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SEQUENTIAL INFECTION AS RISK FACTOR FOR DENGUE HEMORRHAGIC FEVER/DENGUE SHOCK SYNDROME (DHF/DSS) DURING THE 1981 DENGUE HEMORRHAGIC CUBAN EPIDEMIC

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In 1977, a dengue 1 epidemic occurred in Cuba; it was characterized by a mild clinical picture and over 0.5 million individuals were affected. DHF/DSS appeared in the country in 1981, caused by dengue 2 virus and more than 300,000 cases of Dengue fever were reported, among them more than 10,000 cases of Hemorrhagic Dengue and 158 deaths. By October, the epidemic was over (G. Kouri et al., 1989, *Bull WHO, 67*: 375-380). Since approximately 50% of the Cuban population had as their only exposure dengue 1 in 1977-1978 and dengue 2 in 1981 and because *Aedes aegypti* has been controlled with no transmission since then, Cuba provides an unique opportunity for retrospective serologic studies of the secondary infection as risk factor for DHF/DSS epidemic.

In order to test the role of secondary infection to the development of severe disease, three groups of patients with DHF/DSS grades II to IV (children and adults) were studied for the presence of neutralizing antibodies (Nt Abs) to dengue 1 and dengue 2 viruses at 1:30 serum dilution.

From previous studies (data non published) using sera taken before and after 1981, we could demonstrate that 1:30 serum dilution allows to discriminate the presence of Nt Abs to dengue 1 or dengue 2 viruses. Table shows some examples.

Secondary infection fluctuated from 95 to 98.5% in the three groups that was statistically significant ($p < 0.01$) when compared to the maximum percentage of secondary infection expected in the Cuban population.

A seroepidemiological survey carried out in a densely populated municipality of Havana City showed that from 1,295 individuals 26.1% had a mónotypic dengue 1 Nt Abs, 6% had monotypic dengue 2 Nt Abs and 17.6% had Abs to both viruses. Five clinical and serologically confirmed DHF/DSS cases were found in the sample; all of them with a secondary infection. DHF/DSS in children occurred in an infection ratio of 1:23 secondary infections and 1:79.5 in adults. This finding support the hypothesis that the mechanism of hemorrhage in dengue infected children and adults could differ because of the apparent variations in the occurrence of severity of the disease (S.B. Halstead, 1989, *Rev. Infect. Dis, 11*: S830-S839).

All these clinical and seroepidemiological observations done during and after the DHF/DSS Cuban epidemic, support the role of sequential infection as the main individual risk factor for severe disease.

TABLE

Titer of neutralizing antibodies to dengue 1 and dengue 2 viruses in sera obtained before and after 1981

Number[a]	Year[b]	Dengue 1[c]	Dengue 2	Type of infection
1	1980	160	<10	Primary (dengue 1)
2	1980	250	<10	Primary (dengue 1)
3	1980	76	24	Primary (dengue 1)
4	1980	320	26	Primary (dengue 1)
5	1980	42	22	Primary (dengue 1)
6	1983	90	40	Secondary (dengue 1 + 2)
7	1983	60	48	Secondary (dengue 1 + 2)
8	1983	<10	82	Primary (dengue 2)
9	1983	<10	70	Primary (dengue 2)
10	1983	<10	130	Primary (dengue 2)

a: samples 1 to 5: sera from blood donors; samples 6 and 7: sera from donors who referred infections in 1977 and 1981; samples 8 to 10: sera from children of 3 years.
b: year of bleeding.
c: reciprocal of titer of neutralizing antibodies determined by Plaque Reduction Neutralization Technique.

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