REVIEW

HEPATITIS B AND HEPATITIS C VIRUS IN THAI BLOOD DONORS

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Abstract. Hepatitis B virus (HBV) and hepatitis C virus (HCV) are major causes of transfusion-transmitted infection (TTI). In Thailand, the prevalence of HBV infection in new blood donors has decreased gradually from 7.1% in 1988 to 2.6% in 2009. This drastic decline in HBV prevalence is mostly the result of an effective expanded program on immunization (EPI) against HBV; the current coverage rate with HBV vaccine in newborns is more than 98% nation-wide. The prevalence of HCV infection, has decreased at a slower rate due to lack of HCV vaccination. The use of healthy volunteer blood donors and nucleic acid amplification technology (NAT) has also contributed to the steady decrease in rates of HBV and HCV infections. We summarize the current status of the EPI program for preventing HBV and the current strategy of HBV and HCV screening in new blood donors.

Keyword: hepatitis B, hepatitis C, blood donor, Thailand

INTRODUCTION

Hepatitis B virus (HBV) and hepatitis C virus (HCV) are major public health problems worldwide, including in Thailand. Infected patients may progress to chronic liver disease, liver cirrhosis and hepatocellular carcinoma. HBV and HCV are found in blood and secretions, and are transmitted vertically and horizontally, such as by sexual contact, blood transfusion or organ transplantation (Burra, 2009; Liang, 2009; Liaw, 2009; Marcellin, 2009; Myrmel *et al*, 2009; Thomson, 2009). HBV and HCV are common transfusion-transmitted infections (TTI) in Thailand and thus, screening of blood donors plays an important part in the prevention of TTI (Liu *et al*, 2006; Dodd *et al*, 2009). The Ministry of Public Health has recommended universal HBV vaccination of newborns as past of the expanded program on immunization (EPI) since 1992 (Poovorawan *et al*, 2000). There is no vaccine for HCV (Burra, 2009; Myrmel *et al*, 2009; Thomson, 2009). This report describes HBV and HCV prevalence among Thai new blood donors who participated in the screening program conducted at the National Blood Center

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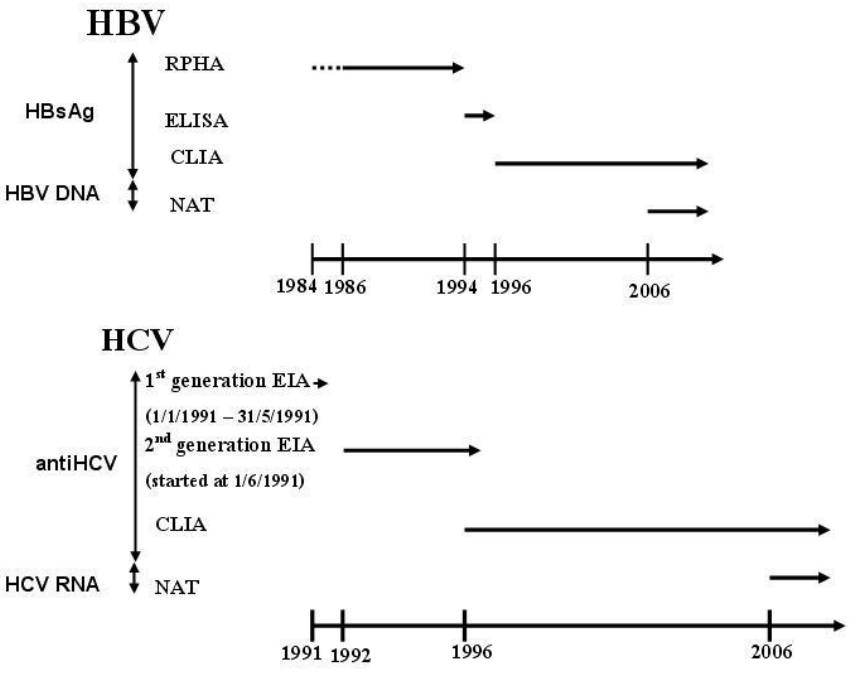

Serology test: RPHA, reverse passive hemagglutination; ELISA, enzyme-linked immunosorbent assay; EIA, enzyme immunoassay; CLIA, chemiluminescent immunoassay; NAT, nucleic acid amplification technology

Fig 1–Evolution of blood screening test at the National Blood Center, Thai Red Cross Society.

