World Journal of Hepatology

Online Submissions: http://www.wjgnet.com/1948-5182office
wjh@wjgnet.com
doi:10.4254/wjh.v3.i2.31

World J Hepatol 2011 February 27; 3(2): 31-37
ISSN 1948-5182 (online)

EDITORIAL

Hepatitis B prevention and control: Lessons from the East and the West

Monica C Robotin

Monica C Robotin, NSW Cancer Council, School of Public Health University of Sydney, Sydney, NSW 2011, Australia
Author contribution: Robotin MC contributed solely to this work.
Correspondence to: Monica C Robotin, MBBS, FRACS, MBA, MIH, M Appl Epid, Medical Director, NSW Cancer Council, Senior Lecturer, School of Public Health University of Sydney, Sydney, NSW 2011,
Australia. monica.robotin@sydney.edu.au
Telephone: +61-2-90367137 Fax: +61-2-93680711
Received: September 13, 2010 Revised: December 13, 2010
Accepted: December 20, 2010
Published online: February 27, 2011

Abstract

Despite being ten times more common than HIV infection, viral hepatitis has so far not commanded the same public health response worldwide, so a global viral hepatitis treatment program is still a long way from becoming a reality. However, much progress has occurred over the last few decades, with the screening of blood products, sound infection control practices and the introduction of disposable needles and syringes leading to significant reductions in nosocomial hepatitis B transmission in the developed world and increasingly in other countries. The introduction of hepatitis B vaccination in the 1980s and its integration into the Expanded Immunization Program have led to substantial reductions in chronic hepatitis B infection rates in children and to millions of lives saved. The availability of effective antiviral treatment has revolutionized treatment prospects, although access to treatment remains a significant challenge for most developed countries and remains out of reach for developing nations. Some of these breakthroughs have occurred in Asian countries, others in the West, but their unifying features are innovative research, timely clinical translation and a commitment to apply their findings to improve the health of populations, not just individuals. This paper reviews some of the challenges and opportunities for hepatitis B control at the end of the first decade of the third millennium and argues for closer East - West collaborations, to bring in fresh perspectives, avoid duplications of effort and in order to help answer many of the remaining challenges in making hepatitis B history.

Key words: Hepatitis B; Hepatocellular cancer; Hepatitis B surveillance; Vaccination; Screening

Peer reviewers: Shahinul Alam, Associate Professor, Department of Hepatology, BSM Medical University, Dhanmobdi R/A, Dhaka 1000, Bangladesh; Janus P Ong, MD, Clinical Associate Professor, Section of Gastroenterology, Department of Medicine, Philippine General Hospital, Taft Avenue, Manila, Philippines; Ioannis Diamantis, MD, PhD, Professor, University of Athens Medical School, Department Internal Medicine, A. Tritsi 26 GR-15238, Athens, Greece

Robotin MC. Hepatitis B prevention and control: Lessons from the East and the West. *World J Hepatol* 2011; 3(2): 31-37 Available from: URL: http://www.wjgnet.com/1948-5182/full/v3/i2/31.htm DOI: http://dx.doi.org/10.4254/wjh.v3.i2.31

INTRODUCTION

In May 2010, the 63rd World Health Assembly of the World Health Organization adopted a resolution calling for a comprehensive approach to the prevention and control of viral hepatitis, which kills over 1 million people every year. Viral hepatitis is 10 times more common than HIV infection[1], but despite the availability of effective treatments, a global viral hepatitis program providing access to treatment for the vast numbers of people with chronic hepatitis B (CHB) infection living in the developing world is far from becoming a reality[2].

Hepatitis B (HBV) infection is endemic in many South-East Asian countries, in some Pacific Islands, and in some African countries[1,3], with sero-prevalence rates in excess

of 8% in the general population leading to 25%-40% of those infected developing cirrhosis or hepatocellular cancer (HCC)[4]. Even in countries of intermediate HBV prevalence, such as in the Mediterranean basin and the Middle East, HBV poses significant challenges, due to the large numbers of affected individuals[5].

