

Changing Seroprevalence of Hepatitis B Virus Markers of Adults in Singapore

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Abstract

Introduction: We presented the findings from 2 seroprevalence studies conducted 6 years apart, so as to determine changes in the hepatitis B surface antigen (HBsAg) positivity rate and immunity to hepatitis B virus (HBV) among Singapore residents aged 18 to 69 years, and to assess the impact of a 4-year catch-up hepatitis B immunisation programme for adolescents and young adults launched in 2001. **Materials and Methods:** Two hepatitis B seroprevalence studies (HBSS) were conducted in 1999 and 2005 based on stored blood samples collected from 4698 participants aged 18 to 69 years during the national health survey (NHS) 1998 and from 3460 participants during the NHS 2004, respectively. Serology for HBsAg, hepatitis B e antigen (HBeAg) and antibody to HBsAg (anti-HBs) were tested by enzyme immunoassay in HBSS 1999 and electrochemiluminescence in HBSS 2005. **Results:** The overall age-standardised prevalence of HBsAg among Singapore residents aged 18 to 69 years decreased significantly from 4.0% in HBSS 1999 to 2.8% in HBSS 2005 ($P = 0.002$). The age-standardised prevalence of HBsAg in males (4.9% in 1999) and Chinese (4.7% in 1999) both decreased significantly to 2.7% and 2.8%, respectively in 2005. The overall age-standardised population immunity to HBV (anti-HBs ≥ 10 mIU/ml) increased from 39.7% in 1999 to 42.1% in 2005 ($P = 0.019$). In particular, the age-specific prevalence of anti-HBs showed a significant increase among those in the age group of 18 to 29 years from 27.9% in 1999 to 41.7% in 2005 ($P < 0.001$) and among those in the age group of 30 to 39 years from 39.9% in 1999 to 44.7% in 2005 ($P = 0.021$). **Conclusion:** There was an overall decline in the HBsAg positivity rate as well as an overall increase in population immunity to HBV. Following the 4-year catch-up immunisation programme, there was a significant increase in the immunity to HBV infection in the younger population aged 18 to 29 years.

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Introduction

In Singapore, epidemiological surveillance and research on hepatitis B virus (HBV) infection were initiated when acute viral hepatitis was made a notifiable disease under the Infectious Diseases Act in 1976. Based on the findings of epidemiological investigations of reported cases and the results of seroepidemiological studies, a national hepatitis B prevention and control programme was formulated and implemented.¹ Immunisation against HBV infection forms the cornerstone of the programme, alongside the other activities which include surveillance, routine antenatal screening and screening of voluntary blood donors for HBV carriers, adoption of universal precautions and public education.²

The hepatitis B immunisation programme, introduced in mid-1983, was initially targeted at the high-risk groups such as healthcare workers but later also included babies born to HBV carrier mothers from 1 October 1985 onwards.² From 1 September 1987, the childhood immunisation programme was extended to include all newborns. The coverage rate for infants who have completed the full course of 3 doses before 1 year of age increased from 50% in 1988 to 91% in 1994 and since 2005, at least 95% of children under 2 years of age have been immunised against hepatitis B.³ The herd immunity of the childhood population, based on a seroprevalence survey conducted in 1998/1999,⁴ was 90% in children below 5 years of age and 77% in children aged between 5 and 14 years of age and no cases of acute

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hepatitis B has been reported in children below 15 years of age since 1997.³ The prevalence of hepatitis B surface antigen (HBsAg) in Chinese children aged between 5 and 9 years was 5.7% in 1972⁵ and 3.4% in 1987¹ but none of the primary school children 6 years of age was tested positive in 1993.⁶

However, HBV infection remains an important public health problem among the adult population in Singapore. A recent study estimated that the annual costs of chronic HBV infection and its complications such as chronic hepatitis, liver cirrhosis and liver cancer amounted to S\$279 million and draws attention to the continuing financial burden of the disease in Singapore.⁷

In 1999, a hepatitis B seroprevalence study (HBSS 1999) of the adult population aged 18 to 69 years was conducted using stored blood sample from the national health survey (NHS) 1998.⁸ A key finding from this study was that the majority of the younger age group of 18 to 29 years old had no immunity to HBV infection as indicated by a low seroprevalence of antibody to HBsAg (anti-HBs) (27.9%) in this age group. Based on these findings, the School Health Services of the Health Promotion Board (HPB) implemented a 4-year hepatitis B catch-up immunisation programme which was targeted at the student population born before 1987 and who were likely to have missed the national hepatitis B childhood immunisation programme. During the same period, the HPB also embarked on a mass media programme to increase public awareness on the risks of HBV infection and the importance of immunisation against hepatitis B. Education materials were distributed to the students, parents and the public together with publicity over the television, radio and newspapers.

