

## **Current situation of hepatitis B and C in Hong Kong** (adopted from **Surveillance of Viral Hepatitis in Hong Kong - Update report 2011.** **Special Preventive Programme, Centre for Health Protection, Department of Health.** **December 2012)**

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### **Pattern of Hepatitis B in Various Communities and its Significance**

Parenterally -transmitted viral hepatitis B resulting in chronic infection state is endemic in Hong Kong. The number of reported acute hepatitis B virus (HBV) infections has been decreasing over the last decade, from 121 cases reported in 2002 to 70 cases reported in 2011. In an epidemiologic study of acute HBV by the Department of Health and Hong Kong Red Cross Blood Transfusion Service (HKRCBTS), 149 of 351 eligible subjects recruited from 2000 to 2003 participated in risk factor assessment with or without blood screening. Repeat blood donors who tested positive for HBsAg for the first time and were then confirmed IgM anti-HBc positive were reported as having acute HBV. There were 43 such clients, yielding an incidence rate of HBV seroconversion in repeat donors as 9.4/100,000 (n=148,366), 9.3/100,000 (n=150,420), 4.6/100,000 (n=151,410) and 3.5/100,000 (n=143,230) in 2000, 2001, 2002 and 2003 respectively. Nearly 70% of the study subjects were male; 99% were Chinese and the mean age was 31 years. Over half could not have risk factor of acute HBV determined despite undergoing a standardized questionnaire interview by nurses. Sexual contact was assessed to be the commonest risk (85%) in the rest. Of 124 subjects who had hepatitis B screening at 6 months post-IgM anti-HBc positivity, 50% developed anti-HBs while 9.7% were HBsAg positive. The results suggested a higher rate of HBV chronicity than what was previously reported in the literature. However, these findings have to be interpreted with extreme caution owing to the relative small number of samples, incompleteness of data and potential biases from the subjects sampling and other study design.

Determining the seroprevalence of hepatitis B surface antigen (HBsAg) sheds light on how common chronic HBV infection is in different communities, as well as informing its chronic disease burden. The various adult communities can be categorized into 3 groups according to the risk of contracting HBV: those (a) without apparent risk, (b) with undetermined risk, and (c) with apparent risk. Groups without apparent risk for which data was available include blood donors, pre-marital/ pre-pregnancy service users, antenatal women, police officers, new health care workers (HCW). Clients seeking post-exposure management and tuberculosis patients are those with undetermined risk. Drug users, HIV/AIDS patients and female sex workers are at apparent risk of contracting HBV related to their risk behaviours.

A majority of the available seroprevalence data in different populations were limited to overall positivity rate of HBV markers. Still, temporal trend can be discerned as most have yearly data for the past decade or so. For groups with some demographic characteristics available, such as age and gender, further analyses have been made per the aggregate data. Several features on the current pattern of HBV could be observed from the serologic investigations, namely (a) chronic HBV infection is in a general declining trend in community groups without apparent risk of contracting HBV, (b) HBV prevalence increases with increasing age, and (c) chronic HBV infection is commoner in male than female. A word of

caution in the interpretation of data though, is that testing for HBV markers has been performed for a variety of reasons in different communities, with heterogeneous mix of population characteristics.

The temporal decline of chronic HBV infection has been most obvious in new blood donors. Its HBsAg prevalence follows a continual falling trend since early 1990s, to a record low of 1.1% in year 2011. The falling trend was also observed in other community groups without apparent HBV risk, albeit less prominent. The HBsAg prevalence in antenatal mothers has been decreasing from over 10% in the early 1990s to 7.4% in 2011. As compared with other groups without apparent risk, the overall HBsAg prevalence in antenatal mothers is higher and confounded by the place of birth. A study of 2480 pregnant women attending the Maternal and Child Health Centre (MCHC) of DH in 1996 found a 13.1% in those born in Mainland China as compared to 8.4% in local mothers [<sup>1</sup>]. Data from Virus Unit, Department of Health also showed a higher prevalence of 12.5% and 13.8% in the subset of non-resident expectant mothers versus the overall positivity rate of 8.5% and 8.6% in 2004 and 2005 respectively. The prevalence in pre-marital/ pre-pregnancy package service users has dropped from 9.6% in 1990 to remain static in the range of 6.4% to 7.4% in the past decade. The prevalence in newly recruited health care workers as determined at pre-HBV vaccination screening showed a drop in the past 3 years from 6.2% in 2009 to 3.2% in 2011 among male, and 4.3% in 2009 to 1.3% in 2011 among female.

