Infection with hepatitis B virus in infancy

A longitudinal study of 8 cases

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SUMMARY  Eight infants who developed HBsAg aged between 1 and 5 months were identified in the greater Copenhagen area during the period 1970–76. 7 had acquired the infection from their mothers and one had received a HBsAg-positive blood infusion. 3 infants had a transient infection lasting 2 to 8 months while the remaining cases developed persistent antigenaemia with evidence of minor liver dysfunction during a follow-up of one to 6 years. HBsAg was persistently present in 4 of 5 infants, indicating infectivity in these patients. Prematurity or administration of specific immunoglobulin at delivery apparently did not affect the course of infection.

Infection with hepatitis B virus is a rare cause of the hepatitis syndrome in infancy (Mowat et al., 1976; Danks et al., 1977). However vertical transmission from an infectious mother to her newborn infant has been recognised as an important mechanism for the maintenance and dissemination of hepatitis B in many areas (Mazzur and Blumberg, 1974; Okada et al., 1975; Stevens et al., 1975), and this type of infection may account for most asymptomatic HBsAg carriers found in adults (Sevens et al., 1975).

In the few series of neonatal infection reported, considerable differences have been observed regarding the infants’ mothers, the clinical features of the infection, and the incidence of persistent infection in the children (Dupuy et al., 1975; Schweitzer, 1975; Stevens et al., 1975). In order to delineate the course of this infection in infants, a prospective study of all recognised cases of hepatitis B in children aged less than one year between 1970 and 1976 in the greater Copenhagen area (population 1·5 million) is presented.

Materials and methods

All obstetric and paediatric departments, and the department of infectious diseases, in the greater Copenhagen area reported any case in which infection with hepatitis B virus was suspected in a pregnant woman or in an infant. By surveying discharge summaries in 1976 we confirmed that no further cases had occurred.

The diagnosis of hepatitis B infection was based on the detection of HBsAg in the blood at age one to 6 months. No case of congenital hepatitis B—i.e. a persistent positive HBsAg reaction from the day of birth—was identified.

Serological evaluation of the children was made in hospitals; children persistently positive for HBsAg were investigated further by regular clinical examination and measurement of the levels of prothrombin, alkaline phosphatases, bilirubin, albumin, immunoglobulin G, A, and M, and (by radioimmunoassay) HBsAg and anti-HBs (Skinhøj et al., 1976). HBsAg and anti-HBs were estimated by agar-gel diffusion (Skinhøj et al., 1976).

Results

The survey resulted in identification of 8 cases of hepatitis B infection (Table).

Origin of infection. The mothers of 7 infants were known to be HBsAg-positive at delivery or less than 2 weeks before. 4 of these mothers had uncomplicated acute hepatitis with transient antigenaemia, while 2 were persistent carriers of HBsAg. One had chronic persistent hepatitis, the other had had a renal transplant and received prednisone and azathioprine; she had two children 3 years apart and both were included in the study.

Case 7 was born to a healthy woman, and the infant required exchange transfusions for neonatal hyperbilirubinaemia. At age 2 months the infant was also given a blood transfusion, for anaemia, from a donor subsequently found to be a healthy carrier of HBsAg.

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The course of infection was unremarkable. Eight cases of hepatitis B infection are summarised in the Table. All infants became antigenaemic within 6 months, but specific hepatitis B immunoglobulin (Skinhoj and Balstrup, 1975) given to 3 infants tended to prolong the incubation period to 12–15 weeks, compared with 6–10 weeks for the untreated infants. In 3 infants (Cases 6, 7, 8) a more than 2-fold increase of s-ALAT was found within one month after development of HBsAg; 2 subsequently eliminated this antigen.

The course of infection in an infant was apparently not influenced by the state of the mother—e.g. HBsAg carrier or transiently infected at delivery (Table)—nor by the infant’s birthweight or mode of delivery.

Follow-up studies. The 5 children still HBsAg-positive at 12 months remained so throughout the period of study. 3 cases had persistently raised s-ALAT values, but other liver function tests remained normal in all infants. HBsAg was present in all 5 infants and remained so in 4. In the transiently infected children, a normal anti-HBs response was observed after elimination of HBsAg.

