The Epidemiology of Hepatitis B in a Defined Urban Thai Population: Longitudinal Epidemiological Data

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OBJECTIVE: To determine the changes in hepatitis B antigen (HBsAg) and antibody (anti–HBsAg) over a nine–month period.

BACKGROUND: For a description of the experimental design and preliminary data of this study see SEATO Medical Research Laboratory Annual Report 1971–1972 and 1972–1973. Samples and information collected from this urban Thai population allowed for determination of the incidence and loss of evidence of hepatitis B virus (HBV) infection between July 1971 and April 1972.

PROGRESS: There were 523 people age one year and older whose paired (July 1971 – April 1972) sera were tested and confirmed by radioimmunoassay (RIA) for HBsAg and by passive hemagglutination (PHA) for anti–HBsAg. The percentage distributions by age and sex of these 523 persons were very similar to the total 683 persons age one year and older in the random sample who were present throughout the nine–month period. Thirty–six (92%) of the 39 people positive for HBsAg in July 1971 remained positive over the nine month period (Table 1). All three who became negative for HBsAg, however, became positive for anti–HBsAg. Four of the 484 people (0.8%) negative for HBsAg in July 1971 (Table 1) had acquired HBsAg by April 1972. Anti–HBsAg titers were negative in both sera of these four individuals.

In terms of antibody (Table 1), 219 (92%) of the 238 persons positive for anti–HBsAg in July 1971 were still positive in April 1972. The 19 anti–HBsAg reverters included 8 males and 11 females. Thirty–one (10.9%) of the 285 persons negative in July 1971 became positive for anti–HBsAg during the interval. Six persons were positive for both HBsAg and anti–HBsAg on one or both collection times.

The paired PHA anti–HBsAg data revealed that, of the 238 people positive for anti–HBsAg in July 1971 (Table 1), 132 (55.5%) had no significant change in titer (less than a four–fold difference) over the ensuing nine months; 67 (28.2%) had a significant titer rise and 39 (16.4%) had a significant titer drop, the latter including the 19 people who reverted to negative (Table 1). If a significant titer rise can be taken to mean a re–exposure to HBV, then it is conceivable that about 20% (102 people) in this sample were exposed to HBV during this period. This percentage resulted from adding the 67 persons above with significant PHA titer rises to the 31 persons converting to anti–HBsAg and the 4 persons converting to HBsAg during this period of observation.

Considering the presence of either HBsAg or anti–HBsAg to be evidence of prior exposure to HBV, antigen and antibody results were combined for these 523 people (Table 2). Over 20% of the children age one to four showed serologic evidence of HBV exposure, with HBV prevalence rapidly rising to over 60% by age 15 and remaining fairly constant in the adult years. Only 39% (220 people) were negative for HBsAg and anti–HBsAg on both dates. Acquistion and loss of evidence of infection over the nine months occurred at every age, but is probably seen to the greatest extent under the age of 5 years. The data in Table 2 suggested that it would be appropriate to try to fit a reversible catalytic curve to the age–prevalence data (1). This is displayed in Figure 1. The HBV prevalence results of Table 2 are shown as a histogram.

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Tabie 1. HBsAg and Anti—HBsAg Results of Sampled Persons in July 1971 and April 1972*

HBsAg		Anti—HBsAg								Total
Jul 71	Apr 72	Jul 71	Apr 72	Jul 71	Apr 72	Jul 71	Apr 72	Jul 71	Apr 72	
		+	+	+	—	—	+	—	—	
+	+	4		2		0		30		36
+	—	0		0		3		0		3
—	+	0		0		0		4		4
—	—	215		17		28		220		480
Total		219		19		31		254		523

* Persons whose paired sera were tested by RIA for HBsAg and PHA for anti-HBsAg.

