

## Study of Hepatitis in a Pediatric Outpatient Department

**Investigators:** Richard A. Grossman, LTC, MC  
Robert B. Cotton, MAJ, MC  
Milton Willhight, SFC  
Dumrong Chiewsilp, M.D.  
Songsri Buranakarl  
Pethal Mansuwan, M.D.\*

**OBJECTIVE:** To determine the proportion of acute hepatitis cases seen in a pediatric outpatient department which are associated with HAA and to determine the duration of antigenemia.

**DESCRIPTION:** HAA has been found much less frequently in inpatient pediatric than adult hepatitis cases in Bangkok. Since available outpatient data suggested that most of the pediatric hepatitis cases are not hospitalized, a study of this population was indicated. By selecting age—and sex—matched case controls and by obtaining sera from family members of both cases and controls, background HAA prevalence could be controlled for and risk factors could be better assessed. The study was performed at the Bangkok Children's Hospital Outpatient Department throughout 1971. Detailed historical information was obtained from all cases, controls and their family members. Controls were of the same sex, age (usually within  $\pm$  one year of the cases), and lived in the same general area of Bangkok—Thonburi (whenever possible) as the cases. Controls were usually selected on the same or following day at the outpatient clinic. Control diagnoses were almost all uncomplicated upper respiratory infections or pertussis. CF testing for HAA and anti-HAA was run on all sera; where CF results (HAA) were questionable, the IEOP test was also performed. An attempt was made to obtain serial sera from the families of all HAA positive persons (whether they were cases, controls or family members).

**PROGRESS:** From January to December, 1971, 71 patients were given a diagnosis of hepatitis. Of these, 62 had a clinical and laboratory picture compatible with the diagnosis. Two pairs of male—female siblings were included, one pair in April, one in November, and each time the sibs became symptomatic within 3 days of each other. None of these 4 cases were positive for HAA. Eleven of the 62 cases were residents of provinces outside the greater Bangkok area—3 from Ayutthaya, 3 from Pathumthani, 2 from Nonthaburi and one each from Chachoengsao, Chainat and Chiangmai. Of the remaining 51 Bangkok area cases, controls were matched for 42 cases (82%)—21 males and 21 females. The Bangkok cases occurred in every month except December. Although no sharp peak occurred, there were noticeably fewer cases in the final 3 months of 1971 (Jan—Mar: 18; Apr—Jun: 19; Jul—Sept: 10; Oct—Dec: 4). The age and sex distribution of these 51 cases is shown in Table 1. Males accounted for 53% of the cases and the males were 1—2 years older, on the average, than females.

**BACKGROUND:** Information on the 42 cases and their controls is summarized in Table 2. Age and sex were, of course, comparable, but so too were household size and other characteristics except for contact with a jaundiced person. The typical symptoms of acute hepatitis are apparent in the case sample while fever was not often present in either group at the clinic visit. The cases were seen 2—15 days after the onset of symptoms (median 5 days). Comparability of non—hepatitis—associated variables is also shown by similar distributions of hemoglobin in cases and controls (Table 3.) Liver function test results are clearly different. The other 9 cases without controls did not differ from the rest of the cases for the variables considered. The liver function test results were very similar between the family members of the 51 Bangkok area cases and the 42 controls (Table 4). Although only a small number of both family groups had slight elevations in these tests, such elevations were more frequent in case family members.

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\* Director, Children's Hospital

Antibody to HAA was not detected in any of sera tested during the study. HAA was detected in 9.5% of the 42 cases and 4.8% of their matched controls (Table 5). Although the difference is not statistically significant, there are two features which point to this being a real difference. First, the rate in the family members of both cases and controls is comparable to that in the controls, which is also approximately the prevalence found in the general Bangkok population (See Huay Khwang Study). Second, and more pertinent to the association of HAA with pediatric hepatitis cases, is the question of persistence of HAA positivity. Our results to date have indicated that HAA is usually a transient phenomenon in symptomatic hepatitis cases while asymptomatic Thais who have been found to have HAA in their sera have usually remained positive for up to 2 years of observation. Table 6 summarizes the serologic history of the 20 HAA positive persons found in the study. Three of the 4 positive cases who were followed past the initial serum collection had titers less than 1:64 and rapidly reverted to negative. The fifth positive case was not followed, but was positive only by IEOP on the initial serum. All but one of the other 14 positive persons (controls and family members) who were followed from 4 to 36 weeks had high, persistent CF titers (almost always  $\geq 1:64$ ). Liver function tests were normal in every HAA-positive control and family member. Without having the necessary preinfection HAA status on the cases and a larger series of cases, it can only be suggested from these data that HAA is associated with a definite, but small proportion of symptomatic pediatric hepatitis cases in Bangkok and that the risk of developing overt hepatitis may be greater in a child who lacks the antigen than in one who is a persistent carrier.

The family of case 42, while interesting of itself, may also provide support for the latter hypothesis of risk. Six of the 8 family members of the case were HAA positive, the 5 positives that were subsequently followed remaining so; they are presumed to be HAA carriers (Table 6). The positives were 2 brothers (ages 13 and 16), 2 sisters (ages 12 and 27), the aunt (age 45) and the uncle (age 47) of the case (a 12 year-old male). Unfortunately, the 27 year-old sister, who had a low titer of 1:8 on the initial serum (study No. 42h), was lost to followup. Negative was a 14 year-old sister and an 18 year-old brother. The case's initial serum was anticomplementary and all subsequent sera were negative. There was no history of transfusions, drug addiction, jaundice or prior exposure to jaundice for any of the 9 family members.

