Hepatitis B Status of Hmong Patients

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Background: **This study was conducted to determine the hepatitis B status, by age, of Hmong patients attending a St. Paul family practice residency clinic.**

Methods: **The clinic records of 1585 Hmong patients 4 years of age and older were reviewed for information about hepatitis B status. Those without evidence of previous serologic testing or vaccination were invited to participate in the study by being tested for three hepatitis B virus (HBV) markers—hepatitis B surface antigen (HBsAg), antibody to HBsAg (anti-HBs), and hepatitis B core antibody (anti-HBc); those whose results were positive for HBsAg and anti-HBc were also tested for hepatitis B e antigen (HBeAg) and alanine aminotransferase (ALT). Patients whose results were positive for only anti-HBc had their serologic tests repeated after 3 or more months, and those patients whose results remained positive for only anti-HBc were offered the vaccine and further follow-up serologic tests.**

Results: **Of the 434 total participants, 77 (18 percent) had acute or chronic infection (HBsAg present). The rate of infection was highest—28 percent—in the group of patients 15 to 19 years old. Of 66 patients with positive test results only for anti-HBc, 33 of 36 (92 percent) who had follow-up serologic tests after 3 or more months had the same result again in the absence of intervention. Six of 8 (75 percent) patients with results positive only for anti-HBc who received hepatitis B vaccine subsequently converted to an immune status (anti-HBs positive). For all age groups, the cost of pretesting patients with an unknown HBV status and vaccinating susceptible patients was less than the cost of vaccinating without pretesting.**

Conclusions: **This study, which confirmed previous findings of a high occurrence of hepatitis B virus infection in Hmong refugee communities, found the highest rate of infection to be among adolescents. Prevaccination testing appeared to be a cost-saving procedure for patients whose hepatitis status was unknown. (J Am Board Fam Pract 1997;10:322-28.)**

Hepatitis B infection is a growing public health concern in the United States. From 1979 to 1989, the reported incidence of hepatitis B virus (HBV) infection in this country increased by 37 percent, and now approximately 4000 to 5000 people die annually from chronic liver disease related to the hepatitis B virus.[1] Among persons at higher risk for hepatitis B infection are those who have emigrated from high-risk regions of the world, such as Southeast Asia. The prevalence of infectious HBV disease (hepatitis B surface antigen [HBsAg] present) in Southeast Asian refugees entering the United States and other developed countries has ranged from 12 to 14 percent,[2] whereas that of the general adult population of the United States is less than 1 percent. While infectious HBV disease represents a substantial risk for all Southeast Asian emigrants, Southeast Asian children are most endangered by this infection. In Asian countries one quarter to one half of the children who become carriers of hepatitis B die of cirrhosis or primary liver cancer during their adult years.[3] Furthermore, the earlier in life a person is infected with hepatitis B, the greater the likelihood that person will become a chronic carrier.[4]

As a result of these risks, the routine screening of pregnant women of Asian descent for HBsAg has been recommended since 1984, and the prophylactic vaccination of newborns of mothers with HBV has been recommended since 1981.[4] In addition, the universal immunization of all infants regardless of maternal hepatitis B virus status has been recommended by the Centers for Disease Control and Prevention and the American Academy of Pediatrics since the early 1990s.[5] Finally, the Canadian Task Force on the Periodic Health Examination and the US Preventive Services Task Force recommend that all persons exposed to or at high risk for HBV infection receive immunization.[1] The full impact of these recent

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recommendations is not expected to be evident for approximately 25 years.[5]

There is growing consensus that the hepatitis B vaccine should be considered for all children in this country as well as for Asian-American adolescents and adults before they become sexually active.[6] It is not clear, however, which age groups should be serologically tested for HBV before vaccination. This question might be answered by knowing the rate of HBV susceptibility for various age groups, the subject of two recent investigations. A Southeast Asian immigrant population residing in Georgia, which included families from Cambodia, Laos, and Vietnam,[4] showed somewhat lower rates of infectivity than a Hmong immigrant group in Wisconsin.[2] For example, in children younger than 9 or 10 years of age, approximately 20 percent of the Georgia group was infected compared with 25 to 42 percent of the Wisconsin group (in both groups, infection was defined as HbsAg positive or hepatitis B core antibody [anti-HBc] positive). Apart from these studies, there is little available information about the hepatitis B status of various age groups of Southeast Asian refugees. Further, it is likely that the hepatitis B status of immigrant populations changes with time, as more children and adolescents become vaccinated.

