

**SURVEILLANCE OF VIRAL
HEPATITIS IN HONG KONG
– 2002 Update Report**

**Department of Health
December 2003**

THE SCIENTIFIC WORKING GROUP ON VIRAL HEPATITIS PREVENTION (SWG VHP)

About SWG VHP

The *Scientific Working Group on Viral Hepatitis Prevention* (SWG VHP) was formed by the Department of Health in 1992. It succeeded the work of the previous *Scientific Working Group cum Advisory Committee on Hepatitis B Vaccination*. Constituted by professionals in microbiology, public health and clinical fields, the SWG VHP has the following terms of reference:

- To keep under review local and international trends of viral hepatitis infection
- To advise the Government on the strategy on the prevention of viral hepatitis in Hong Kong.

The Department of Health's Special Preventive Programme (SPP) provides secretariat support to the SWG VHP.

Membership List (as of December 2003)

Dr SS Lee (Chairman)	Consultant, Special Preventive Programme, Department of Health
Professor NK Leung, <i>BBS, JP</i>	Hon Consultant Paediatrician, Princess Margaret Hospital
Professor CL Lai	Professor, Department of Medicine, The University of Hong Kong
Professor John Tam	Professor, Department of Microbiology, Chinese University of Hong Kong
Dr WL Lim, <i>JP</i>	Consultant Medical Microbiologist, Department of Health
Dr Betty Young	Consultant Paediatrician, Pamela Youde Nethersole Eastern Hospital
Dr CK Lin	Hospital Chief Executive, Hong Kong Red Cross Blood Transfusion Service
Dr HY Lo	Consultant Physician, Queen Elizabeth Hospital
Dr KT Tse	Consultant, Department of Obstetrics and Gynaecology, Queen Elizabeth Hospital
Dr Nancy Leung	Hepatologist, Department of Medicine, Chinese University of Hong Kong
Dr ST Lai	Consultant Physician, Infections Disease Division, Princess Margaret Hospital
Dr LY Tse	Consultant (Community Medicine), Disease Prevention and Control Division, Department of Health

Dr SL Leung Principal Medical Officer, Family Health Service, Department of Health
Dr YY Ho Consultant (Community Medicine), Food & Environmental Hygiene
Department
Mr. Thomas Tam Senior Pharmacist, Department of Health

Secretariat

Dr KH Wong Senior Medical Officer, Special Preventive Programme, Department of
Health
Mr. MK Wong Senior Executive Officer, Special Preventive Programme, Department
of Health

Correspondence

The Secretariat
Scientific Working Group on Viral Hepatitis Prevention
c/o Special Preventive Programme Office,
5/F Yaumatei Jockey Club Clinic,
145 Battery Street, Yaumatei,
Kowloon,
HONG KONG.

Telephone: (852) 2780 8622
Facsimile: (852) 2780 9580

Website: www.hepatitis.gov.hk
E-mail: hepatitis@dh.gov.hk

Research Team

This report* was compiled by the SPP of the Department of Health, on behalf of the SWGVHP. Dr. KL Hau and Ms Crystal Ng assisted in the collection of data, Ms Kathy Cheng compiled and analysed the data, Dr. KH Wong and Dr. SS Lee wrote the report.

*pdf version of the report can also be downloaded from www.hepatitis.gov.hk.

CONTENTS

	Page
The Scientific Working Group on Viral Hepatitis Prevention	1
Contents	3
Tables and Figures	4
Preface	5
Executive Summary	6
1. Introduction	8
2. Data Sources	9
3. Acute Viral Hepatitis	11
4. Falling Prevalence of Hepatitis B Markers	16
5. Hepatitis B mutants	28
6. Hepatitis C Infection	30
7. Tracking Hepatitis A and Hepatitis E	33
8. Hepatocellular carcinoma	36
9. Conclusions	38
Acknowledgements	41
Abbreviations	42
References	43

TABLES & FIGURES

<i>Number</i>	<i>Title</i>	<i>Source</i>	<i>Page</i>
Box 1	No. of cases of viral hepatitis reported to the Department of Health between 1966 and 2002	DH	12
Box 2	Reported viral hepatitis from 1966 to 2002	DH	13
Box 3	Breakdown of different types of reported viral hepatitis from 1996 to 2002	DH	14
Box 4	Types of acute viral hepatitis in patients (n=1304) admitted to a public hospital between 1996 and 1999	PMH	15
Box 5	Prevalence of HBsAg in new blood donors from 1990 to 2002	HKRCBTS	16
Box 6	HBsAg prevalence and its gender and age breakdown in new blood donors in 2002	HKRCBTS	17
Box 7	HBsAg prevalence among university students/staff	CUHC	17
Box 8	HBsAg prevalence among university students/staff	BUHC	18
Box 9	HBsAg prevalence from the Premarital Package Service	FPA	18
Box 10	HBsAg prevalence in antenatal women from 1990 to 2002	FHS & Virus Unit (DH)	18
Box 11	HBsAg prevalence and age breakdown of antenatal mothers	FHS (DH)	19
Box 12	HBsAg prevalence among antenatal mothers of different age groups in 1990, 1995, 2000 – 2002	FHS & Virus Unit (DH)	20
Box 13	Prevalence of hepatitis B markers in police officers from 1996 to 2002	DH	20
Box 14	HBsAg prevalence among male and female police officers of different age groups from 1996 to 2002	DH	21
Box 15	Prevalence of hepatitis B markers in subjects who underwent routine virological investigations in 2001.	Virus Unit (DH)	21
Box 16	Prevalence of hepatitis B markers in newly recruited health care workers in 2001-2002	DH	22
Box 17	Prevalence of hepatitis B markers in drug users from 1990 to 2002	Virus Unit (DH)	23
Box 18	HBsAg prevalence in new HIV/AIDS patients in 1998, 2000-2002	ITC (DH)	24
Box 19	Prevalence of HBsAg from the CRPVH 2001 study	DH	24
Box 20	HBsAg prevalence in different population groups from 1990 to 2002	Multiple sources	26
Box 21	Trends of HBsAg in selected population groups from 1990 to 2002	Multiple sources	27
Box 22	HBV serology at ≥ 6 to < 9 months post IgM anti-HBc positivity	DH	25
Box 23	Anti-HCV prevalence in new blood donors	HKRCBTS	30
Box 24	Anti-HCV prevalence and its gender and age breakdown in new blood donors in 2002	HKRCBTS	30
Box 25	Anti-HCV prevalence in drug users on rehabilitation	Virus Unit (DH)	31
Box 26	Anti-HCV prevalence in HIV/AIDS patients in 2001 and 2002.	ITC (DH)	31
Box 27	Prevalence of anti-HAV in a collection of studies/testings between 1978 and 2002	Multiple sources	34
Box 28	Prevalence of anti-HAV in participants of CRPVH 2001	DH	35
Box 29	Prevalence of anti-HEV in participants of CRPVH 2001	DH	35
Box 30	Time trends of liver cancer incidence and mortality	HKCR	36

PREFACE

At its 7th meeting on 15 May 1995, the Scientific Working Group on Viral Hepatitis Prevention (SWG VHP) deliberated on the issue of hepatitis surveillance in Hong Kong. The discussions in the meeting led to the suggestions of (a) maintaining a database on the seroprevalence of infective hepatitis in Hong Kong, (b) conducting regular epidemiological studies to supplement existing information on the different forms of infective hepatitis, and (c) alerting the Government, health care providers and researchers on the possible emergence of new epidemiological trends of viral hepatitis. Subsequently, in 1996, 1997, 2000 and 2002, local epidemiological data on viral hepatitis were collected and published in an “update report” series. The effort represented the first step towards a coordinated system in the description and dissemination of hepatitis surveillance information in Hong Kong.

This is the sixth report on viral hepatitis surveillance that brings updated information as of the end of 2002, for the information of health care professionals working on various aspects of viral hepatitis prevention. In this Report, data from on-going programmes were updated through year 2002. Also, new data gathered from other sources in year 2002 or before were included. Readers are reminded that this Report, similar to previous ones under the same series, is not a primary study but a collection of secondary data on the subject. The original papers and authors should be consulted in case of queries.

In the course of the preparation of the Report, we have received enthusiastic support from health professionals of different agencies. The publication of the Report would not have been possible without their input. We also reckon that the list in the Acknowledgements may not be exhaustive. Much as we tried to be accurate and concise, we are fully aware of the possibility of errors. We welcome criticisms, suggestions and comments of any kind. These would be important in helping us improve the quality of the next Report.

Secretariat
Scientific Working Group on Viral Hepatitis Prevention
December 2003

EXECUTIVE SUMMARY

This epidemiological report on viral hepatitis in Hong Kong is an integration and analyses of data from four sources: (a) the statutory notification system, (b) statistics from services, (c) seroprevalence studies and (d) publications or abstracts on the subject. The majority of the new information collected in 2002 has focused on hepatitis B, followed by hepatitis A, hepatitis C and hepatitis E.

The statutory notification system has remained a useful mechanism for tracking the pattern of acute viral hepatitis. In recent years, with the exception of the 1992 hepatitis A epidemic, the number of acute viral hepatitis reported per year has been stable at around a few hundred per year. The predominance of HAV, followed by HBV infections among acute viral hepatitis corresponded with the data from hospital inpatient statistics. There were recent data suggesting an increasingly important, though still relatively small, role of hepatitis E (HEV) in Hong Kong. The current system is insensitive in identifying new HCV infections.

The seroprevalence of hepatitis B (HBV) markers in Hong Kong has continued to fall. In antenatal women, however, the drop is less obvious. This observation could be linked to those not born in Hong Kong. Age is an important factor affecting HBsAg prevalence, with a higher proportion of the older population having markers of past infection or becoming chronically infected. The introduction of universal neonatal hepatitis B vaccination in 1988 is expected to lead to a gradual decrease of positive HBsAg rate in the younger age groups. This notion was supported by recent data in young children. As regards populations with high-risk behaviours, the HBsAg positive rate in drug users has generally fallen over the years until 1997, followed by a slowly rising trend again (12.7% in 2002). The prevalence rate in this population is still substantially higher than the general population.

The prevalence of hepatitis A markers has also continued to fall in young people. Data obtained from a community research project done in 2001 showed some 20% and 50% anti-HAV positivity rate in people aged 18-29 and 30-39 years old respectively. This was equivalent to a shifting of the age-specific HAV seroprevalence curve to the right, when compared to the age-specific breakdown data in the 1978/79 and 1987-89 studies. Such cohort effect suggested the absence of major HAV infections in the society in the last two decades, though the methodologies differed across these studies.