Of 1,056 tuberculosis patients attended TB & Chest Clinics, Department of Health between March and May in 2011, 106 (10.0%) were detected HBsAg positive, with the highest prevalence rate in the middle age group (40-59 years old: 14.9%) followed by the more elderly group ( $\geq 60$  years old: 9.4%). The HBsAg positivity rate was also found to be higher in male clients (11.4%) than in female (7.6%). Among clients attended for post exposure management, HBsAg rate was found higher in non-health care workers than in health care workers, which may be partly explained by the success of pre-employment vaccination programme for health care workers.

The HBsAg prevalence in HIV/AIDS patients under care of DH was in the range of 5.6% to 15.9% in the past decade. Due to the underlying immunosuppression, HIV/AIDS patients could be more prone to becoming chronically infected with HBV after acute infection [<sup>2</sup>]. The HBsAg prevalence in female sex workers attending the clinic of Action for REACH OUT in the past five years ranged from 5.0% to 10.4%. The data regarding prevalence of HBsAg in drug users in recent years was hardly able to be interpreted due to the small number of subjects tested since 2006. Overall, the difference in HBsAg prevalence between groups with or without apparent risk of contracting HBV has not been prominent in the past few years.

## **Age and Gender Difference in Prevalence of Hepatitis B**

For some groups, data supported age as an important correlate of HBV infection, with generally a higher proportion of the older and the male population having viral markers or being chronically infected. HBsAg was most common in patients aged 40 or above in TB clinic cohort in 2011. Also in 2011, the HBsAg prevalence of male new blood donors was higher than those of female new blood donors, particularly in those over 40 years old. Moreover, HBsAg prevalence appeared to be lower in antenatal women aged less than 19 years though there was no apparent difference among older subjects. From the 1996 to 2006

data in police officers, the HBsAg rate progressively increased with each 10-year age group, being 4.7% in  $\leq 20$  years old and 9.1% in 51-60 years old subjects.

Male had a higher HBV prevalence than female, as observed in several groups. In 2011, the HBsAg positivity rate among new blood donors was 1.4% in male and 0.9% in female. Among tuberculosis patients treated at chest clinics, the rate in 2011 was 11.4% in male and 7.6% in female. From 1996 - 2006, the HBsAg rate in male police officer (6.6%) was higher than female police officer (4.0%). The 2001 household study also showed that a higher overall HBsAg rate in male.

Perinatal transmission has been the most important factor for existent chronic hepatitis B infections. In 2009, a HBsAg seroprevalence study was conducted among 1913 children aged 12 to 15 years (unpublished DH data). The study found an HBsAg seroprevalence of 0.78% (95% confidence interval 0.39 -1.16%) in these children who were born after the implementation of universal neonatal HBV vaccination programme. This result showed that Hong Kong has already achieved a time-bound goal of reducing chronic HBV infection rate to less than 2% among 5 year-old children by the year 2012, as set by the Western Pacific Regional Office (WPRO) of the World Health Organization (WHO). In July 2011, Hong Kong was verified by WPRO as having successfully achieved the goal of HBV control.

## **Genotypes of Hepatitis B and their Disease Course**

Genotyping studies of HBV in Hong Kong became more common in the last decade. A study of 776 chronic hepatitis B patients seen at the University of Hong Kong Liver clinic from 1999 to mid-2003 found that genotype C was the commonest (486, 62.6%), followed by B (252, 32.5%), with a majority of genotype B belonged to subgroup Ba [3]. Similarly, another study of 426 chronic HBV patients recruited consecutively from 1997 to mid-2000 at the Hepatitis clinic of Princess of Wales Hospital (PWH) found a prevalence of 57% (242) and 42% (179) of genotypes C and B respectively [4].

A study of 49 HBV genotype C ethnic Chinese patients under the care of PWH Hepatitis clinic identified 2 distinct groups with different epidemiological distribution and virologic characteristics - 80% being genotype "Cs" (found mostly in Southeast Asia) and 20% "Ce" (predominated in Far East) [5]. In addition, subgenotype Cs appears to be more common in Hong Kong than other parts of China. In the recent analysis of a cohort of patients with HBeAg-negative chronic liver disease from three different parts of China (Beijing, Shanghai and Hong Kong), 69% of genotype C patients in Hong Kong belonged to subgenotype Cs whereas 97% of genotype C HBV in Shanghai and Beijing belonged to subgenotype Ce ( $P < 0.0001$ ) [6].

