The Epidemiology of Hepatitis—Associated Antigen (HAA) in a Defined Urban Population. I. Prevalence Survey

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OBJECTIVE: To determine the prevalence of HAA in a random sample of urban Bangkok residents and to test the genetic hypothesis of the HAA carrier state.

DESCRIPTION: Our case—control studies of both Bangkok area hepatitis patients and recipients of HAA (+) blood have clearly demonstated the important association with HAA in these populations. A sizeable (>5%) prevalence of HAA has also been found in presumably healthy male blood donors. Although necessary and valuable information is derived from the study of these groups, important questions about host and environmental risk factors involved in the acquisition and persistence of HAA (and anti—HAA) and their relation to subclinical as well as clinical hepatitis can best and most validly be obtained by adequate sampling of the population at risk—in this case, the total Thai population. Since the overall risk of developing hepatitis is greater in urban than in rural populations, we decided to establish a Bangkok study site, perform a cross—sectional, family—directed survey, and, based upon these results, determine the feasibility and need for continuing prospective surveillance.

The study area selected was the Huay Khwang low income housing development. One of the 3 major sections was mapped and found to have exactly 800 houses. The rows of houses (on both sides of 8 blocks) are composed of groups of 5 adjoining houses with several yards separating each of the 5—house clusters. The 160 clusters were taken as the sampling units and 15 such clusters (75 houses) were randomly selected. Thus the sampling process was basically similar to that used in Chiangmai and Mae Sariang. Confidence limits of the various statistics presented were derived from the method for analyzing cluster random samples. In June, 1971, comprehensive interviews were performed with the random sample residents, using standardized questionnaire forms. Special attention was paid to the family relationships in each household so that accurate pedigree analyses could be performed in the testing of whether susceptibility to being an HAA carrier is inherited as an autosomal recessive trait (as Blumberg hypothesizes). In July, 1971, blood was collected from volunteering sample members (over age one year) within a 2—week period; heights and weights were also measured. The following tests were promptly run on the blood specimens: hemoglobin, hematocrit, SGOT, HAA (CF and IEOP tests) and blood typing (ABO, MNS, CDE, Duffy, Kell and Kidd). For very young children and a few who refused venipuncture, peripheral blood was sometimes obtained instead; only a limited number of tests could be performed on these specimens. After the HAA results became known, extra effort was expended to try to get complete (as far as possible) participation of all family members where at least one member had been found to be HAA—positive. Thus numerous extra specimens were obtained from relatives living in the Bangkok—Thonburi area. These non—random sample persons are not included in the prevalence analyses (Tables 1—7), but they are included in the family analyses (Table 8 and 9).

RESULTS: The random sample included a total of 814 people in the 75 houses, or an average of 10.8 people per house. There were 147 separate families residing in these houses (average of 2.0 families per house). The average family size, therefore, was 5.5 persons. The age and sex distributions of the Huay Khwang sample are presented in Table 1. Precision of the sampling process was both good (standard errors approximately 0.01) and comparable over the entire age span. Compared to a typical Thai village, this urban sample has proportionally more young people (median age 1—3 years younger) and fewer males (46% versus the country—wide value of 49%). Nearly 90% of the sample population (over age 1 year) volunteered a blood sample (Table 2). Participation was very good for females and children but only 70% of the adult males submitted specimens.

A total of 695 sera were processed for HAA—55 (7.9%) were positive for the antigen (Table 3); none were positive for anti—HAA. Although it appears that the prevalence may be higher in males (9.5%) than in females (6.8%), this difference is not statistically significant, either in children or in adults (Table 4). An additional 11 persons (1.8%) had anticomplementary CF reactions, but the IEOP test was negative for each specimen. The IEOP procedure proved to be slightly more sensitive than the CF test. Only one of the 55 positives was IEOP—negative, CF—positive, while IEOP was positive in 5 sera which were CF—negative plus 3 more sera which had partial fixation or $\leq$1:2 CF reaction. Overall, 80% of the CF positives had high ($\geq$1:32) titers which are what we have usually found in persistent HAA carriers. (Indeed, followup sera 6 months later on these persons found all such persons tested still positive, at similar high titers).

In general, past histories on HAA—positive persons differed little from those in the whole sample (Table 5). The historical variables considered, therefore, provided no clue as to possible means of HAA acquisition. Only a history of jaundice was elicited in greater frequency in HAA—positives, but only 4 of the 55 positives (7.3%) gave such a history. The HAA—positive group was also similar to the entire sample in distributions of height, weight, hemoglobin and hematocrit (Table 6). (Age adjustment of the positives was not required since the HAA—positives were similarly distributed to the entire sample). Although the mean SGOT for both sexes was higher in the positive group (and worthy of further evaluation), 48 of the 55 HAA—positives had SGOT values below 70 and only 3 were over 90 (highest 104). Differences in the 2 blood typing groups are probably reflecting the clustering of HAA—positives in family members plus the incompleteness of the typing data; these and other important genetically—related data are presently being further evaluated.