Table 2. Prevalence of Hepatitis Virus (HBV) Infection in July 1971 and Incidence and Loss Evidence of HBV Infection between July 1971 and April 1972, by age

Age (years)	No. paired sera tested	HBV Prevalence[1] July 1971		HBV incidence[2] July 1971— April 1972		HBV titer loss[3] July 71— April 72	
		No.	%	No.	%	No.	%
1—4	33	7	21.2	6	23.1	2	28.6
5—9	89	28	31.5	6	9.8	2	7.2
10—14	104	44	42.3	6	10.0	4	9.1
15—19	68	41	60.3	5	18.5	1	2.4
20—29	64	40	62.5	3	12.5	2	5.0
30—39	66	44	66.7	3	13.6	1	2.3
40—	99	67	67.7	3	9.4	5	7.5
Total	523	271	51.8	32	12.7	17	6.2

1 Positive for HBsAg, for anti—HBsAg, or for both

2 Acquisition of either HBsAg or anti—HBsAg in persons negative for both in July 1971

3 Reversion to negative of HBsAg (or anti—HBsAg) without acquisition or continued positivity of anti—HBsAg (or HBsAg)

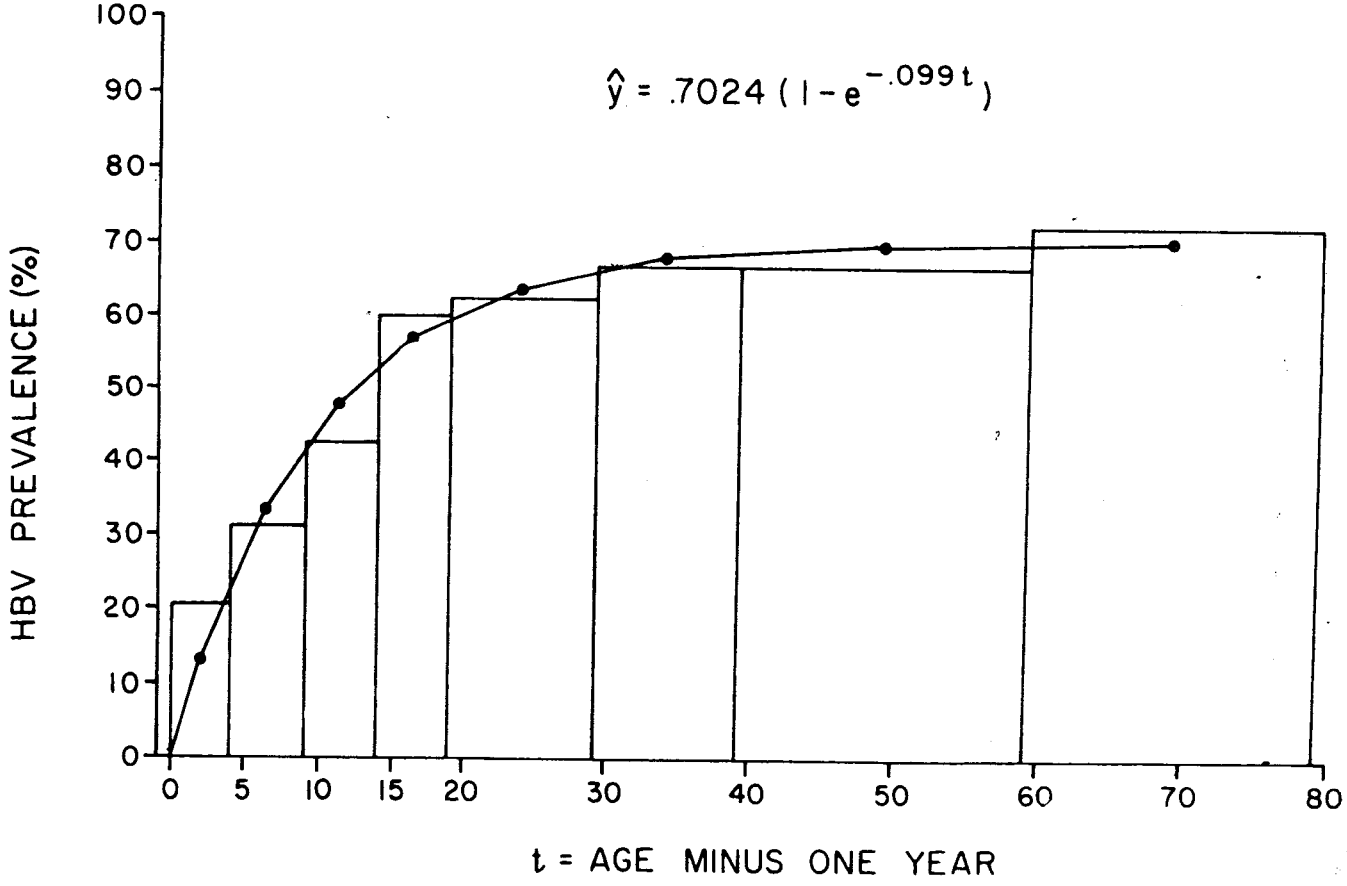

FIGURE 1. HBV PREVALENCE BY AGE (JULY 1971). OBSERVED PREVALENCE PROPORTIONS ARE SHOWN BY THE RELATIVE FREQUENCY HISTOGRAM. THESE DATA WERE FITTED WITH A REVERSIBLE CATALYTIC CURVE (1) WHICH IS SHOWN BY THE SUPERIMPOSED CUMULATIVE RELATIVE FREQUENCY POLYGON, (WITH THE EQUATION ABOVE THE CURVE). NOTE THAT THE TIME SCALE HAS BEEN SHIFTED ONE YEAR TO THE LEFT SO THAT THE EXPERIENCE WITH HBV WOULD BE ESTIMATED FROM BIRTH. (SEE TEXT)

Superimposed on this is the curve fitted to these data using a reversible catalytic model. The fit of this model to the observed data is very good except for somewhat underestimating the prevalence under age 5. (It should be noted that the age scale has been shifted one year to the left in Figure 1 so that prevalence could be estimated from birth). The equation of the fitted curve provides 2 constants: the first, 0.7024, or 70%, is the estimated peak (asymptotic) prevalence attainable under the reversible conditions; the second. 0.099, is a combination of two constants of infection, 0.070 or 7.0% average annual rate of acquisition plus 0.029 or 2.9% average annual rate of loss of evidence of HBV infection. The observed results (Table 2) show a larger gain and loss of evidence of infection over the 9-month observation period than predicted by the model; however, the rates of acquisition and loss estimated by the model express the average of annual rates over the years.