Other examples of family clusters of asymptomatic HAA positives in Thais are presented elsewhere in the Report. Further prospective study is needed to determine whether (as Blumberg hypothesizes) symptomatic hepatitis is more likely to occur in HAA negative than in HAA-positive persons in a population like the Thais where the relatively large numbers of HAA positives may be related to a genetic predisposition to the carrier state.

Table 1.  
Hepatitis Cases at Children's Hospital Outpatient Department In Bangkok—Thonburi Residents, 1971

Age	Male	Female	Total
0-2	3	2	5
3-5	3	6	9
6-8	8	10	18
9-11	7	4	11
12-14	6	2	8
TOTAL	27	24	51
Median	8.8	7.2	7.9

**Table 2.**  
**Comparison of Hepatitis Cases with Controls for Various Background Characteristics**

Background Characteristic	Cases N=42	Controls N=42
Males	21	21
Median Age	7.9	7.5
Household Size — Range	3—12	3—12
Household Size — Median	7	7
Dental work previous 6 mos.	4	5
Medical injections previous 6 mos.	23	28
History of Jaundice	3	2
Contact with jaundiced person previous 6 mos.	9	2
History of Blood Transfusion	1	0
<u>Present Illness</u>		
Vomiting	24	10
Dark Urine	38	5
Light Stool	10	1
Fever (Temp. > 37.5)	3	5
Jaundice	40	0
Enlarged or Tender Liver	30	0

**Table 3.**  
**Comparison of Hepatitis Cases with Controls for Various Laboratory Test Results**

Laboratory Test	No. Pairs Tested	Cases	Controls
Hemoglobin — Range	40	5.6—14.7	7.5—14.5
Hemoglobin — Median	40	11.9	12.1
SGOT — Range	42	72*—1850	11—67
SGOT — Median	42	367	30
Total Bilirubin — Range	42	0.4**—34.4	0.0—0.6
Total Bilirubin — Median	42	6.8	0.3
Alkaline Phosphatase — Range	41	1.6—23.2	2.7—10.0
Alkaline Phosphatase — Median	41	10.1	5.1
HAA Positive	42	4(9.5%)	2(4.8%)

\* All but one value was > 90

\*\* All but 2 values were > 1.8

Table 4.  
Comparison of Family Members of Hepatitis Cases and Controls  
for Various Laboratory Test Results

Laboratory Test	Family Members of 51 Cases* N=186	Family Members of 42 Controls N=111
SGOT — Range	10–104	10–57
SGOT — Median	27.5	27.2
SGOT — No. $\geq 90$	2	0
Total Bilirubin — Range	0.0–1.5	0.1–2.3
Total Bilirubin — No. (%) $\geq 1.0$	12(6.4)	3(2.7)
Alkaline Phosphatase — Range	1.0–16.4	1.0–9.6
Alkaline Phosphatase — No. (%) $\geq 8.0$	7(3.8)	2(1.8)
HAA Positive — No. (%)	8(4.3)	5(4.5)

\* Total of 49 families since 4 cases occurred in 2 families.

Table 5.  
Summary of HAA Positives in Bangkok Area Cases, Controls and Family Members

	No. Tested	HAA Positives					Mean SGOT
		No.	%	No. Male	Age		
					Range	Median	
<u>Cases</u>							
Total	51	5	9.8	3	8–9	9	1045
with Controls	42	4	9.5	2	8–9	8.5	1181
<u>Controls</u>	42	2	4.8	1	10–12	11	34
<u>Family Members</u>							
Of the 51 Cases	186	8	4.3	3	11–47	21.5	27
Of the 42 Controls	111	5	4.5	4	12–37	24	27

Table 6.  
Persistence of HAA Positivity in Cases, Controls and Family Members

	Study Number	Initial CF Titer	No. Weeks Followed	Followup Sera		CF Titer on Last Serum
				No. Tested	No. (+)	
<u>Cases</u> (5)	16	1:16	2	1	0	Neg
	18	$\geq 1:64$	53	13	13	$\geq 1:64$
	40	1:32	4	3	2	Neg
	43	Neg*	0	0	--	--
	61	PF+*	22	8	1	Neg
<u>Controls</u> (2)	C-47	$\geq 1:64$	33	11	11	$\geq 1:64$
	C-65	$\geq 1:64$	16	7	7	$\geq 1:64$
<u>Cases</u> <u>Family Members</u> (8)	27c	$\geq 1:64$	4	2	2	$\geq 1:64$
	42a	$\geq 1:64$	10	4	4	$\geq 1:64$
	42b	$\geq 1:64$	36	10	10	$\geq 1:64$
	42d	$\geq 1:64$	29	7	7	$\geq 1:64$
	42f	$\geq 1:64$	32	9	9	$\geq 1:64$
	42g	$\geq 1:64$	32	9	9	$\geq 1:64$
	42h	1:8	0	0	--	--
	53b	$\geq 1:64$	10	3	0	Neg
<u>Control</u> <u>Family Members</u> (5)	C-32c	$\geq 1:64$	5	2	2	$\geq 1:64$
	C-39d	$\geq 1:64$	4	2	2	$\geq 1:64$
	C-52a	1:16	24	7	7	$\geq 1:64$
	C-65b	$\geq 1:64$	20	7	7	$\geq 1:64$
	C-65c	$\geq 1:64$	20	6	6	$\geq 1:64$

\* IEOP (+).

+ PF = Partial Fixation.