A comprehensive health response to hepatitis B has been slow to develop, probably because the complexity and variable natural history of the disease and its long asymptomatic phase do not command the same emergency response accorded to other infectious diseases. The link between CHB and liver cancer was described some 3 decades ago in Taiwan[6], and we owe much of our current understanding of hepatitis B epidemiology to scientists working in the East. They contributed key research findings on the impact of HBV vaccination on HCC incidence[7], the effect of antiviral therapy (lamivudine) in preventing progression to CHB-related cirrhosis[8] and in demonstrating the link between elevated viral loads and HCC development[9].

Until quite recently, two patterns of disease appeared to co-exist in different parts of the world: a chronic disease associated with significant death and disability in the East and a self-limiting, acute viral infection in the West. The introduction of the hepatitis B vaccine has led to substantial reductions of chronic hepatitis B infection in countries where infection is transmitted in early childhood, but overall, prevention strategies have failed to take into account the multifaceted epidemiology of the HBV infection[10]. An increased migration from high HBV prevalence countries to the industrialized countries in the West in the second half of the last century is linked to increased rates of HCC diagnoses among some migrant populations in the West. For example, Vietnamese American men are 11 times more likely to develop HCC than non-Hispanic Whites[1] and hepatitis-B related HCC has become the most important cancer health disparity affecting Asian Americans[1,11]. These statistics are increasingly being replicated in Australia[12], as well as in other Western countries[13-14].

In the West, HBV infection is usually acquired in adulthood, a long-term carrier state is uncommon and severe complications of chronic hepatitis-B infection remain rare in the general population. Consequently, the public health response to hepatitis B has focused mostly on the prevention and management of acute hepatitis B outbreaks. Hepatitis B surveillance systems exist in most Western countries[15-18], but approximately 50% of acute cases are missed by the infectious disease reporting systems[19], downgrading the importance of hepatitis B as a priority disease in the eyes of policy makers and program planners[2]. In part, this is due to the absence or non-specific nature of symptoms associated with acute hepatitis and compounded by the fact that HBV infection is more common in marginalized populations, with limited contact with health care providers [such as prisoners, men who have sex with men (MSM), intravenous drug users (IVDU) and some migrant populations]. As early as 1991, Margolis emphasized that eliminating HBV transmission was only possible by preventing infections acquired during early childhood, as well as those acquired by teenagers and adults[10]. Change is on the horizon though, with the Institute of Medicine recently publishing recommendations for improving the prevention and control of hepatitis B and C infections, in response to substantial increases in the number of cases of hepatitis B and C in the United States[2]. This comprehensive report is focused on the US situation and systematically examines the progress made in disease surveillance, immunization, knowledge and awareness of viral hepatitis among health care providers and communities, as well as the degree of access to hepatitis services. The Chair of this working group was Dr Palmer Beasley, whose work in Taiwan improved our understanding of disease transmission patterns, elucidated links to HCC and established the effectiveness of HBV vaccination[6,20-23]. One can only speculate how effectively a closer East-West collaboration led by someone who worked closely both in the East and the West may accelerate progress in hepatitis B prevention and control, from the current position where we are running a "a race against time"[24]. In this race, some success stories have already changed practice both in the East and the West, while in many areas, a collective approach uniting East and West may help solve some of the as yet unanswered questions on hepatitis B and its control.

PRIMARY PREVENTION

Significant successes have been recorded both in the East and the West in delivering vaccination programs, although immunization rates in rural, remote and marginalized populations lag behind those of urban populations. Within 10 years of launching the nationwide HBV vaccination program, the HBsAg carrier rate of Taiwanese children decreased 10-fold, from approximately 10% to 1%. This was accompanied by a four-fold reduction in HCC incidence rate in 6-9 year olds, demonstrating for the first time that a mass vaccination program can reduce cancer incidence in humans[7]. Similar trends have been observed in China, where the chronic HBV carrier rate in children fell from 10% in the year universal infant vaccination commenced (1992) to 1%-2% in 2006, thus preventing approximately 30 million new CHB infections[25].

In the US, acute hepatitis B incidence fell by 80% from 1987 to 2004[26], yet approximately 1000 infants (mostly children not born in medical settings- many of them Asian American) still become infected annually as a result of vertical transmission[1-2]. Reaching some of these populations remains a challenge both in the East and the West, as demonstrated by the fact that two consecutive US national surveys did not identify any reductions in hepatitis B prevalence[6], assumed to be related to an increased migration from countries where the disease is endemic[27].