The largely school-based voluntary catch-up immunisation programme was launched in January 2001 for students in secondary schools, junior colleges, centralised institutes, institutes of technical education, polytechnics and universities. In 2001/2002, fulltime national servicemen were also offered hepatitis B screening and immunisation at 35 Singapore Armed Forces medical centres. In 2004, the programme was also extended to the students in 18 special schools.

At the end of the 4-year immunisation programme, a total of 221,873 youths (students and national servicemen) had participated, of whom 127,108 were tested seronegative for various HBV markers. Among the seronegative youths, 108,576 (85.4%) completed at least one dose of hepatitis B immunisation and 99,333 (78.1%) completed all the 3 doses.

We undertook another national seroepidemiological survey on hepatitis B in 2005 (HBSS 2005) to assess the changing seroprevalence of HBV markers in the adult population in Singapore by comparing the findings with those of HBSS 1999. Special reference was made

on the impact of the catch-up hepatitis B immunisation programme.

Materials and Methods

The NHS 1998 and NHS 2004 were national cross-sectional surveys conducted to determine the prevalence of major non-communicable diseases such as diabetes and their associated risk factors among Singapore residents. In each survey, polyclinics geographically well spread out across Singapore were selected. The study population was selected by a combination of disproportionate stratified sampling and systematic sampling. The sample selection was divided into 2 phases. During the first phase, a modified two-stage stratified design was carried out and during the first stage, sampling divisions within close proximity to the selected polyclinics were chosen, followed by systematic sampling of dwelling units of each selected sampling division stratified by house-type during the second stage. House visits were then conducted to enumerate all members of the households within the age group of 18 to 69 years old in NHS 1998 and 18 to 74 years in NHS 2004. During the second phase, a random sample of persons was selected from all the individuals identified in phase 1. The NHS 1998 and NHS 2004 were approved by the Health Promotion Board (HPB)'s Institutional Review Board (IRB) Ethics Committee. The NHS participants included in HBSS 1999 and HBSS 2005 consented to having their residual sera used for further research. Personal identifiers (ID) from the NHS demographic data were permanently removed and survey ID assigned for HBSS 1999 and HBSS 2005. Corresponding survey ID was also tagged to the samples before these samples were sent to the assigned testing laboratories. This process of delinking was to ensure strict anonymity of the study participants.⁹

In HBSS 1999, the sera from 4698 participants had been tested by enzyme immunoassay (EIA) using commercial reagents (Abbott Laboratories, North Chicago, USA; HBsAg was tested by AUSZYME MONOCLONAL, HBeAg by AxSYM HBe and anti-HBs by AUSAB EIA).⁸

In HBSS 2005, a baseline HBsAg prevalence of 3% was used as the premise to estimate the sample size required to detect changes in seroprevalence levels. It was calculated that a sample size of 3460 would be required to detect 10% relative change from the baseline measurement with 95% confidence. For logistical convenience, sera obtained from 4034 participants of the NHS 2004 aged 18 to 69 years who had given consent for future research on their blood specimens were used for the hepatitis B seroprevalence study. The sera which had been collected and stored at -80°C at the Department of Pathology, Singapore General Hospital, were sent to the Department of Laboratory Medicine, National University Hospital for testing. The stored blood sera were first tested for HBsAg

using electrochemiluminescence (by Roche E170, Roche Diagnostics Ltd, Germany). Sera of subjects found to be HBsAg positive were further tested for Hepatitis B e antigen (HBeAg) using electrochemiluminescence (by Roche E170, Roche Diagnostics Ltd, Germany). Those found to be HBsAg negative were screened for anti-HBs using chemiluminescence (OCD Vitros ECI, Ortho-Clinical Diagnostics, USA). Those with anti-HBs levels <10mIU/ml were considered non-immune to the HBV and those with levels \geq 10mIU/ml were considered to have immunity to HBV.

Statistical analysis was performed using the statistical software package, Statistical Package for Social Sciences (SPSS) 15.0. The survey sample data of HBSS 1999 and HBSS 2005 were adjusted to the age, ethnic group and gender distribution of the 2004 Singapore resident population, to ensure that the characteristics of the samples conformed to that of the general population.

Findings from HBSS 2005 were compared with those of HBSS 1999 which involved sera obtained from 4698 participants of the NHS 1998 aged 18 to 69 years. Age-standardisation of prevalence of HBsAg, HBeAg and anti-HBs for HBSS 1999 and HBSS 2005 were calculated by the direct method, using the 2000 census resident population as the standard. Differences between the age-gender-standardised incidence rates of the 3 ethnic groups were computed and tested for statistical significance using the Z-test.¹⁰ Statistical significance was taken as $P < 0.05$ level.

