
Original Article

Assessment of hepatitis B vaccine-induced seroprotection among children 5-10 years old in Ulaanbaatar, Mongolia

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Summary

Hepatitis B virus infection is a serious public health problem. Mongolia is one of the countries with the highest rates of hepatitis B virus infection in the world. The routine immunization with the hepatitis B vaccine began nationwide in 1991. The purpose of this study was to determine the persistence of seroprotection (anti-HBs ≥ 10 mIU/mL) in children 5-10 years old that were immunized with the hepatitis B vaccine as infants. In total, 438 children were selected from six health facilities in Ulaanbaatar through a multistage random sampling method. Vaccination information was confirmed by checking the vaccination records kept in the health facilities. A blood sample was obtained from each child for anti-HBs, HBsAg and anti-HBc. Of 438 children, five (1.1%) were HBsAg positive and 58 (13.2%) were anti-HBc positive. Sixty infected children were excluded and a total of 378 (86.3%) sera were evaluated. The seroprotective antibodies were detected in only one-fourth of the children at the age of ten. Titres of anti-HBs decreased significantly with age (Linear regression $p = 0.01$). This decrease is primarily due to the rapid decrease in children living in ger areas ($p < 0.001$) compared to children living in apartment areas ($p = 0.152$). On the other hand, children living with higher socio-economic status had more exposure to blood-borne pathogens, probably due to inappropriate health-seeking behaviors.

Keywords: Hepatitis B vaccine, Seroprotection, Mongolia

Introduction

Hepatitis B virus (HBV) infection is a serious public health problem. According to the World Health Organization (WHO), two billion people worldwide have been infected with HBV at some time in their lives (1,2). Of these, about 350 million remain chronically infected and become carriers of the virus (1,2). Every year there are over four million acute clinical cases of HBV and one million die from chronic active hepatitis,

cirrhosis or primary liver cancer (2). Hepatitis B is the only type of chronic viral hepatitis that can be prevented by a vaccine. In 1991, the WHO called for all children to receive the hepatitis B vaccine, and 136 countries added this vaccine to their routine immunization program by the end of 2001 (2,3).

Mongolia included the hepatitis B vaccine in their national immunization program in 1991. Two doses of the vaccine were given at the ages of 0 and 2 months until 1996, then the third dose was added, being given at an age of 8 months. In general, the hepatitis B vaccine is recommended as a three-dose series given at the ages of 0, 1 and 6 months (3). The first dose should be given within 24 hours after delivery, and a total of three doses with an interval of at least four weeks, but not more than two months between the first and second doses, are recommended.

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In Western Pacific Regional countries, where hepatitis B vaccination has been included in national immunization programs routinely, seroprevalence of HBV infection has been reduced by over 85% (from 9.8% to 0.7% in Taiwan, from 11% to 0.7% in Fiji, from 10% to 0% in Singapore, from 16.3% to 3.0% in Vanuatu), whereas in Mongolia, it was estimated to decline by only 50% (from 14-39% in 1989 to 6-7% in 1998-1999) (3,4). The incidence of icteric viral hepatitis in Mongolia has also been reduced by more than two times in general, and the HBV carrier rate has been decreased by 3.3 times in the vaccine-age population since the introduction of hepatitis B vaccination (5). However, HBV infection was still prevalent at a relatively high rate of 10% in apparently healthy individuals in 2002 (6). Furthermore, prevalence of antibody to hepatitis B surface antigen (anti-HBs) induced by the vaccine was only 70.2% among 2-year-old children in rural areas compared to 94.2% among children in urban area (7) because of incomplete vaccination and freezing of the vaccine during transportation (8). Although more than 95% of all children received the hepatitis B vaccine in Mongolia, children in rural areas were less likely to complete the recommended doses than children in urban settings, probably due to seasonal difficulties in locating nomadic households (7).

Although the hepatitis B vaccine is highly effective, the duration of protection and indications for its booster dose need to be further investigated (9-11). A study in Taiwan reported that fifteen years after routine immunization with the hepatitis B vaccine, a large proportion of the children exhibited waning immunity (12). The real threat may emerge in the future when the immunized children become older and begin engaging in sexual activity with generations that still have a high HBV carrier rate. Currently, a booster dose of hepatitis B vaccine after the three-dose routine immunization is not recommended because carriers of the virus are rarely found among children who were immunized 10-15 years previously with hepatitis B vaccine (13-17). However, some reports have suggested that boosters are necessary because of the progressive decline of anti-HBs over time and the potential risk for development of HBV infection (12,18,19). Therefore, efficacy of the vaccine, long-term immunity and necessity of a vaccine booster are important issues in endemic areas.