The WHO-led Expanded Immunization Program (EPI) has made great strides in increasing access to the hepatitis B vaccine in the developing world, with 177 countries having nationwide hepatitis B vaccination programs in 2008. While in 1990 only 1% of infants worldwide received all 3 doses of the hepatitis B vaccine, by 2008 this figure had increased to 69%. Regional variations persist, although the proportion of fully immunized infants in South East Asia has been increasing rapidly, from 29% in 2007 to 41% in 2008[28]. Gaps in coverage persist in some countries, particularly in rural areas , with fewer than 21% of newborns in Laos are receiving their first dose of vaccine on time[29].

Substantial challenges remain, as highlighted by a global survey carried out by the World Hepatitis Alliance in conjunction with WHO: 80% of the 135 countries participating in the survey lacked resources to carry out viral hepatitis control, one third lacked any viral hepatitis prevalence data and free hepatitis testing was not available to half their populations[29]. While developed countries have been extremely successful in reducing disease transmission through their blood supply and reducing nosocomial transmission, significant resource limitations and persisting stigma constrain these efforts in many resource-limited settings[29-30].

CHALLENGES IN HEPATITIS B SCREENING AND SURVEILLANCE

Obtaining accurate estimates of the prevalence of HBV infection remains a significant challenge to epidemiological research not only in the US[31], but also in other countries. National population-based surveys can provide reliable estimates of HBV sero-prevalence, but their complexity and cost means that only a few countries such as the US and South Korea have been able to implement such programs[6,32] although, even there, survey coverage remains low in at risk populations. The advent of rapid testing technologies (recently utilised by WHO in Cambodia to evaluate the impact of HBV vaccination)[33] can improve HBV detection rates in hard-to-reach populations both in the East and West, and may provide critical data for program planning[2].

While most European countries (as well as North America and Australia) have in place surveillance systems for hepatitis B and C infection, data are not readily comparable across countries, due to differences in surveillance systems, reporting practices and data collection, as well as to different case definitions[17]. Difficulties arise in the classification of "acute" cases, due to the complex testing required for establishing a hepatitis B diagnosis and the limitations of the current testing systems, where test results are not reliably communicated to surveillance staff. Adopting pragmatic laboratory case definitions for hepatitis B and harmonizing case definitions from Canada, the UK and the US (as done in a pilot program in Manitoba, Canada) could allow more meaningful comparisons between countries and prevention strategies[34].

Although the predictive value of the "traditional" case definitions is low, it too can be improved, using additional criteria, such as specific criteria for ALT and total bilirubin levels. Applying these to the CDC acute hepatitis B cases increased the positive predictive value from 50% to over 95%[19].

In western countries, more or less systematic screening for hepatitis B has been carried out in their indigenous populations, such as in Alaskan natives in the US[35], the Canadian First nation people[36], Australian Aboriginal populations[37] and among Maori populations in New Zealand[18]. Since 1999, New Zealand has had a national screening and follow-up program for hepatitis B targeted at Maori, Pacific and Asian residents, developed in response to the high morbidity and mortality and the significant economic impact of untreated HBV infection in these subpopulations. The program has screened over 170 000 people and is providing ongoing CHB surveillance to more than 12 000 people[18,38].

Since 1996, Taiwan has been offering free hepatitis screening through outreach community-based screening programs, screening over 160 000 people over a 10-year period. Results suggest that a heavy burden of disease related to hepatitis B is to be expected in years to come, as 17% of people born before the vaccination program was instituted were CHB-positive[39].

Recently, demonstration projects have successfully targeted special migrant groups in the West, by linking screening with the provision of free or subsidized vaccination for those identified as susceptible. The programs generally target closely knit populations, defined by religious or other affiliations (e.g. users of ethnic media) and provide targeted information and education to the intended audience[38,40-42]. To be successful, the programs need to be accompanied by a shift in current perceptions of screening from that of a once-off test to to that of a way of entering into a program of regular follow up and timely institution of treatment.

San Francisco is aiming to become the first HBV-free city, with the Hep B Free Campaign providing screening, vaccination and treatment to all Asian and Pacific Islander residents (representing 30% of its population)[1]. To improve disease surveillance, the city has also established a population-based chronic hepatitis B registry, which carries out CHB enhanced surveillance and interviews cases, improving the understanding of transmission patterns and participants' ability to access hepatitis care[43]. However, such programs are very resource- intensive[15], making them unaffordable in resource-limited settings and problematic even for well-resourced countries with a huge infected population, such as China[44].