Regarding HBV disease course, recent studies found that patients infected with genotype C may have a more aggressive clinical course than those infected with genotype B. It was shown that genotype B patients had earlier HBeAg seroconversion than genotype C patients in an early study [14]. Moreover, local studies have shown a higher risk of cirrhosis and HCC development [4,7], as well as more severe histological fibrosis, with genotype C [8]. Among HBV genotype C, subgenotype Cs appears to carry a worse prognosis than subgenotype Ce [6]. In a local study by the Chinese University of Hong Kong, patients infected by subgenotype Cs had the lowest serum albumin and highest alanine aminotransferase levels

compared with subgenotypes Ce and Ba. And, patients infected by subgenotype Cs also had more severe histological necroinflammation than subgenotype Ce [6].

Nevertheless, in a study of end-stage HBV-related liver disease patients requiring transplantation, those with genotype B had significantly more pre-transplant acute flare and worse liver function while genotype C patients had a greater risk and severity of recurrence due to lamivudine-resistant mutants [9].

In a case control study, it was concluded that HCC patients had a significantly higher prevalence of core promoter mutations and genotype C but the association with HCC is mediated via the former [10]. A study of 5080 chronic HBV patients focusing on familial HCC found 22 such families, giving a prevalence of 4.3 families/1000 HBV carriers [11]. Age of onset of HCC is significantly younger in familial HCC than sporadic cases, and it progressively decreased down the generations, suggesting an anticipation phenomenon.

## Current Situation of Hepatitis C

Although HCV shares similar transmission routes with hepatitis B, the two infections may not be of equal prevalence in a locality, as what epidemiological data points to in Hong Kong. While HBV is still prevalent in many populations in Hong Kong, HCV prevails only in isolated communities from available evidence. Conceivably related to the different epidemiology, HCV is of relatively less public health significance regarding chronic liver diseases when compared to HBV in Hong Kong.

From 1996-2011, a total of 31 cases of acute hepatitis C infection were reported to DH under the statutory notification system, with one to eleven cases reported annually. A review by the Centre for Health Protection entitled “Hepatitis C in Hong Kong, 2008 to 2011” [12] showed that among the 22 laboratory confirmed acute hepatitis C cases reported to DH from January 2008 to October 2011, there were 17 males and 5 females, mostly (86%) acquired the infection locally. The median age was 47.5 years. Majority (86%) was ethnic Chinese. Five (23%) of them reported history of injecting drug use while no particular risk factor was identified for the remaining cases.

Data from new blood donors who were mostly adolescents and young adults in the last decade suggested that HCV infection is around 0.1% locally, with the figure in 2011 being 0.1% (95% confidence interval 0.07% - 0.13%). Among the new blood donors, anti-HCV was most commonly detected in males aged 50 years or over, and males were more commonly affected than females. Findings of the household study of the entire spectrum of adult age groups conducted in 2001 further supported the uncommon scene of HCV infection among general population in Hong Kong; the overall positive rate was 0.3% in 936 subjects (95% confidence interval, 0.07%-0.94%). From 1999 to 2010, six of 1191 (0.5%) clients who attended the Therapeutic Prevention Clinic (TPC) at Integrated Treatment Centre (ITC) of CHP, DH for post-exposure management were tested positive for anti-HCV at 6 months. All 6 cases were non-HCW and already HCV infected at time of injury upon retrospective testing of baseline specimens.

From the studies published in the early 1990s, it was shown that anti-HCV was more commonly found in injecting drug users (IDU, 66.8%), haemophilia (56%), haemodialysis

(4.6%) and other patients requiring frequent blood/blood product transfusions but not persons at risk through sexual contact [13]. Another study conducted for 51 haemodialysis patients found that 8 (16%) were positive for anti-HCV by second generation enzyme immunoassay and 1 (2%) for HCV RNA alone, giving an overall infection rate of 18% [14]. This study also found a new infection rate of 4.9% per patient-year upon longitudinal follow up of 19 months. Results of testing non-random samples from drug users under treatment showed a HCV positive rate of 74% in 1988/1989 and 46% in 2000/2001.