Results

The demographics of the participants in HBSS 1999 and HBSS 2005 are comparable and are shown in Table 1. The crude seroprevalence of HBV markers by gender, ethnicity, age group, educational level and main work status in HBSS 1999 and HBSS 2005 are shown in Table 2.

The overall age-standardised seroprevalence of HBsAg among Singapore residents aged 18 to 69 years in HBSS 2005 was 2.8%, significantly lower than that of the HBSS 1999 (4.0%) ($P = 0.002$) (Table 3). The age-specific seroprevalence rate increased from 2.1% in young adults aged 18 to 29 years to 3.4% in the age group of 30 to 39 years (Fig. 1). It then dropped to 2.9% in the age group of 40 to 49 years (nearly half of 5.5% in HBSS 1999) and 1.6% in the age group of 50 to 59 years (nearly one-third of 4.9% in HBSS 1999). The prevalence was highest in the oldest age group of 60 to 69 years (4.0%).

There was no difference in the age-standardised HBsAg prevalence between the genders (2.8% for both genders), contrary to HBSS 1999 when a significant difference between males and females (4.9% vs 3.2%, $P = 0.023$) was observed (Table 3). Among the females, it was observed that the age-specific prevalence of HBsAg in the 18 to 29

Table 1. Demographics of Study Population, HBSS 1999 and HBSS 2005

	HBSS 1999		HBSS 2005	
	No.	%	No.	%
All	4698	100.0	4034	100.0
Gender				
Male	2356	50.1	2002	49.6
Female	2342	49.9	2032	50.4
Ethnic Group				
Chinese	3753	79.9	3190	79.1
Malay	597	12.7	512	12.7
Indian	348	7.4	332	8.2
Age Group				
18-24	513	12.7	654	13.9
25-29	412	10.2	576	12.3
30-34	488	12.1	640	13.6
35-39	508	12.6	674	14.3
40-44	536	13.3	631	13.4
45-49	501	12.4	509	10.8
50-54	410	10.2	351	7.5
55-59	294	7.3	278	5.9
60-64	209	5.2	211	4.5
65-69	163	4.0	174	3.7

years age group has increased from 1.6% to 2.8%, although this increase was not statistically significant.

Among the 3 major ethnic groups, the age-standardised HBsAg prevalence was highest amongst the Chinese (2.9%), followed by the Malays (2.8%) and the Indians (1.6%), but the differences were not statistically significant. This was in contrast to HBSS 1999 in which a significant difference between the Chinese and non-Chinese populations was observed (Table 3).

The age-standardised prevalence of HBsAg in males has decreased significantly to 2.8% from 4.9% in HBSS 1999 ($P = 0.001$) while its prevalence in the Chinese had also decreased significantly to 2.9% from 4.7% in HBSS 1999 ($P < 0.001$) (Table 3).

No significant difference in HBeAg positivity rate among those seropositive for HBsAg was observed in the 2 studies (13.0% in HBSS 1999 vs 11.9% in HBSS 2005). Its age-specific seroprevalence remained the highest among those aged 18 to 29 years (15.8%) and declined in the older age groups. Among the ethnic groups, its age-standardised prevalence in HBSS 2005 was highest in Malays, in contrast to the findings in HBSS 1999 in which Chinese had the highest prevalence (Table 4). All the Indians tested negative for this HBV marker in both surveys. Overall, there were also no significant differences in the age-standardised prevalence

Table 2. Prevalence (%) of HBV Markers by Gender, Ethnicity, Age Group, Educational Level and Main Work Status in Singapore, HBSS 1999 and HBSS 2005

