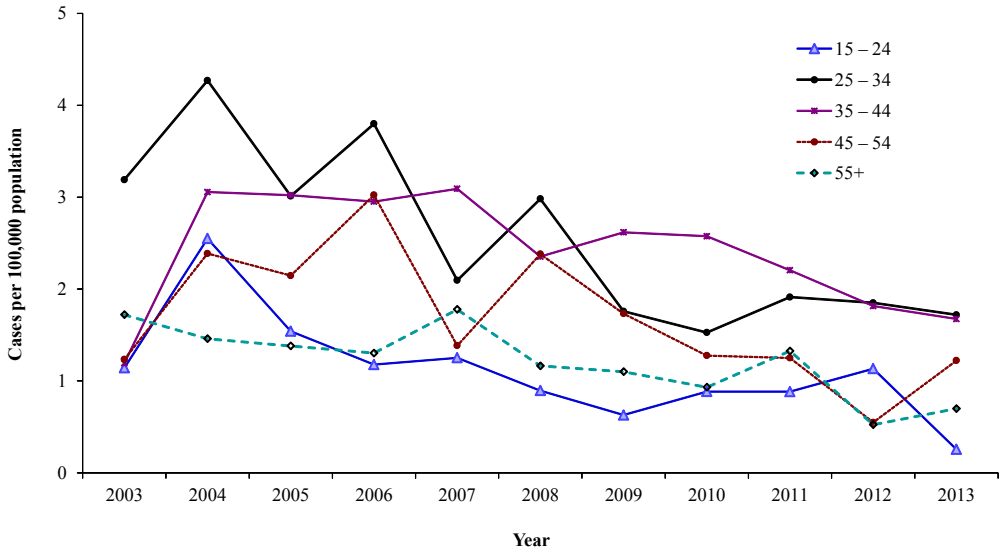
During the period 2003-2013, a total of 829 cases of acute hepatitis B, including 188 imported cases, were reported. The annual proportion of imported cases ranged from 10.2% to 31.0%. Among the imported cases, 24 were tourists and foreigners seeking medical treatment in Singapore, and they were excluded from further analysis. The annual incidence rate of acute hepatitis B was consistently higher in men than in women. Among the 805 cases of acute hepatitis B, there was a male predominance with a male to female ratio of 5:1 in the 11-year period.

The highest incidence of acute hepatitis B was observed among persons aged 25-44 years for both men and women. The incidence per 100,000 population ranged from 1.5 to 4.3 in the 25-34 year age group, while it ranged from 1.2 to 3.1 in the 35-44 year age group (*Fig. 4*). The incidence of acute hepatitis B in children less than 15 years of age declined from 10 cases in 1983 to 0 since 1997.[17] Of all the cases, over one-third (34.2%) occurred in the 25-34 year age group, while another 27.6% were in the age group of 35-44 years.

The ethnic-specific incidence rate of acute hepatitis B is shown in *Fig. 5*. Among 558 cases who were Singapore residents, Chinese constituted over three-quarters (76.7%), while Malays and Indians comprised 12.5% and 7.2%, respectively. Non-residents constituted 30.7% of all the cases in the 11-year period.

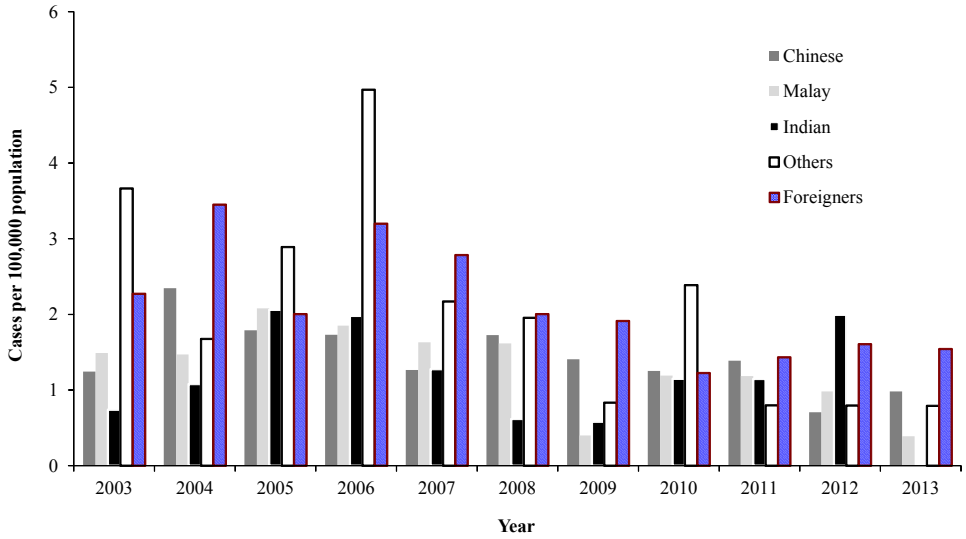
Table 8 shows the results of blood samples obtained from antenatal women screened for HBsAg and HBeAg at KKH from 2003 to 2013. The proportion tested positive for HBsAg ranged from 2.2% to 2.8%. Of those who were HBsAg positive, about 22.6% to 30.2% were also positive for HBeAg.

Figure 4
Age-specific incidence of acute hepatitis B per 100,000 population, 2003-2013*



* Excluding tourists and foreigners seeking medical treatment in Singapore.

Figure 5
Ethnic-specific incidence of acute hepatitis B per 100,000 population, 2003-2013*



* Excluding tourists and foreigners seeking medical treatment in Singapore.

Table 8

Results of blood samples obtained from antenatal women screened at KKH for HBsAg and HBeAg, 2003 to 2013

Year	No. of blood samples screened	% HBsAg positive	% HBeAg positive among the HBsAg positives
2003	13,059	2.4	27.9
2004	13,446	2.3	30.2
2005	14,969	2.2	22.6
2006	14,916	2.4	24.6
2007	16,449	2.8	28.8
2008	17,899	2.4	28.4
2009	19,090	2.5	27.2
2010	18,417	2.4	29.2
2011	19,707	2.2	29.9
2012	18,570	2.2	31.1
2013	19,177	2.3	28.8

Vaccination coverage

The coverage for infants who had completed the full course of three doses of hepatitis B vaccine before one year of age increased from 50% in 1988 to 91% in 1994.[17] Since 2005, at least 95% of children completed the full course of hepatitis B vaccination by 2 years of age (*Fig. 3*).[18]

Prevalence of HBV markers

The overall prevalence of HBsAg was 0.3% (95% confidence interval [CI]: 0.1% – 0.9%) among children and adolescents aged 1-17 years, and 3.6% (95% CI: 2.9% – 4.2%) among adults aged 18-79 years in 2010.

In the NPSS 2008-2010, there was no significant difference in HBsAg prevalence by age group (test for trend, p = 0.066); 0.0% in the 1-6 year-olds, 0.3% in the 7-12 year-olds and 0.8% in the 13-17 year-olds (*Fig. 6*). Based on the residual sera from NHS 2010, HBsAg prevalence was lowest among young adults aged 18-29 years (1.2%) and highest in the age group of 50-59 years (4.5%).