Discussion
In accordance with previous observations in Caucasians (Papaevangelou et al., 1974; Schweitzer,

<table>
<thead>
<tr>
<th>Case</th>
<th>Sex</th>
<th>Birthweight (kg)</th>
<th>Mode of delivery</th>
<th>Source of infection</th>
<th>Immuno-prophylaxis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>1.9</td>
<td>Spontaneous</td>
<td>Mother AHB</td>
<td>None</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>2.8</td>
<td>Caesarean section</td>
<td>Mother RT</td>
<td>None</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>3.0</td>
<td>Caesarean section</td>
<td>CHB HBsAg+</td>
<td>None</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>2.4</td>
<td>Spontaneous</td>
<td>Mother AHB</td>
<td>None</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>2.6</td>
<td>Spontaneous</td>
<td>Mother AHB</td>
<td>None</td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>3.6</td>
<td>Spontaneous</td>
<td>Mother CPHB</td>
<td>HBsAg 0</td>
</tr>
<tr>
<td>7</td>
<td>F</td>
<td>2.3*</td>
<td>Spontaneous</td>
<td>Blood donor healthy</td>
<td>HBsAg carrier</td>
</tr>
<tr>
<td>8</td>
<td>F</td>
<td>2.3*</td>
<td>Caesarean section</td>
<td>Mother AHB</td>
<td>1.5 ml HBIG</td>
</tr>
</tbody>
</table>

*Weight at infection.

AHB = acute hepatitis B; RT = renal transplant, receiving prednisone and azathioprine; CHB = chronic hepatitis B; CPHB = chronic persistent hepatitis B; HBIG = hepatitis B immunoglobulin.

The 4 infants born to mothers with acute hepatitis were all born 4 to 6 weeks before term, but their neonatal course was unremarkable.

Course of infection. The infants showed no physical disorder, although one (Case 8) was slightly jaundiced for 2 weeks.

Laboratory data are summarised in the Figure. All

Numbers above lines give s-ALAT titres (normal upper limit 40 U/l).
Numbers below lines show results of HBsAg tests, + = positive, 0 = negative, e = HBsAg.
HBIG = hepatitis B immunoglobulin, BT = blood transfusion.

Figure Course of hepatitis B infection in 8 infants.
Beasley, R. (1975; Skinhoj et al., 1976) our group of children acquired the infection from their mothers who in severe cases had acute hepatitis, but 3 of the mothers were immunosuppressed because of a renal graft or had chronic persistent hepatitis. This is known to carry a high risk of infectivity and should be separated from the healthy carrier state.

HB$_B$ antigen is usually present in infectious cases. Its presence in the serum in pregnancy is associated with an increased incidence of infection in infants (Okada et al., 1976; Skinhoj et al., 1976; Beasley et al., 1977; Gerety and Schweitzer, 1977).

In contrast with some previous reports (Wright et al., 1970; McCarthy 1973; Dupuy et al., 1975, 1977), our study indicates that some infected children may be expected to eliminate the agent before the age of one year with no major complications.

Our results suggest that s-ALAT may perhaps be a prognostic marker. 2 of the 3 children with abnormal values terminated the infection, while 4 out of 5 without measurable inflammatory reaction became chronic carriers of HB$_B$Ag. Similar findings in adults (Barker and Murray, 1971) suggest that liver damage is related to the immune response rather than to viral replication (Edgington and Chirari, 1975).

With regard to prevention of the infection, neither preterm caesarean section nor withholding breast feeding has been effective (Beasley et al., 1975). Hepatitis B immunoglobulin (Kohler et al., 1974; Schweitzer, 1976) was given to 3 of our patients but all subsequently became infected, and the course was similar to that of the other cases, except that the incubation period tended to be longer.

Similar disappointing results have been obtained in another study (Cossard and Cohen, 1976). Pharmacological immunostimulation with levamisole or similar substance might provide a measure for terminating the prolonged infection. Otherwise, children still positive for HB$_B$Ag at one year are likely to become carriers, and although these children apparently develop normally, the long-term prognosis is unknown, while the persistence of HB$_B$Ag indicates that these individuals will be vectors of hepatitis B virus for many years.

References