This study was conducted at a family practice residency clinic in St. Paul, Minnesota, where approximately 60 percent of the total visits to the clinic were made by Hmong refugees. The procedure used in previous years by this clinic for hepatitis screening and immunization has been as follows. All refugees and pregnant women have been routinely screened for HbsAg since the early 1980s. For those with test results positive for HBsAg, inconsistent attempts have been made to contact family members to request that they be tested and immunized if they are found to be susceptible. Before 1989 all infants born to mothers who tested positive for HBsAg received hepatitis B immune globulin and were begun on the hepatitis B vaccine series. From 1989 to the present, all infants, regardless of their mothers' hepatitis status, have been started on the hepatitis B vaccine series, and as before, those infants whose mothers have tested positive for HBsAg also receive hepatitis B immune globulin. Beginning in 1993, we have attempted to vaccinate nonimmune adolescents seen in the clinic, but this practice has not been consistent for logistic reasons. The current study called for a more consistent effort in screening and vaccinating Hmong children, adolescents, and adults.

The purpose of this study was to determine the hepatitis status, by age, of Hmong patients attending a St. Paul family practice clinic. This information would help us not only to single out susceptible patients requiring vaccination, but also to provide data about the economic usefulness of performing serologic testing before vaccination in various age groups.

Methods

Because all or nearly all patients from this clinic who were younger than 5 years would have received the hepatitis B vaccine through the universal infant vaccination policy of the clinic initiated 5 years earlier, this study targeted Hmong patients 5 years old and older. All such patients who were scheduled to be seen at the clinic for well-child visits or specific health concerns from 17 October 1994 through 16 October 1995 had their charts reviewed before the visit to determine whether they had been previously vaccinated against hepatitis B or had had hepatitis B serologic tests performed. Those without evidence of previous serologic testing or hepatitis B vaccination were assigned to be seen by a Hmong research assistant (a recent medical school graduate) who explained the purpose of the study and asked for their consent to participate. The research assistant also reviewed the charts of Hmong patients who had been seen at the clinic during the previous year and attempted to contact by telephone those who had no evidence of hepatitis B immunity to enlist them in the study.

Initially, the consent process required that the patient or, for patients younger than 18 years, the patient plus a parent sign a consent form before participation. This requirement appeared to make patients overly cautious and was a deterrent to study participation. Consequently, after the second month of the study, the Human Subjects Committee waived the requirement for the participant's signed consent, and verbal consent by the patient (and parent for patients younger than 18 years), witnessed and signed by the research assistant, was considered adequate. Patients who agreed to participate had their blood tested for HBsAg, antibody to HBsAg (anti-HBs), and anti-

Table 1. Hepatitis B Virus Markers and Associated Tests.

Marker or Test	Description
HBsAg (hepatitis B surface antigen)	Indicates infection with hepatitis B virus (HBV)
Anti-HBs (antibody to hepatitis B surface antigen)	Usually indicates immunity to HBV; commonly develops about 5 to 6 months after HBV infection or vaccination
Anti-HBc (hepatitis B core antibody)	Usually develops 6 to 10 weeks after HBV infection as part of immune response; can indicate past or ongoing infection
HBeAg (hepatitis B e antigen)	Marker of the core of the virus—correlates with active viral replication; presence of HBeAg implies a highly infectious state
ALT (alanine aminotransferase)	Marker of hepatocellular dysfunction, which can be caused by HBV

HBc. Those judged to be susceptible to hepatitis B infection (HBsAg negative, anti-HBs negative, anti-HBc negative) were advised to be vaccinated. Patients whose test results were positive for only anti-HBc (HBsAg negative, anti-HBs negative, anti-HBc positive) were asked to return to the clinic for repeated tests in 3 months; those whose results remained positive for only anti-HBc on the second test were then recommended for vaccination and a subsequent qualitative anti-HBs test. For patients with positive test results for HBsAg and anti-HBc, the laboratory was instructed to add measures of the hepatitis B e antigen (HBeAg) and alanine aminotransferase (ALT) to the test profile. Table 1 describes each of the hepatitis B tests used in this study.

During the first month of the study it was very difficult to get patients who had their blood drawn to return to the clinic for their first vaccine. As a result, beginning the second month, we recommended that all patients younger than 18 years be given their first vaccine at the initial visit, after their blood had been drawn. Subsequent vaccines were canceled for those patients who were found to be previously immune or infected. Susceptible patients were asked to return at 1 and 6 months to complete the 3-phase vaccination series.