There were no significant differences in the prevalence of HBsAg by gender among residual sera from NPSS 2008-2010 (p = 0.36) and NHS 2010 (p = 0.93) (*Table 9*). No significant differences in the prevalence of HBsAg were detected among the three major ethnic groups among children and adolescents aged 1-17 years (p = 0.35). In the adult seroprevalence survey, HBsAg prevalence in Chinese (4.4%)

Table 9

Prevalence (%) of HBsAg among children and adolescents aged 1-17 years (NPSS 2008-2010) and adults aged 18-79 years (NHS 2010)

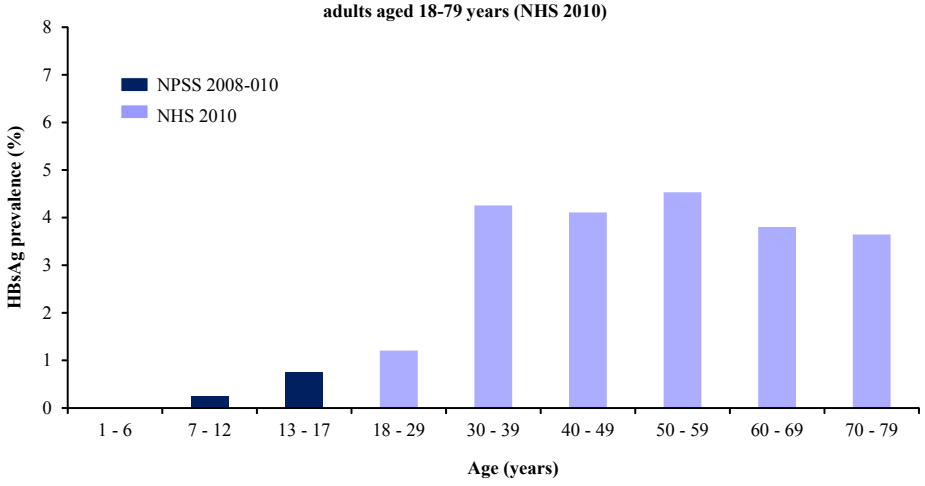
Demographics	Age group	
	1-17 years*	18-79 years#
Gender		
Male	0.5	3.6
Female	0.2	3.6
Ethnic group		
Chinese	0.6	4.4
Malay	0	1.7
Indian	0	0.9
Others	-	2.4

* NPSS 2008-2010

\# NHS 2010

Figure 6

Age-specific HBsAg prevalence (%) among children and adolescents aged 1-17 years (NPSS 2008-2010) and adults aged 18-79 years (NHS 2010)



was significantly higher than that in non-Chinese ($p < 0.01$), while there was no significant difference in HBsAg prevalence between Malays (1.7%) and Indians (0.9%) ($p = 0.41$).

In NPSS 2008-2010, the proportion with immunity to HBV decreased significantly from 63.8% in 1-6 year-olds to 32.8% in the 7-12 year-olds, and 23.5% (95% CI: 19.6% – 27.9%) in the 13-17 year-olds (test for trend, $p < 0.0005$) (*Fig. 7*). There was no linear trend in the immunity to HBV by age among adults aged 18-79 years ($p = 0.26$). The lowest proportion was in the age groups of 18-29 years (42.5%) and 60-69 years (42.7%), and the highest proportion was in the oldest age group of 70-79 years (49.2%).

In the NPSS 2008-2010, the proportion with immunity to HBV did not differ significantly by gender (42.6% in males versus 37.5% in females; $p = 0.077$) (*Table 10*). Among adults aged 18-79 years, the anti-HBs prevalence was significantly higher in women (46.6%) than in men (40.6%) ($p = 0.001$).

There was no significant difference in proportion with immunity to HBV among children and adolescents aged 1-17 years by ethnic group ($p = 0.46$). In the adult seroprevalence survey, there were significant differences in the immunity to HBV among the three main ethnic groups with the highest prevalence in

Table 10

Prevalence (%) of anti-HBs among children and adolescents aged 1-17 years (NPSS 2008-2010) and adults aged 18-79 years (NHS 2010)

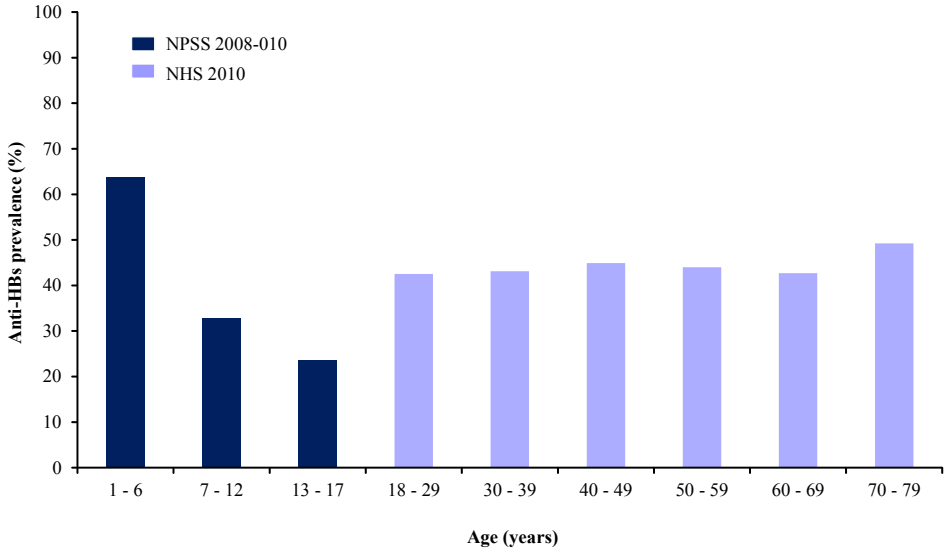
Demographics	Age group	
	1-17 years*	18-79 years#
Gender		
Male	42.6	40.6
Female	37.5	46.4
Ethnic group		
Chinese	40.6	48.7
Malay	37.0	25.2
Indian	42.6	32.6
Others	-	41.6

* NPSS 2008-2010

\# NHS 2010

Figure 7

Age-specific anti-HBs prevalence (%) among children and adolescents aged 1-17 years (NPSS 2008-2010) and adults aged 18-79 years (NHS 2010)



Chinese (48.7%), followed by Indians (32.6%) and Malays (25.2%) ($p < 0.05$).

Among residual sera from NHS 2010, HBeAg was detected in 4.2% of those who were HBsAg positive. About 22.5% (95% CI: 21.1% – 23.9%) of the adults were positive for anti-HBc, indicating recent or past infection. HBsAg was detected in 15.1% of those who were anti-HBc positive. The prevalence of anti-HBc increased with age from 4.5% among young adults 18-29 years of age to 45.6% in the oldest age group of 70-79 years ($p < 0.0005$).

The proportions of adults aged 18-79 years who were seropositive for the different HBV serological markers are shown in a Venn diagram (*Fig. 8*). About 27.5% of the adults had vaccine-induced immunity while 3.5% had chronic HBV infection in 2010.

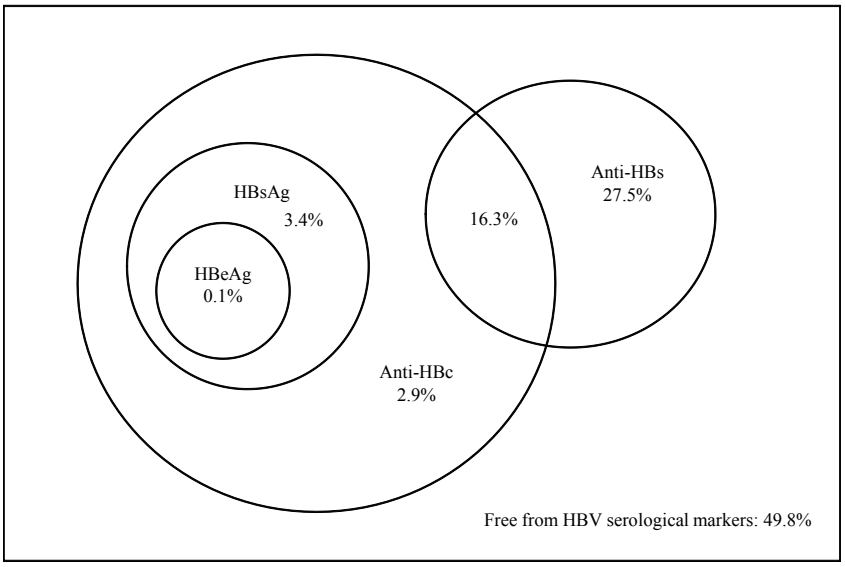
Among adults aged 18-69 years, the overall age-standardised HBsAg prevalence declined from 4.0% in 1998 to 2.7% in 2004, but increased to 3.6% in 2010. The changes in age-standardised HBsAg prevalence were all statistically significant between the consecutive six-yearly NHS ($p < 0.05$).