Devising cost-effectiveness screening and treatment strategies is critical to program success and recent studies have confirmed that routine screening can be cost-effective in Asians and Pacific Islanders in the US[45] and in at-risk migrant populations in the Netherlands[46]. Providing antiviral treatment to people with CHB can be more

Table 1 Challenges and solutions in the public health response to hepatitis B

Challenges	Possible solutions
Lower HBV immunization rates in remote/ marginalized populations	Develop effective outreach vaccination programs Community education
Unresponsive HBV surveillance systems	Develop uniform, pragmatic case definitions for acute HBV infection Redesign surveillance systems
Low rates of HBV screening	Reduce stigma and discrimination Increased awareness and education about HBV Replace once-off screening with systematic follow up
Cost of screening and treatment programs	Develop more cost-effective programs
Access to treatment	Increase treatment access and reduce cost of drugs Seek innovative ways of providing treatment access and know-how for less developed countries

HBV: hepatitis B virus.

cost- effective than liver cancer screening in migrant populations in Australia[47], but more work is needed to develop low-cost screening and treatment programs, which can address the needs of the developing world.

The relative merits of alternative surveillance options, such as carrying out enhanced surveillance intermittently[16] or focusing efforts on specific populations, are worthy of exploring. As early as 1994, Ruth Berkelman recommended a reevaluation of US infectious disease surveillance practices, to ensure they remain responsive to the challenges imposed by a changing disease landscape[48]. This remains as relevant today as it was 16 years ago.

Program design needs to avoid stigma and discrimination associated with testing in specific populations, particularly in certain ethnic groups. Because mandatory hepatitis B testing in mainland China has in the past led to the exclusion of HBsAg positive people from employment and study, Chinese immigrants may have serious misgivings about being tested, out of concern that this could lead to stigmatization and discrimination in their adopted country. A substantial body of research has documented migrant communities' knowledge of hepatitis B and attitudes to screening, particularly in North America[49-57], and this can inform the development of culturally sensitive screening and treatment programs, which take into account the ethnic, racial and socioeconomic disparities associated with chronic hepatitis B infection.

Unfortunately, the low levels of awareness and knowledge about hepatitis B among at-risk populations are also mirrored in low levels of knowledge among health care providers[58-61]. This is a contributing factor to low rates of testing and treatment among at-risk populations and leads to limited clinical support for the allocation of resources for hepatitis B prevention, control and surveillance efforts, even in well-resourced settings (Table 1)[62].

ACCESS TO SERVICES

The differential rates of hepatitis B–related liver cancer between Asian and Pacific Americans and the general US population represents the single most important cancer-related inequality in the US[1,62]. Canadian estimates suggest that 1%-2% of their Southeast Asian migrants have CHB and would benefit from antiviral therapy[63], but that few in this population are aware of their CHB status and of the changing treatment paradigms in hepatitis B. In Australia antiviral treatment can be accessed free of charge, yet only approximately 2% of people with CHB are receiving treatment[64]. These problems are greatly magnified in resource-limited settings by the high cost and long duration of antiviral treatments. Furthermore, identifying the people who stand to benefit the most from antiviral treatments remains problematic both in the West and the East.

WAY FORWARD

In well-resourced settings, a hepatitis B Registry model may improve the quality of CHB surveillance and provide direct links to health services, education, contact tracing and better outcomes[43]. The next step in well-resourced countries may be to integrate CHB into a system of chronic disease surveillance, as piloted in Taiwan. The program uses a specially designed health information system, collecting data on five cancers (cervical, breast, colorectal, cancer of the oral cavity and liver cancer) and three chronic conditions (hypertension, hyperlipidemia and type 2 diabetes)[65]. By the end of 2003, 60 000 participants (representing almost 30% of the target population) were enrolled in the program, demonstrating that an integrated management model of cancer and chronic disease is feasible.