The Hong Kong Red Cross Blood Transfusion Service has been a major source of data on hepatitis C (HCV) in Hong Kong. In the past ten years, the prevalence of anti-HCV in new blood donors has ranged between 0.058% and 0.099%. Two previous local studies suggested that 1b was the most common HCV genotype in Hong Kong.

A community study in 2001 found that HEV prevalence may have fallen compared with a decade ago. Data on HDV and HGV are too limited for any meaningful interpretation of trends.

From available evidence, chronic hepatitis B infection has remained an important cause of hepatocellular carcinoma in Hong Kong.

1. INTRODUCTION

Viral hepatitis is an important group of infectious diseases in Hong Kong. In human, at least five hepatitis viruses have been documented to give rise to liver inflammation. These viruses are named alphabetically in order of the date of their isolation or diagnosis in the scientific community. They are: hepatitis A (HAV), hepatitis B (HBV), hepatitis C (HCV), hepatitis D (delta agent or HDV), and hepatitis E (HEV). In 1995, hepatitis G virus¹ (HGV) was identified. However, its association with clinical diseases is still a subject of debate. More recently, another transfusion-transmitted virus² (TTV) was described, which is also possibly linked with liver diseases.

Since 1992, the *Scientific Working Group on Viral hepatitis Prevention* (SWGVHP) has been monitoring the hepatitis situation in Hong Kong with an aim to support the development of prevention strategy. In 1996 and 1997, reports on the surveillance of viral hepatitis were published and it was decided subsequently that these surveillance reports be prepared on a regular basis. From 2000 to 2002, reports of epidemiological data up to the end of the preceding year were compiled.

The SWGVHP does not undertake surveillance activities directly. This Report is a compilation of surveillance data collected and collated from various sources, largely in the public sector. In the process, the Group reviews the situation and brings the information updated as of the end of year 2002. In compiling the Report, the Secretariat tried to focus on the new information identified and collected in 2002. For details of earlier data, readers should refer to the SWGVHP's five previous update reports dated 1996, 1997, 1999, 2000 and 2001.

2. DATA SOURCES

The production of the 2002 Update Report has relied on the collection and interpretation of data from four major sources:

- (a) Disease notification system,
- (b) Statistics from various services,
- (c) Seroprevalence studies, and
- (d) Published papers or presented abstracts on hepatitis epidemiology or related subjects.

Disease notification system

In Hong Kong, viral hepatitis is a notifiable disease under the *Quarantine and Prevention of Disease Ordinance* (Cap. 141). The notification system is managed by the Department of Health, which publishes an update report in its *Public Health and Epidemiology Bulletin* on a bimonthly basis. This bimonthly update report on notifiable diseases is also posted on the Department's homepage (www.dh.gov.hk).

Statistics from various Services

Seroprevalence data on viral hepatitis in Hong Kong are derived from the statistics of various clinical services and programmes. The main sources of such data for the 2002 Update Report are:

- (a) Screening of blood donors at the Hong Kong Red Cross Blood Transfusion Service;
- (b) Hepatitis B screening programme for antenatal mothers at the Maternal and Child Health Centres, Department of Health;
- (c) Premarital screening programme of the Family Planning Association of Hong Kong;
- (d) City University hepatitis awareness programme;
- (e) Hepatitis screening of drug users, Department of Health;
- (f) Pre-vaccination hepatitis screening for police officers and health care workers at Hepatitis Vaccination Clinic, Department of Health;
- (g) Screening of HIV/AIDS patients followed up at the Integrated Treatment Centre, Department of Health
- (h) Seroprevalence data from Government Virus Unit, Department of Health
- (i) Pattern of acute viral hepatitis admitted to the Princess Margaret Hospital, Hospital Authority
- (j) Hepatitis awareness project of the Baptist University of Hong Kong
- (k) Hong Kong Cancer Registry, Hospital Authority

Seroprevalence studies

Seroprevalence data of a Community Research Project on Viral Hepatitis conducted in 2001, a survey of students and general public, and a project on IgM anti-HBc positive hepatitis B are included in this Report.

Published papers or presented abstracts

In Hong Kong, clinical service providers and academic institutes have shown keen interest in the clinical and public health aspects of viral hepatitis. A review of publications and presentations serves to enrich the information on hepatitis epidemiology. However, some of the information may overlap with those collected from other sources. Also, readers are reminded that they should refer to the original texts for details.

3. ACUTE VIRAL HEPATITIS

The epidemiology of acute viral hepatitis in Hong Kong could be derived from:

- (a) data from the disease notification system and
- (b) hospital inpatient statistics.

Data from disease notification system

Over the years, the disease notification system has remained a useful source of information for viral hepatitis presenting clinically. In Hong Kong, voluntary reporting of viral hepatitis was started in 1966 by the then Medical and Health Department. Viral hepatitis became a notifiable disease in 1974. From 1988 onwards, the notification system has expanded by including the breakdown of viral hepatitis into hepatitis A, hepatitis B, non-A non-B hepatitis and unclassified infection. Under this system, four categories of viral hepatitis are distinguished, based on the following criteria:

- (a) Hepatitis A – IgM anti-HAV positive
- (b) Hepatitis B – IgM anti-HBc positive (excluding known chronic HBV carrier)
- (c) Non-A non-B hepatitis – negative for the above two markers
- (d) Unclassified hepatitis – data on hepatitis markers inconclusive

Since 1996, hepatitis C and hepatitis E can be distinguished in the reported cases. Those cases that would have been classified into non-A non-B and unclassified hepatitis previously is now grouped into 3 categories:

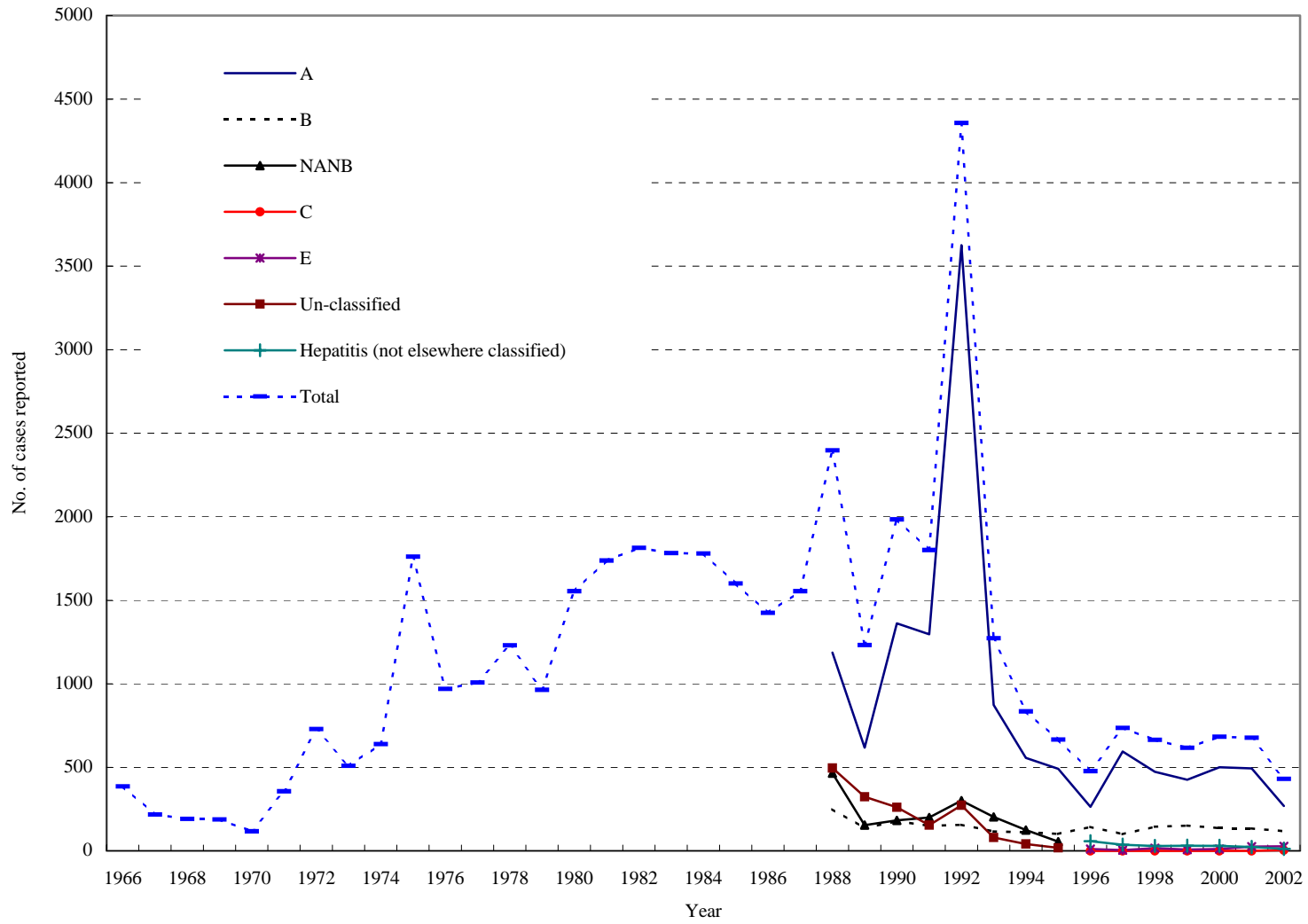
- (c1) Hepatitis C – Anti-HCV positive
- (c2) Hepatitis E – Anti-HEV positive
- (c3) Hepatitis (not elsewhere classified) – includes non-ABCE hepatitis cases and cases which did not have enough serological markers to be classified into any of the above categories.

Box 1 shows the figures for the notified cases in Hong Kong over the past 37 years. Box 2 is a graphical presentation of the time trend of reported hepatitis in the same period. Box 3 shows the breakdown of different types of reported viral hepatitis from 1996 to 2002.