To the best of our knowledge, there has been no study assessing the duration of seroprotection induced by the hepatitis B vaccine in Mongolia. In this paper, we examined the persistence of seroprotection in 5-10 year old children who were immunized with the hepatitis B vaccine as infants and explored the risk factors affecting the efficacy of the hepatitis B vaccine.

Methods

This study was conducted from January to February 2006

in Ulaanbaatar, Mongolia. Through cluster sampling, we selected three of the nine districts in Ulaanbaatar: Songinokhairkhan, Chingeltei and Baganuur. Areas within the districts can be classified into two distinct categories: apartment areas and ger areas. Two health facilities, one from an apartment area and the other from a ger area, were chosen at random from each selected district. Living conditions of the Mongolian population depend primarily on the type of dwelling. In Ulaanbaatar, *gers* (traditional Mongolian dwellings consisting of tent-like wooden structures covered with felt, without inside hygienic facilities) and *houses* (structures with one or more rooms, some with piped water and/or inside hygienic facilities) co-exist on dirt roads in ger areas. In contrast, *apartments* (structures that are provided with piped water, heating systems, and hygienic facilities) are located in areas that have paved roads and often have local shopping centres (20). Children aged 5 to 10 years who had previously received two or three doses of hepatitis B vaccine were selected from 6 health facilities by reviewing vaccination records. The study population in each health facility comprised six age groups with approximately 72 children in each age group, 36 boys and 36 girls: 5 years, 6 years, 7 years, 8 years, 9 years, and 10 years of age.

The dates of administration, number of doses received, and serial numbers of hepatitis B vaccines were confirmed by checking the vaccination records kept in the health facilities. Detailed information was obtained from the children's mothers by a semi-structured questionnaire that included child's age, sex, date of birth, residence, personal history of blood exposure (e.g. previous blood transfusion, operation, intravenous injection and dental manipulation), family history of liver diseases, experience of home injection and toothbrush sharing, and socio-economic status of the child's parents.

A 5 mL blood sample was obtained from each child to test for anti-HBs, hepatitis B surface antigen (HBsAg) and antibody to hepatitis B core antigen (anti-HBc). All blood samples were delivered to the laboratory in Ulaanbaatar on the same day that the blood was drawn. Serum samples were divided into two labeled, sterile Ependorff tubes to avoid repeated freezing and thawing, then were maintained in long-term storage under deep-freeze conditions until processed. Anti-HBs was quantitatively estimated on a mini VIDAS immunofluorometric autoanalyzer manufactured by bioMérieux, France. Levels of anti-HBs were expressed in milli-international units per millilitre (mIU/mL). The range of reliability of the mini VIDAS autoanalyzer is between 5 mIU/mL and 500 mIU/mL. Values of anti-HBs < 10 mIU/mL were considered un-protective, and values \geq 10 mIU/mL were considered protective. The presence of HBsAg, and anti-HBc were determined with ACON immunochromatographic tests (Acon Laboratories, USA).

Statistical analysis was performed using SPSS 12.0.1

for Windows. Linear regression was used to analyze continuous values of anti-HBs titer. The chi-square test was used to test the strength of the relationship between categorical variables, and a *p*-value below 0.05 was considered statistically significant.

This study was approved by the Ethical Committee of the University of Tokyo, Japan, and Ministry of Health, Mongolia. The purpose of the study was carefully explained to children's mothers and written informed consent to participate in the study was obtained before we started the study. The parents were informed of their child's serological results and hepatitis B vaccine booster inoculations were offered to those with un-protective titres.

Results

A total of 438 children and their 438 mothers participated in this study. Children's age, gender, and place of residence were distributed equally (Table 1). We found that 72.1% of mothers and 59.9% of fathers of study children living in an apartment area

had more than 10 years of education, significantly higher than the parents living in ger areas: 28.8% and 16.2%, respectively (*p* < 0.001; Table 2). Similarly, parents living in apartment areas were more likely to be employed and had higher incomes than those living in ger areas. These results were statistically significant (*p* < 0.001; Table 2).

