Hepatitis B Virus Infection Among Americans Residing in Southeast Asia

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OBJECTIVE : To determine the incidence of Hepatitis B virus (HBV) infections in Americans exposed to a population with endemic hepatitis and a high prevalence of Hepatitis B surface antigen (HB_SAg) carriers.

BACKGROUND : Until recently only clinical evidence was available to document infection with agents causing viral hepatitis. Over the past several years, however, the development of new serological tests has allowed for the detection of past infection with HBV. Data has been accumulated on the prevalence of HBV infections in various populations. Epidemiological investigations in Bangkok, Thailand, showed that almost ten percent of an urban Thai population were carriers of HB_SAg and that almost 50% had evidence of HBV infections at some time in the past. Age specific prevalence of infection with HBV in this population increased until the age of 15 at which point it reached a plateau at approximately 70% (1). Studies of rural Thai populations have shown similar age acquisition curves for HBV infection (2).

In recent years, large numbers of Americans, mostly military personnel, have resided in Southeast Asia. These Americans came from an area in which HB_SAg has been found in only 0.1 to 1.0% of the population and evidence of HBV infection has been found in only five to twenty percent (3, 4.)

This study was designed to determine the risk of becoming infected with hepatitis B, to define environmental and behavioral factors which increase the risk of infection, and to determine the ratio of clinically apparent to inapparent infections in a population of American enlisted men residing in Thailand,

DESCRIPTION : A description of the design of this study appeared in the SEATO Medical Research Laboratory Annual Report 1974-1975.

Subjects : Subjects were drawn from service men aged 18-27 years in enlisted grades E 1-E 5. These men were assigned to either the United States Army Support Group, Thailand or the United States Air Force 635 th Combat Support Group. Shortly after arriving in Thailand a questionnaire was administered to volunteers to determine personal, demographic and medical information. During the ensuing year these men were interviewed three times at approximately four month intervals regarding social, behavior and medical problems.

Serology : Serum was obtained initially and at the time of each interview. Serum was tested for HB_SAg by a counterimmunoelectrophoresis (CIEP) technique (SEATO Medical Research Laboratory Annual Report 1973-1974) and a commercially available radioimmune assay AUSRIA (Abbott Laboratories) using appropriate absorption procedures (1). CIEP positive sera were subtyped for HB_SAg determinants d. y, w and r, using a immunodiffusion technique (SEATO Medical Research Laboratory Annual Report 1972-1973). Antibody to HB_SAg (anti-HB_S) was detected by a commercially available radioimmune assay (AUSAB, Abbott Laboratories). This test was confirmed by a passive hemagglutination test using red blood cells coated with purified HB_SAg of subtype ad (Electronucleonics Laboratories) or by inhibition of the radioimmune assay by absorption of antibody activity with

HB_SAg. All sera from each individual found to have HB_SAg or anti-HB_S at any time were retested simultaneously. The presence of either HB_SAg or anti-HB_S was taken as evidence of prior infection. Sequential sera from a sub-set of the men followed for one year in Thailand were submitted to the Walter Reed Army Institute of Research (WRAIR) to be screened for antibody to Hepatitis B core antigen (Anti-HB_C). Screening was done by a Radioimmuno assay Inhibition test developed at WRAIR.

PROGRESS :

Study Sample : Subjects were enrolled in this study between April and December 1973. Initial questionnaires were completed in December 1973 and the three follow-up interviews were completed in April, August, and December 1974 respectively. The first interview occurred 12 to 24 weeks, the second 24 to 38 weeks, and the last 39 to 65 weeks after entering Thailand. Individuals who missed interviews or whose interviews fell outside of the established time periods were considered incompletely collected for purposes of this study.

Demographic Data : There were 413 men who completed the initial questionnaire and submitted blood shortly after their arrival in Thailand. Examination of the questionnaires showed that 78 % were white, 21 % were black, and 1 % were oriental. Although the age range was set from 18 through 27 years, over 80 % of the men were between the ages of 20 and 24 years. Three quarters of the men had graduated from high school while five percent had completed college. Seventy-three percent of the men were enlisted rank E 4 and above, but 12.5 % were E 2 reflecting the number of recently enlisted personnel.

Approximately 60 % of the men were enlisted in the Army, and the remainder were in the Air Force. The Air Force personnel tended to be older ; all of the men in grade E 2 were in the Army. All of the Air Force and approximately two thirds of the Army were stationed in a large military complex on the east shore of the Gulf of Thailand near the town of Sattahip. The bulk of the remaining Army personnel were located in Bangkok, but a few were stationed at military posts further to the north. Contact with Thai civilians was available to all of these men.