The overall age-standardised prevalence of anti-HBs among adults aged 18-69 years in 2010 (43.3%) was significantly higher than that in 1998 (40.1%) ($p = 0.004$), but it was not statistically different from that in 2004 (42.0%) ($p = 0.29$).

Comments

The burden of HBV-related morbidity and mortality among all the WHO regions is known to be disproportionately high in the Western Pacific Region (WPR) where Singapore is located. While one quarter of the world population resides in the WPR, this Region accounts for about half of chronic hepatitis B infections.[19] Chronic hepatitis B infection is endemic in the WPR. The majority of chronic HBV carriers in intermediate (2%-8% HBsAg positivity) and high endemic (8%-20% or higher HBsAg positivity) areas

Figure 8
Distribution of hepatitis B serological markers in Singapore residents aged 18-79 years (NHS 2010)



of the WPR acquire HBV infection in early childhood from HBsAg-positive carrier mothers.[20,21] In September 2005, the WPR became the first WHO region to adopt a regional goal of hepatitis B control, and the aim was to reduce the prevalence of chronic HBV infection to below 2% among children aged 5 years or older by 2012.[22] In September 2012, the Region's Expanded Programme on Immunization Technical Advisory Group and Hepatitis B Expert Resource Panel recommended setting 2017 as the target year for the goal to reduce hepatitis B infection rates to less than 1%.[23] The key strategy for reaching these targets is the achievement of high immunisation coverage of three or more doses of hepatitis B vaccine, including the first dose given within 24 hours of birth. As the prevalence of HBsAg was found to be 0.4% (95% CI: 0.2–1.1%) among children and adolescents aged 5-17 years from NPSS 2008-2010, Singapore has thus achieved the target set by the WHO WPR to reduce the prevalence of chronic HBV infection to below 2% among children aged 5 years or older by 2012.

When the results from the NPSS among children and adolescents aged 1-17 years during the period 2008-2010 and the seroprevalence study among adults aged 18-79 years in 2010 were combined, we estimated an overall HBsAg prevalence of 2.9% in the general Singapore resident population aged 1-79 years. Hence, Singapore is still classified as an area of intermediate HBV endemicity. In countries of intermediate endemicity, the WHO has recommended catch-up vaccination strategies targeting at older age groups or groups with risk factors for acquiring HBV infection, in addition to routine infant vaccination.[24]

In Singapore, adults are at risk of acquiring HBV as evidenced by highest age-specific incidence rate of acute hepatitis B in those aged 25-44 years. Medical practitioners should routinely enquire the hepatitis B vaccination status of their patients, and recommend screening and vaccination for those who have not been immunised. In Asia, vertical transmission is believed to be the leading cause of endemicity of hepatitis B. With effective childhood immunisation programmes, sexual transmission is likely to overtake as the leading cause of HBV infection in healthy susceptible adults, similar to what has occurred in the West.[25] Hence, it is important that prevention programmes are actively targeted at the susceptible adult population, especially those who engage in high-risk behaviour and activities, so as to reduce horizontal transmission via sexual contact.

Based on the three national seroprevalence studies conducted by MOH, about 43.6% of Singapore residents aged 18-69 years had immunity to HBV in 2010, which was a continued improvement from 39.5% in 1998 and 42.0% in 2004. However, more than half of the population remained at risk of HBV infection. As the universal hepatitis B immunisation was implemented as part of the NCIP in September 1987, those born before 1987 may not have adequate immunity against hepatitis B, and hence they are encouraged to seek medical advice and be vaccinated against hepatitis B, if necessary.

During the Liver Disease Awareness Week jointly organised by the Hepatopancreatobiliary Association Singapore and the Hepatitis B Support Group of Singapore in July 2013, free hepatitis B screenings were provided.[26] Blood tests conducted on nearly 800 people revealed the prevalence of hepatitis B among those aged 50 years and older was 4%.[27] This was similar to the HBsAg prevalence of 4.2% among adults aged 50 years and older who participated in NHS 2010. Men aged 45 years and older who may not

have been vaccinated against hepatitis B are deemed as the most at-risk group and they are encouraged to be screened for hepatitis B, as HBV is often a precursor to liver cancer which is the fourth most common cancer among men in Singapore.[27] A total of 2,110 men were diagnosed with liver cancer between 2009 and 2013, with crude incidence of 22.6 per 100,000 Singapore resident population.[28]

The national hepatitis B prevention and control programme in Singapore has been largely successful, as evidenced by the decline in HBV carrier rate and sustained decline in incidence rate of liver cancer (*Table 11*). There was a significant increase in the proportion with immunity to HBV infection in the younger population aged 18-29 years following the four-year catch-up immunisation programme in 2001.[10] This highlighted the importance of immunisation programmes in our national hepatitis B prevention and control efforts. In addition to ensuring high hepatitis B immunisation coverage rates of at least 95% for the national childhood immunisation programme, vaccination against hepatitis B should also be continued to be actively promoted among adults.

Hepatitis B vaccinations have been fully subsidised for all Singaporean children at the polyclinics since 1 June 2013.[26] In addition, adults can use their Medisave for hepatitis B vaccination. This ensures that all children and adults in Singapore have access to hepatitis B vaccination and are adequately protected against HBV. As part of the health education and promotion efforts by HPB, pamphlets on hepatitis B are available at polyclinics for the public, and talks have been conducted by the Primary Care Academy at workplaces. The population immunity against hepatitis B is continually monitored to assess if the health education and promotion efforts have been effective and adequate.

Table 11
Gender-specific age-standardised incidence of liver cancer per 100,000 Singapore resident population*

Period	Gender	
	Male	Female
1968-1972	28.6	7.9
1973-1977	27.4	6.9
1978-1982	27.7	6.9
1983-1987	23.0	6.7
1988-1992	19.0	5.4
1993-1997	19.0	4.9
1998-2002	19.1	4.9
2003-2007	18.5	5.0
2008-2012	17.1	4.8

* Segi's world population was used in direct age-standardisation.
Data source: Singapore Cancer Registry, National Registry of Diseases Office

(Reported by Ang LW[1], James L[1], Cutter J[2], Epidemiology & Disease Control Division[1], and Communicable Diseases Division[2], Ministry of Health, Singapore)

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The 2014 Ebola virus disease outbreak in West Africa: assessment of risk of importation into Singapore