(NBC), Thai Red Cross Society, Bangkok, Thailand from 1988 to 2009.

BLOOD DONOR SCREENING PROGRAM

The blood donor screening program comprises donor self selection, general examination by health care providers, blood screening test and record collection. The donor ages range from 17 to 70 years old (NBC, 1989; Kunanusoon, 1991; NBC, 2009). Since 1985, all blood donations have been obtained from volunteers. Prisoners were excluded in 1986. Donor self selection is based on a screening questionnaire aimed at excluding donors at high risk for TTI: promiscuity without taking precautions, sex workers, homosexual men, prisoners, tattooing, and recipients of blood transfusion from donors (NBC, 1989; Kunanusoon, 1991; NBC, 2009). Until recently, serological techniques were applied for routine blood screening by the National Blood Center, Thai Red Cross Society. The HBV marker was HBsAg whereas the HCV marker was anti-HCV. Evolution of the screening test is shown in Fig 1. The reliability of these tests is limited since they do not detect viruses during the window

Table 1
Serology negative/NAT positive blood samples for HBV and HCV during 2008-2009.

	2008	2009
HBV	175 (1:2,800)	165 (1:3,300)
HCV	1 (1:490,000)	0 (0)

period nor occult hepatitis. The window period of HBV and HCV infections constitutes the acute phase of infection during which serological markers cannot be detected. Occult hepatitis has been described with both HBV and HCV. During the occult HBV stage, infected patients test negative for HBsAg irrespective of the presence or absence of HBV antibodies (anti-HBc and/or anti-HBs). Nevertheless, HBV DNA is present in the liver. A negative test result for HBsAg may be due to a low HBsAg titer, escape mutants of the surface gene region or, insufficient sensitivity of the screening tests (Allain, 2004; Liang, 2009; Ozaslan and Purnak, 2009). Anti-HBc is detected in many occult HBV patients but is not used for routine blood screening because Thailand is an area endemic for HBV and adults born prior to HB vaccine integration into the EPI display a high prevalence of anti-HBc. Occult HCV infection is characterized by a diseased liver and HCV RNA in peripheral blood mononuclear cells irrespective of the detection of HCV RNA in the serum, anti-HCV detection and/or abnormal liver enzyme levels (Carreño *et al*, 2009; De Marco *et al*, 2009; Pham *et al*, 2010).

Serology negative blood samples have been screened by nucleic acid amplification technology (NAT) since 2006. To enhance protection from TTI, the routine screening test was combined with NAT which can detect viruses during the window period and help identify donors with occult hepatitis (Allain *et al*, 2004; Liu *et al*, 2006; Carreño *et al*, 2009; De Marco *et al*, 2009; Phikulsod *et al*, 2009; Pham *et al*, 2010). Virus detection in serology negative/NAT positive blood samples is depicted in Table 1. The window period and occult hepatitis cannot be discriminated from each other by this screening program. Further investigation is required to confirm the diagnosis by establishing a complete serologic profile and blood donor follow-up. The Chiron Procleix Ultrio test (Gen-Probe, San Diego, CA) on the TIGRIS platform (Chiron, Emeryville, CA) was used as the routine NAT in 2006. Subsequently, the Roche cobas TaqScreen Multiplex (MPX) test (Roche Molecular Systems, Branchburg, NJ) on the cobas s201 platform (Roche Instrument Center, Rotkreuz, Switzerland) was introduced to the National Blood Center, Thai Red Cross Society. Evaluation of both tests was performed in 2007. The result of one study showed both these tests are acceptable as routine screening tests for TTI (Phikulsod *et al*, 2009) (Table 2). Upon analyzing cost-effectiveness, the routine NAT was abandoned in favor of the Roche cobas TaqScreen Multiplex (MPX) test (Roche Molecular Systems, Branchburg, NJ) on the cobas s201 platform (Roche Instrument Center, Rotkreuz, Switzerland) in 2008.