To follow on from Ruth Berkelman's recommendations, the "new look surveillance" in the 21st century may combine core surveillance with targeted surveillance of specific population groups. It may involve sentinel networks[48], linking health care providers and laboratories to a central data collection and processing center by using primary care networks, as is currently done for influenza surveillance. The information provided by this system could be augmented by enhanced surveillance in at-risk populations, such as migrants, indigenous people, MSM, prisoners, or institutionalizedgroups. The creation of international networks to monitor and investigate HBV infection could increase the effectiveness of public health interventions and promote collaborative research. Survei-

Table 2 Ways to improve outcomes in hepatitis B

Ways forward
Develop Registry model of hepatitis B surveillance, linked to health service delivery and education
Integrate CHB surveillance with surveillance for other chronic diseases
Develop responsive HBV surveillance systems
Create international networks for hepatitis B monitoring
Integrate surveillance and clinical data
Develop collaborations to enhance sharing of information

CHB: chronic hepatitis B; HBV: hepatitis B virus.

llance data coupled with clinical information obtained from publicly available databases recording hospital discharge as well as morbidity and mortality, could provide a comprehensive picture of the burden of disease related to HBV infection in different populations. Sharing economic models across different countries could assist in devising cost-effective health care delivery models, commensurate with the level of available resources.

International collaborations, such as that currently trialed by the National Institute of Diabetes and Digestive and Kidney Diseases which is implementing an action plan for liver disease research across the National Institute of Health, could lead to a more efficient utilization of resources and information sharing and to the speeding up of progress (Table 2)[31].

Increasing East - West collaboration can provide new perspectives, avoid the duplication of effort and help answer the many remaining challenges posed by this protean disease. Over the last decade, WHO has supported the development of comprehensive cancer control programs in many countries, based upon four pillars: cancer prevention, early detection, appropriate treatment and relevant research. These four principles apply equally well to hepatitis B prevention and control and to this list we can add a fifth pillar: international collaboration. They are all essential in the process of "making hepatitis B history".

ACKNOWLEDGMENTS

Many thanks for Professor Jacob George, for reviewing the manuscript and to Ms Yaping Liu for her continued support with literature searches.