**Box 1. No. of cases of viral hepatitis reported to the Department of Health
between 1966 and 2002 (Data source: DH)**

Year	A	B	NANB	C	E	Un- classified	Hepatitis (not elsewhere classified)	Total
1966		<i>voluntary reporting since 1966</i>						386
1967								218
1968								191
1969								188
1970								117
1971								357
1972								729
1973								509
1974		<i>notifiable since 1974</i>						639
1975								1761
1976								969
1977								1008
1978								1230
1979								964
1980								1554
1981								1738
1982								1814
1983								1783
1984								1780
1985								1601
1986								1425
1987								1554
1988	1187	250	465			496		2398
1989	618	136	154			324		1232
1990	1362	178	183			261		1984
1991	1297	150	200			154		1801
1992	3626	157	301			273		4357
1993	874	116	203			80		1273
1994	557	112	125			41		835
1995	491	102	55			18		666
1996	264	144	-	-	11	-	58	477
1997	595	100	-	-	4	-	37	736
1998	474	145	-	-	16	-	29	664
1999	426	152	-	-	8	-	31	617
2000	505	137	-	-	11	-	30	683
2001	494	134	-	-	26	-	23	677
2002	269	119	-	4	28	-	10	430

Box 2. Reported viral hepatitis from 1966 to 2002 (Data source: DH)



Box 3. Breakdown of different types of reported viral hepatitis from 1996 to 2002. (Data source: DH)



The last hepatitis A epidemic occurred in 1992, with over 3600 reported cases. There were some 1300 total cases of acute viral hepatitis in 1993, which then fell to between 500 and 800 annually afterwards. In 2002, 430 cases of viral hepatitis have been reported, the majority (62.6%) of which were still hepatitis A. Both the numbers of all new cases and hepatitis A appear to be lower than those of year 2001. With improvements in sanitation, housing and economic standards, hepatitis A has shifted from an asymptomatic childhood infection to a clinical disease in young adults. The lack of immunity against the virus and the consumption of contaminated food contributed to the reported acute hepatitis A in recent years.

On the other hand, hepatitis B is endemic in Hong Kong, with a high proportion of adults already carrying some markers signifying past infection or chronicity of infection. With the introduction of universal neonatal hepatitis B vaccination in 1988, hepatitis B infection in childhood is conceivably becoming very uncommon. These factors account for the relatively smaller number of acute symptomatic hepatitis B, and the predominance of hepatitis A in the overall reported numbers.

Since the inclusion of hepatitis C in the classification system, for the first time 4 cases were reported in year 2002. However, the reporting of acute viral hepatitis may not be an effective means of studying hepatitis C epidemiology.

The number of hepatitis E cases reported yearly varied from 4 to 28 in the past 7 years.

Hospital inpatient statistics

The pattern of reported hepatitis corresponded with the trend depicted in hospital inpatient statistics. In a study of 1304 patients with acute viral hepatitis admitted to a public hospital between 1996 and 1999 (Box 4), episodes due to hepatitis A, B, C, D, E and non-A-E were 723 (55.4%), 425 (32.6%), 3 (0.2%), 0 (0%), 80 (6.1%) and 73 (5.6%) respectively³. (Box 4) However, it should be noted that a distinction between acute and acute-on-chronic hepatitis B infection is difficult in these cases in the absence of previous testing for hepatitis markers.

Box 4. Types of acute viral hepatitis in patients (n=1304) admitted to a public hospital between 1996 and 1999 (Data source: PMH)

Type of viral hepatitis	No. of patients (%)	
A	723	(55.4%)
B	425	(32.6%)
C	3	(0.2%)
D	0	(0%)
E	80	(6.1%)
Non-A-E	73	(5.6%)

The pattern largely echoed those reported to the disease notification system. Hepatitis A, followed by hepatitis B, was the most important causes of acute viral hepatitis. Acute symptomatic hepatitis C was unlikely to be very common in Hong Kong. Acute hepatitis E (HEV) was present in Hong Kong, the trend of which has to be tracked with time.

4. FALLING PREVALENCE OF HEPATITIS B MARKERS

Hepatitis B infection is monitored through the testing of serological markers resulting from the infection. The commonest markers monitored are:

- (a) HBsAg – present in chronic carriers and also during active acute infection;
- (b) Anti-HBs – indicative of immunity to the virus;
- (c) Anti-HBc – an indicator of natural infection.

Over the past years, serological data on hepatitis B have been collected from different sources. Many of these were statistics from services for young adults while others were tests on populations with higher risk of exposure.

Hepatitis B markers in young adults

Data on hepatitis B markers in young adults have come mainly from the following ongoing programmes:

- (a) Blood donor screening at the Hong Kong Red Cross Blood Transfusion Service,
- (b) Antenatal testing at the Department of Health's Maternal and Child Health Centres,
- (c) Pre-marital package service of the Family Planning Association of Hong Kong, and
- (d) Hepatitis awareness project of the City University's Health Centre and
- (e) Hepatitis awareness project of the Baptist University's Health Centre.

New blood donors

The majority of blood donors in Hong Kong are between the age of 16 and 30. Data from the Hong Kong Red Cross Blood Transfusion Service revealed a declining trend of HBsAg prevalence in this group of young adults, from 7.97% in 1990 to 3.63% in 2002 in new donors. (Box 5) However, this population may be a biased one because some known carriers may not go for blood donation, which could account for the low rate in the new donors. The prevalence in repeat donors was 0.14%.

Box 5. Prevalence of HBsAg in new blood donors from 1990 to 2002 (Data source: HKRCBTS)

Year	% HBsAg +
1990	7.97
1991	8.04
1992	7.38
1993	6.70
1994	5.87
1995	5.99
1996	5.62
1997	5.20
1998	4.89
1999	4.44
2000	4.15
2001	3.98
2002	3.63

Box 6. HBsAg prevalence and its gender and age breakdown in new blood donors in 2002 (Data source: HKRCBTS)

First Time donors in 2002	Male			Female		
	Age Group	No. tested	HBsAg No. positive %	No. tested	HBsAg No. positive %	%
16-19	12856	428	3.3%	13483	342	2.5%
20-29	4901	277	5.7%	4620	220	4.8%
30-39	1716	90	5.2%	2115	41	1.9%
40-49	841	63	7.5%	1213	46	3.8%
>49	249	15	6.0%	319	13	4.1%

As shown in Box 6, there was no specific age pattern for HBsAg positivity among new blood donors in 2002. However, the prevalence was consistently higher in male for all age groups, with an overall rate of 4.2% and 3.0% in male and female donors respectively. The odds ratio of HBsAg positivity in male was 1.46 (95% CI, 1.31-1.62).

University students and staff

The prevalence figures obtained from the ongoing hepatitis awareness project for students and staff of the City University of Hong Kong from 1994 to 2002 (Box 7) were similar to those of the new blood donors. The highish 6% of HBsAg prevalence in those aged below 21 in 2002 may be related to the small number tested.

Box 7. HBsAg prevalence among university students/staff (Data source: City University Health Centre)

Year	Aged below 21			Aged 21 - 30		
	Total no. of cases	HBsAg+ve		Total no. of cases	HBsAg+ve	
		No.	%		No.	%
1994	305	7	2.3	830	29	3.5
1995	324	10	3.1	768	33	4.3
1996	348	4	1.1	762	30	3.9
1998	371	5	1.3	608	21	3.5
2000	230	7	3.0	391	12	3.1
2001	288	6	2.1	610	18	3.0
2002	134	8	6.0	306	9	2.9

Since 2001, data from the Baptist University Health Awareness Programme (Box 8) was included. In 2002, the HBsAg prevalence rate was 1.5% in persons below 21 years old and 2.3% in those aged 21-30.

Amongst 1328 students (aged 18-25) of the Chinese University of Hong Kong tested in 2001/2002, 3.6% were positive for HBsAg, with a corresponding rate of 3.2% in males (n=505) and 4.4% in females (n=823). The HBsAg prevalence was 2.9% in 3457 secondary school students tested in 2001/2002.⁴

**Box 8. HBsAg prevalence among university students/staff
(Data source: Baptist University Health Centre)**

Year	Aged below 21		Aged 21 – 30			
	Total no. of cases	HBsAg+ve		Total no. of cases	HBsAg+ve	
		No.	%		No.	%
2001	220	7	3.2	204	10	4.9
2002	132	2	1.5	177	4	2.3

Clients of the Pre-marital package service of the Family Planning Association

The falling trend of HBsAg in young adults was also evident in data from the Pre-marital Package Service of the Family Planning Association. (Box 9) The prevalence rates were comparable though somewhat higher than the HBsAg positive rates reported in new blood donors and young university students and staff. However, the rates were in general lower than those of antenatal mothers (see below). In 2002, for example, the HBsAg prevalence of young adults attending the Family Planning Association was 6.9%, compared to that of 9.0% in the expectant mothers attending antenatal clinics.

Box 9. HBsAg prevalence from the Premarital Package Service (Data source: FPA)

Year	Total no. of cases	HBsAg +ve	
		No.	%
1990	17,251	1,659	9.6
1991	19,142	1,831	9.6
1992	18,445	1,708	9.3
1993	19,193	1,661	8.7
1994	16,466	1,210	7.3
1995	16,798	1,320	7.9
1996	19,959	1,575	7.9
1997	17,109	1,301	7.6
1998	13,163	897	6.8
1999	12,686	851	6.7
2000	15,348	862	5.6
2001	16,611	844	5.1
2002	15,077	1,033	6.9

Antenatal mothers

The HBsAg prevalence in antenatal mothers has also been falling over the years. The observation carries significant implication as it could be used to predict the future trend of perinatal infection. Results from antenatal screening demonstrated a steady decline from over 10% in the early 1990s to 9.0% in 2003 (Box 10). Those between the age of 15 and 19 had a lower prevalence of 5.0%, compared to that of 8.1% above the age of 34 in 2002 (Box 11). The results of clients younger than 15 years of age should however be interpreted with care because:

- (a) of the small number involved, and

Box 10. HBsAg prevalence in antenatal women from 1990 to 2002 (Data source: FHS and Virus Unit, DH)

Year	No. tested	HBsAg +	
		No.	%
1990	31749	3574	11.3
1991	30075	3278	10.9
1992	31394	3391	10.8
1993	34221	3456	10.1
1994	32470	3247	10.0
1995	30962	3016	9.7
1996	31508	3072	9.7
1997	25892	2417	9.3
1998	24678	2223	9.0
1999	23934	2114	8.8
2000	19090	1701	8.9
2001	23373	2142	9.2
2002	22202	2005	9.0

- (b) the dataset has actually included abortion cases and non-pregnant clients from sources other than the Maternal and Child Health Centres who attended for screening of sexually transmitted disease (STD)

Box 11. HBsAg prevalence and age breakdown of antenatal mothers

(Data source: FHS, DH)

Year	No. tested (% positive HBsAg) according to age group					
	<15*	15-19	20-24	25-29	30-34	>34
1990	447 (6.9)	1044 (10.3)	4671 (13.4)	15228 (10.7)	7639 (12.6)	2780 (12.9)
1991	86 (5.8)	987 (10.7)	4620 (10.7)	13151(10.4)	8168 (11.5)	3063 (11.8)
1992	50 (4.0)	928 (9.6)	5065 (11.4)	13093 (10.6)	8788 (10.6)	3470 (11.7)
1993	30 (10.0)	984 (9.0)	5589 (10.5)	12345 (10.3)	9395 (11.6)	3798 (11.0)
1994	50 (6.0)	951 (7.8)	5723 (9.8)	11590 (9.7)	10158 (10.6)	3998 (10.4)
1995	474 (4.3)	922 (8.4)	4979 (9.7)	10619 (9.6)	10112 (9.8)	4283 (10.3)
1996	97 (6.2)	842 (7.8)	4765 (10.3)	10137(9.5)	9759 (9.5)	5908 (10.6)
1997	9 (0)	902 (7.1)	4207 (9.3)	8895 (9.6)	7982 (9.3)	3897 (9.3)
1998	104 (11.5)	911 (5.8)	3887 (9.2)	8507(9.3)	7418 (8.8)	2851 (9.3)
1999	124 (11.3)	794 (7.7)	3777 (8.6)	8068 (9.3)	7196 (8.2)	3975 (9.3)
2000	22 (9.1)	618 (6.8)	2974 (10.1)	6466 (9.5)	5818 (8.0)	3192 (8.7)
2001	17 (5.9)	659 (7.3)	3516 (9.5)	8330 (10.1)	6936 (8.3)	3915 (9.0)
2002	4 (25.0)	484 (5.0)	2829 (9.7)	9120 (9.7)	6351 (8.5)	3414 (8.1)

* The dataset for those aged below 15 included abortion cases and non-pregnant clients attended for STD screening from sources other than the Maternal and Child Health Centres.