EXPANDED PROGRAM ON IMMUNIZATION OF HBV VACCINE

The HBV vaccine was approved by the US Food and Drug Administration in 1982 (CDC, 1982). Plasma derived hepatitis B and recombinant yeast derived vaccines have been used in Thailand for more than 25 years. Both vaccines have proven highly effective in preventing HBV infection, including in high risk neonates born to carrier

Table 2
Comparison of nucleic acid amplification technologies (NAT).

Test	Technique	Lower limit of detection [a] (IU/ml)		Sensitivity (%)	Specificity (%)
		HBV	HCV		
Chiron TIGRIS/Procleix Ultrio	Individual sample	10	3	>95	99.9
Roche Cobas s 201/Cobas TaqScreen Multiplex	Pooled sample (1:6)	3	10	>95	99.9

[a]Lower limit of detection, sensitivity and specificity were evaluated by the National Blood Center, Thai Red Cross Society; the serology test served as the gold standard.

Table 3
National HBV vaccine coverage in Thailand.

	HBV vaccine coverage					
Year	1994	1995	1996	1999	2003	2008
Percentage	77.4	88	93.4	95.4	96	98.3

mothers. The plasma derived vaccine has become obsolete. Many reports show HBV vaccination reduces the HBV carrier rate in the general population (Zanetti *et al*, 2008; Liang *et al*, 2009a, b; Ni and Chen, 2010; Park *et al*, 2010). The most effective way to reduce the carrier rate in the population is with mass vaccination of newborns with HBV vaccine at birth. In 1988, the universal HBV vaccination program for newborns in Thailand was started. A pilot project was performed in 2 provinces: Chiang Mai and Chon Buri. The program was expanded to include 10 additonal provinces in 1990 and was expanded to nationwide vaccination in 1992 (Chunsuttiwat *et al*, 1997; Poovorawan *et al*, 2000; Jutavijittum *et al*, 2005). The HBV vaccine is recommended to be administered to all newborns at 0, 1-2, and 6 months. Hepatitis B immunoglobulin (HBIG) was added for newborns of HBV carrier mothers. The combined HBV and DTP vaccine (DTP-HB) was included in the EPI in 2007. The alternative dose administration recommended for newborns is at 0, 2, 4 and 6 months (Bureau of General Communicable Disease, 2004, 2005, 2007, 2008; Tharmaphornpilas *et al*, 2009). To reduce HBV carrier status in high risk newborns an additional monovalent HB vaccine was added at one month for newborns with HBsAg positive mothers (Tharmaphornpilas *et al*, 2009). National vaccine coverage of HBV increased from 77.4% in 1994 to 98.3% in 2005 (Table 3) (Bureau of General Communicable disease, 2004, 2005, 2007, 2008; Tharmaphornpilas *et al*, 2009). The prevalence of HBsAg in the general population had declined to 4% in 2004. In comparison with children born prior to the EPI, those born after the EPI have a lower HBV carrier rate (Chongsrisawat *et al*,

Table 4
Prevalence of coinfection in Thai new blood donors during 2000-2009, *n* (%).

Year	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
Total number	66,340	70,139	73,017	82,818	96,720	84,875	92,460	96,773	84,216	89,311
Type of coinfection										
HBV/HCV	31 (0.047)	33 (0.047)	38 (0.052)	33 (0.040)	42 (0.043)	26 (0.031)	30 (0.032)	19 (0.020)	15 (0.018)	21 (0.024)
HBV/HIV	25 (0.038)	10 (0.014)	11 (0.015)	23 (0.028)	22 (0.023)	21 (0.025)	19 (0.021)	22 (0.023)	20 (0.024)	13 (0.015)
HCV/HIV	32 (0.048)	41 (0.059)	28 (0.038)	31 (0.037)	46 (0.048)	20 (0.024)	19 (0.021)	19 (0.020)	6 (0.007)	11 (0.012)
HBV/HCV/HIV	1 (0.002)	2 (0.003)	6 (0.008)	3 (0.004)	1 (0.001)	1 (0.001)	1 (0.001)	0 (0)	1 (0.001)	0 (0)

