

The Epidemiology of Viral Hepatitis in Americans in Southeast Asia

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OBJECTIVE : To study the epidemiology of hepatitis in American military personnel exposed to populations with endemic hepatitis and a high prevalence of hepatitis B surface antigen (HB_s Ag) carriers.

BACKGROUND : In order to make decisions about disease control, the epidemiology of the disease must be understood. Viral hepatitis has long been a major military problem. In the Vietnam conflict, it was the second most frequent cause for the loss of man hours. Until recently, only historical evidence was available to document infection with agents causing hepatitis. In the past decade, however, serological tests have been devised which identify both hepatitis A and hepatitis B virus infection. This report is the conclusion of a study reported in previous annual reports (1). Here we report data on the subtype specificities of antibody to hepatitis B surface antigen (anti-HB_s) in those people who developed antibody, a partial analysis of behavioral patterns associated with the development of hepatitis B and data on the incidence and prevalence of hepatitis A infections.

METHODS : Subjects were drawn from servicemen aged 18-27 years in enlisted grades E-1 to E-5. These men were assigned to 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 volunteers to determine personal demographic and medical information. During the ensuing year these men were interviewed 3 times at approximately 4 month intervals regarding social, behavior and medical problems. Serum samples were collected at the time of each interview and submitted for serological tests for evidence of hepatitis A and B virus infections. Data on the prevalence and incidence of HBV infections were presented previously (1).

The radioimmune assay inhibition test used to identify the subtype of anti-HB_s was similar to that published by Hoofnagle et al. (2). This utilized the commercially prepared solid phase radioimmune assay for anti-HB_s (AUSAB, Abbott Laboratories, North Chicago, Ill). Subtype specificity of anti-HB_s was identified by incubation of aliquots (0.1 ml) of serum containing anti-HB_s with equal volumes (0.1 ml) of serum containing known HB_s Ag subtypes, adr_s, adw and ayw. A control sample incubated with normal human serum was included. Following 2 hours incubation at room temperature, test beads (coated with HB_s Ag) supplied

in the commercial kit, were added and the test proceeded according to the instructions of the manufacturer. The counts per minute resulting from the mixture of the serum with each subtype and that resulting from the mixture with normal human serum were compared. Subtype specificity of antibody could be identified if the counts per minute were reduced by the addition of any HB_s Ag subtype to less than 50% of that at the normal human serum control. The serum was considered to contain antibody to the shared subtype determinants if 2 or more HB_s Ag subtypes reduced the counts per minute by approximately equal degrees.

Hepatitis A antibody was detected by the specific immune adherence technique described by Miller et al. (3). These tests were kindly performed for us by Drs. P.J. Provost and M.R. Hilleman of the Division of Virus and Cell Biology Research, Merck Institute for Therapeutic Research, in West Point, Penna.

RESULTS : Of 18 people who acquired anti-HB_s during a year follow up period, 16 yielded sufficient serum for testing. In 14 of these men we were able to detect antibody to 2 subtype determinants and in 8 we were able to identify antibody to 3 subtype determinants. Ten persons had antibody directed against the ad determinants. In 6 of these, antibody to the third determinant could be identified, one against adw and five against adr. Four of the 10 people who developed antibody against ad had it by the end of the first 3 months of their stay in Thailand. The remaining 6 acquired it later.

There were 4 persons who developed antibodies to ay subtypes. Three of these persons developed them during their first 3 months in Thailand. These individuals probably did not acquire their hepatitis B infections from contact with the Thai population, as Thais carry almost exclusively ad subtypes.

Computer analyses of behavioral data compiled at the time of interview have identified 4 major areas of activity which correlate with development of hepatitis B infection during the course of one year in Thailand.

Individuals acquiring HBV infections had significantly more social and sexual contact with the Thais than did those who were not infected. The infected individuals usually lived in the Thai community and were more likely to be marijuana smokers. (Table 1 shows those variables which were significantly associated with the acquisition of HBV).

Serum collected on arrival and after one year in Thailand from 176 people were tested for antibody to hepatitis A. Of these, 35 (19.8%) had antibody on arrival in Thailand. Of a number of variables tested, including educational levels, size of home towns and age, only race (that is, being black) was significantly associated with prior hepatitis A infection.

There were 5 people who developed antibodies to hepatitis A while in Thailand, 4 of these had subclinical infections. One man was hospitalized with icteric hepatitis. This man was one of 6 who had clinical hepatitis; the other 5 were diagnosed as hepatitis B (1). Because of the few cases of hepatitis A, no behavioral correlates of hepatitis A acquisition could be defined.

This completes the laboratory work and the computer analysis on this project. The data will be prepared for publication.

Table 1. Significance Level¹ of Variables Associated with Hepatitis B Virus Infections

Variable	Probability ²
1. Race (being black)	a
2. Use of Thai language	a
3. Weeks off base first three months	b
4. Ever living off base second time	a
5. Ever living off base in tour	c
6. Weeks with hired wife first three months	b
7. Ever having hired wife second three months	c
8. Ever having hired wife in tour	d
9. Total of hired wives in tour	b
10. Total cases VD (or NGU) in tour	c
11. Total sex contacts first three months	a
12. Total sex contacts second three months	a
13. Total sex contacts third three months	d
14. Total sex contacts in tour	a
15. Marijuana use second three months	b
16. Total marijuana use in tour	a
17. Having friends of hired wife using marijuana	a

¹ In each case, individuals with hepatitis B virus infections had significantly more of the behavior in question.

² a) $p \leq .05$ b) $p \leq .02$ c) $p \leq .01$ d) $p \leq .001$

REFERENCES :

1. Scott, R.M., Schneider, R.J., Snitbhan, R., Karwacki, J.J., and Bancroft, W.H. Hepatitis B Virus Infections among Americans Residing in Southeast Asia. SEATO Medical Research Laboratory Annual Report, 1976, Pages 40-43.
2. Hoofnagle, J.H., Gerety, R.J., Smallwood, L.A., and Barker, L.F., 1977. Subtyping of Hepatitis B Surface. Antigen and Antibody by Radioimmunoassay, *Gastroenterology*, 72:290-296.
3. Miller, W.J., Provost, P.J., McAleer, W.J., Ittensohn, O.L., Villarejos, V.M., and Hilleman, M.R., 1975. Specific Immune Adherence Assay for Human Hepatitis A Antibody. Application to Diagnostic and Epidemiologic Investigations (38783). *Proc. Soc. Exp. Bio. and Med.*, 149:254-261.