Of 438 children, 5 (1.1%) were HBsAg positive, indicating current infection or carrier status, and all 5 were male, school-age children (Table 3). Three of the 5 children were also anti-HBc positive. The presence of anti-HBc without HBsAg is indicative of past infection. The overall anti-HBc positive rate was 13.2% (58/438), with 7.9% (12/152) of preschool-age children and 16.1% (46/286) of school-age children testing positive for anti-HBc. There was a significant difference in anti-HBc seroprevalence between children of preschool age and school age (*p* < 0.05; Table 3). Surprisingly, all 60 infected children were documented to have received at least 2 doses of the hepatitis B vaccine.

We excluded the 60 children with evidence of HBV infection from the analysis of vaccine-induced seroprotection. A total of 378 (86.3%) sera were evaluated and titres of anti-HBs decreased significantly with age (Linear regression *p* = 0.01; Table 4). Protective titres (≥ 10 mIU/mL) of anti-HBs were detected in 184 (48.7%) children. There was a significant difference in the percentage of children with protective anti-HBs between age groups: 63.0% for 5-year-olds, 61.2% for 6-year-olds, 58.9% for 7-year-olds, 45.0% for 8-year-olds, 35.5% for 9-year-olds, and 25.0% for 10-year-olds (*P* < 0.001; Table 4). This decrease is primarily due to the rapid decrease in children living in ger areas (*p* < 0.001) compared to children living in apartment areas (*p* = 0.152).

Two children with incomplete vaccination records were excluded from the analysis of seroprotection rate due to vaccination. Of the remaining 376 children without HBV infection, 23.1% received two doses of the vaccine and 76.9% received three doses (Table 5).

Table 1. Study population characteristics (*n* = 438)

		<i>n</i>	%
Gender	Male	222	50.7
	Female	216	49.3
Age in years	5	79	18.0
	6	73	16.7
	7	75	17.1
	8	70	16.0
	9	70	16.0
	10	71	16.2
District	Songinokhairkhan	146	33.3
	Chingeltei	147	33.6
	Baganuur	145	33.1
Residential area	Apartment	220	50.2
	Ger	218	49.8
Activity of child	At home	23	5.3
	At kindergarten	105	24.0
	At school	310	70.8

Table 2. Household socioeconomic characteristics

		Apartment (<i>n</i> = 220)		Ger area (<i>n</i> = 218)		<i>p</i> -value*	
		<i>n</i>	(%)	<i>n</i>	(%)		
Parental educational years	Mother:	≥ 10 years	158	72.1	62	28.8	< 0.001
		< 10 years	61	27.9	153	71.2	
	Father:	≥ 10 years	121	59.9	30	16.2	
		< 10 years	81	40.1	155	83.8	
Parental occupation	Mother:	working	161	73.5	122	56.7	< 0.001
		not working	58	26.5	93	43.3	
	Father:	working	185	91.6	142	75.9	
		not working	17	8.4	45	24.1	
Monthly family income (togrog ^a)	$\leq 70,000$	30	14.1	104	49.3	< 0.001	
	70,001 - 100,000	53	24.9	79	37.4		
	100,001 - 250,000	90	42.3	24	11.4		
	> 250,000	40	18.8	4	1.9		

* By chi-square test; ^a 1000 togrog is equivalent to approximately US\$1.

Table 3. Prevalence of HBsAg and anti-HBc

	Total n (%)	HBsAg n (%)	Anti-HBc n (%)
Total	438 (100)	5 (1.1)	58 (13.2)
Gender:			
Male	222 (50.7)	5 (2.3)	25 (11.3)
Female	216 (49.3)	0 (0)	33 (15.3)
Age groups:			
Preschool-age (5-6)	152 (34.7)	0 (0)	12 (7.9)*
School-age (7-10)	286 (65.3)	5 (1.7)	46 (16.1)
Number of received vaccine ^a :			
2 doses	99 (22.7)	1 (1.0)	12 (12.1)
3 doses	377 (77.3)	4 (1.2)	46 (13.6)
Residential area			
Apartment	220 (50.2)	3 (1.4)	28 (12.7)
Ger	218 (49.8)	2 (0.9)	30 (13.8)

* $p < 0.05$ by chi-square test; ^a 2 children were excluded due to incomplete vaccination records.

