PRIMARY AND SECONDARY TYPE SEROLOGIC RESPONSES IN PATIENTS WITH ISOLATION CONFIRMED DENGUE INFECTIONS, 1971-1979

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OBJECTIVE : To determine, by retrospective data review, if there is an association between virus type isolated and the pattern (primary versus secondary) of the antibody response in patients with DHF.

BACKGROUND : Scott et al. clearly demonstrated that DHF and DSS could occur during a child's first exposure to dengue viruses (i.e. during a primary infection). In the two cases cited in that report which were documented by virus isolation from the patient or sibling blood, one yielded dengue type 1, and another dengue type 3. As the vast majority of dengue virus isolates obtained at the AFRIMS/SEATO Lab over the past decade have been dengue type 2, Scott et al's report suggested a possible association between primary DSS and D1 and D3. A similar association had been noted by Halstead in 1962-1964. We therefore performed a retrospective data review to determine if we could detect an association between the virus type isolated and the pattern of the serologic response.

METHODS : SEATO/AFRIMS laboratory records were reviewed for the years 1971 through 1979 and a list was compiled of all typed dengue viruses isolates from patients with a clinical diagnosis of DHF. Next, the age and all available data on the HAI antibody responses of these patients was tabulated.

As all patients did not have paired sera obtained on the same days after onset of illness, two types of data analysis were performed;

1. In the first type of analysis, it was simply noted if the patient had any detectable HAI antibodies (HAI 1:20) to D1, 2, 3 or 4 in the acute serum obtained on the day of admission and blood sampling for virus isolation, and the results tabulated as negative or positive. All 257 cases from which dengue virus isolates had been obtained during the years 1971-1979 were included in this analysis.

2. The second analysis included only children over 12 months of age from whom data was available on the HAI antibody titers to D1, 2, 3 and 4 in both acute serum and in a second sample obtained 10 to 19 days later. Patients for whom convalescent antibody titers were available but were obtained on days outside the stated intervals, and children less than 1 year old, were excluded from analysis. 135 cases were available using these criteria. The distribution of antibody titers in acute and convalescent sera was graphed and tabulated for each type. Next cases were defined as having a primary or secondary type antibody response based on the following definitions :

	Acute titer to D1, 2, 3, 4	Convalescent titer to D1, 2, 3, 4
Primary	< 1:10	1:20 - 1:640

Secondary	≥ 1:20	≥ 1:2560

and the proportion of cases showing either a primary or a secondary type antibody response as determined for each virus type.

RESULTS : Table I shows that the proportion of cases of isolate proven infections which lacked detectable HAI antibody in the acute serum sample were 56, 16, 64 and 70%, for D1, 2, 3 and 4 respectively. The differences show statistical significance as noted in Table I. For the years 1971 through 1975, a period when D1, D2, and D3 were all isolated in approximately equal numbers using identical techniques, the proportions of antibody negative acute sera were 64, 31 and 87%.

Table 2 shows the distribution of the highest acute and day 10-19 convalescent HAI antibody titers in the 135 cases analyzed.

Table 3 shows the number of isolate proven cases with each type meeting the stated criteria for primary or secondary infections

Table 1. Antibody present or absent in acute sera (all isolates, N = 257)

Year	Virus type D1		Virus type D2		Virus type D3		Virus type D4	
	-	+	-	+	-	+	-	+
71	1	2	5	11	1	0	-	-
72	-	-	1	1	-	-	-	-
73	3	2	4	9	3	1	-	-
74	4	1	1	4	4	0	-	-
75	1	0	3	6	6	1	-	-
76	-	-	1	7	1	0	0	5
77	-	-	1	36	3	8	2	17
78	-	-	7	24	0	1	0	5
79	0	2	6	56	-	-	0	1
Total	9	7	29	154	18	10	2	28

Statistical significance 1971 - 1979, chi-squared analysis

D1 vs D2	$p < .001$
D1 vs D3	p N.S.
D1 vs D4	$p < .001$
D2 vs D3	$p < .001$
D2 vs D4	p N.S.
D3 vs D4	$p < .001$

Statistical significance 1971 - 1975, chi-squared analysis

D1 vs D2	$p = .03$
D1 vs D3	p N.S.
D1 vs D4	$p < .001$

Table 2. Highest acute and convalescent HAI antibody titers in 135 isolation positive cases of DHF, 1971 - 1979.

Reciprocal Highest HAI titer	D1		D2		D3		D4		Total	
	Acute	Conv	Acute	Conv	Acute	Conv	Acute	Conv	Acute	Conv
<10	4	0	3	0	6	0	0	0	13	0
10	0	0	3	0	0	0	0	0	3	0
20	0	0	2	0	1	0	0	0	3	0
40	0	1	5	0	2	0	0	0	7	1
80	0	1	7	0	3	0	1	0	11	1
160	1	0	6	1	3	0	1	0	11	1
320	0	2	14	0	1	4	2	0	17	6
640	0	0	7	0	1	1	2	0	10	1
1280	0	0	12	1	0	0	2	0	14	1
2560	0	0	15	1	0	1	5	0	20	2
5120	0	0	9	11	0	1	0	4	9	16
10240	0	1	10	79	0	10	7	16	17	106
	5	5	93	93	17	17	20	20	135	135

Table 3. DHF among children one year or older, 1971 - 1979 : Distribution of HAI antibody response according to virus isolate type

	1°	2°	?	Total
D1	4	1	0	5
D2	2	87	4	93
D3	5	11	1	17
D4	0	20	0	20
	11	119	5	135

Statistical significance, chi-squared analysis

D1 vs D2	$p < .001$
D1 vs D3	p N.S.
D1 vs D4	$p < .001$
D2 vs D3	$p < .001$
D2 vs D4	p N.S.
D3 vs D4	$p < .001$