Background

The *ebolavirus*, discovered in 1976, is one of the causes of viral haemorrhagic fever, and is among the most virulent pathogens for humans, with high fatality rates from 50% to 90% in infected individuals. Despite being relatively rare, the dramatic deaths that frequently accompany Ebola virus disease (EVD, previously known as Ebola haemorrhagic fever) outbreaks invoke immense fear and profound psychological impact on affected communities. In addition, outbreaks are intensely reported and publicised as a global threat devastating large populations. The public perception that the 1995 EVD outbreak in Kikwit, the Democratic Republic of the Congo (DRC), could spread to the rest of the world was one of the factors that built political momentum leading to the revision of the International Health Regulations (IHR) in 2005, requiring countries to develop public health capacities to detect and respond to outbreaks.[1] Although EVD outbreaks have been documented since 1976, the frequency of reported outbreaks has increased substantially post 2000.[2,3] Recent outbreaks in Central Africa include three independent, near-simultaneous outbreaks in 2012 – two EVD outbreaks in Uganda and one in the DRC - and a 2014 outbreak in the DRC.[4, 5] Nonetheless, EVD outbreaks in Central Africa have thus far been relatively limited in size and confined to rural areas or small towns, the largest of which occurred in Gulu and Mbarara in Uganda with 425 cases and 224 deaths reported over three months from October 2000 to January 2011.[6]

The current EVD outbreak affecting West Africa is the first outbreak in the sub-region, and has become far larger than all previous outbreaks combined. The origin of the outbreak was retrospectively traced to initial cases in Guinea's southeastern Forest Region in December 2013, which was not recognised and officially notified to the World Health Organization (WHO) until March of 2014.[7] In August, the WHO declared the outbreak to be an "extraordinary event" and a Public Health Emergency of International Concern (PHEIC) in view of the scale of the outbreak, its potential for further international spread, and the seriousness of such consequences.[8] Also in September, the United Nations Security Council adopted a resolution declaring this epidemic a threat to international peace and security.[9] As of 28 November 2014, the WHO reported a total of 16,203 clinical cases including 6,943 deaths from six affected countries (Guinea, Liberia, Sierra Leone, Mali, Spain and the United States (US)), and two previously affected countries (Nigeria and Senegal). Transmission remains widespread and intense in Guinea, Liberia and Sierra Leone, with the true burden of disease likely to be underestimated due to under-reporting.[10]

While spread of the infection from Guinea to Sierra Leone, Liberia, Senegal and Mali had occurred due to porous land borders, the exportation of cases to Nigeria, Spain and the US were linked to commercial air travel, a returning volunteer healthcare worker, and autochthonous transmission following care of imported or repatriated EVD cases.[9, 11-16] An acutely

ill Liberian air-passenger who flew from Liberia to Nigeria against medical and travel advice in July was Nigeria's index case. He sparked a three-generation chain of transmission among his contact networks resulting in 20 confirmed and probable cases in Lagos and Port Harcourt. [16,17] In October, Spanish health authorities confirmed the first autochthonous case in a nurse who had participated in the medical care of an infected missionary priest repatriated from Sierra Leone, representing the first human-to-human transmission of EVD outside of Africa.[17] On 30 September, the US confirmed the first EVD case diagnosed in the country, involving a Liberian national who travelled to Dallas, Texas from Liberia and developed symptoms four days after arrival. Two Texas nurses who had cared for the case subsequently contracted the infection.[18] In October, an American healthcare worker who had volunteered with Medicins Sans Frontieres (MSF) in Guinea tested positive for EVD, six days after his return to New York city.[18]

Virology and epidemiology

The genus *ebolavirus* contains five distinct species – Zaire, Sudan, Taï Forest (previously known as Côte d'Ivoire), Bundibugyo and Reston – each named for the location at which it was first identified. All *ebolaviruses* can cause severe disease in both human and non-human primates, with the exception of Reston *ebolavirus* which causes haemorrhagic fever in non-human primates but appear to be non-pathogenic for humans.[19] EVD presents with a sudden onset of non-specific symptoms including fever, malaise, anorexia, headache, sore throat, abdominal pain, vomiting, diarrhoea, myalgia, arthralgia, and rash, after a two to 21-day incubation period. Haemorrhagic symptoms such as epistaxis, petechiae, bleeding from mucous membranes, and internal bleeding may develop later.[20] No licensed vaccine or specific treatment is currently available, although several promising experimental interventions were used on a small number of international healthcare workers who contracted the infection during the 2014 West Africa outbreak.[21] Nonetheless, appropriate supportive care, especially during early stages of illness, can improve clinical outcome.[22]

The *ebolavirus* is zoonotic, naturally residing within an animal host. As the virus is dependent on an animal host for transmission, the endemic range of the disease is typically limited geographically, constrained by the ecological and climatic requirements of specific host species.[23,24] The natural maintenance cycle of the virus remains unclear. Arthropods have generally showed resilience to infection; bats and possibly rodents have been successfully infected; and frequent successful but fatal infections have been observed in various species of nonhuman primates.[25]

Although the natural reservoir of the *ebolavirus* is currently unknown, in Africa, outbreak appearance and ebolavirus transmission from bats to other animal species appear to coincide with increased prevalence of ebolavirus circulation in bats, suggesting that bats are the most likely source.[26] The observation that EVD outbreaks in great apes and humans were closely associated with sharply drier conditions at the end of the rainy season also suggested seasonal enviroclimatic influences *of ebolavirus* transmission.[27,28] Also, increased deaths in the Central African wildlife, particularly the great apes and duikers (a type of antelope), tend to precede and be linked to spillover *ebolavirus* infections in humans. Humans are not natural reservoirs for any of these viruses but can be infected accidentally

when the activities of the infected reservoir hosts and humans overlap.[25]

Secondary human-to-human transmission can occur once an initial person acquires the infection. This can occur directly through close contact with infected ill persons or their bodily fluids, or indirectly through contact with objects contaminated with infected bodily fluids. The *ebolavirus* has been found to be shed in a wide variety of bodily fluids not visibly contaminated by blood including saliva, breast milk, stool and tears during the acute phase of illness. However, it has been suggested that the virus is rapidly inactivated by salivary enzymes, and the oral cavity is unfavourable for virus persistence and replication. *Ebolavirus* has also not been detected in urine specimens, and prevalence on skin is low supporting previous empirical observations that risk of secondary transmission from causal contact is minimal. However, the *ebolavirus* has been isolated from breast milk (15 days post disease onset) and semen (82 days post disease onset) of convalescent patients after clearance from blood suggesting delayed viral clearance from immunologically protected sites. Due to the potential prolonged presence of the virus in these sites, precautions should be taken to avoid spreading the disease during convalescence – sexual abstinence or use of a condom, avoidance of breastfeeding and contact with the mucous membrane of the eye for at least three months after recovery are recommended to avoid possible exposure. [29,30]

The transmissibility of *ebolavirus* increases as the disease progresses; infected individuals are unlikely to transmit the infection prior to the onset of symptoms.[31] While asymptomatic human infections have been documented, these individuals are not a significant source of transmission due to very low viral loads.[32,33] Nonetheless, build-up of sporadic cases can lead to onward transmission among household and healthcare contacts, resulting in community outbreaks and nosocomial infections.[34] The highest risk activities are those that bring the infected individual into close contact with others, such as the health- and home-care settings, and funeral preparations. Hence opportunities for sustained transmission are culturally and contextually dependent.[2]

Risk factors for infection and outbreak

Close human-animal interface

To date, almost all human EVD cases have been linked to the handling of susceptible animal species.[30] A typical EVD epidemic chain arises from a given index individual who handles infected animal carcasses found in the forest (mainly gorillas, chimpanzees and duikers), and then transmits the infection through the community.[3] There is currently no firm proof that humans can be infected by the reservoir species (most likely bats) directly although the possibility cannot be excluded. The findings from a surveillance study of EVD conducted in the DRC from 1981 to 1985 to estimate the incidence of human infection suggest that sporadic human infection from nature occurs relatively frequently; however, outbreaks tend to be self-limiting due to high mortality and do not regularly amplify into large epidemics.[35]