	HBsAg		HBeAg		Anti-HBs	
	1999	2005	1999	2005	1999	2005
All	4.1	2.7	0.5	0.3	39.5	42.0
Gender						
Male	4.9	2.7	0.5	0.3	38.5	41.1
Female	3.3	2.7	0.5	0.3	40.5	43.0
Ethnic Group						
Chinese	4.7	2.8	0.6	0.3	44.3	42.3
Malay	2.1	2.7	0.2	0.6	19.7	41.5
Indian	0.5	1.8	0.0	0.0	22.1	40.5
Age Group						
18-24	1.4	1.9	0.3	0.4	27.2	43.4
25-29	2.6	2.2	0.3	0.2	28.9	39.6
30-34	4.5	3.1	0.9	0.2	40.2	45.4
35-39	4.6	3.7	0.6	0.8	39.7	44.1
40-44	5.4	3.2	0.8	0.4	43.7	42.8
45-49	5.5	2.6	0.4	0.4	44.8	39.1
50-54	5.4	2.2	0.3	0.0	47.0	40.2
55-59	4.0	0.7	0.0	0.0	50.9	42.5
60-64	3.3	4.3	0.5	0.5	47.8	43.5
65-69	4.6	3.7	0.0	0.0	43.0	36.0
Educational Level						
No formal education / Primary	4.7	2.3	0.6	0.4	38.7	36.9
PSLE ⁺ / Secondary	3.2	3.9	0.1	0.1	33.2	41.4
'O' level / 'N' level	3.4	2.4	0.5	0.2	34.4	42.9
'A' level / Diploma / Professional qualifications	3.4	3.0	1.0	0.6	37.9	44.7
Degree	3.0	2.1	0.2	0.3	40.6	43.7
Main Work Status over Last 12 Months						
Working	4.1	2.8	0.5	0.4	39.5	42.4
Student	1.7	2.4	0.3	0.0	22.7	46.3
National service	1.4	0.0	0.0	0.0	27.0	34.6
Homemaker / Housewife	2.9	3.1	0.5	0.6	37.2	42.2
Retired	2.2	5.5	0.0	0.0	39.0	42.6
Unemployed	3.4	1.7	0.0	0.0	31.4	36.2

⁺ Primary School Leaving Exam

of HBeAg by gender and by ethnic group (Table 4).

The overall age-standardised seroprevalence of anti-HBs in HBSS 2005 was significantly higher than that in HBSS 1999 (42.1% vs 39.7%, $P = 0.019$) (Table 5). Among the

different age groups, younger adults aged 18 to 29 years (41.7%) and 30 to 39 years (44.7%) had the highest anti-HBs prevalence (Fig. 1). This was in contrast to HBSS 1999 when the level of immunity was lowest in these 2 age groups. The age-specific prevalence of anti-HBs showed a significant increase among those in the age group of 18 to 29 years (41.7% vs 27.9%, $P < 0.001$) and among those in the age group of 30 to 39 years (44.7% vs 39.9%, $P = 0.021$) compared to HBSS 1999. As in HBSS 1999, there was no significant gender difference in the prevalence of anti-HBs.

The age-standardised prevalence of anti-HBs also did not show any statistically significant difference by gender. A significant increase in its prevalence by 22.4% and 19.1%, in Malays and Indians, respectively ($P < 0.001$) was observed (Table 5).

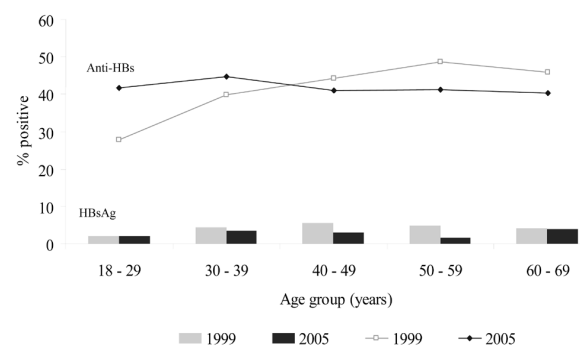


Fig. 1. Age-specific seroprevalence (%) of HBsAg and anti-HBs among adults in Singapore, HBSS 1999 and HBSS 2005.

Discussion

There has been a declining trend in the HBsAg prevalence in the adult population in Singapore. Prior to the implementation of the national childhood immunisation programme, the HBsAg prevalences of specific adult population groups were high: family contacts of chronic hepatitis B carriers (38%),⁵ spouses of HBsAg/HBeAg carrier women (15.7%),⁵ multiple transfused patients (13%),¹¹ Chinese males above 35 years of age (10%),¹² dental surgeons (11.4%),¹³ male prostitutes (14.9%)¹⁴ and female prostitutes (6.3%).¹⁵ In 1972, the HBsAg prevalence by immuno-electrophoresis was 8.5% in adult Chinese but this decreased to 6.2% in 1987.⁵ The overall prevalence among voluntary blood donors in 1975 was 9.1% by the reverse passive haemagglutination method,¹⁶ with a prevalence of 13.6% in Chinese, 7.3% for Malays and 6% for Indians but the corresponding figures by enzyme immunoassay in 1986 decreased to 3.9%, 4.6%, 1.6% and 0.9%, respectively.¹⁷ The prevalence in national servicemen had also declined from 8.1% in 1984 to 4.4% in 1988.⁵ Moreover, the prevalence