Table 4. Distribution of anti-HBs titers in children living in apartment and ger area by age ($n = 378$)

Age in years	Anti-HBs titer		Anti-HBs		Anti-HBs (+)	
	Median	(IQR 25% - 75%)	(-) ^a n (%)	(+) ^b n (%)	Apartment area n (%)	Ger area n (%)
Total	8	(3.0 - 37.0)	194/378 (51.3)	184/378 (48.7)	103/191(53.9)	81/187 (43.3)
5	15	(4.5 - 44.5)	27 (37.0)	46 (63.0)	26 (72.2)	20 (54.1)
6	14	(3.0 - 55.0)	26 (38.8)	41 (61.2)	18 (56.2)	23 (65.7)
7	18	(6.0 - 42.7)	23 (41.1)	33 (58.9)	16 (57.1)	17 (60.7)
8	7	(2.2 - 34.5)	33 (55.0)	27 (45.0)	15 (48.4)	12 (41.4)
9	4	(1.7 - 27.0)	40 (64.5)	22 (35.5)	14 (43.7)	8 (26.7)
10	4	(1.2 - 10.2)	45 (75.0)	15 (25.0)	14 (43.7)	1 (3.6)
<i>p</i> -value	0.01 [†]		<0.001*	<0.001*	NS	<0.001*

IQR: interquartile range; [†] By linear regression analysis; * By chi-square test; ^a Anti-HBs < 10 mIU/mL; ^b Anti-HBs ≥ 10 mIU/mL.

Table 5. Distribution of anti-HBs among children depend on the number of received doses of hepatitis B vaccine

	Total ($n = 376^a$)		<i>p</i> -value*
	2 doses n (%)	3 doses n (%)	
Total	87 (23.1%)	289 (76.9%)	
Age in years:			
5	1 (1.4)	71 (98.6)	< 0.001
6	0 (0)	67 (100)	
7	1 (1.8)	55 (98.2)	
8	10 (16.7)	50 (83.3)	
9	36 (58.1)	26 (41.9)	
10	39 (66.1)	20 (33.9)	
Anti-HBs:			
Total	(-) ^b 66 (75.9) (+) ^c 21 (24.1)	126 (43.6) 163 (56.4)	< 0.001
9 year-olds	(-) 28 (77.8) (+) 8 (22.2)	12 (46.2) 14 (53.8)	0.01
10 year-olds	(-) 32 (82.1) (+) 7 (17.9)	12 (60.0) 8 (40.0)	< 0.05
Apartment area	(-) 26 (65.0) (+) 14 (35.0)	61 (40.7) 89 (59.3)	< 0.01
Ger area	(-) 40 (85.1) (+) 7 (14.9)	65 (46.8) 74 (53.2)	< 0.001

* By chi-square test; ^a 2 children were excluded because of incomplete vaccination records; ^b Anti-HBs < 10 mIU/mL; ^c Anti-HBs ≥ 10 mIU/mL.

There was a significant difference in seroprotection rate (anti-HBs) between children that received two doses (24.1%) and three doses (56.4%) of the vaccine ($p <$

0.001; Table 5). More than half of the children aged nine and ten received only two doses of the vaccine, due to the two-dose policy in effect at the time they were receiving their vaccinations. The protective anti-HBs were detected in a significantly higher proportion of 9-year-olds that received three doses (53.8%) of the vaccine compared to 9-year-olds that received two doses (22.2%; $p = 0.01$; Table 5), and a similar difference was found in 10 year-olds: 17.9% for two doses and 40% for three doses ($p < 0.05$; Table 5). In addition, this difference in protective anti-HBs due to the number of received doses was the same, regardless of living in an apartment area ($p < 0.01$) or in a ger area (< 0.001 ; Table 5).