In general, the populations most at risk in endemic areas are those with close contact with animals and their products such as slaughterers and hunters; and those with occupations that involve work in areas with enzoonotic transmission such as mining or forestry work.[36] A recent analysis on the zoonotic niche for EVD transmission has predicted that 22.2 million people in Central and West Africa currently

inhabit areas suitable for zoonotic transmission of EVD, the vast majority of which are in rural as opposed to urban or peri-urban areas. Nonetheless, EVD outbreaks remain relatively rare compared to other high burden disease prevalent in the region, despite the widespread practice of bushmeat hunting in these predicted areas.[2]

Weak healthcare systems and healthcare settings with poor infection control practice

The sporadic nature of EVD and its occurrence in geographically remote or politically unstable regions of the developing world are major challenges to the control of the disease. Problems include weak capacity of public health systems in these regions, insufficient funds, and limited availability of trained human resources in the area of surveillance and response.[37] The notion that poor hospitals are key amplifiers, especially in early stages of the outbreak, has been a central tenet of understanding the dynamics of EVD in Africa.[38] Onward transmission typically resulted from inadequate supplies, unsafe procedures, use of contaminated medical devices including needles and syringes, and poor adherence to infection control measures in resource poor setting.[39] Retrospective analysis of the 1995 Kitwit, DRC outbreak showed that individuals who were at significant risk of infection were those who came into direct physical contact with body fluids of patients. They were mostly family caregivers, nurses, and those who prepared a body for burial. The greatest threat of disease dissemination came from cases in the late stage of illness, and the bodies of the recently deceased as the bodies would contain copious amounts of viral particles at these points of time.[50] Similarly, in the 2000 Gulu, Uganda outbreak, the most important risk factor was direct repeated contact with a sick person's body fluids during the provision of care. Simple physical contact, such as shaking hands with the sick, was neither necessary nor sufficient for transmission, and the use of gloves during care was able to reduce the transmission risk even before strict barrier nursing was implemented. Significantly more females than males were affected in this outbreak, largely because the women generally took more responsibility in caring for the sick.[40]

While EVD transmission via heavily contaminated fomites is possible,[42,41] environmental contamination and fomites do not appear to pose a significant risk provided that infection control guidelines are adhered to.[16] The virus is susceptible to a wide range of disinfectants such as household bleach, alcohol-based hand rubs, and soap; and survives only a short time on surfaces that are in the sun or have dried.[42,43] Although the possibility of airborne transmission cannot be completely ruled out, it appears to be a minor mode of transmission, if any.[42]

Socio-cultural factors that belies the biomedical model of infection

Certain religious or cultural factors specific to the endemic regions are also seen to contribute to the emergence and spread of EVD including the consumption of bush meat, traditional treatment methods, and traditional African burial practices, such as hugging or touching the body of infected corpses.[7,40,44-46] African traditions also reject the notion of infection and transmission, and members of a family stay even more closely together during times of crisis than they do in normal times, taking food from the same plates, sleeping close to each other, and giving care to sick family members.[43] Socio-cultural factors can also affect the implementation or effectiveness of intervention measures. Top-down, standardised response and

control measures have sometimes proven culturally inappropriate leading to strong resistance from local populations. Particularly sensitive were the prevention of customary burial practices, and the hiding of sick and dead people behind tarpaulins in isolation units, which led to the suspicion that their body parts were being stolen.[1] The belief of witchcraft, and not the *ebolavirus*, as the cause of deaths continues to persist in some rural African communities as evidenced by difficulties faced by field response teams even in recent outbreaks.[47]

Nonetheless, all previous EVD outbreaks have been successfully controlled via the institution of contact tracing, quarantine and barrier nursing measures, without the use of specific airborne precautions. EVD patients can be managed effectively without undue risk to medical staff by employing standard patient isolation, and barrier nursing procedures.[48]

Features of the 2014 West Africa outbreak

Prior to the 2014 EVD in West Africa, the subregion was not considered to be an area in which the *ebolavirus* was endemic given that West Africa had only reported a single case of human infection with Taï Forest *ebolavirus* in the Ivory Coast in 1994. Major investigations that were carried in and around the Taï Forest region in response to this case failed to identify the reservoir of this *ebolavirus* species.[49] While virological investigations have identified the Zaire *ebolavirus* as the causative agent in the current outbreak, phylogenetic analyses reveal that the virus is distinct from strains from the DRC and Congo, and had not been introduced from these countries into Guinea.[9] In addition, a recent study on blood samples collected during 2006-2008 from patients with acute viral febrile illnesses in Sierra Leone provided serological evidence that *ebolaviruses* were circulating and infecting humans in Sierra Leone.[50] These studies suggest that the *ebolavirus* could have been present in the West Africa sub-region for some time. Nonetheless, previous ecological niche modelling of EVD outbreaks and sporadic cases estimates that the potential geographical distribution of *ebolaviruses* spreads across the humid rainforests of Central and Western Africa.[27] Notably, the presumed first case of the West Africa outbreak has been traced to a child in Guéckédou prefecture in Forested Guinea.[9]

The similarities in both the ecological circumstances leading to the initial Guinea outbreak, and the phylogeny of the causative Zaire *ebolavirus* compared to previous outbreaks support the notion that the scale of the current outbreak is more heavily influenced by patterns of human-to-human transmission rather than any expansion of the zoonotic niche or continued human-reservoir exposure[2,3]. Genomic surveillance suggests that the outbreak began from a single transmission from the natural reservoir with subsequent sustained human-to-human spread.[51] A comprehensive analysis of epidemiological surveillance data conducted by the WHO Ebola response team has shown that clinical manifestations, course of infection, as well as the transmissibility of the virus are similar to that observed in previous EVD outbreaks (*Table 12*).[8] Other earlier studies have similarly demonstrated that the early transmission dynamics in Guinea, Sierra Leone and Liberia was consistent with prior outbreaks in Central Africa, suggesting that the unprecedented scale of the current outbreak was a result of insufficient surveillance and containment measures, and population attributes rather than biological characteristics of the new EVD strain.[52-55]

Table 12

Clinical characteristics of the EVD outbreak in West Africa[8]

Common signs and symptoms	Fever (87.1%), fatigue (76.4%), loss of appetite (64.5%), vomiting (67.6%), diarrhoea (65.6%), abdominal pain (44.3%) and unexplained bleeding (18%)
Case-fatality ratio (CFR)	70.8% among case-patients with definitive outcomes (as of 14 September)
Mean incubation period	11.4 days
Mean serial interval	15.3±9.3 days
Duration of illness	Mean time from onset of symptoms to hospitalisation 5.0±4.7 days Mean time to death after admission to the hospital 4.2±6.4 days Mean time to discharge after admission to the hospital 11.8±6.1 days
Estimates of basic reproduction number (R_o) during initial exponential growth	Guinea 1.71 Liberia 1.83 Nigeria 1.20 Sierra Leone 2.02

The massive scale and complexity of the 2014 West Africa EVD outbreak is attributable to several factors unique to the region. Porous borders between Guinea, Sierra Leone and Liberia and the extensive movement of people, as well as the transport of bodies by relatives have led to the rapid spread of the disease across extremely large areas and present a huge challenge in contact tracing. It was estimated that during early June, one to two transnational transmissions per single primary case had occurred; estimates in August showed a declined but non-negligible number of cross-border transmissions between Guinea, Sierra Leone and Liberia.[54]