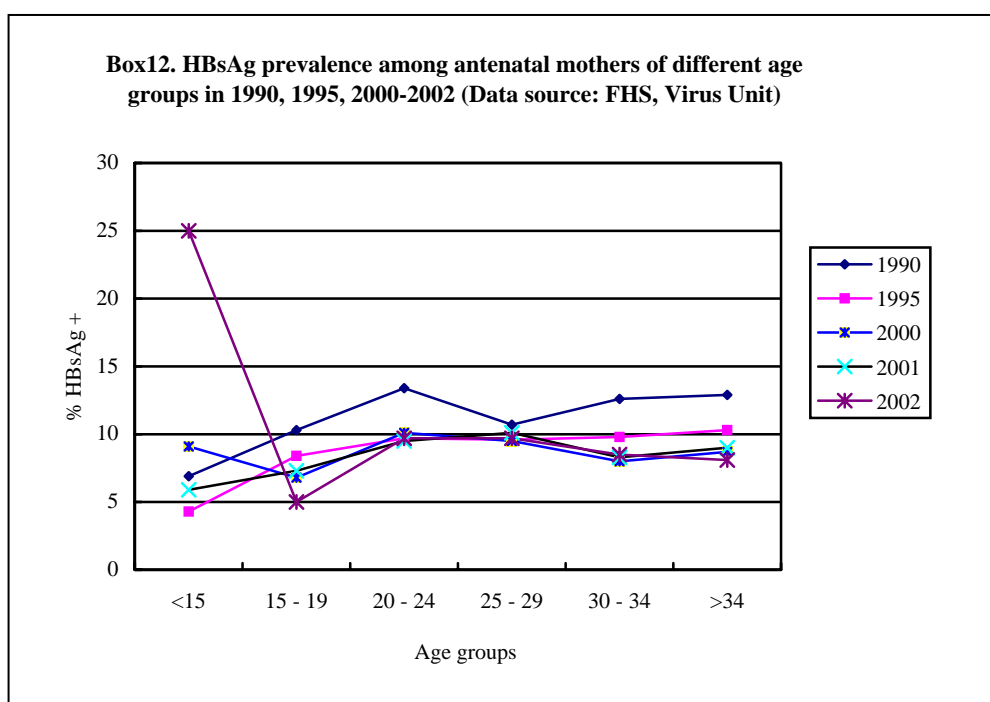
Despite the young age of the antenatal population, the HBsAg rate was generally higher than that in new blood donors, young university students/staff and clients of pre-marital package. One of the confounding factors may be the place of birth of the individual. A study on 2480 pregnant women attending the MCHC in 1996 showed a difference in HBsAg positive rate between locally and non-locally born antenatal mothers⁵. Those born in Hong Kong had a HBsAg prevalence of 8.4%, versus that of 13.1% in those born in Mainland China.

Age and hepatitis B markers

There is a positive correlation between age and the prevalence of hepatitis B markers from natural infection in a population. Generally speaking, the older a person is, the higher the chance of having been exposed to hepatitis B virus and thus harbouring markers of the infection. This association was illustrated by the HBsAg figures for antenatal mothers in the early 1990s (Box 11 & 12). However, this relationship disappeared after 1998, the reason for which is unclear.

Another more compelling piece of evidence that confirmed this finding was derived from the hepatitis B pre-vaccination screening done for the police force between 1996 and 2002 (Box 13 & 14). The results demonstrated a positive correlation between age and HBV markers. Furthermore, the HBsAg positivity rate correlates with age in males. In addition, similar to the new blood donors, men had a higher prevalence of HBsAg than women for all age groups (Box 14), or were tested positive for any HBV markers in a higher proportion of the subjects. However, it must be

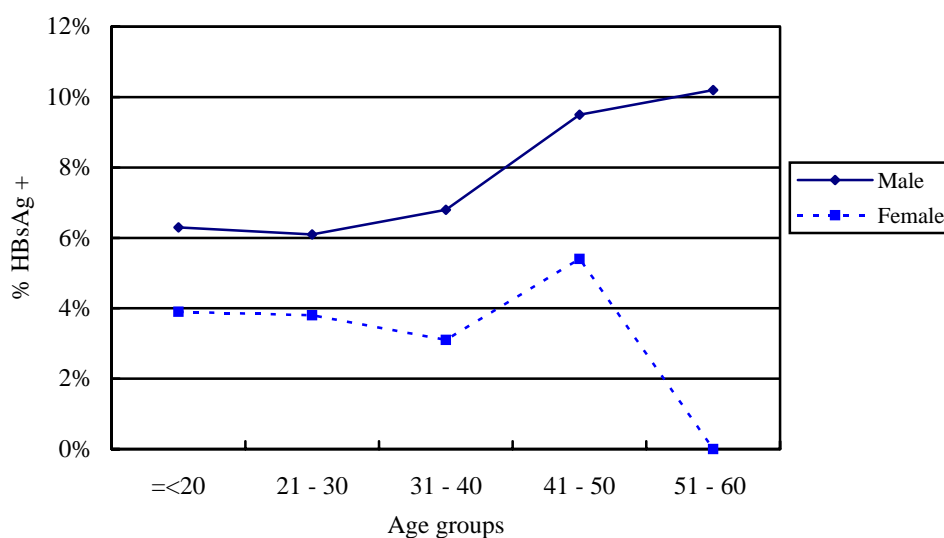
cautioned against extrapolating these figures to the general population because it was a highly selected sample.



Box 13. Prevalence of hepatitis B markers in police officers from 1996 to 2002 (Data source: DH)

Age	Male					Female				
	No. tested	+ve for HBV markers		+ve for HBsAg		No. tested	+ve for HBV markers		+ve for HBsAg	
		No.	%	No.	%		No.	%	No.	%
≤20	412	128	31.1	26	6.3	103	27	26.2	4	3.9
21-30	5156	1602	31.1	308	6.0	1343	423	31.5	56	4.2
31-40	5307	2113	39.8	369	7.0	427	147	34.4	13	3.0
41-50	2535	1401	55.3	244	9.6	340	142	41.8	20	5.9
51-60	344	212	61.6	36	10.5	13	8	61.5	0	0.0
Total	13754	5456	39.7	983	7.1	2226	747	33.6	93	4.2

Box 14. HBsAg prevalence among male and female police officers of different age groups from 1996 to 2002 (Data source: DH)



*The zero prevalence in the 51-60 years old female group could be result of the small number involved.

In the screening of laboratory samples left over from routine virological investigations in 2001, it was found that HBsAg was absent in those below 10 years old. However, anti-HBc rose markedly from 1.3% in persons of 1-4 years old to 7% in those of 5-9 years old (Box 15).

Box 15. Prevalence of hepatitis B markers in subjects who underwent routine virological investigations in 2001. (Data source: Virus Unit, DH)

Age group	No. tested (% +ve)		
	HBsAg	Anti-HBs*	Anti-HBc*
1-4	100 (0)	91 (78)	80 (1.3)
5-9	99 (0)	91 (40.7)	86 (7)
10-14	100 (4)	90 (54.4)	87 (5.7)
15-19	100 (2)	96 (32.3)	94 (14.9)
20-24	100 (11)	88 (36.4)	83 (19.3)
25-29	99 (10.1)	86 (46.5)	85 (28.3)
30-34	100 (7)	91 (44.0)	94 (14.9)
35-39	100 (15)	82 (50.0)	79 (34.1)
>39	99 (11.1)	81 (51.9)	74 (46.0)

*Specimens positive for HBsAg were not tested for anti-HBs and anti-HBc

Hepatitis B serology in occupationally exposed professionals

Health care workers are at risk of HBV infection because of potential occupational exposure to blood and body fluids. In 1983, a study in Hong Kong reported a higher rate of HBsAg in those who had been in service for over 10 years (10.8%) versus those at entry (7.5%)⁶. The rates for anti-HBs were 43.1% and 20.3% respectively.

The HBsAg prevalence was lower in subsequent studies. In 1992 and 1993, HBsAg and anti-HBs were positive in 4.4% and 38.2% respectively of 5825 health care workers screened⁷. The corresponding figures were 7% and 36.3% in data collected in a vaccination campaign of the Department of Health in 1995. Again, in all instances, the HBsAg prevalence varied positively with age.

As shown in Box 16, the prevalence of HBsAg in new recruits of public service health care workers in 2002 was 5.0%. Again, the positivity rate was lower than those of earlier studies in the 1980s. However, since Sep 2000, HBV screening procedure of new recruits has been changed from an opt-in to opt-out approach. Thus, this change could have affected the HBV results in 2001 and 2002, as compared with earlier years.

Box 16. Prevalence of hepatitis B markers in newly recruited health care workers in 2001-2002 (Data source: DH)

Year	Male			Female		
	No. tested	+ve for HBsAg No.	%	No. tested	+ve for HBsAg No.	%
2001	440	27	6.1	613	36	5.9
2002	499	23	4.6	730	38	5.2

Risk behaviours and Hepatitis B markers

Unprotected sex and needle sharing (in injecting drug users) are known routes of HBV transmission. Three programmes offered data on hepatitis B infection in people who were more likely to have engaged in high risk behaviours predisposing to HBV transmission - drug users, commercial sex workers and HIV-infected patients.