Of 58 children with evidence of past infection (anti-HBc positive), 23 (39.7%) had protective titres of anti-HBs, and 35 (60.3%) had non-protective titres of anti-HBs (Table 6). The prevalence of potential carriers (positive for anti-HBc, but without protective anti-HBs) was 8% (35/438), and of the suspected 35 carriers, 23 (65.7%) children lived in an apartment area (Table 6). Based on interviews of 434 children, 261 (60.1%) had at least one exposure to a risk factor for HBV infection in the past, such as having a blood transfusion (1.6%), operation (6.2%), intravenous injection (28.9%) or dental manipulation (44.4%; Table 6). In particular, children living in apartment areas were significantly more likely to be exposed to intravenous

Table 6. Comparison of positive cases of anti-HBc and the risk factors between residential areas

	Total n (%)	Apartment n (%)	Ger n (%)	p-value*
Past infected cases:	58/438 (13.2)	28 (48.3)	30 (51.7)	0.001
Anti-HBc (+) and anti-HBs (-)	35/58 (60.3)	23 (65.7)	12 (34.3)	< 0.01
Anti-HBc (+) and anti-HBs (+)	23/58 (39.7)	5 (21.7)	18 (78.3)	
Existence of past exposure:	261/434 (60.1)	151 (57.9)	110 (42.1)	< 0.001
Blood transfusion	7/438 (1.6)	3 (42.9)	4 (57.1)	NS
Operation	27/436 (6.2)	15 (55.6)	12 (44.6)	NS
Intravenous injection	126/436 (28.9)	76 (60.3)	50 (39.7)	< 0.01
Dental manipulation	193/435 (44.4)	114 (59.1)	79 (40.9)	0.001
Sharing toothbrush	50/435 (11.5)	12 (24.0)	38 (76.0)	< 0.001
With family history of liver diseases	180/438 (41.1)	101 (56.1)	79 (43.9)	< 0.05
Practiced injection at home	155/436 (35.6)	95 (61.3)	60 (38.7)	0.001

* By chi-square test.

injection ($p < 0.01$) or dental manipulation ($p = 0.001$) than children living in ger areas. In addition, 41.1% (180/438) of children had family members with a history of liver disease, with a higher proportion (56.1%) found in apartment children compared to ger children (43.9%; $p < 0.05$; Table 6). Also, 35.6% (155/436) lived in families which practiced self injection at home, with 61.3% living in apartment areas and 38.7% in ger areas ($p = 0.001$). There was significant difference ($p < 0.01$) in the history of liver disease between families which practiced injection at home (77/155; 49.7%) compared to families which had never practiced home injection (102; 36.3%).

Discussion

As far as we know, this is the first study designed to determine the long-term persistence of seroprotection induced by hepatitis B vaccination among children aged 5-10 who were immunized as infants in Mongolia. This study revealed that only 48.7% of children had seroprotective antibody levels in connection with hepatitis B vaccination administered 5-10 years earlier. This was higher than a previous study among the immunized 0-7 year olds (39.7%) in Ulaanbaatar in 1998-1999 (21). However, one of our important findings was that the seroprotective rate markedly declined with age so that as time after vaccination increases, the seroprotection rate decreases. The protective anti-HBs were absent in more than half of children at the age of 8, and only 25% of children had seroprotective antibodies at the age of 10. Moreover, the decline occurred earlier than in other countries. Among 10-years-olds who received three doses of the vaccine, 40% had seroprotective antibodies, which was lower than the findings of a study conducted in Taiwan (a hyperendemic country), where a 50% seroprotection rate was found among 13-15 year-old children (11).

A possible reason for the earlier decline of seroprotection was the number of doses received by the children. We found that children vaccinated with three doses had higher titres of seroprotective antibodies than children vaccinated with two doses. The importance of

a third dose for protective anti-HBs was also confirmed by comparisons within the 9-year-old and 10-year-old age groups. The third dose of the vaccine in the infant immunization schedule produces a large and rapid rise in antibody titres and therefore, might be considered as a booster dose (13,22).

This study reported that children living in ger areas were more likely to lose seroprotection than children living in apartment areas. The result is similar to a study among two-year-old Mongolian children comparing urban (Ulaanbaatar) and seminomadic rural areas (7) reporting that rural children had lower seroprotection than urban children. Although our study was carried out only in Ulaanbaatar, infrastructures of ger areas are similar to seminomadic settings and the people are probably living in relatively low socioeconomic conditions, including poor nutrition. Our study reported that people living in ger areas had characteristics associated with low socioeconomic status such as low education level, employment rate and income. In the city, vaccines are distributed from the National Center for Communicable Diseases (NCCD) to each district once a month, to health centers located in both apartment and ger areas monthly, and are stored by the health centers in a refrigerator. Even though there were different formulations of the hepatitis B vaccine, such as Hepavax B, Hepavax Gene, and Engerix B, in use at the time when our study children were born, all children in this study were immunized with the same vaccine in a given month, regardless of living area. None of the children received the hepatitis B vaccine through mobile services. In addition, many studies have shown that high socioeconomic status positively affects health status, morbidity, and mortality (23,24). Thus, we suppose that low socioeconomic status and poor nutrition might affect the persistence of anti-HBs induced by the vaccine.