Of the 413 men initially studied, 376 (91 %) were seen at the first interview, 340 (83 %) at the second, 326 (79 %) at the third (Table 1). Some men were lost to follow-up due to curtailment of assignment in Thailand or to temporary duty elsewhere. There were 271 men who were followed at all interviews (Table 2).

Table 1. Experience with Hepatitis B Infection Among American Enlisted Men Followed at Four Month Intervals for One Year

Observation	Initial	1st Interview	2nd Interview	3rd Interview
Weeks in Thailand	0	13-25	26-39	40-65
Total number studied	413	376	340	326
Prior HBV infection	31 (7.5)*	28 (7.4)	26 (7.6)	21 (6.4)
Acquired HBV infection	—	11 (1.9)	14 (4.1)	20 (6.1)
Total HBV infection	31 (7.5)	39 (10.3)	40 (11.8)	41 (12.5)

* Percent of total number studied enclosed in parentheses

Table 2. Experience with Hepatitis B Infection Among 271 American Enlisted Men Followed at Four Month Intervals for One Year

Observation	Initial	1st Interview	2nd Interview	3rd Interview
Weeks in Thailand	0	13-25	26-39	40-65
Prior HBV infection	17 (6.2)*	17 (6.2)	17 (6.2)	16 (5.8)
Acquired HBV infection				
By interval	–	7 (2.5)	5 (2.0)	6 (2.2)
Cumulative	–	7 (2.5)	12 (4.5)	18 (6.7)
Total HBV infection	17 (6.2)	24 (8.7)	29 (10.7)	34 (12.5)

*Percent of total number studied enclosed in parentheses

Prior Infections: Evidence of prior infections with HBV was detected in 31 (7.5%) of the 413 men studied on arrival in Thailand (Table 1). Examination of questionnaires revealed that 156 (38%) of these men reported a previous Asian assignment. HBV infections were significantly associated with experience in Asia (Table 3).

Table 3. Prevalence of Experience with Hepatitis B Infection Among 413 American Enlisted Men on Entering Thailand: The Importance of a Prior Asian Tour

Prior Asian Tour	Prior Hepatitis B Experience		
	Yes	No	Total
Yes	20	136	156
No	11	246	257
Total	31	382	413

Chi square (1 df) = 9.0053
$p > 0.05$

New Infections: There were six men who were hospitalized for icteric hepatitis during their one year in Thailand. If the 413 men initially studied were taken as the largest denominator, the minimum attack rate for clinical hepatitis was 14.6 cases/1000 men/year. Five of the six clinically apparent cases of hepatitis proved on serological testing to be HBV infections. In twenty additional men HBV infections were identified serologically by the development of either HB_SAg and/or anti-HB_S. Although these twenty infections were clinically mild, four men reported non-

specific symptoms at approximately the time of infection. Thus, 83.3% of clinically diagnosed viral hepatitis in this group of young men during one year in Thailand proved to be HBV infections. The ratio of clinically inapparent to apparent HBV infections was 4 : 1, only 20% of HBV infections in this population manifested themselves clinically.

Development of HB_SAg : HB_SAg was detected in ten individuals at one time or another during the observation period. In two people, HB_SAg was detected in the initial serum. One, a 19 year old white man, had cleared the HB_SAg and developed anti-HB_S by the first interview, four months after his arrival in Thailand. This man had been hospitalized for hepatitis just before coming to Thailand and admitted intravenous drug use prior to becoming ill. The second, a 22 year old black man, carried HB_SAg throughout his tour in Thailand. He denied any prior drug use or clinical hepatitis.

HB_SAg was first detected in eight individuals while they were residing in Thailand. HB_SAg was found in serum of one individual at the first follow-up bleed, three individuals at the second, and four at the third. All four of the men who developed antigen at the first and second follow-up bleed had cleared the antigen by the subsequent bleed and three of the four had developed anti-HB_S.

Subtypes of HB_SAg : Of the ten HB_SAg detected, subtypes were identified in six. Two were from individuals in whom antigen was detected upon arrival in Thailand. In the long term carrier, adw was detected while ayw was found in the man recovering from hepatitis. In four of the eight men who developed HB_SAg while in Thailand, adr was identified.