Tables 7 and 8 present attempts to describe the distribution of HAA positives in families. The 55 positives (and presumed persistent HAA carriers) were present in 11 of the 15 five—house clusters and in 23 of the 75 houses. Although these figures do not suggest a marked clustering effect, analysis by blood relatives (i.e., families) in these houses definitely suggests a degree of clustering within families which is not necessarily shared between families or between houses. Whereas almost 1/3 of the houses had at least one HAA(+)resident, only 18.4% of the families showed this. As expected, the % of positive families increased with increasing family size, but so too did the proportion of positive people in positive families (Table 7, c/b). There were several examples of houses with 2 large (5—7) families residing together where only one family had HAA—positives. Although one family could still conceivably be sharing an environmental HAA ascertainment factor not shared by the other family, contact between both families' members is extremely close at all social levels and results such as these appear to better support a theory of familial predisposition to HAA—carriage. Table 8 shows that at least one offspring was positive in each of the 6 families in which the mother was positive compared to only 8 out of 75 families in which the mother was negative and the father was either negative or not tested. The method used by Blumberg to test the genetic hypothesis was applied to these family data (Table 9). The segregation of HAA—positive offspring in matings where one parent is HAA—positive (upper table) shows a very close fit to the expected distribution and provides further support for the hypothesis that predisposition to the HAA—carrier state is inherited as an autosomal recessive condition. The fit is poor, for matings where both parents are negative (lower table).

However, the numbers are quite small and in 7 of the 12 families HAA results are known for only one parent (the other parent was assumed to be negative). Further data may be forthcoming from a repeat serum collection from the total random sample which is being obtained in April, 1972.

Available sera from the random sample cohorts from Mae Sariang and Chiangmai Valley (see 1969—70 and 1970—71 Annual Reports) provided the opportunity to determine (by IEOP test) the prevalence of HAA in these Northern Thai populations. In Mae Sariang and in 3 of the 4 Valley villages, prevalence was lower than in Huay Khwang. The schoolchildren in urban Chiangmai (age 6-8) had a similar prevalence to Huay Khwang and one village (C) had 9 of 46 males (20%) HAA—positive. The 9 were clustered in 4 families. Each of the 22 HAA—positives in Chiangmai had persistent IEOP—positive reactions over the 2 years (Nov 69—Nov 71) of surveillance and had normal SGOT values.

Table 1.

Sex and Age Distributions of Huay Khwang Random Sample

Age	Male		Female		Total				
	Frequency	Relative Freq. (%)	Frequency	Relative Freq. (%)	Frequency	Relative Freq. (%)	Cumulative Relative Frequency (%)	Sp*	95% CL+
0—4	58	15.4	46	10.5	104	12.8	12.8	.0100	10.6—14.9
5—9	55	14.6	58	13.2	113	13.9	26.7	.0155	23.3—30.0
10—14	63	16.8	67	15.3	130	15.9	42.6	.0167	39.1—46.2
15—19	45	12.0	59	13.5	104	12.8	55.4	.0126	52.7—58.1
20—29	51	13.6	78	17.8	129	15.8	71.2	.0134	68.4—74.1
30—39	40	10.6	56	12.8	96	11.8	83.0	.0110	80.7—85.4
40—49	42	11.2	38	8.7	80	9.9	92.9	.0055	91.7—94.0
50—	22	5.8	36	8.2	58	7.1	100.0	— —	— —
Total	376	100.0	438	100.0	814	100.0	100.0	— —	— —
Median Age	16.3		19.1		17.9				

* Standard error of the sample proportion.

\+ 95% confidence limits of the sample proportion.

Table 2.

Participation of Huay Khwang Random Sample in Giving Blood Specimens

Age	Male		Female		Total	
	No. Sera	%*	No. Sera	%	No. Sera	%
1–9	89	89.0	87	94.6	176	91.7
10–19	100	92.6	120	95.2	220	94.0
20–29	38	74.5	71	91.0	109	84.5
30–39	27	67.5	53	94.6	80	83.3
40–49	27	64.3	37	97.4	64	80.0
50–	16	72.7	32	88.9	48	82.8
Total	297	81.8	400	93.9	697	88.3
Median Age	15.0		19.3		17.4	

* %Giving blood specimen.

Table 3.
Prevalence of HAA by Age and Sex

Age	Male			Female			Total		
	No. Tested	HAA (+)		No. Tested	HAA (+)		No. Tested	HAA (+)	
		No.	%		No.	%		No.	%
1—4	34	1	2.9	31	2	6.4	65	3	4.6
5—9	54	5	9.2	56	7	12.5	110	12	10.9
10—14	61	8	13.1	66	2	3.0	127	10	7.9
15—19	39	6	15.4	54	3	5.5	93	9	9.7
20—29	38	5	13.2	70	4	5.7	108	9	8.3
30—39	27	0	0.0	53	4	7.5	80	4	5.0
40—	43	3	7.0	69	5	7.2	112	8	7.2
Total	296	28	9.5	399	27	6.8	695	55	7.9*
Median	15.0	15.0		19.3	19.2		17.4	16.4	

* 95% confidence limits 4.5—11.3%.