Ranked 178, 174 and 177 out of 186 countries, respectively, for human development, the weak healthcare systems of Guinea, Liberia and Sierra Leone - largely destroyed or severely disabled following years of civil war and conflict - lacked funding, infrastructure and technical capabilities to respond to the outbreak.[56] In Liberia, a mere 51 doctors served the population of 4.3 million before the outbreak.[57] In addition to human resource constraints, healthcare workers were also inexperienced in dealing with EVD. Infection and control practices were inadequate with healthcare workers constituting around 4% of cases in the outbreak.[12] General mistrust in the government and international response teams, as well as suspicions about the care patients were receiving in treatment centres were also major issues that have led patients to evade treatment and even removal of confirmed cases from health facilities by families.[58-60] Furthermore, transmission in rural communities was facilitated by strong cultural practices and traditional beliefs leading to high-risk actions including hiding patients, treating them at home, and handling dead

bodies according to local customs. More than 300 cases were linked to one funeral of a well-known traditional healer in Sierra Leone. In Guinea, 60% of cases have been linked to traditional burials.[61]

In Liberia, the outbreak was driven mainly by case importations during the first epidemic month. However, an exponential growth in the number of cases, reflecting self-sustaining transmission was subsequently observed.[54] In contrast, onward transmission was limited in Nigeria, despite the introduction of the virus into large, populous cities of Lagos and Port Harcourt, underscoring the importance and effectiveness of prompt and rigorous control measures. In particular, Nigeria benefited from its recent experiences in outbreak responses including a mass lead poisoning incident in 2010 and initiatives implemented for polio eradication in 2012. In Senegal, which recorded only one EVD case, prompt notification about the case by Guinean health authorities leading to a rapid containment response was key as the case had not disclosed his recent travel or contact history with EVD patients.[62]

An estimated net reproduction number (R_t, the estimated net reproduction number measures the average number of secondary cases generated by a typical primary case at a given time, accounting for incomplete host susceptibility to infection and control measures in place) remaining above 1 in Guinea, Liberia and Sierra Leone as of early September suggested that while the epidemic was still expanding in these areas, containment could be achieved by preventing just over half of the secondary transmissions per primary case.[8] A modelling tool, EbolaResponse, developed by the US Centers for Disease Control and Prevention estimates that the tipping point to start a rapid decline in cases in Sierra Leone and Liberia requires approximately 70% of EVD patients to be isolated in treatment facilities or in home or community settings such that there is a reduced risk of transmission.[63] In September 2014, only 10% of patients were in such settings, with the demand for patient care outstripping available resources in many regions.[64,65] In early November, the figure was 20% in Liberia and 13% in Sierra Leone.

Risk of international spread

Given that the incubation period of EVD may last up to three weeks, an infected individual can travel without detection while asymptomatic or showing early unspecific signs of infection, as experienced in the US. Nonetheless, the WHO notes that the risk of a tourist or business person contracting EVD during a visit to areas affected by the current outbreak is extremely low, even if the visit included travel to local areas from which primary cases have been reported. The type of contact with infected living or dead persons or animals required for transmission are all unlikely exposures for the average traveller. Likewise, the risk for travellers visiting friends and relatives in affected countries is similarly low, unless the traveller has direct physical contact with a sick or dead person or animal infected with the virus.[66]

However, travellers whose activities overlap with settings at risk for EVD are at particular risk. In the context of this outbreak, as of 30 November 2014, 17 expatriate healthcare and humanitarian workers involved in outbreak responses in Liberia and Sierra Leone, and a cameraman providing media coverage of the outbreak in Liberia were known to have contracted the infection and were subsequently evacuated to the US, the United Kingdom (UK), Germany, Spain, France, Norway, Switzerland, and

Italy (Six patients were evacuated to the US, three to Germany, two each to Spain and France, and one each to the UK, Norway, Switzerland, and Italy). With the exception of one secondary case involving a nurse in Spain, the remaining evacuated patients were successfully managed.

While there were only a few EVD infected travellers who reported being symptomatic during commercial air travel, there is currently no indication of EVD transmission during air travel on board an aircraft.[67] The WHO considers the risk of transmission of EVD during air travel to be low.[68] Nonetheless, the occurrence of EVD cases and transmission in populous capital cities with major commercial airports including Conakry, Freetown, Monrovia, and Lagos have fuelled concerns about further international spread via air travellers and prompted travel and immigration restrictions by several countries, as well as curtailed or temporary suspension of air travel by some regional and international air carriers.[69] Some restrictions have since been eased following caution that flight limitations have undermined relief efforts, and could worsen the EVD epidemic. The reduction in scheduled commercial air traffic capacity between 1 September and 31 December 2014 were estimated to be by 51% for Liberia, 66% for Guinea and 85% for Sierra Leone.[70]

In 2013, prior to the EVD outbreak, air travellers departing from Guinea, Sierra Leone, and Liberia combined accounted for only 0.05% of the total international air traffic volume worldwide.[72] Travellers departing from these countries predominantly travel to African destinations, followed by Europe, and the Eastern Mediterranean. The South-East Asia and the Western Pacific regions receive less than 5% of passenger volume combined.[71] A recent study assessing the potential for international dissemination of EVD via commercial air traffic based on global mobility and EVD prevalence estimated that with unrestricted travel conditions and the absence of exit screening, one EVD infected international air traveller would leave Guinea every 2.7 months, Liberia every 0.2 months, and Sierra Leone every 2.7 months, with a combined average of 2.8 infected travellers departing these three countries monthly. The non-African countries among the top final destination countries of travellers departing from the three countries included the UK, France, Belgium, China, the US, India, Germany, Lebanon, Canada and Italy.[72] Nevertheless, a study by Brockmann *et al.* highlighted the presence of differences in the distribution propensity and the most likely route of spread from each of the airports in EVD-affected countries, given the heterogeneities in flight connections and air travel networks (*Table 13*). On this basis, the authors estimated the probability of an infected individual arriving in Singapore from West Africa to be extremely low even in the absence of flight restrictions (highest from Nigeria at 0.13%; lowest from Liberia at 0.03%) (*Table 14*).[72] (The relative import probability is the probability that an infected individual arrives at any location in the worldwide air-transportation network as a product of (i) the probability that an infected individual boards a plane at an outbreak location; and (ii) the probability that an infected person arrives at point Y given that the person boards the plane at point X. The actual import risk, which is dependent on factors at outbreak sites, is much lower than the relative import probability.)

A Global Epidemic and Mobility model by Gomes *et al.*, which took into consideration airline passenger traffic, disease aetiology, and evolution of the outbreak, had found the projected probability of an infected individual arriving at non-African coun-

Table 13

Relative risk of importation of an infected individual from EVD affected countries based on outbreak airport location, by region

Airport location	Cumulative relative import probability (%)				
	Africa	Europe	Asia	Americas	Oceania
Conakry, Guinea	84.517	10.866	2.836	1.722	0.059
Freetown, Sierra Leone	79.94	15.427	2.431	2.16	0.043
Monrovia, Liberia	89.997	7.644	1.407	0.906	0.025
Dakar, Senegal	53.48	32.648	8.572	5.155	0.145
Lagos, Nigeria	69.969	12.442	11.763	5.62	0.206
Port Harcourt, Nigeria	93.791	2.522	2.502	1.144	0.042
Combined	71.239	14.788	8.611	5.207	0.155

Source: Adapted from Brockmann et al. 2014

Table 14

Relative risk of importation of an infected individual from EVD affected countries into Singapore, based on outbreak airport location with and without flight restrictions

Airport location	Cumulative relative import probability[iii] (%)				
	No flight restrictions	CKY-CDG knockout	FNA-LHR knockout	FNA-LGW knockout	ROB-ACC knockout
Conakry, Guinea	0.0526	0.0162			
Freetown, Sierra Leone	0.0807		0.0203	0.0838	
Monrovia, Liberia	0.0255				0.0224
Dakar, Senegal	0.0773				
Lagos, Nigeria	0.1303				
Port Harcourt, Nigeria	0.1303				