Patients younger than 18 years who refused or whose parents refused serologic testing were offered the hepatitis B vaccine without previous screening.

Table 2. Characteristics of Nonparticipants.

Characteristics	No.
Charts reviewed, never contacted for study	
Record of previous hepatitis B vaccine	267
Record of natural immunity to hepatitis B	70
Could not be reached by telephone	224
Missed appointment	158
Missed by research assistant in clinic	72
Moved to another clinic	33
Died (gastric and pancreatic carcinoma)	2
Patients contacted who did not participate	
Refused participation	319
Canceled appointment for hepatitis screening	6
Total	1151

Results

A total of 1585 clinic charts were reviewed. Of these charts, 826 patients were never contacted about the study for reasons shown in Table 2. Of the remaining 759 patients who were seen and invited to participate, 325 refused, and 434 agreed to participate, giving a response rate of 57 percent. The participants' mean age was 27.7 years (SD = 17.1); 293 (67.5 percent) were female, and 141 (32.5 percent) were male.

Table 3 shows the hepatitis status of participants by age. Although the study was geared to patients aged 5 years and older, 4 children younger than 5 years whose hepatitis status was unknown were tested and therefore included in the study; all 4 were found to be immune to hepatitis B by previous vaccination (anti-HBs positive). Between the ages of 5 and 14 years, 55 of 104 (53 percent) patients were found to be susceptible to hepatitis B virus (HBsAg negative, anti-HBs negative, anti-HBc negative), and thus were vaccine-eligible. On the other hand, 47 of 104 (45 percent) of the children aged 5 to 14 years were either infected or immune to hepatitis B and, therefore, would not have benefited from the vaccine. Patients from 15 to 19 years of age showed the highest frequency of acute or chronic hepatitis B infection (HBsAg positive)—28 percent compared with 18 percent of the entire sample. For patients aged 20 years and older, 17 per-

Table 3. Hepatitis B Status of Hmong Patients, by Age.

Age (y)	Infectious (HBsAg Positive) No. (%)	Immune (Anti-HBs Positive) No. (%)	Susceptible (All Markers Negative) No. (%)	Anti-HBc Positive No. (%)	Total No.
0-4	0	4 (100)	0	0	4
5-9	2 (7)	12 (40)	15 (50)	1 (3)	30
10-14	13 (1)	20 (27)	40 (54)	1 (1)	74
15-19	15 (28)	17 (31)	20 (37)	2 (4)	54
≥ 20	47 (17)	130 (48)	33 (12)	62 (23)	272
Total	77 (18)	183 (42)	108 (25)	66 (15)	434

cent were infectious and 48 percent were immune to HBV.

Patients With Acute or Chronic Infection

Seventy-seven patients (18 percent) had positive test results for HBsAg, indicating acute or chronic infection. Of the 77 infected patients, 35 had positive HBeAg test results, indicating greater infectivity, and 13 had elevated ALT levels, evidence of hepatocellular dysfunction. Repeated test results for 18 of these patients with HBeAg-positive results after 3 or more months were identical to the initial results in all but 1 patient, whose HBeAg became nonreactive.

Four of the 76 patients who had HBsAg-positive and anti-HBc-positive results also had anti-HBs positive results. Three of these 4 patients who tested positive for all three markers were tested for HBeAg, which was also found to be positive.

Positive Only for Anti-HBc

Sixty-six patients had test results positive only for anti-HBc. Although this group of patients spanned all age categories, most of them were adults; 62 (94 percent) were 20 years old or older (16 were 20 to 29 years old, 19 were 30 to 39 years old, 10 were 40 to 49 years old, 6 were 50 to 59 years old, and 11 were 60 years old or older). Figure 1 displays follow-up testing and vaccination of patients whose test results were positive only for anti-HBc. Thirty-seven of the 66 patients had one to two follow-up serologic tests, with a mean time lapse of 4.5 months between the first and second test. For 33 of these 37 patients, the first set of follow-up test results remained the same (positive only for anti-HBc); 3 of the remaining 4 patients converted to anti-HBc positive, anti-HBs positive spontaneously, and 1 converted after vaccination. Of 7 patients who received hepatitis B vaccine after their second positive anti-HBc test result, 5 had results that converted to anti-HBs positive, anti-HBc positive, and 2 had results that remained positive only for anti-HBc. Of the 8 patients with results positive only for anti-HBc who received hepatitis B vaccine and subsequent serologic testing, 6 (75 percent) converted to an immune state.