A HCV seroprevalence study in 2006 conducted in methadone clinics targeting IDU echoed the high prevalence rate of HCV in this community [15]. Of 567 IDU participants recruited in 2006, 84% were male and 98% were ethnic Chinese. The median age was 49 years and median injection duration was 17 years. Two-thirds (62%) admitted ever sharing injecting equipments. Prevalence of anti-HCV was 85% (95% confidence interval 82.5 - 88.3%). Injection duration, recent injection, ever sharing injecting equipments and concomitant use of other drugs were independent factors associated with HCV infection.

HIV/AIDS patients, with a proportion being IDU, is another group with consistent data showing a comparatively high HCV prevalence. From 2000 to 2011, HCV-HIV coinfection among patients attending ITC ranged from 7% to 25%. The prevalence rate appears to be higher in male than female patients, likely related to the differential risk of parenteral and blood product exposure. While HCV infection is present in 1 - 7 % of HIV/AIDS patients infected due to sexual contact, HCV was nearly universal in patients infected through drug injection. It should be noted that, among patients infected due to sexual contact, the relatively high HCV prevalence (7%) in male patients infected via heterosexual route was attributed to a significant proportion (64%) having past history of drug use. While there has been overseas data supporting sexual transmission of HCV among HIV-infected men who have sex with men [16], the anti-HCV prevalence of subjects who contracted HIV via homosexual or bisexual contact in the DH HIV/AIDS patient cohort remained below 2% from screening since 2005. The overall higher HCV prevalence, coupled with the hastened liver disease progression in HIV-infected patients [17], would no doubt result in a unique HCV/HIV coinfection that demands attention.

Since 2003, laboratory surveillance for HCV in Hong Kong was enhanced to monitor the trend of anti-HCV among selected population groups in the local community, including blood donors from HKRCBTS, and selected in-patients from the Princess Margaret Hospital (PMH) and Prince of Wales Hospital (PWH, joined since 2005). Some 180,000-240,000 new and repeated blood donors of HKRCBTS were tested for anti-HCV each year, among which the prevalence was consistently low at less than 0.1% since 2003. Whereas among the selected hospital patients tested in the past nine years, the overall anti-HCV prevalence was 3.2%. Anti-HCV was most commonly found in drug users, of which 49.2% were found positive, followed by patients with history of blood transfusion at 10.3%. Overall, the male-to-female ratio of HCV positive subjects was about 2.3 to 1, with a mean age of 48.3 years old.

Genotypic studies in Hong Kong has identified that 1b and 6a were the prevalent HCV genotypes locally, a scenario different from that in western countries where 1a predominated [18]. In an early study of 212 blood donors tested anti-HCV positive from 1991 to 1994, the commonest genotype found was 1b (58.8%), followed by 6a (27.0%) [19]. In another study of hospitalized patients with HCV testing for clinical indications 1b was the commonest type

found in patients with chronic liver diseases and chronic renal failure [20]. According to a local study of patients on renal replacement therapy, the predominant genotype was 1b, followed by 1a and 6a [21]. Yet, the commonest genotype in intravenous drug users was genotype 6. A retrospective analysis of 106 intravenous drug users and 949 non-drug users with samples collected between December 1998 and May 2004 also confirmed the significant high prevalence of genotype 6a in drug users (58.5%) followed by 1b (33.0%), in contrast to 63.6% for 1b and 23.6% for 6a in non-drug users [22]. Besides intravenous drug use, age and sex were independent factors associated with HCV genotypes in this study. In a methadone clinic-based study published in 2011, out of 273 IDUs with different periods of initiating injection, 52% had genotype 6a and 38% had 1b. Both genotypes 1b and 6a were prevalent among older injectors, while subtype 3a was more common in young injectors and those initiating injection more recently during 1995-2006. Moreover, phylogenetic analysis revealed no specific clustering of any subtype or genotype, which did not suggest any outbreak of HCV among the study population. The extensive use of methadone widely available since 1980s may have protected Hong Kong from the emergence of HCV clusters among injection drug users [23].

The natural history of 138 HCV genotype 1 patients (median age: 50 years) was compared with that of 78 HCV genotype 6 patients (median age: 46.5 years) in Queen Mary Hospital [24]. Both genotypes share a similar natural history based on liver biochemistry, HCV viral load, and on probability of cirrhotic complications and mortality after a median follow-up period of over 5 years.