ACC: Kotoka International Airport, Accra, Ghana
CDG: Charles de Gaulle airport, Paris, France
CKY: Conakry International Airport, Conakry, Guinea
FNA: Lungi International Airport, Freetown, Sierra Leone
LHR: Heathrow Airport, London, United Kingdom
LGW: Gatwick Airport, London, United Kingdom
ROB: Roberts International Airport, Monrovia, Liberia

Source: Adapted from Brockmann et al. 2014

tries to be extremely low (<5%), with the exception of France, the US (which have already experienced imported cases), the UK, and Belgium. An 80% reduction of air traffic to and from the affected countries generated only a three to four week delay in the timeframe for the probability of an imported case if the outbreak was not contained. Nevertheless, the expected size of any subsequent cluster resulting from international spread was small in all non-African countries, with outbreaks involving more than 10 individuals considered to be statistically rare events.[57,73]

Conclusion

Increasing human population in EVD risk areas and changes in land use resulting in penetration into previously remote areas of the rainforest increases the opportunities for human-animal exposure, and consequently, the risk of spillover events. In addition, at-risk populations have become more mobile and better connected internationally leading to increased opportunities for international spread. The West Africa outbreak demonstrated that factors such as poor health infrastructure, lack of timely, effective interventions and local customs can transform a limited outbreak into a massive, nearly uncontrollable epidemic.[74]

The EVD epidemic in West Africa is likely to continue for several more weeks, if not months. In view of global trade and travel, the importation of a human case of EVD into Singapore is theoretically possible. However, the likelihood of such an event is considered to be low due to the low level of travel connectivity between Singapore and EVD affected regions in West Africa. Continued suspension of flight services to West Africa by some airlines further reduces passenger traffic, and demands for flights to Africa from Asia have fallen as well.[75] In addition, the risk of acquisition and subsequent transmission of EVD can be significantly reduced if travellers and healthcare providers are informed and aware of the risk, and if basic hygiene and precautionary measures are followed, and infection prevention and control measures are practised. Currently, travellers departing from the affected West African countries are subject to temperature screening, visually assessed for potential illness and are required to respond to a health questionnaire. Furthermore, most illnesses in returned travellers from the affected regions are more likely due to other more common infectious diseases including malaria, dengue or enteric fevers, which have similar initial presentation. As of early October, around 36,000 departing passengers have been screened in Guinea, Sierra Leone and Liberia, among whom, 77 had symptoms compatible with EVD; none of these persons tested positive for EVD with the majority suffering from malaria which is endemic in the region.[76]

Nonetheless, the potential for healthcare associated transmission of EVD necessitate a high index of suspicion, particularly those with a relevant travel history, and a standardised risk assessment approach to febrile travellers. Current vigilance and awareness of the EVD situation in West Africa is exceptionally high worldwide, as evident by numerous media reports of testing of suspected cases with compatible travel histories. Persons at the greatest risk of secondary infection would be those who come into direct physical contact with the body fluids of infected persons during the period of acute illness, including healthcare workers; family caregivers or other individuals who had provided direct nursing care for the case prior to diagnosis; laboratory workers handling specimens; as well as persons who prepared the body of infected persons for burial. Both autochthonous

infections in Spain and the US had occurred in the healthcare setting following the provision of care to EVD patients. Initial investigations suggested the accidental exposures had likely occurred as a result of improper de-gowning of contaminated personal protective equipment (PPE).[77,78]

Preparedness against EVD is dependent on the core strength of health systems.[79] In Singapore, there is a robust infectious disease surveillance system and well-established infection control practices in our healthcare institutions. Nonetheless, the occurrences of secondary cases among healthcare workers in Spain and the US highlight the importance of strict adherence to infection control measures and minimization of high-risk procedures when providing care to EVD patients, and monitoring of healthcare workers involved in such care. While the occurrences of a few additional cases among close contacts of an imported case cannot be excluded, countries with well-developed health systems and services are unlikely to see much, if any, onward transmission of EVD.

(Contributed by Public Health Intelligence Branch, Epidemiology and Disease Control Division)

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Prevalence of past dengue virus infection among children and adults in Singapore

Introduction

Dengue is endemic in Singapore, and the vectors, *Aedes aegypti* and *Aedes albopictus,* breed throughout the year. A comprehensive nationwide *Aedes* prevention and control programme incorporating source reduction, health education and law enforcement was launched in 1969. It has been successfully implemented since 1973, as evidenced by a sharp reduction in *Aedes* premises index (percentage of premises found to be breeding *Aedes* mosquitoes) and low dengue incidence.[1] However, since the 1980s, dengue epidemics have occurred on a six-year cycle in 1986/7, 1992, 1998, 2004/5, 2007 and 2013/4. During the 11-year period between 2004 and 2014, excluding the epidemic years, the dengue incidence per 100,000 population ranged from 87.2 in 2012 to 145.3 in 2008.[2]

Seroprevalence surveys supplement disease notification in monitoring the changing immune status against dengue virus (DENV) infection and assessing the effectiveness of the national *Aedes* control programme. The first serological survey representative of the adult resident population aged 18-74 years was based on the residual sera of participants of the National Health Survey (NHS) in 2004; it showed an overall prevalence of past DENV infection of 59.0% (95% confidence interval [CI]: 57.5% – 60.5%).[3]

To assess the impact of past dengue epidemics on the Singapore resident population, we undertook another national seroepidemiological study involving children and adolescents aged 1-17 years over a 24-month period from 2008 to 2010, and adults aged 18-79 years in 2010.

Materials and methods

Seroprevalence surveys

There are two parts to our study. The Ministry of Health (MOH) conducted a national paediatric seroprevalence survey (NPSS) between August 2008 and July 2010 involving prospective collection of residual sera following completion of routine biochemical investigations by the diagnostic laboratories in two public acute hospitals, KK Women's and Children's Hospital and National University Hospital of Singapore.[4] This survey was carried out in accordance to Section 7 of the Infectious Diseases Act, which provides for the use of residual blood samples for the purpose of public health surveillance. The selection of residual sera was confined to Singapore residents (citizens and permanent residents) of Chinese, Malay and Indian ethnicity aged 1-17 years attending inpatient services or day surgery at the two hospitals. Sera of patients known to be immunocompromised, on immunosupressive therapy, or who had been diagnosed with infectious diseases such as dengue were excluded. A total of 1,200 sera were collected, comprising 400 in each of the three age groups of 1-6 years, 7-12 years and 13-17 years.

The adult seroprevalence survey was based on 3,293 residual sera from Singapore residents aged 18-79 years who participated in the NHS 2010. The NHS was a population-based cross-sectional survey conducted by the MOH to determine the prevalence of major non-communicable diseases and their associated risk factors among Singapore adult residents.[5] The fieldwork for the NHS was carried out over a

three-month period from 17 March to 13 June 2010. There was no increase in dengue incidence during this period. A total of 4,337 persons aged 18-79 years participated in the NHS 2010, yielding an overall response rate of 57.7%. Of these respondents, 3,293 (75.9%) with sufficient amount of residual sera for laboratory testing were analysed. The adult seroprevalence survey was approved by the Ethics Committee of the Health Promotion Board. Only sera from NHS participants who had consented to having their residual sera used for further research were included in this study.

The sera in these two surveys were tested for IgG antibodies against DENV by ELISA using commercial test kits (EUROIMMUN, Germany) according to the manufacturer's recommended procedure. Levels ≥ 20 RU/mL were considered to be reactive.