Table 3. Crude and Age-Standardised Seroprevalence (%) of HbsAg in Adults in Singapore by Gender and Ethnic Group, HBSS 1999 and HBSS 2005

	1999		2005		Difference in age-std prevalence [2005 – 1999]
	Crude prevalence	Age-std prevalence (95% CI)	Crude prevalence	Age-std prevalence (95% CI)	
All	4.1 (3.5, 4.7)	4.0 (3.4, 4.6)	2.7 (2.2, 3.2)	2.8 (2.2, 3.3)	-1.3†
Gender					
Males	4.9 (4.0, 5.8)	4.9 (3.9, 5.9)	2.7 (2.0, 3.4)	2.8 (2.0, 3.6)	-2.1†
Females	3.3 (2.6, 4.0)	3.2 (2.5, 3.9)			
Ethnic Group					
Chinese	4.7 (4.0, 5.4)	4.7 (3.9, 5.4)	2.8 (2.2, 3.4)	2.9 (2.3, 3.5)	-1.8‡
Malay	2.1 (1.0, 3.2)	2.1 (1.1, 3.1)	2.7 (1.3, 4.1)	2.8 (1.7, 3.9)	0.7
Indian	0.5 (0.0, 1.2)	0.5 (0.0, 1.0)	1.8 (0.4, 3.2)	1.6 (0.6, 2.6)	1.1*

* 0.01 < P < 0.05

† 0.001 < P < 0.01

‡ P < 0.001

Table 4. Crude and Age-Standardised Seroprevalence (%) of HBeAg in Adults in Singapore by Gender and Ethnic Group, HBSS 1999 and HBSS 2005

	1999		2005		Difference in age-std prevalence [2005 – 1999]
	Crude prevalence	Age-std prevalence (95% CI)	Crude prevalence	Age-std prevalence (95% CI)	
All	0.5 (0.3, 0.7)	0.5 (0.3, 0.7)	0.3 (0.1, 0.5)	0.4 (0.2, 0.6)	-0.1
Gender					
Males	0.5 (0.2, 0.8)	0.5 (0.2, 0.8)	0.3 (0.1, 0.5)	0.4 (0.1, 0.6)	-0.1
Females	0.5 (0.2, 0.8)	0.5 (0.2, 0.8)	0.3 (0.1, 0.5)	0.4 (0.1, 0.6)	-0.2
Ethnic Group					
Chinese	0.6 (0.4, 0.8)	0.6 (0.3, 0.9)	0.3 (0.1, 0.5)	0.4 (0.1, 0.6)	-0.2
Malay	0.2 (0.0, 0.6)	0.2 (0.0, 0.6)	0.6 (0.0, 1.3)	0.6 (0.1, 1.1)	0.3
Indian	0.0	0.0	0.0	0.0	-

Table 5. Crude and Age-Standardised Seroprevalence (%) of Anti-HBs in Adults in Singapore by Gender and Ethnic Group, HBSS 1999 and HBSS 2005

	1999		2005		Difference in age-std prevalence [2005 – 1999]
	Crude prevalence	Age-std prevalence (95% CI)	Crude prevalence	Age-std prevalence (95% CI)	
All	39.5 (38.1, 40.9)	39.7 (38.2, 41.1)	42.0 (40.5, 43.5)	42.1 (40.5, 43.7)	2.5*
Gender					
Males	38.5 (36.5, 40.5)	38.6 (36.5, 40.8)	41.1 (38.9, 43.3)	41.1 (38.8, 43.5)	2.5
Females	40.5 (38.5, 42.5)	40.7 (38.7, 42.6)	43.0 (40.9, 45.2)	43.1 (40.9, 45.3)	2.4
Ethnic Group					
Chinese	44.3 (42.7, 45.9)	44.5 (42.8, 46.3)	42.3 (40.6, 44.0)	42.3 (40.4, 44.2)	-2.3
Malay	19.7 (16.5, 22.9)	19.5 (16.9, 22.2)	41.5 (37.2, 45.8)	41.9 (38.5, 45.3)	22.4†
Indian	22.1 (17.7, 26.5)	21.8 (18.6, 25.0)	40.5 (35.5, 45.8)	40.9 (37.0, 44.8)	19.1†

* 0.01 < P < 0.05

† P < 0.001

of HBsAg in women monitored through routine screening of antenatal mothers at public healthcare institutions had declined significantly from 4.4% in 1980 to 1981, to 4.1% in 1983 to 1985, 3.4% in 1987 to 1990 and 2.3% in 2003 to 2004.¹⁸