REFERENCES

1 **McBride G**. Hepatitis B virus-induced liver cancer in Asian Americans: a preventable disease. *J Natl Cancer Inst* 2008; **100**: 528-529
2 IOM (Institute of Medicine). Hepatitis and liver cancer: a national strategy for prevention and control of hepatitis B and C. In: IOM, editor. Washington DC: Institute of Medicine, 2010
3 **Lavanchy D**. Hepatitis B virus epidemiology, disease burden, treatment, and current and emerging prevention and control measures. *J Viral Hepat* 2004; **11**: 97-107
4 **Lavanchy D**. Chronic viral hepatitis as a public health issue in the world. *Best Pract Res Clin Gastroenterol* 2008; **22**: 991-1008
5 **Custer B**, Sullivan SD, Hazlet TK, Iloeje U, Veenstra DL, Kowdley KV. Global epidemiology of hepatitis B virus. *J Clin Gastroenterol* 2004; **38**: S158-S168
6 **Beasley RP**, Hwang LY, Lin CC, Chien CS. Hepatocellular carcinoma and hepatitis B virus. A prospective study of 22 707 men in Taiwan. *Lancet* 1981; **2**: 1129-1133
7 **Chang MH**, Chen CJ, Lai MS, Hsu HM, Wu TC, Kong MS, Liang DC, Shau WY, Chen DS. Universal hepatitis B vaccination in Taiwan and the incidence of hepatocellular carcinoma in children. Taiwan Childhood Hepatoma Study Group. *N Engl J Med* 1997; **336**: 1855-1859
8 **Liaw YF**, Sung JJ, Chow WC, Farrell G, Lee CZ, Yuen H, Tanwandee T, Tao QM, Shue K, Keene ON, Dixon JS, Gray DF, Sabbat J. Lamivudine for patients with chronic hepatitis B and advanced liver disease. *N Engl J Med* 2004; **351**: 1521-1531
9 **Chan HL**, Sung JJ. Hepatocellular carcinoma and hepatitis B virus. *Semin Liver Dis* 2006; **26**: 153-161
10 **Margolis HS**, Alter MJ, Hadler SC. Hepatitis B: evolving epidemiology and implications for control. *Semin Liver Dis* 1991; **11**: 84-92
11 The Office of Minority Health. Chronic Hepatitis B in Asian Americans, Native Hawaiians and other Pacific Islanders. Editor: US Department of Health and Human Services., 2008. Accessed 12/07/2010. Available from: URL: http://minorityhealth.hhs.gov/templates/browse.aspx
12 **Supramaniam R**, O'Connell DL, Tracey E, Sitas F. Cancer incidence in New South Wales migrants 1991 to 2001. Report. Cancer Council NSW: Sydney, 2006
13 **Haworth EA**, Soni Raleigh V, Balarajan R. Cirrhosis and primary liver cancer amongst first generation migrants in England and Wales. *Ethn Health* 1999; **4**: 93-99
14 **Visser O**, van Leeuwen FE. Cancer risk in first generation migrants in North-Holland/Flevoland, The Netherlands, 1995-2004. *Eur J Cancer* 2007; **43**: 901-908
15 **Fleming DT**, Zambrowski A, Fong F, Lombard A, Mercedes L, Miller C, Poujade J, Roome A, Sullivan A, Finelli L. Surveillance programs for chronic viral hepatitis in three health departments. *Public Health Rep* 2006; **121**: 23-35
16 **Forssman BL**, Gupta L. Enhanced surveillance of hepatitis B infection in inner-western Sydney. *NSW Public Health Bull* 2007; **18**: 115-118
17 **Rantala M**, van de Laar MJ. Surveillance and epidemiology of hepatitis B and C in Europe - a review. *Euro Surveill* 2008; **13**: 18880
18 **Robinson T**, Bullen C, Humphries W, Hornell J, Moyes C. The New Zealand Hepatitis B Screening Programme: screening coverage and prevalence of chronic hepatitis B infection. *N Z Med J* 2005; **118**: U1345
19 **Klompas M**, Haney G, Church D, Lazarus R, Hou X, Platt R. Automated identification of acute hepatitis B using electronic medical record data to facilitate public health surveillance. *PLoS One* 2008; **3**: e2626
20 **Beasley RP**, Hwang LY, Lee GC, Lan CC, Roan CH, Huang FY, Chen CL. Prevention of perinatally transmitted hepatitis B virus infections with hepatitis B virus infections with hepatitis B immune globulin and hepatitis B vaccine. *Lancet* 1983; **2**: 1099-1102
21 **Beasley RP**, Hwang LY, Lin CC, Leu ML, Stevens CE, Szmuness W, Chen KP. Incidence of hepatitis B virus infections in preschool children in Taiwan. *J Infect Dis* 1982; **146**: 198-204
22 **Beasley RP**, Hwang LY, Stevens CE, Lin CC, Hsieh FJ, Wang KY, Sun TS, Szmuness W. Efficacy of hepatitis B immune globulin for prevention of perinatal transmission of the hepatitis B virus carrier state: final report of a randomized double-blind, placebo-controlled trial. *Hepatology* 1983; **3**: 135-141
23 **Hwang LY**, Roggendorf M, Beasley RP, Deinhardt F. Perinatal transmission of hepatitis B virus: role of maternal HBeAg and anti-HBc IgM. *J Med Virol* 1985; **15**: 265-269
24 **Leeder S**, Raymond S, Greenberg H, Liu H, Esson K. A race against time. The challenge of cardiovascular disease in de-

