

Hepatitis B Virus Infections in Americans
in Southeast Asia

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OBJECTIVE: To determine the epidemiology of hepatitis in American military personnel exposed to populations with endemic hepatitis and a high prevalence of HB_sAg carriers.

BACKGROUND: Until recently only historical evidence was available to document infection with agents causing viral hepatitis. In the past 10 years, however, investigations of hepatitis B, initially stimulated by the discovery of hepatitis B surface antigen, have provided serological evidence of infections with hepatitis B virus in a number of populations. In tropical Southeast Asia studies at the SEATO Medical Research Laboratory have documented serological evidence of prior HBV infection in up to 75% of Bangkok residents and a carrier prevalence of HB_sAg of approximately 9% (1). In recent years a large number of Americans, largely military personnel, have been stationed in Southeast Asia. These Americans came from an area in which HB_sAg is found in only 0.1 to 1.0% of the population and evidence of prior HBV infection in only 5 to 20% (2, 3).

A study of Americans entering and leaving the Republic of Vietnam in 1970 showed that troops arriving for an initial tour and those leaving after approximately one year had had equal experience with hepatitis B virus (Table 1). Troops arriving in Vietnam for a subsequent tour, however, had significantly greater experience with hepatitis B virus. The data suggested that previous experience in Vietnam was related to a greater experience with hepatitis B virus. This study was designed to determine the environmental and host factors which lead to the development of clinical and subclinical hepatitis among American troops in Southeast Asia.

DESCRIPTION: A description of the design of this study appeared in the SEATO Medical Research Laboratory Annual Report 1973-1974. Briefly the population studied was drawn from servicemen aged 18-25 years in grades E1-E5 entering either the United States Army Support Group, Thailand or the United States Air Force 635th Combat Support Group. Shortly after arrival in Thailand a questionnaire was administered to these men to determine, among other things, their previous duty station, previous tropical experience and their prior experience with hepatitis. During the ensuing year these men were interviewed three times at approximately four month intervals. The interviews contained questions of social behavior and medical experience. Serum samples were collected at the time of each interview and were submitted for detection of hepatitis B surface antigen (HB_sAg) by complement fixation (CF), immunoelectrophoresis (IEOP) and radioimmune assay (RIA). Antibodies against hepatitis B surface antigen (anti-HB_s) were detected by a radioimmune assay inhibition (RIAI) and confirmed and titered by a passive hemagglutination test (PHA). Methods for these assays have appeared elsewhere (SEATO Medical Research Laboratory Annual Reports 1971-1972, 1972-1973 and 1973-1974).

PROGRESS: Subjects were enrolled in this study between April and December 1972. Initial questionnaires were completed in December 1972. The first of three follow-up interviews was completed in April 1973, the second in August 1973 and the third in December 1973. The three follow-up interviews and bleeds were divided according to timing into groups. The time of the first interview fell between 12 and 24 weeks (3 and 6 months), the second between 24 and 38 weeks (6-9.5 months) and the last between 39 and 65 weeks (9.5-16 months). Individuals whose interviews fell outside of these time periods were excluded from the study. With these stipulations, there were 418 individuals who completed the

initial questionnaire and from whom blood was obtained. Of these, 385 (92%) were seen at the first follow-up, 317 (76%) at the second and 326 (78%) at the third. Two hundred and seventy-one people (61%) were completely followed with all three interviews and bleeds. Table 2 shows the prevalence of past experience with hepatitis B virus at each bleed and the incidence of infection for the period of time from the first bleed. Table 3 shows similar data for 271 people who were completely followed with all three interviews and four bleeds.

Table 1. Evidence of Hepatitis B Virus Infection in American Military Personnel in the Republic of Vietnam

Military Personnel	HB _s Ag	Anti-HB _s
Inprocessing		
Initial tour	0.39% (4/1004)	3.50% (7/200)
Subsequent tour	2.42% (7/289)	11.28% (22/195)
Outprocessing	0.46% (5/1072)	3.1% (6/189)
TOTAL	0.68% (16/2365)	6.0% (35/584)

Table 2. Experience* with Hepatitis B Virus in American Enlisted Men at Three Month Intervals Throughout One Year's Tour in Thailand

Bleed	1st	2nd	3rd	4th
Weeks in country	0	13-25	26-39	40-65
Total number studied	418	385	316	326
Persistent evidence	—	16 (4.2%)	15 (4.8%)	14 (4.3%)
Incidence	—	8 (2.0%)	12 (3.7%)	17 (5.2%)
Prevalence	18 (4.3%)	24 (6.2%)	27 (8.5%)	31 (9.5%)

* Experience is determined by presence of HB_sAg or anti-HB_s.