During the 6-year period between HBSS 1999 and 2005, the overall HBsAg prevalence declined further from 4.1% to 2.7%. The decline was significant for the 2 subgroups: males and the Chinese ethnic group. A prevalence of 2.7% was much lower than that of other countries in Asia (e.g. Thailand and China) where the prevalence ranged between 8% and 20%.¹⁹ However, even with this reduced seroprevalence, Singapore is still classified by the World Health Organisation (WHO) as a country with intermediate HBV endemicity (i.e. HBsAg prevalence ranging from 2% to less than 8%).^{19,20} In contrast, other developed countries such as the United States, Canada, Australia, United Kingdom and several other Western European countries have much lower prevalence of HBsAg between 0.2% and 0.5%.¹⁹ Nevertheless, Singapore is already within WHO Western Pacific Region's goal of reducing the HBsAg seroprevalence in children at least 5 years of age to less than 2% by 2010.²¹

Based on this prevalence, it is estimated that there are 63,900 persons aged 18 to 69 years being positive for HBsAg among Chinese, Malay and Indian resident population in 2004, of whom 11% are highly infectious as indicated by HBeAg positivity. These HBeAg positive people are the most infective group and represent a high infectivity risk to the susceptibles in the community.

In the general population, ad hoc surveys carried in the 1980s showed that the age-specific prevalence of HBsAg was highest in the 35 to 44 year-old age group (6.3%).⁵ However in the HBSS 2005, we noticed that the prevalence in the 35 to 44 year-old age group had declined to 3.4%.

Compared to the findings of HBSS 1999, there was a significant decrease in the age-standardised HBsAg prevalence for males (from 4.9% to 2.8%) but not for females (3.2% and 2.8%, respectively). The change in HBsAg prevalence was only observed among the Chinese ethnic group, but not in the other ethnic groups. In fact, the age-standardised HBsAg prevalence for the Indian ethnic group had increased significantly from 0.5% to 1.6%. The reasons for these findings are unknown.

Among the 3 major ethnic groups, it had been found that the prevalence of HBsAg was significantly higher among the Chinese compared to the non-Chinese although the frequencies of anti-HBs were of the same order. It was suggested that this could be due to differences in immunological responsiveness to HBsAg which is genetically determined.^{22,23} With the declining prevalence of HBsAg over the years, no significant difference between Chinese and non-Chinese was observed in HBSS 2005.

There was also no significant difference between gender.

While HBeAg positivity among female HBV carriers in the reproductive age of 18 to 44 years had dropped from 18.2% in HBSS 1999 to 12.8% in HBSS 2005, this group warrants close monitoring in view of the high-risk of perinatal transmission from HBsAg/HBeAg positive mothers to the newborns if post-exposure prophylaxis is not administered accordingly.²⁴⁻²⁶ In such situations of a lack of post-exposure prophylaxis, there is a 70% to 90% risk of infants infected developing chronic carrier state.²⁵

The impact of the hepatitis B prevention and control programme in adults is also indicated by the declining incidence of acute hepatitis B which dropped from 9.2 per 100,000 in 1985 to 3.4 per 100,000 in 1999 and 1.7 per 100,000 in 2007.³ As there has been no routine adult hepatitis B immunisation except for healthcare workers and the catch-up immunisation programme for students in secondary schools, colleges, university and national servicemen aged from 15 years to below 30 years, other public health measures could also have contributed to the decline in HBsAg prevalence. These include health education to generate greater awareness of the disease and its modes of transmission, routine screening of blood donors for HBV carrier status, universal use of disposable needles and syringes in healthcare institutions and trade premises (e.g. tattoo parlours, beauty salons) and universal blood precautions.¹ Since the routine screening of voluntary blood donors for HBsAg was implemented in 1973, post-transfusion hepatitis B has virtually disappeared. The introduction of disposable needles and syringes in healthcare institutions has brought about a significant decline in the proportion of acute hepatitis B with a recent history of exposure to various parenteral procedures such as injection, dental treatment, venepuncture, acupuncture and tattooing from 62.1% in 1977 to 5.9% in 1988 and 0% since 1999.²⁷ It is interesting to note that the primary liver cancer incidence rates had been dropping even before the national control programme was implemented, from 27.8 per 100,000 per year during 1978 to 1982 to 18.9 per 100,000 per year from 1993 to 1997.²⁸ For the period 1998 to 2002, the age-standardised incidence rates of liver cancer further decreased to 18.5 per 100,000 per year for males and 4.6 per 100,000 per year for females.²⁹ It is interesting to note that the primary liver cancer incidence rates had been dropping even before the national control programme was implemented. Among males, the rates dropped from 27.7 per 100,000 per year between 1978 and 1982 to 19.0 per 100,000 per year between 1993 and 1997.²⁸ For the period 1998 to 2002, the age-standardised incidence rate of liver cancer among males further decreased to 18.5 per 100,000 per year.²⁸ For the females, the age-standardised incidence rate of liver cancer had decreased from 7.0 per 100,000 per