veloping countries. New York: The Center for Global Health and Economic Development, 2004
25 **Zhou YH**, Wu C, Zhuang H. Vaccination against hepatitis B: the Chinese experience. *Chin Med J (Engl)* 2009; **122**: 98-102
26 **Daniels D**, Grytdal S, Wasley A. Surveillance for acute viral hepatitis - United States, 2007. *MMWR Surveill Summ* 2009; **58**: 1-27
27 **Gish RG**, Gadano AC. Chronic hepatitis B: current epidemiology in the Americas and implications for management. *J Viral Hepat* 2006; **13**: 787-798
28 WHO. Global immunization coverage in 2008. Editor: World Health Organization 2009. Accessed on 2010-07-12. Available from: URL: http://www.who.int/immunization/newsroom/GID_english.pdf
29 **Parry J**. At last a global response to viral hepatitis. *Bull World Health Organ* 2010; **88**: 801-802
30 **Gust ID**. Epidemiology of hepatitis B infection in the Western Pacific and South East Asia. *Gut* 1996; **38** Suppl 2: S18-S23
31 **Kim WR**. Epidemiology of hepatitis B in the United States. *Hepatology* 2009; **49**: S28-S34
32 **Lee DH**, Kim JH, Nam JJ, Kim HR, Shin HR. Epidemiological findings of hepatitis B infection based on 1998 National Health and Nutrition Survey in Korea. *J Korean Med Sci* 2002; **17**: 457-462
33 **Soeung SC**, Rani M, Huong V, Sarath S, Kimly C, Kohei T. Results from nationwide hepatitis B serosurvey in Cambodia using simple and rapid laboratory test: implications for National Immunization Program. *Am J Trop Med Hyg* 2009; **81**: 252-257
34 **Hong Z,** Smart G, Zaniewski G, Wu H, Wu J, Goedhuis N, Giulivi A, Kaita K, Dawood M. Epidemiological study of hepatitis B infection in Manitoba, Canada, 1992-2003. *Eur J of Clin Microbol Infects Dis* 2005; **24**, 464-470
35 **McMahon BJ**, Bulkow L, Harpster A, Snowball M, Lanier A, Sacco F, Dunaway E, Williams J. Screening for hepatocellular carcinoma in Alaska natives infected with chronic hepatitis B: a 16-year population-based study. *Hepatology* 2000; **32**: 842-846
36 **Minuk GY**, Uhanova J. Viral hepatitis in the Canadian Inuit and First Nations populations. *Can J Gastroenterol* 2003; **17**: 707-712
37 **Nguyen VT**, Dore GJ. Prevalence and epidemiology of hepatitis B. In: Matthews G, Robotin M, editors. B Positive- all you wanted to know about hepatitis B. Sydney: Australasian Society for HIV Medicine (ASHM), 2008: 13-23
38 **Gane E**. Screening for chronic hepatitis B infection in New Zealand: unfinished business. *N Z Med J* 2005; **118**: U1344
39 **Lazarus R**, Klompas M, Campion FX, McNabb SJ, Hou X, Daniel J, Haney G, DeMaria A, Lenert L, Platt R. Electronic Support for Public Health: validated case finding and reporting for notifiable diseases using electronic medical data. *J Am Med Inform Assoc* 2009; **16**: 18-24
40 Screening for chronic hepatitis B among Asian/Pacific Islander populations--New York City, 2005. *MMWR Morb Mortal Wkly Rep* 2006; **55**: 505-509
41 **Rein DB**, Lesesne SB, Leese PJ, Weinbaum CM. Community-based hepatitis B screening programs in the United States in 2008. *J Viral Hepat* 2010; **17**: 28-33
42 **Custer B**, Sullivan SD, Hazlet TK, Iloeje U, Veenstra DL, Kowdley KV. Global epidemiology of hepatitis B virus. *J Clin Gastroenterol* 2004; **38**: S158-S168
43 Communicable Disease Control & Prevention Section, San Francisco. Chronic hepatitis B surveillance report 2007-2008, San Francisco. Chronic viral hepatitis Registry project San Francisco, 2009
44 **Liu J**, Fan D. Hepatitis B in China. *Lancet* 2007; **369**: 1582-1583
45 **Hutton DW**, Tan D, So SK, Brandeau ML. Cost-effectiveness of screening and vaccinating Asian and Pacific Islander adults for hepatitis B. *Ann Intern Med* 2007; **147**: 460-469
46 **Veldhuijzen IK**, Toy M, Hahné SJ, De Wit GA, Schalm SW, de Man RA, Richardus JH. Screening and early treatment of migrants for chronic hepatitis B virus infection is cost-effective. *Gastroenterology* 2010; **138**: 522-530
