

The Effect on the Offspring of Maternal
Hepatitis B Surface Antigenemia

Principal Investigators:

Robert McNair Scott, MAJ, MC
Dumrong Chiewsilp, MAJ, MC, RTA
Suchitra Nimmannitaya, M.D.¹
William H. Bancroft, LTC, MC

Associate Investigators:

Karoon Mansuwan, M.D.²
Pethal Mansuwan, M.D.¹
Rapin Snitbhan, M.D.
Vandee Ningsanonda, M.D.¹

OBJECTIVE: To study the effect on the offspring of chronic hepatitis B antigenemia in the mother.

BACKGROUND: Clinical hepatitis B developing during the latter part of pregnancy has been associated with an increased perinatal mortality, a high incidence of premature delivery and a high frequency of virus transmission from mother to infant (1). Information on the effect of asymptomatic maternal hepatitis B antigenemia is conflicting. It has been suggested that the incidence of prematurity and perinatal mortality is also increased in infants born of these mothers (2). Transmission of virus from antigenemic mothers to their infants appears to be an uncommon event in mother infant pairs studied in the West (3, 4). However, a strong association between antigenemia in mothers and their children has been shown in cross sectional population studies in the Far East (5, 6). This study was designed to investigate the effect of maternal antigenemia on pregnancy and the offspring in a population with a high prevalence of antigen carriers.

DESCRIPTION: This study was divided into two phases. A description of the initial phase may be found in the SEATO Medical Research Laboratory Annual Progress Report, March 1974.

Population: Antigen positive mothers and their families were sought for follow-up 1½-2½ years after initial collection in the delivery room. Temporal controls were matched to each family that could be located. Temporal controls were members of families of women who were collected in the delivery room and whose delivery dates were as close as possible to those of the antigen positive mothers. Each control mother was delivered within two days of an antigen positive mother. Interim family histories were obtained on all families studied and these included the duration of breast feeding, the medical and dental history of the child and the person who cares for the child most of the time. Family relationships were determined and other members of the family living in the household were sought. Each infant was examined by a physician and height and weight measurements were recorded.

Sera were collected on antigen positive and control mothers, their infants, and as many family members as could be found. Saliva was also collected from all mothers.

Laboratory Studies: Sera were submitted for determinations of transaminase and bilirubin concentrations. They were tested for hepatitis B antigen by radioimmune assay (Abbott Laboratories, Ausril), counterelectrophoresis and complement fixation. A radioimmune assay inhibition technique was used to screen for antibody against HB_sAg and positives were titrated and confirmed by a passive hemagglutination test (PHA, Electronucleonics).

1 Children's Hospital, Bangkok, Thailand

2 Women's Hospital, Bangkok, Thailand

PROGRESS: As reported in the SEATO Medical Research Laboratory Annual Report 1973-1974, of 1,625 mothers screened in the delivery room at Women's Hospital, 93 or 5.7% were found to be positive. Of the 93, 47 were located, 30 were not located and 16 lived outside of Bangkok.

Ninety-four families were followed, 47 with antigen positive mothers and 47 temporal controls. There were no significant differences between the antigen positive family and the temporal control found in family variables such as household size and income. Five families of antigen positive mothers who resided outside of Bangkok, returned to the city for follow-up. If these five were discounted, then the distribution within the city of the families of antigen positive mothers and controls was similar. Maternal factors such as age, parity, history of past abortion, infant mortality and transaminase levels also showed no significant differences. Further, there were no significant differences seen in the weight, length or transaminase levels of the infant at birth, nor in the number of infants born prematurely or the infant mortality rate over the first year of life. In the 94 families followed, five infants had died. Two deaths were recorded within the control families and the other three in families of antigen positive mothers. Three of these deaths occurred at or shortly after delivery. Two were related to complications of delivery and one to prematurity. Two children died during the first year of life. One child of an antigen positive mother died at four months of age during an episode of diarrhea for which no medical aid was sought. A child of a control mother died of pneumonia at six months of age.

Table 1. Experience with Hepatitis B Virus 18-30 Months After Birth

Mother	Offspring			
	No. Tested	Evidence of Infection		
		HB _s Ag	Anti-HB _s	Total
HB _s Ag Positive	44	13 (30%)	3 (7%)	16 (37%)
HB _s Ag Negative	45	0 (0%)	1 (2%)	1 (2%)

Table 2. Maternal Antigen Titer and the Percent of Positive Offspring

Mothers		Offspring	
CF Titer	No. Tested	HB _s Ag Positive	
		No.	%
≤ 1:16	60	0/60	0
1:32	7	1/7	14
1:64	12	5/12	42
> 1:128	10	7/10	70
Total	89	13/89	14

All mothers who were antigen positive at delivery were still positive at the time of follow-up $1\frac{1}{2}$ to $2\frac{1}{2}$ years later. In general the complement fixation titers of these mothers were within four-fold of the titer found at delivery. None of the temporal control mothers or their infants had developed antigen; however, 13 of 44 (29.5%) of surviving infants of antigen positive mothers were found to be positive (Table 1).

Despite what would appear to be abundant hepatitis B virus exposure in infants of HB_sAg positive mothers, the incidence of antibody conversion in this group was low (Table 1). There were no significant differences in the incidence of antibody conversion in infants with positive mothers and in those of control mothers; however, there were three times as many converts in the antigen positive group and the lack of significance might reflect only the small number of infants examined.

There appeared to be a direct relationship between the maternal complement fixation titer at delivery or follow-up and the prevalence of antigen in the serum offspring for follow-up (Table 2). The maternal titer on all 13 infants found to be positive was greater than or equal to 1:32. None of the offspring of mothers with titers less than 1:32 were positive.

At the time of follow-up, the physical status of children of antigen positive mothers and antigen negative controls was documented. None of these children were chronically ill, nor with one exception did any exhibit any biochemical or physical evidence of hepatitis at the time of examination. When compared to normal values established for Southern Chinese children (7), average deviations of height and weight for these two groups of children were not significantly different. The one exception was the antigen positive son of an antigen positive mother whose only sign of illness was a moderate elevation in the transaminase concentrations (SGOT to 136 Sigma Frankel units, SGPT to 90 Sigma Frankel units).

DISCUSSION: As reported in the SEATO Medical Research Laboratory Annual Report 1973-1974, there were no gross differences seen in the prematurity and perinatal mortality rates of infants of antigen positive mothers and antigen negative mothers. Further, there were no apparent differences in the maternal history of pregnancy and child birth between these two groups; however, subtle differences could not be excluded.

Transmission of hepatitis B virus occurred from mother to offspring. In this study only infants of positive mothers were found to be positive at $1\frac{1}{2}$ to $2\frac{1}{2}$ years of age. This does not exclude the possibility of virus transmission and development of the carrier state in children of antigen negative mothers; indeed this must happen in order to maintain the high prevalence of antigen carriers seen in this population. These data do suggest that the infection of infants of negative mothers is a relatively rare event when compared to that of children of antigen positive mothers. The phenomenon of hepatitis B virus transmission appears to be directly related to the antigen titer of the positive mothers. The prevalence of antigen positive offspring increased as the HB_sAg titer in the mother increased.

Maternal antigenemia did not grossly effect the growth or the development of the child. Children who developed HB_sAg were not significantly different in height and weight from children without HB_sAg, whether or not they had HB_sAg positive mothers.

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