Immunization of Participants

Of the 174 patients who were found to be susceptible (all 3 markers negative) or possibly susceptible (positive only for anti-HBc) to HBV, 129 received hepatitis B vaccine during the course of the study (63 received all 3 vaccines; 41, 2 vaccines; and 25, 1 vaccine during the course of the study).

Discussion

Hepatitis B infection was quite prevalent in this population, as seen by the 18 percent frequency of HBsAg positivity, a rate slightly higher than the 15 percent figure cited by the Centers for Disease Control for Hmong immigrants in this country.[6] Within this population, the group of adolescents aged 15 to 19 years had the highest rate of infection—28 percent. Although this study did not examine mechanisms for hepatitis B transmission, possible causes for this observed increased rate of infection among adolescents include sexual activity and use of nonsterile acupuncture needles. This finding points to the need to vaccinate Hmong children before they reach adolescence.

Evidence of current or past infection among younger children, though less common, was not

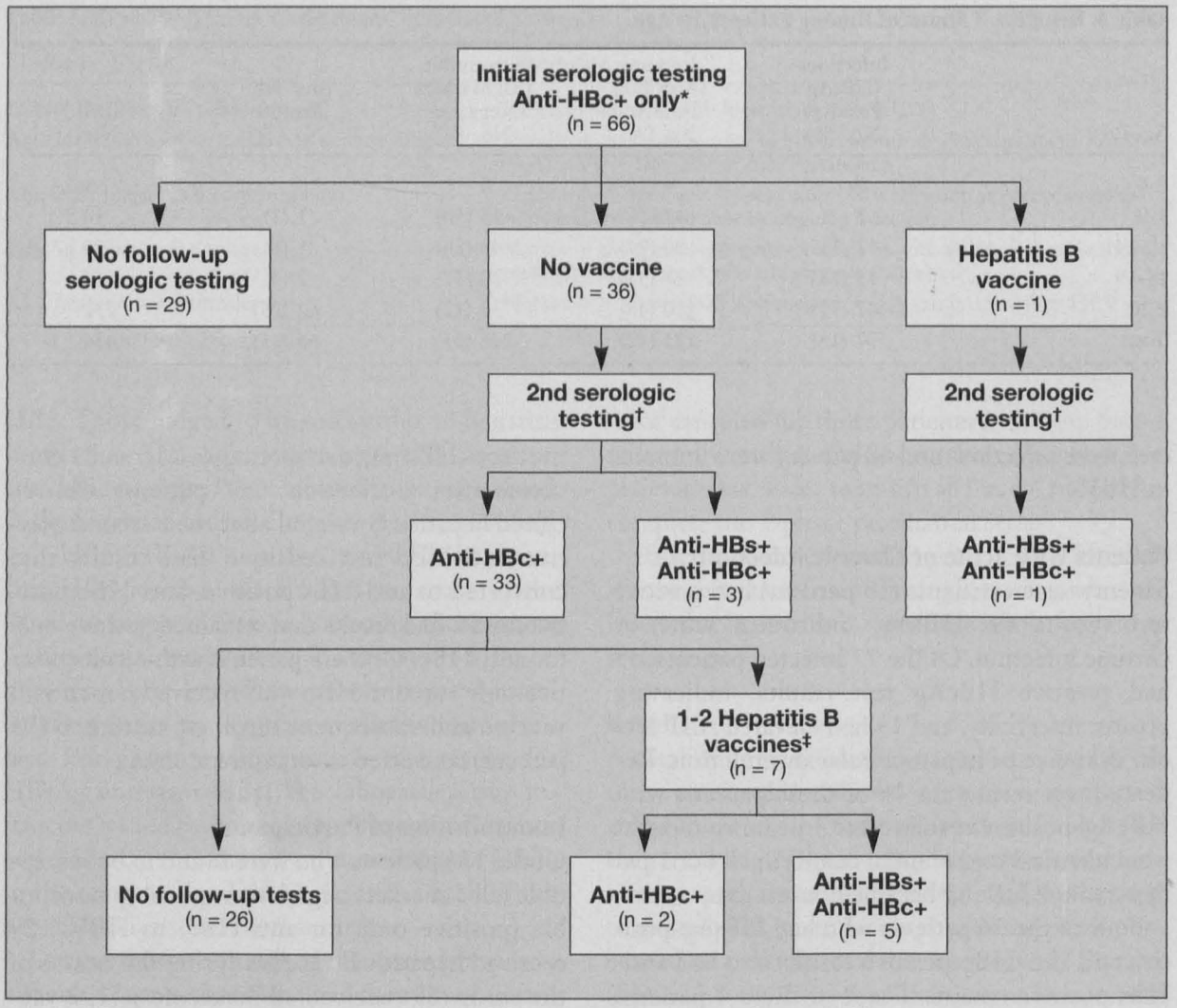

Figure 1. Follow-up of patients with test results positive for anti-HBc only.