47 **Robotin MC**, Kansil M, Howard K, George J, Tipper S, Dore GJ, Levy M, Penman AG. Antiviral therapy for hepatitis B-related liver cancer prevention is more cost-effective than cancer screening. *J Hepatol* 2009; **50**: 990-998
48 **Berkelman RL**, Bryan RT, Osterholm MT, LeDuc JW, Hughes JM. Infectious disease surveillance: a crumbling foundation. *Science* 1994; **264**: 368-370
49 **Butler LM**, Mills PK, Yang RC, Chen MS Jr. Hepatitis B knowledge and vaccination levels in California Hmong youth: implications for liver cancer prevention strategies. *Asian Pac J Cancer Prev* 2005; **6**: 401-403
50 **Chrusch C**, Minuk GY. Public knowledge about hepatitis B related issues in a high risk population. *Arctic Med Res* 1991; Suppl: 374-376
51 **Ma GX**, Shive SE, Fang CY, Feng Z, Parameswaran L, Pham A, Khanh C. Knowledge, attitudes, and behaviors of hepatitis B screening and vaccination and liver cancer risks among Vietnamese Americans. *J Health Care Poor Underserved* 2007; **18**: 62-73
52 **Ma GX**, Shive SE, Toubbeh JI, Tan Y, Wu D. Knowledge, attitudes, and behaviors of Chinese hepatitis B screening and vaccination. *Am J Health Behav* 2008; **32**: 178-187
53 **O'Connor CC**, Shaw M, Wen LM, Quine S. Low knowledge and high infection rates of hepatitis in Vietnamese men in Sydney. *Sex Health* 2008; **5**: 299-302
54 **Taylor VM**, Choe JH, Yasui Y, Li L, Burke N, Jackson JC. Hepatitis B awareness, testing, and knowledge among Vietnamese American men and women. *J Community Health* 2005; **30**: 477-490
55 **Taylor VM**, Jackson JC, Pineda M, Pham P, Fischer M, Yasui Y. Hepatitis B knowledge among Vietnamese immigrants: implications for prevention of hepatocellular carcinoma. *J Cancer Educ* 2000; **15**: 51-55
56 **Taylor VM**, Tu SP, Woodall E, Acorda E, Chen H, Choe J, Li L, Yasui Y, Hislop TG. Hepatitis B knowledge and practices among Chinese immigrants to the United States. *Asian Pac J Cancer Prev* 2006; **7**: 313-317
57 **Yokoe DS**, Mermel LA, Anderson DJ, Arias KM, Burstin H, Calfee DP, Coffin SE, Dubberke ER, Fraser V, Gerding DN, Griffin FA, Gross P, Kaye KS, Klompas M, Lo E, Marschall J, Nicolle L, Pegues DA, Perl TM, Podgorny K, Saint S, Salgado CD, Weinstein RA, Wise R, Classen D. A compendium of strategies to prevent healthcare-associated infections in acute care hospitals. *Infect Control Hosp Epidemiol* 2008; **29** Suppl 1: S12-S21
58 **Ferrante JM**, Winston DG, Chen PH, de la Torre AN. Family physicians' knowledge and screening of chronic hepatitis and liver cancer. *Fam Med* 2008; **40**: 345-351
59 **Lai CJ**, Nguyen TT, Hwang J, Stewart SL, Kwan A, McPhee SJ. Provider knowledge and practice regarding hepatitis B screening in Chinese-speaking patients. *J Cancer Educ* 2007; **22**: 37-41
60 **Stein AD**, Makarawo TP, Ahmad MF. A survey of doctors' and nurses' knowledge, attitudes and compliance with infection control guidelines in Birmingham teaching hospitals. *J Hosp Infect* 2003; **54**: 68-73
61 **Walsh K**. Online educational tools to improve the knowledge of primary care professionals in infectious diseases. *Educ Health (Abingdon)* 2008; **21**: 64
62 IOM (Institute of Medicine). Hepatitis and liver cancer: a national strategy for preovention and control of hepatitis B and C. Washington DC. Editor: Institute of Medicine, 2010
63 **Wong WW**, Minuk GY. A cross-sectional seroepidemiologic survey of chronic hepatitis B virus infections in Southeast Asian immigrants residing in a Canadian urban centre. *Clin Invest Med* 1994; **17**: 443-447

64 National Centre in HIV Epidemiology and Clinical Research. HIV/AIDS, viral hepatitis and sexually transmitted infections in Australia. Annual Surveillance Report. Sydney. Editor: National Centre in HIV Epidemiology and Clinical Research, 2007

65 **Chiu YH**, Chen LS, Chan CC, Liou DM, Wu SC, Kuo HS, Chang HJ, Chen TH. Health information system for community-based multiple screening in Keelung, Taiwan (Keelung Community-based Integrated Screening No. 3). *Int J Med Inform* 2006; **75**: 369-383

S- Editor Zhang HN **L- Editor** Hughes D **E- Editor** Liu N