Drug users

Tests for hepatitis B markers were offered to drug users who had registered with methadone clinics or other drug rehabilitation services. Box 17 shows the prevalence of various hepatitis B markers among drug users in the last 13 years. HBsAg positivity rate has gradually fallen from over 13% in 1990 to a nadir of 6.6% in 1997. However, the rate then increased again to about 11% in 1999 and remained similar at around 12-13% in the last 2 years. In the past, around 90% of drug users were positive for at least one of the three markers (HBsAg, anti-HBs and anti-HBc); this has dropped to 53.4% in 1997 and then slowly rose over the last few years, to 72.3% in 2002. Readers must be cautioned that the number of drug users surveyed from 1995 to 1998 was small compared with other years, and the data were collected from multiple sources. Generally speaking, hepatitis B markers were still detected in a large proportion of drug users.

Box 17. Prevalence of hepatitis B markers in drug users from 1990 to 2002. (Data source: Virus Unit, DH)

Year	No. tested	% +ve			Any marker
		HBsAg	Anti-HBs	Anti-HBc*	
1990	1067	13.4	59.0	15.7	90.8
1991	1517	14.4	54.4	20.5	89.3
1992	832	13.9	49.0	21.4	84.4
1993	744	14.4	43.4	16.4	69.2
1994	607	12.9	38.1	13.5	64.1
1995	190	10.5	36.8	12.1	58.9
1996	358	8.7	43.0	12.6	62.8
1997	290	6.6	36.2	15.9	53.4
1998	290	10.0	43.4	7.9	59.3
1999	725	11.2	44.8	13.8	67.2
2000	892	11.4	42.5	15.8	67.8
2001	654	11.6	41.3	17.3	70.2
2002	553	12.7	43.0	16.6	72.3

* Specimens positive for HBsAg were not tested for anti-HBc

Co-infection with HDV has been reported in injecting drug users. Local data on HDV infection is lacking in recent years. In a report⁸ published in 1995, the prevalence of HDV has fallen from 63.1% of 149 HBsAg +ve injecting drug users in 1985-1986 to 28.8% of 153 HBsAg +ve injecting drug users in 1992-1993. There was a greater decline in infection rate in those with five or less years of illicit drug use history compared to those on drugs for over 5 years. The decrease in HDV prevalence is probably related to a general fall in HBV carriage, an observation reported in overseas studies⁹. No additional information on the pattern of HDV infection was published subsequently. Overall, epidemiological information on HDV in other population groups is scarce.

Female commercial sex workers

From 1995 to 1998, the government Social Hygiene Service which provides free treatment for sexually transmitted diseases (STD) conducted a study to examine the prevalence of hepatitis B markers in female commercial sex workers in Hong Kong. The complete study had involved a total of 1020 female commercial sex workers recruited at one Social Hygiene Clinic on Kowloon side. The prevalence of the serological markers was: 69 (6.8%) positive for HBsAg; 551 (54.0%) positive for anti-HBs; and 400 (39.2%) negative for either. An analysis on 100 commercial sex workers was published¹⁰.

HIV-infected patients

Testing for HBV markers has been offered to clients attending the HIV clinic of the Department of Health. As HIV shares the same routes of transmission with HBV, it is not surprising to find a high HBsAg positivity rate in newly seen HIV-infected patients – 9.3% (2000), 10.9% (2001) and 10.6% (2002). (Box 18) Again, the rate was substantially higher in male than female.

Box 18. HBsAg prevalence in new HIV/AIDS patients in 1998, 2000-2002.
(Data source: Integrated Treatment Centre, DH)

Year	Male		Female		Total	
	No. tested	No. HBsAg + (%)	No. tested	No. HBsAg + (%)	No. tested	No. HBsAg + (%)
1998	140	22 (15.7)	16	2 (12.5)	156	24 (15.4)
2000	87	9 (10.3)	21	1 (4.8)	108	10 (9.3)
2001	75	10 (13.3)	26	1 (3.8)	101	11 (10.9)
2002	119	14 (11.8)	22	1 (4.5)	141	15 (10.6)

Current situation in general population

The Viral Hepatitis Preventive Service of the Department of Health, the Department of Microbiology of the University of Hong Kong and the Department of Paediatrics of the Pamela Youde Nethersole Eastern Hospital conducted a territory-wide Community Research Project on Viral Hepatitis (CRPVH) 2001 to study the epidemiology of viral hepatitis in Hong Kong. Through a standardised telephone sampling survey, Chinese-speaking household members aged 18 or above were interviewed in 2001. Of the 5017 successful telephone respondents, 1610 agreed to attend and eventually 936 (18.7%) turned up for blood screening.

The HBsAg prevalence is shown at Box 19, with age and gender breakdown. The overall prevalence was 8.8% (95% CI, 7.1% to 10.7%), with again a higher rate of 10.4% for male as compared with 7.7% for female. There was no definite age pattern observed in this study. Unexpectedly, the rate was only 5.8% in those aged over 50. Two (2.5%) of the 81 HBsAg positive persons were anti-HDV positive, representing 0.2% of the total cases. The results have to be interpreted with caution as the blood-screened subjects were significantly over-represented by people aged 30-59, those who had received formal schooling and people without paid work.

Box 19. Prevalence of HBsAg from the CRPVH 2001 Study (Data source: DH)

Age Group	Male			Female			Total		
	No. tested	HBsAg +ve		No. tested	HBsAg +ve		No. tested	HBsAg +ve	
		No.	%		No.	%		No.	%
18-30	72	6	8.3	87	6	6.9	159	12	7.5
31-40	93	5	5.4	144	20	13.9	237	25	10.5
41-50	100	20	20.0	183	10	5.5	283	30	10.6
51 & Over	111	8	7.2	146	7	4.8	257	15	5.8
Total	376	39	10.4	560	43	7.7	936	82	8.8

In another study conducted by the Chinese University of Hong Kong on subjects attending a Regional Council Health Festival for general public, the HBsAg positivity rate was 8.3% for 1929 people of 18-60 years old; the respective prevalence in male and females were 10.8% (n=539) and 7.3% (n=1390).⁴

Composite data on HBsAg prevalence

Box 20 and 21 show the HBsAg data collected from various sources between 1990 and 2002. A general declining trend is evident. Comparison across datasets should be cautioned in view of the different methodology employed in the studies. Readers may refer to the report published in 1996, 1997, 2000, 2001 and 2002 for details of some of the data included in the composite table and graph.

Hepatitis B e antigen-negative chronic hepatitis B

A local study¹¹ published in 2000 examined the features of e antigen-negative chronic HBV infection. Cross-sectionally, 69% (243/350) were HBeAg negative, of whom 15% had clinical cirrhosis and another 22% had elevated transaminases. Overall, 17 % of the HBeAg negative patients were viraemic and had evidence of chronic liver disease. Only 45% of the e Ag negative chronic hepatitis B patients were found to have pre-core stop codon mutation.

Study on IgM anti-HBc +ve Hepatitis B

Upon the recommendation of the SWGVHP, the Department of Health introduced in 2000 a new surveillance mechanism on acute HBV infection, in collaboration with the Hong Kong Red Cross Blood Transfusion Service (HKRCBTS). The following subjects were eligible for recruitment into a study project from the notification system: (a) acute hepatitis B, and (b) repeat donors of Red Cross who tested positive for HBsAg for the first time and who were also positive for IgM anti-HBc.

In 2000, 2001 and 2002, 99, 107 and 96 eligible cases were identified. The cases detected in HKRCBTS were 14 each for 2000 and 2001, and 7 for 2002. The incidences of seroconversion were 9.4/100,000 (n=148,366), 9.3/100,000 (n=150,420) and 4.6/100,000 (n=151,410) for repeat donors in 2000, 2001 and 2002 respectively. Of the Chinese subjects recruited for blood testing at ≥ 6 to < 9 months post IgM anti-HBc positivity, some 9-15% of the subjects were still tested HBsAg positive while about half had become anti-HBs positive (Box 22).

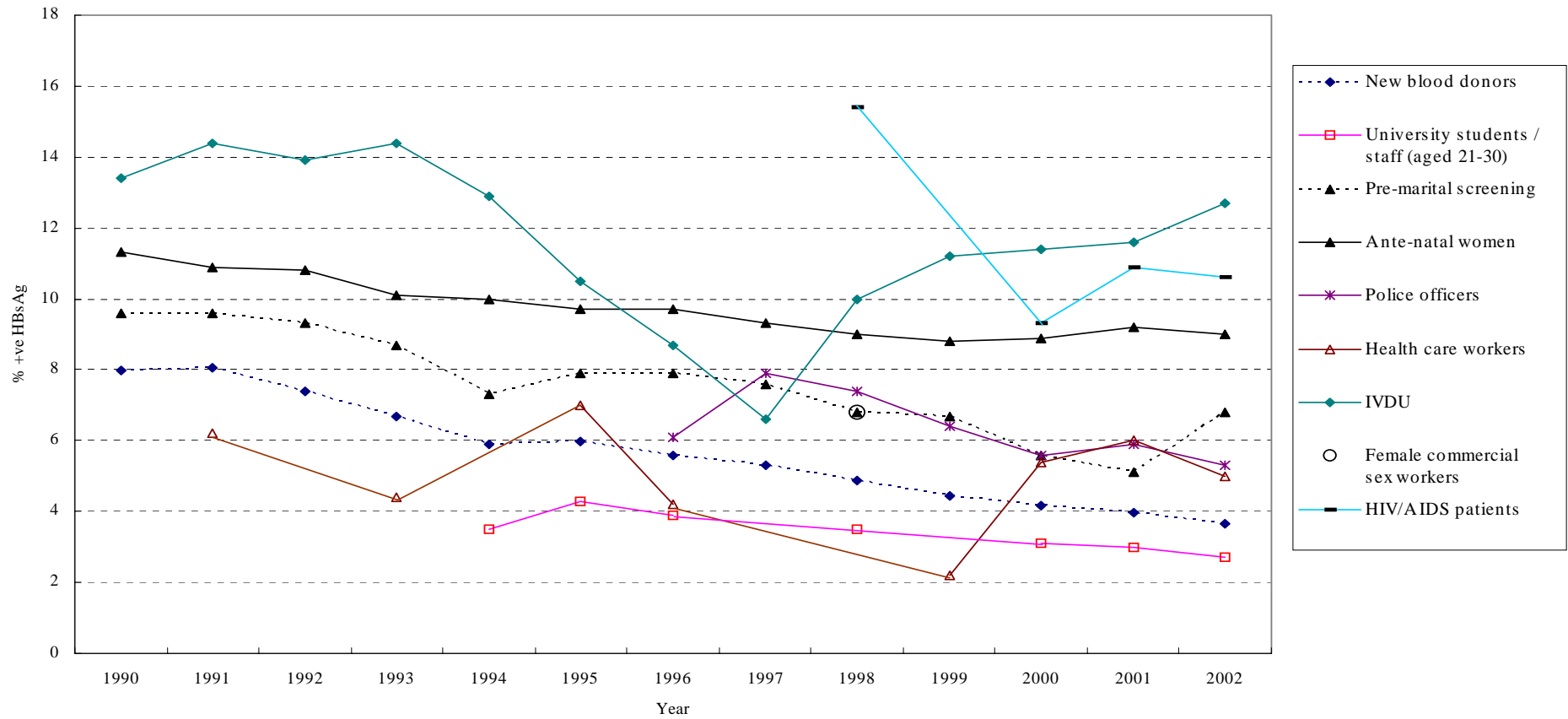
Box 22. HBV serology at ≥ 6 to < 9 months post IgM anti-HBc positivity (Data Source: DH)