Antibody to Hepatitis B Core Antigen : Sequential sera from 334 men were submitted for anti-HB_C screening Anti-HB_C was found in the initial sera of 19 of these men. It was associated with anti-HB_S in 15 individuals. In three sera, anti-HB_C was detected alone ; in ten sera only anti-HB_S was found (Table 4).

Table 4. Frequencies of HB_SAg, Anti-HB_S and Anti-HB_C in Sera Collected on Arrival in Thailand from 334 American Enlisted Men

	Anti-HB_C		Total
	Positive	Negative	
HB_SAg Positive	1	1	2
HB_SAg Negative			
Anti-HB_S Positive	15	10	25
Anti-HB_S Negative	3	304	306
Total Studied	19	315	334

The two individuals in whom HB_SAg was identified on arrival in Thailand were included in the 334 men tested for anti-HB_C. Anti-HB_C was found only in the initial blood of the 22 year old

HB_SAg / adw carrier. In the 19 year old who was convalescing from HBV infection, anti - HB_C had appeared by the end of the first four months at a time when the HB_SAg had been replaced by anti - HB_S.

Among the 334 men screened for anti - HB_C, 24 developed HBV infection while in Thailand as evidenced by the appearance in their serum of HB_SAg and/or anti - HB_S. In two men, transferred to Thailand from Vietnam, anti - HB_C appeared in the initial serum four months prior to the time when anti - HB_S was detected. These men clearly had developed their HBV infections prior to entering Thailand despite the fact that the anti - HB_S was not present at the time of their arrival.

In eight of the remaining 22 men who developed HBV infection, HB_SAg was detected. Anti - HB_C was demonstrated in only three of the eight at the time the antigen was detected. In four of the eight, HB_SAg was first detected in serum collected at the last follow - up interview and no further follow - up could be carried out,

In the four men who could be followed HB_SAg had cleared by the time of the subsequent bleed. Although anti - HB_S was detected in only three of these men anti - HB_S was present in all of them by this time. Seventeen men developed anti - HB_S. Anti - HB_C was found, usually in the same sera, in 12 of them ; in five, however, no evidence of anti - HB_C could be found. Once anti - HB_C was detected in an individuals serum, it was found to be present in all subsequent sera tested. Although the identification of anti - HB_C indicated an alteration of the time of infection in a few cases, screening for this antibody did not diagnose any additional infections other than those detected by HB_SAg and / or anti - HB_S,

HBV infections and Behavioral and Environmental Factors : Two hundred and seventy one men were studied four times at the correct intervals during their one year assignment in Thailand. Seventeen (6.3%) had experienced hepatitis B infection prior to their assignment but 18 (6.7%) acquired HBV infections while in Thailand (Table 2). Figures for the acquisition of HBV infection in 271 individuals who were completely followed were not statistically different from those obtained from men bled at each interview, suggesting that the acquisition of hepatitis B infection in Thailand was not related to any behavior which led to curtailment of assignment.

Among the 271 men, the incidence of hepatitis B infections was approximately equal for each four month period (Table 2). However, if the population was limited to the 167 men who had no previous Asian experience, a difference in the incidence for each time period could be defined (Table 5). This difference probably reflected the large number of men who had been directly transferred to Thailand from elsewhere in the Far East and who may have been exposed to HBV prior to their arrival in Thailand.

Table 5. Experience with Hepatitis B Infection Among 167 American Enlisted Men with no Asian Experience Studied at Four Month Intervals for One Year

Observation	Initial	1st Interview	2nd Interview	3rd Interview
Weeks in Thailand	0	13 - 25	26 - 39	40 - 65
Acquired HBV infection Cumulative	–	1 (0.6)	3 (1.8)	6 (3.6)

Questionnaire and interview data on these 271 men were examined for patterns of behavior which were associated with the development of HBV infections in Thailand. There was no statistically apparent relationship between the development of HBV infection and age, rank, educational level or marital status. Blacks enlisted in the Army tended to have an increased risk of infection. Two patterns of behavior, which may be related, were statistically associated with HBV infection : residence in the Thai community, off post, and the use of drugs, especially cannabis.

SUMMARY : A group of American enlisted men were followed at four month intervals for a one year period in Thailand. The prevalence of prior HBV infection in these men was 7.5 %. HBV infection was significantly associated with prior Asian experience. The incidence of HBV infection among men in this group with no prior Asian experience was 6 %, with 90 % of infections falling after the sixth month. Residence in the Thai community and to a lesser extent drug use, especially cannabis, significantly increased the risk of HBV infections in these men. Clinical evidence of disease was only found in 20 % of those individuals who experienced HBV infections in Thailand.

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