year between 1978 and 1982 to 4.6 per 100,000 per year between 1998 and 2002.²⁸

The HBSS 2005 showed that a large proportion of the adult population aged 18 to 69 years remained highly susceptible to HBV infection with less than half (42%) possessing immunity (anti-HBs ≥ 10 mIU/ml). The age-standardised anti-HBs prevalence increased significantly from 39.7% in HBSS 1999 to 42.1% in HBSS 2005. The most significant increase in the prevalence of anti-HBs from 27.9% to 41.7% was observed in young adults aged 18 to 29 years. This age group had missed the neonatal hepatitis B immunisation programme implemented nationwide since 1987 and represented the cohort that the catch-up immunisation programme targeted. Among those identified who required hepatitis B immunisation, 85.4% completed at least one dose. Therefore, we attribute the increased immunity in this age group to the catch-up hepatitis B immunisation programme implemented from 2001 to 2004. It is important however to note that applying the anti-HBs threshold level of 10 mIU/ml could lead to an underestimation of the true population immunity against HBV. This is because an anti-HBs level of less than 10 mIU/ml does not mean that an individual does not have immunity against HBV. It is a well-known fact that despite waning anti-HBs levels to below 10mIU/ml after primary immunisation, most vaccinated individuals are still protected against HBV infection because of immunological memory.^{24,29,30} Another limitation in our study also comes from the fact that the serological tests used in HBSS 1999 employed the EIA method whereas the HBSS 2005 used the electrochemiluminescence method. However, one study has shown that there is a relatively high concurrence rate between the 2 serology tests kits especially for HBsAg and HBeAg (concurrence between AxSYM and E170 was 97.8% for HBsAg, 98.4% for HBeAg and 91.1% for anti-HBs). Significant differences for anti-HBs were mainly observed at low levels.³¹

Adults continued to be at risk of acquiring HBV as evidenced by the high incidence rate of acute hepatitis B in the age group of 25 to 34 years from 1999 to 2007.³² As such, medical practitioners should routinely enquire the hepatitis B vaccination status of their patients and those who have not been vaccinated should be screened and immunised. In Asia, vertical transmission is believed to be the leading cause of endemicity of hepatitis B. However, with effective childhood immunisation programmes, sexual transmission is likely to emerge as the leading cause of HBV infection in healthy susceptible adults, as in the West.³² Hence, it is important that prevention programmes are actively targeted at the susceptible adult population, especially those who indulged in high-risk behaviour, to reduce horizontal transmission via sexual contact.