	No. (%)		
	HBsAg-/Ab+	HBsAg-/Ab-	HBsAg+/-
2000	14 (50.0%)	11 (39.3%)	3 (10.7%)
2001	14 (42.4%)	14 (42.4%)	5 (15.2%)
2002	19 (57.6%)	11 (33%)	3 (9.1%)

Box 20. HBsAg prevalence in different population groups from 1990 to 2002 (Data source: multiple sources)

Year	% HBsAg+								
	New blood donors	University students/staff (aged 21-30)	Pre-marital screening	Ante-natal women	Police officers	Health care workers	Drug users	Female commercial sex workers	HIV/AIDS patients
1990	7.97	-	9.6	11.3	-	-	13.4	-	-
1991	8.04	-	9.6	10.9	-	6.2	14.4	-	-
1992	7.38	-	9.3	10.8	-	-	13.9	-	-
1993	6.70	-	8.7	10.1	-	4.4	14.4	-	-
1994	5.87	3.5	7.3	10.0	-	-	12.9	-	-
1995	5.99	4.3	7.9	9.7	-	7	10.5	6.8	-
1996	5.62	3.9	7.9	9.7	6.1	4.2	8.7		-
1997	5.20	-	7.6	9.3	7.9	-	6.6		-
1998	4.89	3.5	6.8	9.0	7.4	-	10.0		15.4
1999	4.44	-	6.7	8.8	6.4	2.2	11.2	-	-
2000	4.15	3.1	5.6	8.9	5.6	5.4	11.4	-	9.3
2001	3.98	3.0	5.1	9.2	5.9	6.0	11.6	-	10.9
2002	3.64	2.7	6.8	9.0	5.3	5.0	12.7	-	10.6

Box 21. Trends of HBsAg in selected population groups from 1990 to 2002 (Data source: multiple sources)



5. HEPATITIS B MUTANTS

Hepatitis B virus (HBV) is the smallest known DNA virus that infects man but the genomic organization of the virion is complex.¹² Over the years, vaccination has been recognised as one of the most efficient ways of preventing hepatitis B infections. Effective hepatitis B vaccines normally contain highly immunogenic viral surface antigens while a wide variety of mutations have been discovered in some viral proteins. The phenomenon has led to the public health question of whether the current vaccine would continue to fulfill its roles in the future.¹³ The anti-HBs-mediated immune pressure on HBV seems to have precipitated the emergence and selection of immune escape HBV mutants in spite of adequate antibody titers. Data available so far have documented that HBV mutants are viable. Some 37 mutations and variants of HBsAg have been reported from Taiwan, China, Japan, Hong Kong, Singapore, Thailand, India, Germany, the UK, the USA, Brazil, West Africa, and elsewhere.^{14,15,16}

In another study, two precore variants of hepatitis B virus were identified in chronic carriers in the Chinese community in Hong Kong. One variant had the serine at amino acid (aa) 15, and the other was characterised by a stop codon at aa 28, which inhibits production of hepatitis B e antigen.¹⁷

In patients with e-antigen negative chronic hepatitis B (e-CHB) in Hong Kong precore stop codon mutation was noted, while some had core promoter changes. Forty-five percent of the patients with e-CHB had the precore stop codon mutation, and an additional 41% had core promoter changes. e-CHB may thus be a heterogeneous condition and is not invariably associated with the precore HBV mutant.¹¹

The prevalence of precore mutations among hepatitis B e antigen (HBeAg)-positive patients was high at 44.2%. There was no difference in the prevalence of precore mutations between patients with and without chronic liver complications. However the prevalence of core promoter mutations was higher among patients with complications than among those without complications (90.5% vs. 69.3%, respectively; $P=0.003$).¹⁸

With the use of new antiviral agents, e.g. lamivudine, famciclovir, lobucavir and adefovir, drug-resistant mutants involving the HBV polymerase gene emerged, leading to breakthrough infection was reported in some patients who had received long courses (≥ 12 months) of treatment.¹⁹

In HBeAg-positive patients, approximately 16% of patients treated with lamivudine seroconverted within the first year. This was associated with significant improvement in liver histology. Long-term treatment induces further HBeAg seroconversion, but overall clinical benefit is undermined by continuous emergence of drug-resistant

YMDD mutants. At 1 year, YMDD variants were detected in 81 (24%) of 335 patients who received lamivudine in 4 controlled studies²⁰. YMDD mutants may cause a flare of hepatitis, resulting in the deterioration of liver histology and liver failure.²¹

6. HEPATITIS C INFECTION

Anti-HCV seroprevalence

Hepatitis C is transmitted through parenteral route. One early study in 1988 reported a prevalence of 0.5% in the general population and 66.8% in injecting drug users²². The CRPVH done in 2001 found that 3 (0.32%) out of 936 subjects aged 18 or over was tested anti-HCV positive.

New blood donors

With the implementation of anti-HCV screening at the Hong Kong Red Cross Blood Transfusion Service, a regular source of epidemiological information has become available. Box 23 shows the anti-HCV prevalence in new blood donors, which ranged from 0.035% to 0.099% in the last twelve years. Data per gender and age breakdown for year 2002 is shown at Box 24.

Box 23. Anti-HCV prevalence in new blood donors (Data source: HKRCBTS)

Year	No. of new donors	Anti-HCV+	
		No.	%
1991	48769	17	0.035
1992	43674	28	0.064
1993	36146	36	0.099
1994	38077	24	0.063
1995	39778	28	0.070
1996	40875	24	0.059
1997	40419	35	0.087
1998	43756	29	0.066
1999	40960	40	0.097
2000	41166	24	0.058
2001	43415	30	0.069
2002	42292	34	0.080

Box 24. Anti-HCV prevalence and its gender and age breakdown in new blood donors in 2002. (Data source: HKRCBTS)

First Time donors in 2002	Male			Female		
	Age Group	No. tested	Anti-HCV No. Positive	%	No. tested	Anti-HCV No. Positive
16-19	12856	2	0.02%	13483	1	0.01%
20-29	4901	7	0.14%	4620	5	0.11%
30-39	1716	5	0.29%	2115	3	0.14%
40-49	841	4	0.48%	1213	3	0.25%
>49	249	3	1.20%	319	1	0.31%
Total	20563	21	0.10%	21750	13	0.06%

Drug users

Left-over serum from samples submitted to the Government Virus Unit from methadone clinics and in-patient drug rehabilitation centres were tested for HCV antibody. A comparison of the results obtained from samples in early 1990s and early 2000s showed an overall decline in HCV prevalence in this 10-year period. (Box 25)

Box 25. Anti-HCV prevalence in drug users on rehabilitation. (Data source: Virus Unit, DH)

Year	No. tested	Anti-HCV+	
		No.	%
1991/1992	134	99	73.9
2000/2001	210	97	46.2

HIV-infected patients

The prevalence of anti-HCV was the same at 7.9% amongst new HIV/AIDS patients seen by the Department of Health in 2001 and 2002, with a male preponderance. (Box 26) Though lower than that of drug users, the rate was substantially higher than the new blood donors.

Box 26. Anti-HCV prevalence in new HIV/AIDS patients in 2001 and 2002. (Data source: Integrated Treatment Centre, DH)

Year	Male		Female		Total	
	No. tested	Anti-HCV + (%)	No. tested	Anti-HCV + (%)	No. tested	Anti-HCV + (%)
2001	75	7 (9.3)	26	1 (3.8)	101	8(7.9)
2002	118	10 (8.5%)	22	1 (4.5%)	140	11 (7.9)

HCV genotypes

As regards the genotyping of HCV in Hong Kong, a serotyping study among 212 blood donors who tested positive for anti-HCV in 1991 to 1994 provided very useful information²³. This study revealed that the commonest genotype was 1b (58.8%), followed by type 6a (27.0%). A significantly greater number of donors infected with type 6a reported a history of drug abuse, compared with those infected with type 1b. In western countries, type 1 is most commonly reported.

A comparison of the distribution of genotypes in the study in Hong Kong and another study in the United States²⁴ is as follows:

<u>Genotype of HCV</u>	<u>Hong Kong²¹</u>	<u>United States²²</u>
1a	6.2%	56.7%
1b	58.8%	17.0%
2a	1.4%	3.5%
2b	1.4%	11.4%
3a	1.9%	7.4%
4	-	0.9%
6	27% (6a)	3.2%

Another local study²⁵ looking at renal failure patients and non-renal failure controls also showed the predominance of genotype 1b, followed by 1a and 6a.

<u>Genotype of HCV</u>	<u>Renal failure (n=50)</u>	<u>Non-renal failure (n=26)</u>
1a	10%	4%
1b	78%	69%
2a	2%	4%
2b	4%	4%
4a	2%	0
6a	8%	19%
Mixed	4%	0

7. TRACKING HEPATITIS A AND HEPATITIS E

Both HAV and HEV are transmitted through faecal-oral route. The following is a compilation of the local sero-prevalence studies on HAV and HEV in Hong Kong over the past years.

Hepatitis A infection

Hepatitis A infections in a population can be monitored by the testing of serological markers. Total or IgG anti-HAV is a marker for previous exposure to the virus; IgM anti-HAV is a specific marker for recent infection.

In the past, a number of studies had been conducted in Hong Kong to examine the seroprevalence of hepatitis A in the general population. Box 27 shows results of a collection of studies and other testings over the years. Whereas about half (44.8%) of the adolescents and young adults developed anti-HAV when they reached the age of 11-20 in 1978²⁶, this proportion had dropped to 17.1% in 1987, 11.2% in 1989²⁷, 11.1% in 1993²⁸ and 7% in 1996²⁹. There is therefore, the suggestion of a right shift of the age-specific prevalence curve over the last two decades. The populations and methodologies were, however, different in the various studies.

Amongst 936 subjects screened in the CRPVH 2001, 665 (71.0%) were positive for anti-HAV. There was a positive correlation between prevalence and age. (Box 28) Despite differences in methodologies, a cohort effect was clearly evident when the data of the two studies conducted in 1978/79 and 1987/89 were compared with that of CRPVH 2001. This suggested no occurrence of major new HAV infections in the past 2 decades in Hong Kong.