Table 3. Experience with Hepatitis B Virus in 271 American Enlisted Men Completely Followed Throughout One Year's Tour in Thailand

Bleed	1st	2nd	3rd	4th
Weeks in country	0	13-25	26-39	40-65
Persistent evidence	—	13 (4.7%)	13 (4.7%)	13 (4.7%)
Incidence	—	7 (2.5%)	12 (4.4%)	16 (5.9%)
Prevalence	13 (4.7%)	20 (7.3%)	25 (9.2%)	29 (10.7%)

Three hundred and twenty-six individuals were followed with at least a first and a fourth bleed. At the risk of falsely inflating the prevalence and incidence of hepatitis B infection, six additional individuals were added. These six men were followed with at least two bleeds; three had evidence of prior HBV infection on the first bleed and three developed antibody during the study. Table 4 illustrates the number of HBV infections recorded in these 332 men over the one year period.

Table 4. Hepatitis B Infections Recorded in 332 American Enlisted Men Followed Through One Year's Tour of Duty in Thailand

HBV Serology	Follow-up Blood Sample				
	1st	2nd	3rd	4th	Total
HB _s Ag positive	2 (0.6%)	1 (0.3%)	3 (0.9%)	4 (1.2%)	10 (3.0%)
Anti-HB _s positive	16 (4.8%)	7 (2.1%)	5 (1.5%)	5 (1.5%)	33 (9.9%)
Total HBV Experience (HB _s Ag + Anti-HB _s)	18 (5.4%)	8 (2.4%)	7*(2.1%)	8*(2.4%)	41 (12.3%)

* Two persons who developed antigen followed by antibody are counted only once in the total HBV experience.

Six clinical cases of hepatitis were diagnosed in these 332 men during the periods between bleeds (Table 5). There were four individuals in whom clinical hepatitis was associated with HBV. No HB_sAg was identified in one of these but anti-HB_s developed in the convalescent period by the time of the second bleed. In the second case, HB_sAg was detected in the second blood specimen at the time of clinical disease and anti-HB_s was found in the third. The two remaining cases were diagnosed in the third period; in both of them HB_sAg was detected in the fourth blood sample. No further follow-up samples were obtained from either of them. There were two cases of hepatitis diagnosed with no detectable evidence of HBV infection. These are listed as HBV non-associated hepatitis; however, these individuals may have had HBV infections which might have been detected by more sensitive tests.

In this group of 332 men, HBV associated hepatitis was diagnosed in four of them. Serological evidence of inapparent infection was documented in an additional 19 men. The incidence of HBV infection over the one year period was 23/332 or 6.9% and the apparent to inapparent infection ratio was 4:19.

In analysing these figures, those men who were entering a tropical area for the first time were compared to those who had prior experience in the tropics. Tables 6 and 7 document the differences seen in these two groups.

Table 5. Clinical Hepatitis Infections Recorded in 332 American Enlisted Men Followed Through One Year's Tour of Duty in Thailand

Type of Hepatitis	Four Month Interval			
	1	2	3	Total
HBV Associated	1	1	2	4
HBV Non-associated	1	1		2
Total Clinical Hepatitis	2	2	2	6

These data have been coded for computer analysis. Cross tabulations of hepatitis experience with variables, such as drug use, mixing with the indigenous population and sexual experience will be computed to determine if hepatitis in these troops is associated with any identifiable behavioral pattern.

DISCUSSION: In a group of 332 young American military personnel followed in Thailand, clinically recognizable hepatitis occurred in six (18/1000) over a one year period. Of these six, four (12/1000) had detectable serological evidence of association with hepatitis B surface antigen, the remaining two did not. Screening of these men for the development of HB_sAg or anti-HB_s revealed an additional 19 who had inapparent hepatitis B infection. Thus for HBV infections the apparent: inapparent ratio was as high as 4:19 or nearly 1:5. In other words, 82% of all HBV infections were asymptomatic.

The men in this study demonstrated a direct relationship between previous tropical experience and prior HBV infection as was found in the earlier study in Vietnam. In men without serological evidence of prior HBV infection, however, the incidence of new infection during the current study period was the same, whether or not they had previous tropical experience.

Information on the association of hepatitis B virus infection with social and physical behavior has not yet been analyzed. It is possible that routes of transmission of hepatitis B virus between indigenous populations and United States military personnel may be demonstrated and ways of preventing this infection may be suggested.

Table 6. Prevalence of Demonstrable Experience with Hepatitis B Virus on Entering Thailand: A Comparison of Those With and Without Prior Experience in a High Prevalence Area

Prior Experience	Number of Men	HB _s Ag	Anti-HB _s	Total HBV Experience
Yes	119	2 ^a (1.6%)	11 (10.1%)	13 (10.9%)
No	213	0 (0.0%)	5 (2.3%)	5 (2.3%)
Total Population	332	2 (0.6%)	16 (4.8%)	18 (5.4%)

a. One man had HB_sAg with a complement fixing titer of 1:64 and carried it throughout his stay in Thailand. The carrier rate = 0.3%

Table 7. Incidence of HBV Infection During a One Year Tour in Thailand: A Comparison of Those With and Without Prior Experience in a High Prevalence Area

Prior Experience	Number of Men Susceptible	HB _s Ag	Anti-HB _s	Total HBV Experience
Yes	105	1 (1.0%)	7 (6.6%)	8 (7.6%)
No	208	5 (2.4%)	10 (4.8%)	15 (7.2%)
Total Population	313	6 (2.0%)	17 (5.4%)	23 (7.3%)

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