REFERENCES

- Goh KT. Epidemiology and Control of Hepatitis B Virus infection in Singapore. Tokyo: Southeast Asian Medical Information Center, 1992.
- Goh KT, Doraisingam S, Tan KL, Oon CJ, Ho ML, Chen AJ, et al. The hepatitis B immunization programme in Singapore. *Bull World Health Organ* 1989;67:65-70.
- Ministry of Health. Communicable Diseases Surveillance in Singapore 2007.
- Committee on Epidemic Diseases. Prevalence of hepatitis B virus markers in Singapore. *Epidemiol News Bull* 2000;26:1-2.
- Goh KT. Prevention and control of hepatitis B virus infection in Singapore. *Ann Acad Med Singapore* 1997;26:671-81.
- Committee on Epidemic Diseases. Serological survey on hepatitis B virus infection in school children in Singapore. *Epidemiol News Bull* 1996;22:57-9.
- Ong SC, Lim SG, Li SC. How big is the financial burden of hepatitis B to society? A cost-of-illness study of hepatitis B infection in Singapore. *Viral Hepat* 2009;16:53-63.
- James L, Fong CW, Foong BH, Wee MK, Chow A, Shum E, et al. Hepatitis B seroprevalence study 1999. *Singapore Med J*. 2001;42:420-4.
- Ministry of Health Singapore. National Health Survey 2004. Available at: <http://www.moh.gov.sg/mohcorp/publicationsreports.aspx?id=2984>. Accessed 12 October 2009.
- Armitage P, Berry G. *Statistical Methods in Medical Research*. 2nd ed. Oxford: Blackwell Scientific, 1987.
- Ng HW. Liver dysfunction in haemophilia A, B and other hereditary haemorrhagic disorders. *Ann Aca Med Singapore* 1984;13:524-6.
- Phoon WO, Fong HP, Lee J, Leong HK. A study on the prevalence of hepatitis B surface antigen among Chinese adult males in Singapore. *Int J Epidemiol* 1987;16:74-8.
- Goh KT, Chan YW, Wong LYM, Kong KH, Oon CJ, Guan R. The prevalence of hepatitis B virus markers in dental personnel in Singapore. *Trans R Soc Trop Med Hyg* 1988;82:908-10.
- Goh CL, Rajan VS, Chan SH, Kamarudin A. Hepatitis B infection in prostitutes. *Int J Epidemiol* 1986;15:112-5.
- Goh CL, Kamarudin A, Chan SH, Rajan VS. Hepatitis B virus markers in prostitutes in Singapore. *Genitourin Med* 1985;61:127-9.
- Ong YW. Some clinical and epidemiological aspects of HBsAg antigenaemia and alpha-feto protein levels in Singapore. In: *Liver Cancer and Cancer Problems in Asian Countries*. Proceedings of the AFOCC 2nd Asian Cancer Conference, Singapore, 1976:57-60.
- Chan SH. Hepatitis B infection in Singapore. *Epidemiol News Bull* 1977;3:15-6.
- Committee on Epidemic Diseases. A review of viral hepatitis B surveillance in Singapore, 1999-2004. *Epidemiol News Bull* 2005;31:27-31.
- World Health Organization. Diseases Covered by EPR. Hepatitis B. Available at: <http://www.who.int/csr/disease/hepatitis/whocdscsrlyo20022/en/index1.html>. Accessed 4 December 2009.
- World Health Organization. Position paper on hepatitis B vaccines. *Weekly Epidemiol Rec* 2009;84:405-20.
- Rani M, Yang B, Nesbit R. Hepatitis B control by 2012 in the WHO Western Pacific Region: rationale and implications. *Bull World Health Organ* 2009;87:707-13.
- Yap EH, Ong YW, Simons MJ, Okochi K, Mayumi M. Australia antigen in Singapore II: differential frequency in Chinese, Malays and Indians. *Vox Sang* 1972;22:371-5.
- Simons MJ, Yu M, Shanmugaratnam K. Hepatitis B antigenaemia, specific immune deficiency and hepatocellular carcinoma. *Tumour Res* 1973;8:120-6.

24. Centers for Disease Control and Prevention. Hepatitis B. In Atkinson W, Hamborsky J, McIntyre L, Wolfe S, eds. *Epidemiology and Prevention of Vaccine-Preventable Diseases*. 10th ed, 2nd printing. Washington DC: Public Health Foundation, 2008.
 25. Mast EE, Margolis HS, Fiore AE, Brink EW, Goldstein ST, Wang SA, et al; Advisory Committee on Immunization Practices (ACIP). A comprehensive immunization strategy to eliminate transmission of hepatitis B virus infection in the United States: recommendations of the Advisory Committee on Immunization Practices (ACIP) part 1: immunisation of infants, children and adolescents. *MMWR Recomm Rep* 2005;54(RR-16):1-31.
 26. Chan SH, Tan KL, Goh KT, Lim C, Tsakok M, Oon CL, et al. Maternal-child hepatitis B virus transmission in Singapore. *Int J Epidemiol* 1985;14:173-7.
 27. Committee on Epidemic Diseases. Prevention and control of hepatitis B virus infection in Singapore. *Epidemiol News Bull* 2002;28:31-4.
 28. Seow A, Koh WP, Chia KS, Shi LM, Lee HP, Shanmugaratnam K. Trends in cancer incidence in Singapore 1968-2002. *Singapore Cancer Registry Report No. 6*, 2004.
 29. Goh KT, Tan KL, Kong KH, Oon CJ, Chan SH. Comparison of the immune response of four different dosages of a yeast-recombinant hepatitis B vaccine in Singapore: a four-year follow-up study. *Bull World Health Organ* 1992;70:233-9.
 30. Goh KT, Oon CJ, Heng BH, Lim GK. Long-term immunogenicity and efficacy of a reduced dose of plasma-based hepatitis B vaccine in young adults. *Bull World Health Organ* 1995;73:523-7.
 31. Chen Y, Wu W, Li LJ, Lou B, Zhang J, Fan J. Comparison of the results for three automated immunoassay systems in determining serum HBV markers. *Clin Chim Acta* 2006;372:129-33. Epub 2006 May 19.
 32. Heng BH, Goh KT, Chan R, Chew SK, Doraisingam S, Quek GH. Prevalence of hepatitis B virus (HBV) infection in Singapore men with sexually transmitted diseases and HIV infection: role of sexual transmission in a city state with HBV intermediate endemicity. *J Epidemiol Community Health* 1995;49:309-13.
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