Box 27. Prevalence of anti-HAV in a collection of studies/testings between 1978 and 2002 (Data sources: Multiple sources.)

Age groups	1978	1987	1989	1993	1995	1996		1998	2000	2001	2001	2002
0 – 10	12.9%	5.3%	6.8%	59.4% (M)	8.3%	-	6.1%	5.4%	9.3%	4.58%	-	5.3%
11 – 20	44.8%	17.1%	11.2%		7.0%	11.3%	-	11.8%	7.6%	17.5%	13.2%	26.8%
21 – 30	75.0%	53.8%	58.8%	53.3% (F)	49.0%	-	37.7%	40.8%	35.0%	41.3%	53.2%	46.7%
31 – 40	82.9%	85.1%	83.5%	94.5% (M)	70.5%	-	58.6%	66.7%	60.0%	71.1%	88.3%	58.1%
41 – 50	91.1%	94.7%	91.1%			91.0% (F)					-	
>50					93.9%							
Data source	A ²⁶	A ²⁶	B ²⁷	C ²⁸	D ³⁰	E ²⁹	D ³⁰	D ³⁰	D ³⁰	D ³⁰	F ³¹	D ³⁰

Data sources:

- A. Study on stored sera of 702 healthy subjects, by Chin et al of University of Hong Kong.
- B. Study on 1028 serum samples collected from individuals attending a health exhibition, by Lim et al of Department of Health.
- C. Seroprevalence results reported in the press by Lai et al of University of Hong Kong.
- D. Pre-vaccination screening on students and staff of City University of Hong Kong: 553 (1995), 669 (1996), 608 (1998), 395 (2000), 592 (2001), 372 (2002) and students and staff of Baptist University of Hong Kong 240 (2001), 259 (2002).
- E. Seroprevalence study in school children by Lee A of the Chinese University of Hong Kong.
- F. Community Research Project on Viral Hepatitis 2001

Box 28. Prevalence of anti-HAV in participants of CRPVH 2001 (Data source DH)

Age group	No. Tested	Anti-HAV +ve	
		No.	%
18-29	137	27	19.7
30-39	223	116	52.0
40-49	291	248	85.2
50-59	170	161	94.7
60 & over	115	113	98.3
All	936	665	71.0

As evidenced from the notified cases, HAV is an important cause of acute viral hepatitis. The consumption of contaminated shellfish is one of the causes for the occasional hepatitis A outbreak in Hong Kong. A recent study cited the experience of Tam JS, who reported the detection of HAV by RT-PCR in 6% of clams, 14% of mussels and 30% of oysters in winter. The corresponding figures of summer for clams and mussels were 0% and 26% respectively³².

Hepatitis E infection

In Hong Kong, studies on the seroprevalence of HEV are limited.

A retrospective study published in 1992 testing samples collected in 1989-1991 reported that 16.1% of the healthy subjects were positive for anti-HEV³³. The age-specific prevalence increased with age, from below 10% in people aged below 20, to about 30% in those aged above 40.

Another study published in 1995 reported a prevalence of 18.2% in 77 healthy subjects in southern China³⁴.

Amongst 934 subjects screened in the CRPVH 2001, 176 (18.8%) were positive for anti-HEV. A higher HEV positivity rate was observed in people aged above 40. (Box 28) Despite differences in methodologies, the overall and age-group specific prevalence in 2001 decreased when compared with the previous study.³³

Box 29. Prevalence of anti-HEV in participants of CRPVH 2001 (Data source DH)

Age group	No. Tested	HEV +ve	
		No.	%
18-29	137	11	8.0
30-39	222	32	14.4
40-49	290	70	24.1
50-59	170	39	22.9
60 & over	115	24	20.9
All	934	176	18.8

8. HEPATOCELLULAR CARCINOMA

Cancer is the leading cause of death in Hong Kong. Among various causes of cancer deaths, liver cancer ranked second in male (15.7%) and fourth in female (8%). Liver cancer affects male more than female, with a male-to-female ratio of 3.4. Of the various histological subtypes, hepatocellular carcinoma (HCC) accounted for over half of the cases.³⁵ The outcome of liver cancer remained poor with high mortality: the incidence ratio was around 0.9.

Hepatitis B virus infection is one important aetiological factor in HCC. Studies had shown that some 85.3% to 91.6% of symptomatic HCC cases had evidence of previous hepatitis B infection in Hong Kong.^{36, 37}

There were attempts to achieve early detection of HCC, with the hope of improving its management outcome. In an alpha fetoprotein screening programme conducted in Hong Kong, 1.34% of Chinese patients with chronic HBV infection seen over a 5 year period developed HCC.²⁹ All cases were picked up under the programme. The figures were similar in some Taiwan studies.

HCV infection is another viral hepatitis agent causing HCC. However, it was of relatively minor epidemiologic significance in Hong Kong where HBV infection is overwhelming. In a study published in 1992, among patients with HCC, 7% were found anti-HCV positive. This figure included 3% from HBV-HCV co-infection and 4% HCV infection alone.³⁸

Over the period of 1995 to 1999, the Hong Kong Cancer Registry (HKCR) recorded a drop in the number of new cases of liver cancer in both sexes and in the mortality in male in Hong Kong (Box 29).³⁵

Box 30. Time trends of liver cancer incidence and mortality (crude rate in bracket) (Data source: HKCR)

	New cases				Deaths			
	Male		Female		Male		Female	
1995	1184	(38.4)	405	(13.2)	916	(29.7)	300	(9.8)
1996	1338	(41.6)	400	(12.4)	997	(31.0)	289	(9.0)
1997	1289	(39.8)	412	(12.7)	979	(30.3)	285	(8.8)
1998	1298	(39.9)	380	(11.5)	1016	(31.3)	320	(9.7)
1999	1217	(37.3)	355	(10.6)	1069	(32.7)	351	(10.5)
2000	1221	(37.3)	363	(10.7)	1094	(33.4)	330	(9.7)
1991-2000 average	1249	(40.0)	374	(12.0)	963	(30.8)	292	(9.4)

Note:

- All rates are expressed per 100,000.
- Crude rate is defined as the total number of new cases or deaths in the calendar year divided by the estimated total population in the area at the middle of the year and expressed per 100,000 population.

9. CONCLUSIONS

In the process of compiling the update report series, the SWGVHP has been given an opportunity not only to examine and analyse the hepatitis situation but also appraise the strengths and weaknesses of the existing surveillance mechanism regarding viral hepatitis in Hong Kong. The efforts have also brought a dedicated group of professionals together to develop consensus, and to recommend on prevention strategies and means of enhancing the existing surveillance system.

Patterns of viral hepatitis in Hong Kong

Hepatitis B

As in the last five reports, an obvious pattern observed in the 2002 update report was the decline of hepatitis B markers in most of the community groups studied over the past years. The decline was observed in new blood donors, university students/staff, and police officers. The HBsAg rate has remained high at about 9% in antenatal mothers from 1999 to 2002. The rate in drug users who probably had risk exposure in the past was higher at 12.7% in 2002. Hence, whereas it is still customary to quote an HBsAg carriage rate of 10% in Hong Kong, evidence has emerged to support that it could be much lower.

It can be inferred that perinatal infection has been the commonest cause of HBV transmission in Hong Kong, based on the observation that HBsAg was high in young adults in the general population. With the universal neonatal hepatitis B vaccination programme in place since 1988, infection and carriage in childhood would most likely continue to decline. This was supported by the absence of HBsAg positivity in samples obtained from children below 9 years old in 2001. There is a possibility that sexual contact may become the next common mode of HBV transmission in the future.

Hepatitis C

Hepatitis C shares the transmission routes with hepatitis B. Worldwide, HCV prevalence and its main transmission routes vary from place to place. These may not be in synchrony with the HBV situation. Data from new blood donors suggested that it is below 0.1% in young adults in Hong Kong, much lower than that of HAV, HBV and HEV. Experiences of clinicians and virologists have previously confirmed that HCV was common in injecting drug users and haemophilia patients. Results of testing non-random samples from drug users under treatment suggested a decline in

the rate of HCV infection from over 70% in 1991/1992 to below 50% in 2000/2001. There was epidemiological evidence that 1b was the commonest genotype in Hong Kong, unlike western countries.

Hepatitis A and E

The faecal-orally transmitted viral hepatitis - HAV and HEV - are likely to continue to be important causes of symptomatic infectious hepatitis. The declining level of HAV antibodies reflects the diminishing immunity of the population against the virus. Taken together the findings of the CRPVH 2001 and studies done one and two decades ago, a cohort effect was clear. There was no evidence of major new HAV epidemics locally in this time period. Knowledge of such age-specific anti-HAV prevalence in Hong Kong would be one useful parameter to help decide on the future vaccination strategy for Hong Kong. The epidemiological importance of HEV is less clear though more acute HEV infections were reported in recent years. Some 19% of people aged over 18 in 2001 had anti-HEV, a seemingly lower prevalence than that found a decade ago.

Other viral hepatitis

Local data on other parenterally transmitted viruses like HDV, and HGV are scarce. A meaningful assessment cannot be drawn at this stage.

Hepatocellular carcinoma (HCC)

In Hong Kong, over half of liver cancer was HCC. Hepatitis B infection is an important cause of HCC. The crude rate of HCC as derived from the Cancer Registry has remained at high levels over years. There is, however, a statistically significant decline in overall cases and mortality in male.

Hepatitis B mutants

Reports had shown the emergence of hepatitis B mutants. The relevance of the observation, both in clinical and public health contexts, would need to be determined in future.

Limitations of existing surveillance mechanisms

The current statutory reporting system provides a regular monitoring mechanism for describing *acute* viral hepatitis. The system is useful in tracking symptomatic infections like hepatitis A and hepatitis E in adults but its usefulness in monitoring the other viral hepatitis is doubtful. Reporting of acute viral hepatitis serves little in depicting the epidemiology of hepatitis C infection because of the large proportion of asymptomatic infection and the difficulty in identifying acute infection. Generally speaking, although the disease notification system has remained a useful source of information for acute viral hepatitis over the years, its usefulness in assessing the burden of hepatitis, in particular chronic infections, in the community is limited.

On the other hand, serosurveillance plays a crucial and complementary role in the surveillance of viral hepatitis. In the last six years, the SWGVHP has been able to collect a wide range of data to help describe hepatitis epidemiology in Hong Kong. There are, however, problems in the use of the existing data sets. Many of these studies are not specifically designed to collect epidemiological data. Some are

figures extracted from service activities or health promotion projects (for example, pre-vaccination screening in police officers, testing of drug users, antenatal testing of pregnant women). The methods of subjects selection, e.g. for administrative purposes, are prone to generate bias if generalization is attempted. There are research projects that provide useful one-off epidemiological data. They are, however, of little use in projecting longitudinal trends.