Table 4.

Comparison of HAA Prevalence Between Males and Females

Age	HAA Prevalence (%)		x^2 (1 DF)
	Male	Female	
<15	9.4	7.2	0.48 NS*
≥15	9.5	6.5	1.19 NS
Total	9.5	6.8	1.19 NS

* NS = Not Significant

Table 5.

Comparison of Historical Characteristics between HAA—positive Persons and Total Sample

History of	HAA (+) N=55 (%)	Total Sample* N=697 (%)
Hospitalizations	16.4	16.8
Medical injections previous 6 mos.	23.6	20.2
Dental work previous 6 mos.	5.4	4.4
Tattoo	3.6	4.7
Blood donations	1.8	2.7
Blood transfusions	3.6	3.2
Jaundice	7.3	3.6

* Total sample submitting serum specimen

Table 6.

Comparison of HAA—positive Persons with Total Sample for Various Measurement and Laboratory Test Results

Statistic		HAA (+) Group N=55*	Total Sample N=697*
Mean Height (cm)	Male	142.8	140.8
	Female	138.6	140.6
Mean Weight (Kg)	Male	37.9	38.6
	Female	38.4	41.7
Mean Hemoglobin (g%)	Male	11.9	12.6
	Female	11.2	11.6
Mean Hematocrit (%)	Male	38.0	38.7
	Female	35.2	36.2
Mean SGOT (sf units)	Male	39.0	24.7
	Female	37.0	26.8
Blood Type	% O	29.6	33.9
	% A	25.9	26.0
	% B	27.8	31.1
	% AB	16.7	8.9
	% M	50.9	43.2
	% N	14.5	13.2
	% MN	34.5	43.6

* No. results slightly less for some tests

Table 7.

Distribution of HAA—positive Families and People by Family Size

Family Size*	a No. Families	b No. Families HAA (+)+	b/a (%)	c No. People HAA (+)	c/b
1—2	47	2	4.3	2	1.0
3—5	47	10	21.3	15	1.3
6—8	40	8	20.0	16	2.0
9—11	8	4	50.0	5	1.2
12—14	4	3	75.0	17	5.7
19	1	0	0.0	0	—
Total	147	27	18.4	55	2.0
Median	4.7	6.4	—	7.5	—

* No. in family submitting sera
\+ One or more HAA (+) person in family

Table 8.

HAA Results in Families

Offspring*	Mother		Total
	HAA (+)	HAA (—)	
≥1 HAA (+)	6	12+	18
All HAA (—)	0	67	67
Total	6	79	85

* At least 2 offspring per family (Median=4)
\+ Father was HAA (+) in 4, HAA (—) in 4 and unknown in 4 families

Table 9.

Segregation of HAA—positives in Families with at Least One HAA—positive Offspring

No. Offspring in Family	No. of Families	No. HAA (+)		Variance
		Observed	Expected	
MATING TYPE: HAA (+) x HAA (—)				
1	2	2	2.000	0.000
2	4	5	5.332	0.888
3	2	4	3.428	0.980
4	1	1	2.133	0.782
6	1	1	3.048	1.379
7	1	6	3.528	1.667
8	1	4	4.016	1.945
Total	12	23	23.485	7.641
		χ^2 (1 DF) = 0.033 p ~ 0.85		
MATING TYPE: HAA (—) x HAA (—)				
1	2	2	2.000	0.000
2	1	1	1.143	0.122
3	1	1	1.297	0.263
4	3	3	4.389	1.260
5	2	3	3.278	1.184
6	1	2	1.825	0.776
8	2	2	4.446	2.344
Total	12	14	18.378	5.949
		χ^2 (1 DF) = 3.222 p ~ .075		

Table 10.

Prevalence of HAA in Northern Thailand Study Groups

Study Area*	Age Range Tested	No. Tested	No. HAA (+)	HAA Prevalence (%)		
				Male	Female	Total
Chiangmai Valley						
Village A	1—69	84	0	0.0	0.0	0.0
Village B	1—39	84	1	2.0	0.0	1.2
Village C	1—39	80	9	19.6	0.0	11.2
Village D	1—39	91	1	2.3	0.0	1.1
Urban School E	6—8	161	11	7.5	6.2	6.8
Mae Sariang Town	1—79	177	5	4.9	1.0	2.8

* All samples were randomly selected except for school E.
Blood collected June, 1969 in Mae Sariang; others in July, 1971.