DISCUSSION: The most important result of this study is the evidence that clinically inapparent infection by HBV is a very common occurrence in this population (Table 2). Infections occurred in every age group during the study and between 60 and 70 per cent of subjects age 15 or over showed serological evidence of having been infected at least once in the past. The data suggested that 20% of the population were exposed to HBV during the nine months of observation. Of these, two-thirds showed evidence of re-exposure. Therefore, it is probable that nearly everyone in this community will be infected at least once, if not many times, during his or her lifetime. Further attesting to the widespread exposure and susceptibility to HBV is the finding that nearly every sampled family throughout the study area had at least one member positive for HBsAg or anti-HBsAg. Thus, it may be assumed that the whole population is exposed to HBV from earliest childhood and that susceptibility to infection is universal. Since people of all ages lost serological evidence of HBV infection (s) during the study period, it may also be assumed that reinfections (with or without intervening loss of serologic evidence of infection) are common events. The excellent agreement with the reversible catalytic curve fitted to the July 1971 HBV prevalence data (Figure 1), which requires these same assumptions of universal exposure and reversible susceptibility, further support the conclusion of continuous or at least frequent exposure of all ages to HBV. Because there is also frequent loss of serologic evidence of infection, HBV prevalence by age understandably cannot ever reach one hundred per cent. Indeed, in Huay Khwang, HBV prevalence reaches a plateau in adults close to the 70% maximum predicted by the catalytic model.