

PAPERS AND SHORT REPORTS

Prognosis of children who are carriers of hepatitis B

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Abstract

Fifteen children who had become positive for hepatitis B surface antigen (HBsAg) by perinatal transmission were traced and re-examined after a mean of 8.1 years; all had been born in England to mothers from ethnic minorities who were carriers of HBsAg. Fourteen of the children remained carriers of HBsAg; of these, more girls than boys developed antibody to hepatitis B e antigen (anti-HBe). Those children whose transaminase activities had been above normal within the first three years of life were more likely to have developed anti-HBe.

The earlier production of anti-HBe suggests that girls have a more effective immune response. Increased transaminase activity early in the course of asymptomatic carriage of HBsAg may be a favourable prognostic sign.

Introduction

The infection by a mother who is a carrier of hepatitis B of her baby in utero or during the perinatal period is an important route of transmission, which in some parts of the world may account for 40% of carriers.¹ Because a fairly high proportion of infected infants become carriers the risk of development of chronic liver disease and hepatocellular carcinoma^{1,5} in this group is greater than that in infected adults, who more often clear the infection.³ The probability of an infant becoming a carrier of hepatitis B is related to the mother's ethnic origin and her hepatitis B e antigen (HBeAg) state.^{6,7}

We undertook a follow up study of 17 children, born in the United Kingdom, who had become carriers of hepatitis B as a result of perinatal infection by their mothers, who were carriers.

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Patients and methods

In 1978 we reported on babies born in the West Midlands to 122 mothers who were carriers of hepatitis B surface antigen (HBsAg).⁶ Seventeen of these babies (all born to parents of ethnic minorities; table I), who were followed up for over three months, remained positive for HBsAg. After a mean of 8.1 (range 6.9-9.1) years we traced 15 of these children.

TABLE I—Ethnic origin and sex of 17 children who became positive for HBsAg after perinatal infection

	Boys	Girls	Total
Asian*	1	3	4
Afro-Caribbean	2	2	4
Chinese†	5	4	9
Total	8	9	17

* Includes children of Indian, Pakistani, and Bangladeshi parents.

† All children of Hong Kong Chinese parents.

A medical history was obtained, clinical examination performed, and venous blood taken to be analysed for the presence of markers of infection with hepatitis B virus and for liver function tests. Tests for HBsAg, antibody to surface antigen (anti-HBs), and antibody to core antigen (anti-HBc) were carried out using radioimmunoassay (a modified Blood Products Laboratory radioimmunoassay for HBsAg and anti-HBs⁸ and an in house radioimmunoassay for anti-HBc). Tests for HBeAg and antibody to HBeAg (anti-HBe) were carried out using a Public Health Laboratory enzyme immunoassay.⁹ Tests for delta antigen and antibody were carried out using enzyme immunoassay (Noctech Ltd). Aspartate aminotransferase and alanine aminotransferase activities and total protein, albumin, and bilirubin concentrations were estimated by standard biochemical methods.

Results of liver function tests in a control group of children under 3 years old had been obtained in the original study.

Results were analysed by Fisher's test of exact probability, the Mann-Whitney U test, and Wilcoxon's matched pairs signed ranks test.

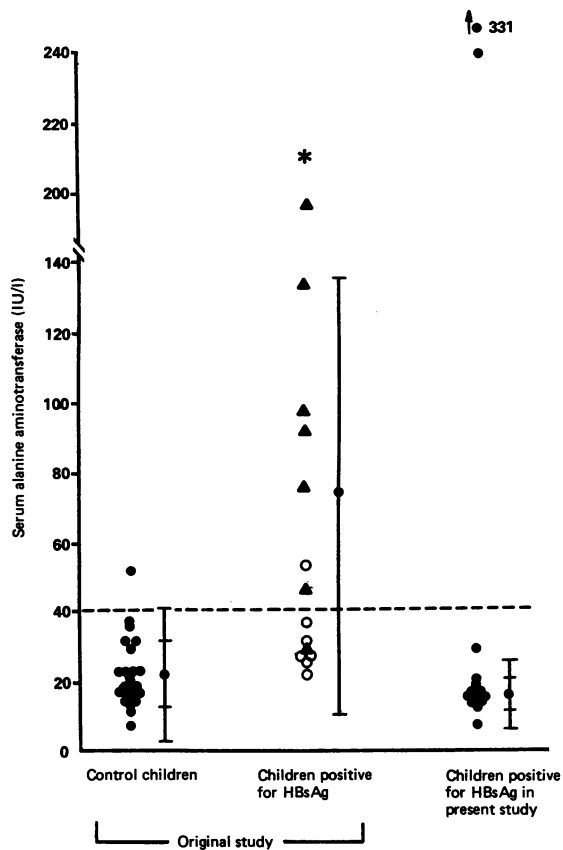
Results

All the children seen were well, and none had features of liver disease. The two untraced children, both Chinese, were believed to have left the country.

All children remained positive for HBsAg except one Asian girl, who had developed anti-HBs (table II). During the initial study the difference in the HBe state between boys and girls was not significant, but on follow up, among those children still positive for HBsAg, the girls were more likely to have developed anti-HBe ($p=0.012$) (table II).

All children had normal concentrations of total protein, albumin, and bilirubin. Originally, the control and carrier children (<3 years old) had shown a significant difference in serum alanine aminotransferase activity

($p<0.0003$). The activity of this enzyme had fallen to normal in 13 of the 15 children at follow up (figure). This reduction reached significance only when the two clearly abnormal children (both boys; one Pakistani and one Chinese) were excluded from the analysis (when $p<0.005$). The Pakistani boy had already developed anti-HBe and was newly returned from an extended stay in Pakistan; recent infection with hepatitis A was excluded by the absence of specific IgM antibody in the serum. The Chinese boy was positive for HBeAg but was clinically well. Neither boy had markers of delta infection. Both remained under review.