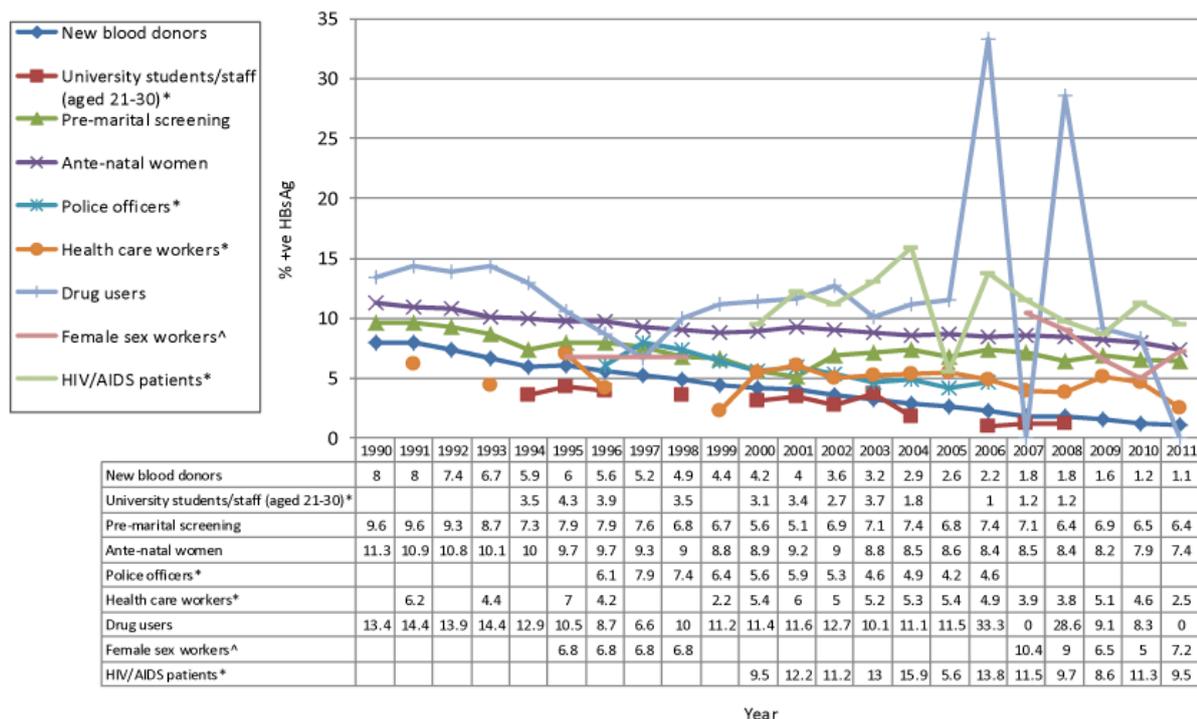
## **Liver Cancer - Major Morbidity and Mortality from Viral Hepatitis**

Chronic HBV and HCV infection are important risk factors for cirrhosis and liver cancer. Globally 700 thousand people died of liver cancer in 2008, and HBV and HCV accounted for 78% of liver cancer cases [25]. Local studies showed that 75-80% of hepatocellular cancers in Hong Kong were related to chronic HBV infection, and 3-6% cases were related to chronic HCV infection. HBV and HCV co-infection accounted for another 0.4-3% [26]. Among 76 liver transplants performed in Queen Mary Hospital due to cirrhosis from 1999 to 2000, 51 and 7 were related to hepatitis B and C respectively [27].

Apart from chronic HBV and HCV infection, other risk factors for liver cancer include excessive alcohol consumption, consumption of aflatoxin contaminated food, etc [28]. In Hong Kong, the age-standardized incidence rate and death rate of liver cancer is higher in male. According to the data from the Hong Kong Cancer Registry [26], liver cancer, including neoplasm of liver and intrahepatic bile ducts, was the fourth commonest cancer in men and seven commonest cancer in women in 2010. There were 1863 new registered cases of liver cancer, with 1398 cases of males and 465 cases of females, which accounted for 10.1% and 3.7% respectively of all new cancer cases in the same year. The median age was 62 years for male and 71 years for female. There was a downward trend for the age-standardized incidence rate for male in the past decade whereas that for female has remained static. The figures were 27.1 for male and 8.1 for female per 100 000 standard population in 2010.

In 2010, liver cancer was the second and fourth leading cause of cancer deaths in men and women respectively in Hong Kong. There were 1530 registered mortality from liver cancer, with 1113 cases of males and 417 cases of females, which accounted for 14.2% and 8% respectively for all cancer deaths. The median age was 66 years for male and 75 years for female. There was a downward trend for the age-standardized mortality rate for both sexes in the past decade. The figures were 21.2 for male and 6.5 for female per 100 000 standard population in 2010 [29].