The Way Forward: Meeting future surveillance needs

Despite these shortcomings, a systematic approach to collate and analyse available data is a useful exercise for better understanding hepatitis epidemiology. However, in order to better reflect the hepatitis situation in Hong Kong, the current surveillance mechanisms need to be enhanced.

Over the past few years, the SWGVHP has discussed means of enhancing the capacity of Hong Kong's surveillance mechanism on viral hepatitis. The main suggestions are:

- (a) Seroprevalence studies would need to be conducted regularly to track the changes over time.
- (b) A pilot surveillance system could be established to monitor the clinical and epidemiological patterns of hepatitis C.
- (c) Liver complications from chronic hepatitis infections shall be regularly tracked to discern public health impacts on morbidity and mortality
- (d) Epidemiology of various HBV mutants shall be tracked, and
- (e) Impacts of universal vaccination programme shall be systematically assessed.

To take these recommendations further, some information on (a), (c) and (d) has been included in this Report. Systematic data collection, analysis and reporting would need to be strengthened in the long term.

ACKNOWLEDGEMENTS

The SWGVHP wishes to thank the following agencies for their input, suggestions or comments in the course of preparing the 2002 Update Report:

Government Virus Unit, Department of Health
Disease Prevention and Control Division, Department of Health
Special Preventive Programme, Department of Health
Family Health Service, Department of Health
Family Planning Association of Hong Kong
Hong Kong Red Cross Blood Transfusion Service
CHC-Group Medical Practice
Health Service of City University of Hong Kong
Princess Margaret Hospital
Health Service of Baptist University of Hong Kong
Department of Microbiology, Chinese University of Hong Kong
Department of Microbiology, University of Hong Kong
Pamela Youde Nethersole Eastern Hospital
Hong Kong Cancer Registry, Hospital Authority

ABBREVIATIONS

AIDS	Acquired immune deficiency syndrome
Anti-HAV	Antibody against hepatitis A virus
Anti-HBc	Antibody against hepatitis B core antigen
Anti-HBs	Antibody against hepatitis B surface antigen
Anti-HCV	Antibody against hepatitis C virus
Anti-HDV	Antibody against hepatitis D virus
Anti-HEV	Antibody against hepatitis E virus
BUHC	Baptist University Health Centre
CRPVH	Community Research Project on Viral Hepatitis
CUHC	City University Health Centre
DH	Department of Health
FHS	Family Health Service
FPA	Family Planning Association
HBsAg	Hepatitis B surface antigen
HAV	Hepatitis A virus
HBV	Hepatitis B virus
HCV	Hepatitis C virus
HDV	Hepatitis D virus
HEV	Hepatitis E virus
HGV	Hepatitis G virus
HIV	Human immunodeficiency virus
HKCR	Hong Kong Cancer Registry
HKRCBTS	Hong Kong Red Cross Blood Transfusion Service
IgG	Immunoglobulin G
IgM	Immunoglobulin M
IDU	Injecting drug users
ITC	Integrated Treatment Centre
MCHC	Maternal and Child Health Centre
PMH	Princess Margaret Hospital
RT-PCR	Reverse transcriptase – polymerase chain reaction
STD	Sexually transmitted disease
TTV	Transfusion transmitted virus

REFERENCES

-
1. Linnen J, Wages Jr J, Zhang-Keck Z-Y, Fry KF, Krawczynski KZ, Alter H et al. Molecular cloning and disease association of hepatitis G virus: a transfusion-transmissible agent. *Science* 1996;271:505-8.
 2. Simmonds P, Davidson F, Lycett C, Prescott LE, MacDonald DM, Ellender J et al. Detection of a novel DNA virus (TTV) in blood donors and blood products. *Lancet* 1998;352:191-95.
 3. Chau TN, Princess Margaret Hospital. Personal communication. 2001
 4. Leung NW, Tam JS, Kan P, Chan L, Chu KW. Decline in viral hepatitis B infection in Hong Kong in the past 20 years:1983-2002. [Abstract] AASLD 2002, 53rd Annual Meeting and Postgraduate Course, Boston, USA, 1-5 Nov 2002.
 5. Kwan LC, Ho YY, Lee SS. The declining HBsAg carriage rate in pregnant women in Hong Kong. *Epidemiol Infect* 1997;119:281-283.
 6. Yeoh EK, Lo HY, Chang WK, Lee SH. Hepatitis B vaccination in health care personnel in a region of high prevalence. *Hepatology* 1983;3:1079 [abstract]
 7. Lim WL, Wong DA, Cheng KC. Immune response to hepatitis B vaccine in health care workers in Hong Kong. *HK Med J* 1996;2:138-140.
 8. Lim WL, Lo JYC, Lee SH. Changing prevalence of hepatitis B virus and hepatitis D virus infection among injecting drug users in Hong Kong indicating a change in high risk behaviour. *AIDS* 1995;9:9.
 9. Gaeta G, Stroffolini T, Chiaramonte M, Ascione T, Sornaiuolo Lobello S et al. Chronic hepatitis D: a vanishing disease? An Italian multicentre study. *Hepatology* 2000;32:824-827.
 10. Yu CW, Chong LY, Lo KK, Ng PS. The epidemiology of hepatitis B infection in commercial sex workers in Hong Kong. *Southern China J Dermato-venereology* 1998;5:47-49. [in Chinese]

-
11. Chan HLY, Leung NWY, Hussain M, Wong ML, Lok ASF. Hepatitis B e antigen-negative chronic hepatitis B in Hong Kong. *Hepatology* 2000;31:763-768.
 12. Lauder IJ, Lin HJ, Lau JYN, Siu TS, Lai CL. The variability of the hepatitis B virus genome: statistical analysis and biological implications. *Mol. Biol Evol* 1993;10:457-470.
 13. Francois G, Kew M, Van Damme P, Mphahlele MJ, Meheus A. Mutant hepatitis B viruses: a matter of academic interest only or a problem with far-reaching implications? *Vaccine* 2001;19:3799-3815.
 14. Zuckerman AJ, Zuckerman JN. Molecular epidemiology of hepatitis B virus mutants. *J Med Virol* 1999; 58:193-95.
 15. Carman WF, Thomas HC, Zuckerman AJ, Harrison TJ. Molecular variants of hepatitis B virus. In :Zuckerman AJ, Thomas HC, eds . *Viral hepatitis*, 2nd edn. London: Churchill Livingstone, 1998:141-72.
 16. Carman WF, Van Deursen FJ, Mimms LT, et al. The prevalence of surface antigen variants of hepatitis B virus in Papua New Guinea, South Africa and Sardinia. *Hepatology* 1997;26:1658-66.
 17. Boner W, Schlicht HJ, Hanrieder K, Holmes EC, Carman WF. Further characterization of 2 types of precore variant hepatitis B virus isolates from Hong Kong. *J Infect Dis* 1995;171:1461-7.
 18. Yuen MF, Sablon E, Yuan HJ, et al. Relationship between the development of precore and core promoter mutations and hepatitis B e antigen seroconversion in patients with chronic hepatitis B virus. *J Infect Dis.* 2002;186:1335-8.
 19. Hussain M. Mutations in the hepatitis B virus polymerase gene associated with antiviral treatment for hepatitis B. *J Viral Hepat* 1999;6:183-194.
 20. Lai CL, Dienstag J, Schiff E, et al. Prevalence and clinical correlates of YMDD variants during lamivudine therapy for patients with chronic hepatitis B. *Clin Infect Dis.* 2003;36:687-96.
 21. Leung N. Treatment of chronic hepatitis B: case selection and duration of therapy. *J Gastroen Hepatol* 2002;17:409-14.
 22. Chan GCB, Lim WL, Yeoh EK. Prevalence of hepatitis C infection in Hong Kong. *J Gastroen Hepatol* 1992;7:117-120.
 23. Prescott LE, Simmonds P, Lai CL, Chan NK, Pike I, Yap PL et al. Detection and clinical features of hepatitis C virus type 6 infections in blood donors from Hong Kong. *J Med Virol* 1996;50:168-175.
 24. Alter MJ, Kruszon-Moran D, Nainan OV, Mcquillan GM, Gao F, Moyer LA et al. The prevalence of hepatitis C virus infection in the United States, 1988 through 1994. *N Engl J Med* 1999;341:556-562.
 25. Chan TM, Lau JYN, Wu PC, Lai CL, Lok ASF, Cheng IKP. Hepatitis C virus genotypes in patients on renal replacement therapy. *Nephrol Dial Transplant* 1998;13:731-4.

-
26. Chin KP, Lok ASF, Wong LSK, Lai CL, Wu PC. Current seroepidemiology of hepatitis A in Hong Kong. *J Med Virol* 1991;34:191-193.
 27. Lim WL, Yeoh EK. Hepatitis A vaccination. *Lancet* 1992;339:304.
 28. Lai CL. Hepatitis A risk heightened. Data quoted in *United Daily News* dated 10 June 1994.
 29. Lee A, Cheng F, Lau L, et al. Changing hepatitis A epidemiology among Hong Kong Chinese adolescents: what are the implications? *Public Health* 1999; 113(4):185-8.
 30. Data from CHC-Group Medical Practice, 1995, 1996, 1998, 2000, 2001, 2002.
 31. Data from Special Preventive Programme, Department of Health, 2001.
 32. Lai JY. Hepatitis A and E in Hong Kong. *HK Med J* 1997;3:79-82.
 33. Lok ASF, Kan WK, Moechli R et al. Seroepidemiological survey of hepatitis E in Hong Kong by recombinant-based enzyme immunoassays. *Lancet* 1992;340:1205-1208.
 34. Tan D, Im SWK, Yao JL, Ng MH. Acute sporadic hepatitis E virus infection in southern China. *J Hepatol* 1995;23:239-245.
 35. Cancer incidence and mortality in Hong Kong - 1998-1999. Hong Kong Cancer Registry, Hospital Authority.
 36. W Shiu, Dewar N, Leung N, et al. Hepatocellular carcinoma in Hong Kong: clinical study on 340 Cases. *Oncology* 1990;47:241-245.
 37. C.L. Lai, JYN Lau, PC Wu, et al. Subclinical hepatocellular carcinoma in Hong Kong Chinese. *Oncology* 1992;49:347-353.
 38. Leung NW, Tam JS, Lai JY, et al. Does hepatitis C virus infection contribute to hepatocellular carcinoma in Hong Kong? *Cancer* 1992;70:40-4.