Serum alanine aminotransferase activity in 25 control children aged under 3 and 15 children positive for HBsAg aged under 3 in original study, and in 14 children positive for HBsAg in present follow up study (mean age 9 years 9 months). Vertical bars indicate means and SD; horizontal broken line shows upper limit of normal paediatric range. (Activities in children positive for HBsAg in original study are mean values.)

*=Subsequently became positive for anti-HBs. ▲=Subsequently became positive for anti-HBe. ○=Remained positive for HBeAg at follow up.

TABLE II—Numbers of children in whom markers of hepatitis B virus were detected in original study and in present study according to ethnic origin and sex

Ethnic origin and sex	HBsAg					
	HBsAg		Anti-HBe		Anti-HBs	
	Original study	Present study	Original study	Present study	Original study	Present study
Asians	Boys *	0	*	1	*	0
	Girls †	0	0	2	0	1
Afro-Caribbean	Boys	2	2	0	0	0
	Girls	2	1	0	1	0
Chinese	Boys	4	3	0	1	0
	Girls	3	1	0	2	0
Totals	Boys	6	5	0	2	0
	Girls	6	2	0	5	1
Both sexes		12	7	0	7	1

* The single Asian boy was not tested in the original study.
† Two Asian girls did not have any markers of HBe in the original study.

TABLE III—Mean alanine aminotransferase activity during first three years of life related to HBe state in present, follow up study

Alanine aminotransferase	HBe state on follow up		Total
	Positive for HBeAg	Positive for Anti-HBe	
Above normal range	1	6	7
Within normal range	6	1	7
Total	7	7	14

Those carrier children who had had raised transaminase activities in the first three years of life (figure) were significantly more likely to have developed anti-HBe on follow up than those whose transaminase activities had been normal ($p=0.014$ for alanine aminotransferase (table III) and $p=0.02$ for aspartate aminotransferase). The one child who had cleared HBsAg completely had had the highest single set of transaminase values in the initial study; because of the interval between the initial study and follow up we could not tell at what age she became immune.

Discussion

A proportion of carriers of hepatitis B will develop liver disease.^{2 10 11} The 15 children in this study (all first generation British residents) were in good health and without symptoms of liver disease. In the absence of histological evidence, however, the existence of important liver disease, or its possible future development, cannot be excluded even in children positive for anti-HBe.¹²

Persistence of the carrier state is more common in boys.^{1 13} In this study more of the girls had developed anti-HBe, suggesting a greater ability of girls to produce an effective immune response to the virus. We regard the girls' production of anti-HBe as a prelude to their future clearance of the infection. The reasons for the difference in response to chronic infection with hepatitis B virus between the sexes remain obscure, but this difference has been widely reported.¹³⁻¹⁶ There is evidence, too, that boys suffer greater morbidity than girls in other types of viral infection.¹⁷

Although a difference in the persistence of HBeAg was observed among our three ethnic groups (Asians cleared HBeAg more effectively), this may be partly explained by the higher proportion of girls in this group.

After the development of anti-HBe previously raised transaminase activities may decrease to normal values.^{18 19} Raised transaminase activities may be attributed to immune mediated destruction of infected liver cells, which gives rise to "spillage" of enzymes.²⁰ Our finding that those children with raised transaminase activities in the first three years of life were more likely to be positive for anti-HBe on follow up suggests that they were the children who were mounting an effective immune response early in the course of their infection. A similar pattern was observed by Skinhoj in a small number of children infected early in life,²¹ and we believe that in asymptomatic patients raised transaminase activities in the early stages of carriage may be a favourable prognostic sign.

The Pakistani boy with raised transaminase activities during this study probably acquired an acute non-A non-B hepatitis in Pakistan, from which he subsequently recovered, as adjudged by a later fall in activity. His condition remained under review, as although he was positive for anti-HBe the presence of liver disease

associated with hepatitis B virus was possible. Without liver biopsy the question of whether viral DNA has become integrated into the host genome of hepatocytes remains unanswered.

Continued study of carriers in the West may clarify the relative importance of the hepatitis B virus and genetic and environmental factors in causing liver disease.²²

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Psychiatric disorder and gynaecological symptoms in middle aged women: a community survey

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Abstract

In a community survey 521 women aged 35-59 were selected at random from all patients registered in two group practices. They were interviewed at home and assessed by means of standardised psychiatric measures and detailed gynaecological inquiry. Levels of psychiatric morbidity were found to be within the expected range for such a sample. Both psychiatric morbidity and the personality dimension of neuroticism were significantly

associated with gynaecological symptoms, including dysmenorrhoea and premenstrual tension, some symptoms of excessive menstruation, and flushes and sweats but not disappearance of menstruation for over six months. Current psychiatric state was significantly associated with recent adverse life events and with indices of psychiatric vulnerability (neuroticism and previous psychiatric history), suggesting possible aetiological links with gynaecological symptoms.

The findings of this study have implications for the management of gynaecological complaints in general practice.

Introduction

Clinical experience has led some gynaecologists and psychiatrists to conclude that gynaecological symptoms are commonly linked with psychiatric disorder.^{1,4} For example, an American gynaecologist maintained that "many patients present gynaecological symptoms without being sick gynaecologically. Their illness represents a psychic conflict sailing under a gynaecological flag."²

There is some research to support these clinical impressions. In three recent studies⁵⁻⁷ women attending gynaecological clinics were assessed with the self rated general health questionnaire.⁸ In each study about half the women were identified as probable psychiatric cases. These levels of morbidity seem impressively high, but they are difficult to evaluate without comparable information on women attending other kinds of medical or surgical clinic.

Conversely, there is some evidence for increased gynaecological

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