**Box 35. Trends of HBsAg in selected population groups from 1990 to 2011 (Data source: multiple sources)**



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**Test paper - Current situation of hepatitis B and C in Hong Kong**

Expiration Date: 23 December 2013

CME point: 1 / CNE point: 1 / PEM point: 1 (not direct-midwifery related)

- Please indicate one answer to each question.
- 

1. HCV infection was more prevalent in the following group, except?
  - (a) injecting drug users
  - (b) haemophilia patients
  - (c) patients on haemodialysis
  - (d) blood donors
  - (e) patients with frequent blood transfusions, especially in the old days
2. Which of the following is not true of hepatitis B control in Hong Kong?
  - (a) World Health Organisation verified Hong Kong achieving the goal of HBV control in 2010
  - (b) a study of school children aged 12-15 years revealed a HBsAg prevalence of <2%
  - (c) control of HBV in children is contributed by the universal neonatal hepatitis B vaccination programme
  - (d) screening of blood donors minimizes HBV transmission via blood transfusion
  - (e) none of the above
3. Which of the following is not true of HBV genotypes and liver complications?
  - (a) some studies found a higher risk of cirrhosis and hepatocellular carcinoma with genotype C
  - (b) genotype C and B were the commonest in Hong Kong
  - (c) genotypes and their subtypes differed across geographic territories
  - (d) familial hepatocellular carcinoma has an earlier age of onset than sporadic cases
  - (e) none of the above
4. Which of the following is not true regarding latest hepatitis C infection in Hong Kong?
  - (a) most of acute hepatitis C cases were sporadic without identifiable risk factor
  - (b) injecting drug use remained an important cause
  - (c) acute hepatitis C ranked first in the notified hepatitis cases
  - (d) male predominated for acute hepatitis cases
  - (e) in general less than 10 hepatitis C cases were notified each year
5. Which of the following is not true of the HCV genotypes situation in Hong Kong?
  - (a) genotype 6a was seen more commonly than western countries
  - (b) genotypes differed across community/patient groups infected with HCV
  - (c) genotype 1 was the commonest found in drug users
  - (d) genotype 1 was the commonest found in renal transplant patients
  - (e) phylogenetic studies did not reveal clustering or outbreak of HCV infections in drug users
6. Which is not true about the transmission, epidemiology and prevention of hepatitis B and C?
  - (a) both HBV and HCV are transmitted via parenteral routes

- (b) an effective vaccine for HBV is available whereas no vaccine exists for HCV
  - (c) vertical transmission is believed to be the most important route for both HBV and HCV locally
  - (d) infection control measures can effectively reduce risk of blood-borne infections for both viruses
  - (e) none of the above
7. Which of the following was not a characteristics of local HBV infection?
- (a) the infection was generally less common than hepatitis C
  - (b) place of birth could affect the prevalence
  - (c) HBsAg prevalence was not remarkably higher in female sex workers than antenatal women
  - (d) drug users were at increased risk
  - (e) none of the above
8. Which of the following is not a pattern of hepatitis B epidemiology discerned in Hong Kong?
- (a) there was a general declining trend of chronic hepatitis B among communities without apparent risk
  - (b) HBsAg prevalence increased with older age in TB patients and police officers
  - (c) chronic HBV infection was more common in male, e.g. in blood donors, TB patients and people sampled from household survey
  - (d) HIV/AIDS patients had a high prevalence
  - (e) none of the above
9. Which of the following is not true of HCV situation in injecting drug users in Hong Kong?
- (a) a high prevalence of about 80% was found in local injecting drug users
  - (b) most of the hepatitis C infected drug users were male Chinese
  - (c) sharing of injecting equipment was a common risk factor
  - (d) duration of drug injection and concomitant drug use are both factors associated with HCV positivity
  - (e) none of the above
10. Which of the following is not true of the liver cancer situation in Hong Kong?
- (a) chronic hepatitis B is the single most important underlying condition of hepatocellular cancer
  - (b) studies estimated that less than 10% of liver cancers were accounted by hepatitis C
  - (c) liver cancer, including that of liver and intrahepatic ducts, was the second commonest and seventh commonest cancer in male and female respectively in 2010
  - (d) liver cancer was an even more important cause of death than its occurrence frequency in both male and female patients, probably related to late diagnosis
  - (e) hepatitis B and C were important cause of liver transplants