PASSIVELY ACQUIRED ANTIBODY TO FLAVIVIRUS IN THAI INFANTS

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INTRODUCTION

Flavivirus infections, particularly dengue, are highly endemic in Thailand; virtually all adults show serological evidence of previous infection. By child bearing age, almost 90% of healthy Thai females have developed antibodies to flaviviruses. The present study was undertaken to determine the prevalence and the decay kinetics of passively acquired antibody to flaviviruses in healthy Thai infants.

MATERIALS AND METHODS

Plasma specimens were collected at a well baby clinic at Children's Hospital in Bangkok during July 1979-March 1980, from healthy children on whom routine hematocrits were being checked. Blood was obtained by finger tip lancination and collected in 75 mm heparinized hematocrit capillary tubes. After centrifugation and hematocrit value recording, 30-40 microliters of plasma were salvaged for antibody studies. The total of 280 chil dren, 1-18 months old, were studied. All were residents of the Bangkok metropolitan area and were generally of lower to middle class social status.

Using standard hemagglutination inhibition microtiter techniques, plasma specimens were tested in serial dilution starting at 1:10 against flavivirus antigens Dengue 1-4 (DEN 1-4) and Japanese encephalitis (JEV).

RESULTS

The prevalence of antibody to flaviviruses is shown in Fig. 1 as the individual highest

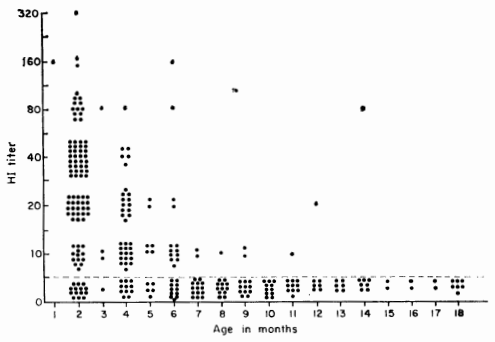

Fig. 1—Highest flavivirus HI antibody in serum of 280 healthy Thai infants.

HI titer to any of the antigens tested versus the child's age. Of the 98 infants age 1-2 months tested, 86% had antibody. The percentage of children with antibody progressively fell with increasing age: 75% at 4 months and 54% at 6 months, then dropping to 10% in the age group 7-12 months. Of 27 infants examined between the age of 13-18 months only one 14 month old had detectable antibody (4%).

The titers of the antibodies detected varied with the children's ages. The highest titers were observed in the youngest age group tested, 1 to 2 month old infants. A few had titers of 1:160 in this age group, 14% had titers of 1:80, 65% of the children positive had titers of 1:20-1:40 and 15% had titers of 1:10.

The antibody titers gradually decreased with increasing age. At the age of 6 months there were more children with titers of 1:10 (9/13) than with higher titers, and thereafter almost all antibody positive children had

a low titer of 1:10. A titer of 1:80 was noted in one of the 14 month old.

The broad reactivity of these passively acquired flavivirus antibodies is demonstrated

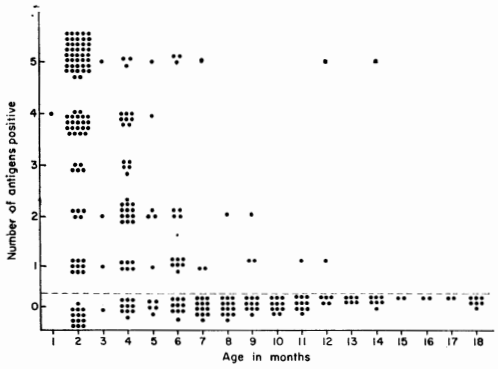

Fig. 2—Age distribution of children with positive flavivirus antibody and number of responding antigens.

in Fig. 2 as the number of reacting antigens versus the age of the child. 50% of infants 1-2 months had broadly reacting antibodies to all 5 antigens tested. In the majority of infants at this age (83%), the antibody responses were positive to 3 or more antigens. A monotypic response was however, observed in about 10% (9/85). Among patients with antibodies reactive to less than five antigens almost all reacted with dengue antigens and not JEV. The percentage of children with antibody to all 5 antigens fell to 12% in the age group 4-6 months and thereafter there were more of children with monotypic response than with broad reactivity. Of particular interest is a 14 month old child whose antibody were positive to all 5 antigens with the highest titer being 1:80 as noted in Fig. 1.

DISCUSSION

Our studies show that most healthy Thai children have circulating antibodies to flaviviruses in early infancy; presumably these antibodies are acquired transplacentally then gradually disappear until age 12-14 months when antibodies to flaviviruses are no longer detectable. The unusual broad reactive antibody response of a rather high titer noted in a single 14 month baby is likely to be post natally acquired. Variations between children of the same age group of the antibody levels and the breadth of reactivity of these passively acquired antibodies are probably related to the maternal antibody status. The decay kinetics of passively acquired antiboby to flaviviruses appear to be in the same pattern as other transplacentally acquired antibodies.

In Bangkok the association of DHF with secondary or repeated dengue infection is a well known phenomenon but occasionally DHF is observed in children with primary dengue, particularly in infants under the age of one year. The age distribution curve of DHF cases seen in Bangkok shows two modal ages, one at 4 to 11 months of age and the other at 7 years of age. Between these two modal age peaks, there appears to be a nadir at around one year, the time by which passively acquired antibodies to flaviviruses, as shown in our studies, can no longer be detected. This is strikingly in contrast to other viral diseases of childhood as it appears to be the "silent period" for DHF.

From these epidemiological observation it seems that passively acquired antibodies to flaviviruses with their broad reactivity may not render these infants immune or completely immune to DHF. On the contrary, these antibodies may enhance dengue infections (and hemorrhagic fever) as hypothesized by Halstead (1980).

REFERENCE

HALSTEAD, S.B., (1980). Dengue haemorrhagic fever-A public health problem and a field for research. *Bull. WHO., 58* : 1.