Although hepatitis B is usually minimally symptomatic in early childhood, the carrier state (the infectious reservoir for hepatitis B) is likely to occur if the infection is acquired at a young age. Our finding of only 1.1% HBsAg seroprevalence shows the substantial improvement in the reduction of HBV infection from

the previous prevalence rate of 2.6% among 0-7 aged immunized children in 1998-1999 (21) and 10% among the healthy adult population in 2002 (6). This would be attributable to two major interventions in the Mongolian health program that began in 1991: the introduction of the hepatitis B vaccine to the national immunization program and an end to the practice of reusing needles for injection. Currently, all such needles are sterile, individually packaged and disposable (25). Also, our finding that none of the 5-year-olds had HBsAg indicates a step towards achieving the Western Pacific Regional goal of reducing HBsAg seroprevalence to less than 1% in 5-year-old children immunized with the hepatitis B vaccine (3,4).

The prevalence of current infection or the carrier state (HBsAg) decreased, however, past infection (anti-HBc) prevalence remained high. A previous study conducted in Mongolia between 1998 and 1999 revealed that the positive anti-HBc rate was 2.6% among 2-year-olds (7) while this study found anti-HBc positive rates of 7.9% in preschool-age children and 16.1% in school-age children. Although these data were derived from different study subjects, the risk of HBV infection appears to increase with age. Moreover, WHO defines children who have positive anti-HBc and negative anti-HBs as low-level HBV carriers with undetectable HBsAg (26). In this study, the prevalence of anti-HBc without anti-HBs was 8%, which was higher than the prevalence reported from a similar study in Taiwan (1.2%) (11). The above findings suggest that Mongolian children were exposed more often to HBV. Children in apartment areas, with comparatively better socioeconomic status, had a higher proportion of anti-HBc without anti-HBs, indicating that they had more exposure to risk factors for blood-borne pathogens than children in ger areas. We speculate that it might be related to frequent dental manipulation, intravenous and unsafe injections, and exposure to infected family members.

In developing countries, most injections are unnecessarily given for nonspecific symptoms such as colds, fatigue, dizziness, diarrhea, abdominal pain, and fever, although oral alternative medicines could be used (24,27). This also occurs in Mongolia. The practice of home injection in our study included 35% of the families, which was similar to the findings of a previous study (27) where 32% of the Mongolian general population living near 20 health facilities occasionally administered injections themselves to relatives at home. Used injection devices were disposed with the home garbage, leading to an increased risk of spreading blood-borne pathogens through unsafe injections and medical waste. Our finding of a higher prevalence of home injections in apartment families might also cause a higher prevalence of liver diseases. A current study in Mongolia reported that hepatitis B accounted for more than one-third of several types of hepatitis (28). Thus,

family members with a positive history of liver disease can be a source of HBV infection to children.

We also revealed that a higher proportion of children in ger areas were sharing toothbrushes with family members, classmates and playmates. This may also be a mode of transmission of the virus through contact with mucous membranes or open skin breaks, since HBV can survive for at least one week on inanimate surfaces (29).

Conclusion

This study has shown that seroprotection induced by hepatitis B vaccination decreases earlier in Mongolian children compared to other hyperendemic countries and that a third dose is important for preserving the efficacy of the vaccine. Children living in poorer areas are more likely to lose the seroprotection, probably due to low socioeconomic status and poor nutrition. However, children living in areas with higher socioeconomic status had more exposure to blood-borne pathogens because of inappropriate health-seeking behaviors such as home injections, frequent dental manipulations and intravenous injections. This study recommends emphasizing the use of disposable medical supplies and appropriate disposal systems, the sterilization of reusable supplies and equipment, and strict adherence to and enforcement of safe and standard medical practices. In addition, community-based education highlighting various modes of transmission and prevention of HBV and the risk factors for blood-borne pathogens is needed for the general population in Mongolia. Finally, further prospective studies are needed to determine the duration of protection, and the necessity and timing of booster doses.

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