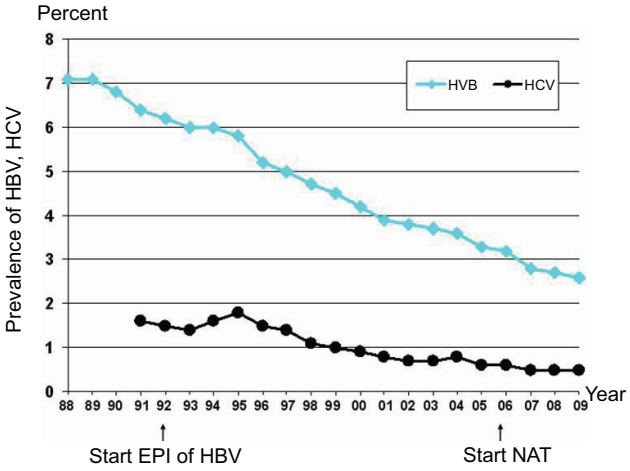

Fig 2–Prevalence of HBV and HCV in Thai new blood donors during 1988-2009 (HCV screening test was started in July, 1990).

2006). The carrier rate of children born after HB vaccine integration into the EPI has declined to 0.7%. Long-term immunity in response to the HBV vaccine has been observed for up to 20 years (Poovorawan *et al*, 2010a,b). Transient infection may have occurred but, no symptomatic cases have been reported (Poovorawan *et al*, 2010, 2011).

PREVALENCE OF HBV AND HCV IN THAI BLOOD DONORS

The prevalence of HBV in Thai new blood donors exceeds that of HCV (Fig 2). In 1978, HBV prevalence amounted to 7.14%, and gradually decreased to 2.63 % in 2009. HCV prevalence was lowest in 1990 (0.12%) according to the HCV screening test started in July. HCV infection prevalence increased from 1.6% in 1991 to 1.86% in 1994, then decreased to 0.51% in 2009. Although the NAT has been used since 2006, no major changes have been observed with either virus. HBV prevalence had reduced considerably faster than HCV. Coinfections have been found among new blood

donors, such as HBV/HCV, HBV/HIV, HCV/HIV and HBV/HCV/HIV (Table 4). Various factors explain the reduction in HBV prevalence. First, Thailand has an effective HBV immunization program and nearly all newborns have received HBV vaccine since 1992; thus, HBV prevalence in the community has drastically declined. Second, several techniques of blood donor screening have been applied to detect infected donors. Finally, all blood donors of the National Blood Center, Thai Red Cross Society have been safe volunteer blood donors since 1987. Blood donor recruitment and screening for HCV is similar to HBV, but HCV prevalence has reduced at a slower rate due to the higher risk of chronic infection and lack of a HCV vaccine. Over the past two decades, blood screening programs and prevention of blood-borne infections in the general population have improved, which eventually may lead to reduced HCV prevalence in new blood donors.

CONCLUSION

Thailand is an area endemic for HBV and HCV. Infected blood donors cause TTI in recipients which may lead to serious complications, such as acute hepatitis, chronic hepatitis, liver cirrhosis and hepatocellular carcinoma. An effective screening program for blood donors is essential to decrease TTI. In order to decrease HBV and HCV prevalence in new blood donors HBV and HCV prevalences have to be reduced in the community.

ACKNOWLEDGEMENTS

We would like to thank the National Blood Center, Thai Red Cross Society for providing the data for this study, the Commission on Higher Education, CU Centenary Academic Development Project, the King Chulalongkorn Memorial Hospital and the Center of Excellence in Clinical Virology, Chulalongkorn University, Bangkok, Thailand for supporting the study. We also thank Ms Petra Hirsch for reviewing the manuscript.

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