Statistical analysis

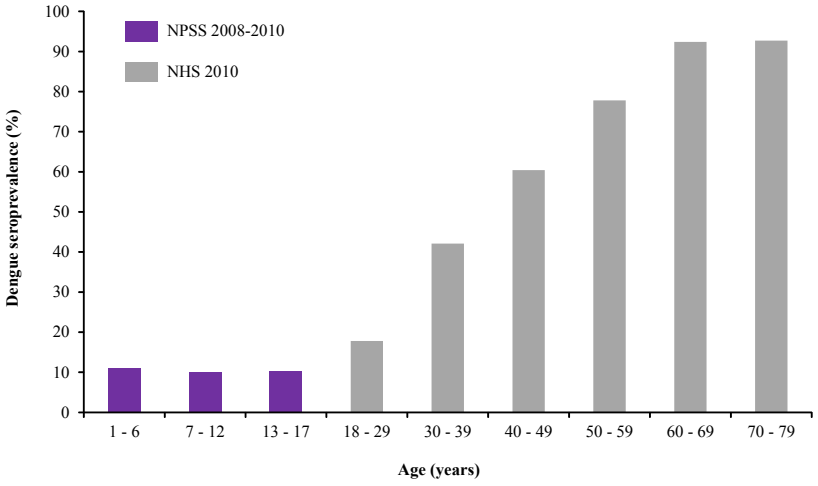
Dengue seropositive rates between any two groups were compared using two-sample independent z-test. The Mantel-Haenszel Chi-square test for trend was used to evaluate the difference in seroprevalence across age groups. Statistical analysis was performed using the statistical software package, SPSS Statistics software, version 19.0 (IBM, USA). All statistical tests were two-sided. A p value < 0.05 was considered statistically significant.

Results

The overall prevalence of past DENV infection was 10.4% (95% CI: 8.7 % – 12.1%) among children and adolescents aged 1-17 years, and 56.8% (95% CI: 55.1% – 58.5%) among adults aged 18-79 years.

In the NPSS 2008-2010, there was no significant difference in seroprevalence by age group (test for trend, p = 0.73); 11.0% in the 1-6 year-olds, 10.0% in the 7-12 year-olds and 10.3% in the 13-17 year-olds (*Fig. 9*). In the adult survey, the seroprevalence increased significantly from 17.8% in young adults aged 18-29 years to 77.8% in those aged 50-59 years (test for trend, p < 0.0005). The seroprevalence was

Figure 9
Age-specific prevalence (%) of past DENV infection among children and adolescents aged 1-17 years and adults aged 18-79 years



maintained at 92.4% or higher in older age groups of 60-69 years and 70-79 years. The age-standardised prevalence of past DENV infection among adults was significantly lower at 54.4% in 2010 compared to 63.1% in 2004 ($p < 0.005$).[6] When the results from the two surveys were combined, we estimated an overall seroprevalence of 44.4% in the general population aged 1-79 years.

The seroprevalence among children and adolescents aged 1-17 years did not differ significantly by gender (11.3% in males versus 9.6% in females; $p = 0.35$) (*Table 15*). Among adults aged 18-79 years, the seroprevalence was significantly higher in males (61.5%) than in females (53.2%) ($p < 0.0005$).

In the NPSS 2008-2010, there was no significant difference in seroprevalence by ethnic group ($p = 0.40$). In the adult survey, among the three major ethnic groups, the seroprevalence in Chinese (57.0%) and Indians (62.0%) was similar ($p = 0.09$), while Malays had a significantly lower seroprevalence (50.2%) than that of Chinese ($p = 0.01$) and Indians ($p = 0.001$).

In the adult survey, the seroprevalence was lowest at 18.9% among those who were studying or doing national service.[6] The seroprevalence was 70.9% among homemakers/housewives, and it was highest at 93.5% in retirees.

While the prevalence of past DENV infection was highest among adults staying on landed residential properties at 60.2%, there was no significant difference by type of dwelling ($p = 0.34$).[6] Among adults living in public and private housing apartments, there was no significant difference in the seroprevalence by floor level ($p = 0.25$).

No significant difference was detected among adults by residency status (57.4% in Singapore citizens versus 53.4% in permanent residents; $p = 0.10$).

Table 15

Prevalence (%) of past DENV infection among children and adolescents aged 1-17 years (NPSS 2008-2010) and adults aged 18-79 years (NHS 2010)

Demographics	Age group	
	1-17 years*	18-79 years#
Gender		
Male	11.3	61.5
Female	9.6	53.2
Ethnic group		
Chinese	10.3	57.0
Malay	12.1	50.2
Indian	7.8	62.0
Others	-	61.6

* NPSS 2008-2010
\# NHS 2010

Comments

In Singapore, young adults are deemed to have a higher risk of acquiring dengue infection, as evidenced by the age-specific incidence rate of dengue being highest in those aged 15-24 years during the dengue epidemics in 2004/5 and 2013/4. The prevalence of past DENV infection in young adults aged 18-24 years was 17.2% in 2004[3] and 17.6% in 2010.

The proportion of children and adolescents aged 1-17 years with evidence of past DENV infection (10.4%) remained low. In a past dengue serological survey conducted on 1,068 children below 16 years of age at the National University Hospital (NUH) during an 18-month period between 1996 and 1997, about 6.7% aged 6-15 years tested positive for anti-DENV IgG antibodies by PanBio dengue IgG ELISA (PanBio, Brisbane, Australia).[7] After more than one decade, the dengue seroprevalence in 2008-2010 was 9.1% in this age group, which was not significantly different from the finding in 1996-1997 ($p = 0.123$).

The herd immunity of the adult population in Singapore is low, as about 43.2% remained susceptible to DENV infection in 2010. As a result of the successful implementation of the comprehensive nationwide *Aedes* surveillance and control programme since the 1970s, the overall *Aedes* premises index had decreased drastically from more than 25% in the 1960s to 1-2% since 1985.[1,8] Based on a mathematical modelling study using local seroprevalence data, the rise in dengue incidence in Singapore was attributed to a declining trend in the force of infection, partly due to a vector-control-driven reduction in herd immunity and an increase in the average age of first infection.[9] Since the 1980s, dengue epidemics in Singapore tend to occur more frequently and with greater intensity, which could be partly attributed to declining herd immunity of the human population over the decades with less exposure to infected female *Aedes* mosquitoes.

It has been recognised that dengue poses a significant socioeconomic and disease burden on many tropical and subtropical regions of the world.[10-12] Dengue was classified by the World Health Organization (WHO) as the "most important mosquito-borne viral disease in the world" again in 2012.[13] The WHO Western Pacific Region (WPR) and Southeast Asia Region (SEAR) together constitute about three-quarters of the global dengue disease burden.[14] The number of reported dengue cases has continued to increase over the past decade in the WPR.[15] In the Asian subregion of the WHO WPR, Singapore was one of the six countries with the greatest burden of dengue.[16] The dengue situation is expected to worsen due to various factors such as the modern dynamics of climate change, globalisation, travel, trade, socioeconomics, as well as viral evolution.[16] Sustainable vector control is one element of the Global Strategy for Dengue Prevention and Control, 2012-2020, and the Integrated Vector Management (IVM) is the strategic approach promoted by the WHO as a rational, cost-effective, and optimal decision-making process for vector control programmes.[13]

Based on the recent national seroprevalence surveys among children and adults, the Singapore population is highly susceptible to dengue epidemics despite its aggressive *Aedes* prevention and control programme. In the absence of a commercially available dengue vaccine which is safe and effective against all the four dengue serotypes, vector suppression through heightened vigilance and concerted efforts of all stakeholders in the community remains the key strategy in the prevention and control of dengue transmission in Singapore.

(Reported by Ang LW, James L, Epidemiology & Disease Control Division, Ministry of Health, Singapore)

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