*HBsAg negative, anti-HBs negative, anti-HBc positive.
†Mean elapsed time between first and second serologic testing was 4.5 months.
‡Mean elapsed time between second and third serologic testing was 8.7 months.

unusual. In fact, only 53 percent of children 5 to 14 years of age remained susceptible to the hepatitis B virus and would therefore have benefited from the vaccine. Given the high cost of administering the vaccine series at the time of the study ($255 for a child 12 years and younger, and $385 for an adult) and the comparatively low cost of testing for the three hepatitis markers ($56), it appears that in this community pretesting all vaccine candidates (with the exception of newborns) would be more cost-effective than administering the vaccine without previous testing (Table 4). Prevaccination testing is not likely to be cost effective for low-risk populations, however.[7]

Health care providers often question which serologic markers should be used to screen for hepatitis B. The answer to this question depends somewhat on the purpose of screening. If one wishes to know whether a patient is currently infectious—valuable information for a pregnant woman who might expose her newborn—it would be most important to screen for HBsAg. If, on the other hand, one wishes to know whether the patient could potentially benefit from the hepatitis B vaccine (ie, has neither been previously infected or immunized), HBsAg and anti-HBs determinations would both be relevant.

Whether anti-HBc should be added to the screening profile depends on the clinical importance of the state reflected by test results positive only for anti-HBc. Several investigators have speculated about the importance of this serotype,

Table 4. Costs for Pretesting or Vaccinating Compared With Vaccinating Only (n = 434).

Age Group (y)	Pretesting All and Vaccinating Susceptible Patients	Cost ($)	Vaccinating All	Cost ($)
0-9	Pretesting—$56 × 34*	1,904		—
	Vaccinating—$225 × 16†	4,080	$225 × 34*	8,670
	Total	5,984		8,670
10-15	Pretesting—$56 × 128*	7,168		—
	Vaccinating—$385 × 63†	24,255	$385 × 128*	49,280
	Total	31,423		49,280
≥ 20	Pretesting—$56 × 272*	15,232		—
	Vaccinating—$385 × 95†	36,575	$385 × 272*	104,720
	Total	51,807		104,720

*Total number of participants in age group.
†Total number susceptible in age group.

and have suggested that it could be due to previous HBV infection with undetectable levels of anti-HBs (either a window phase of recovery or a distantly immune state), chronic HBV infection without detectable HbsAg levels (a carrier state), or cross-reaction with other agents (false positive).[8-10] In this study, 6 of 8 patients who had test results positive only for anti-HBc responded to hepatitis B vaccine by converting to anti-HBs positive. It seems, therefore, that in our population the distantly immune state was the most common explanation for test results positive only for anti-HBc. We do not know whether these patients would have been protected from HBV with their own low natural antibody titers, and if not, whether the boosted immunity conferred by vaccine would have been lasting. These questions should be investigated in future studies. On the surface, however, it appears that vaccinating Hmong patients whose test results are positive only for anti-HBc might be beneficial.

Other confusing serologic outcomes include the coexistence of HBsAg and anti-HBs, which occurred in 4 of our patients. Sjogren[8] believes that this uncommon picture at times represents low levels of heterotypic antibody and is of no major clinical importance. At other times, it might indicate a disturbed immunologic response, an immunocomplex formation, or an association with renal disease. In this population, 3 of 4 patients who had positive test results for all three markers also had HBeAg-positive results; therefore, patients in our study who had positive test results for all 3 markers (HBsAg positive, anti-HBs positive, anti-HBc positive) had a high likelihood of being infectious.

Limitations of this study include its single geographic location and its modest response rate, the latter resulting from the reluctance of this population to undergo procedures, including venipunctures. Nevertheless, our finding of an 18 percent overall rate of infection—identical to the Wisconsin rate[2]—suggests that these patients might indeed be representative of Hmong immigrants in the Upper Midwest.

These data document the prevalence of hepatitis B infection in a Hmong refugee community and the usefulness of prevaccination screening for all patients (except newborns) for whom hepatitis B serologic or vaccination information is not available. The study also underlines the importance of vaccinating Hmong children against hepatitis B before they reach adolescence, a stage associated with relatively high rates of infection.

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