Hepatitis B e antigen and antibody in hepatitis B surface antigen positive blood donors

A. Barr1, S. H. Black2, C. J. Burrell2, B. Dow1, and I. Macvarish1

From the 1Glasgow and West of Scotland Regional Transfusion Centre, Law Hospital, Carluke, Lanarkshire, and the 2Hepatitis Reference Laboratory, Department of Bacteriology, Edinburgh Medical School, Edinburgh, UK

SUMMARY In a study of 105 asymptomatic HBsAg positive blood donors, 9 (8.6%) were found to have HBeAg, 38 (36.2%) anti-HBe, and the remaining 58 (55.2%) neither marker detectable by gel diffusion. There was no correlation between HBeAg/anti-HBe status and HBsAg sub-types, Gm allotypes, the presence of anti-Gm, red cell antibodies, or rheumatoid factor. Rheumatoid factor activity could be removed from anti-HBe positive sera without removing anti-HBe activity, indicating that separate entities were involved.

HBeAg was found only in donors under the age of 30 (p < 0.005), while anti-HBe did not show an age-related trend. HBeAg was also found less commonly in donors of blood group A than in the total carrier population (p < 0.05), indicating an apparent protection in carriers of group A. The blood group distribution for the 105 HBsAg positive donors was similar to that of the general population.

The possibility that the host genetic make-up may influence the type of response to human hepatitis B infection has led to a search for allotypic markers linked to certain types of response. For example, evidence has been presented for (Arndt-Hanser et al., 1974) and against (Rundle et al., 1975) an association between specific ABO blood groups and persistent hepatitis B surface antigen (HBsAg) carriage. In multiply transfused thalassaemic patients, Blumberg et al. (1972) described an association between the development of anti-HBs (that is, successful virus elimination) and the presence of both anti-Gm antibodies and relative homozygosity with respect to Gm immunoglobulin markers. Hillis et al. (1977) have reported a positive association between certain locus B HLA types and HBs antigenaemia in dialysis patients. Finally, it has been proposed that a tendency to HBsAg carriage after hepatitis B virus (HBV) infection may be inherited as a simple autosomal recessive gene (Blumberg et al., 1969), although convincing evidence against this hypothesis in its simplest form has been presented (Vyas, 1974; Mazzur, 1976).

Among chronic carriers of HBsAg, the additional presence of HBeAg (Magnius and Espmark, 1972) is associated with a greater likelihood of infectivity and progressive liver damage. Early in acute hepatitis B infection HBeAg can usually be detected, to be replaced later by anti-HBe in a majority of cases (Frösner et al., 1978; Miyakawa and Mayumi, 1978); the persistence of HBeAg indicates a more serious prognosis. Thus the presence of HBeAg or anti-HBe in HBsAg carriers allows an additional serological distinction between different clinical responses to HBV infection, which might show a clear relationship to the above allotypic markers.

In addition, evidence was presented by Neurath and Strick (1977) that HBeAg itself may be an idio- typic IgG molecule and anti-HBe an anti-idiotype. However, more recent work (Takahashi et al., 1978) has shown that HBeAg activity can exist in serum as a molecule smaller than IgG, as well as in association with IgG. Nevertheless, the possibility that the HBeAg/anti-HBe system might be associated with the Gm system, or with naturally occurring rheumatoid factor, warranted investigation.

In this paper we have examined the HBeAg/anti- HBe status of 105 asymptomatic HBsAg positive blood donors detected at routine screening and correlated our findings with age, ABO and Rhesus (D) blood groups, HBsAg subtype, Gm allotype, the presence or absence of rheumatoid factor, anti-Gm, and red cell antibodies.

Received for publication 7 August 1978
Methods

HBsAg was detected by reverse passive haemagglutination (RPHA, Wellcome) or radioimmunoassay (RIA, Abbott). Five of the 105 donors were positive by RIA but negative by RPHA. HBeAg and anti-HBe were detected by gel diffusion after threefold concentration of test sera; all positive results gave a line of identity with a positive control reaction, and gave no precipitin lines with negative control sera of groups AB and O. Sera were tested for rheumatoid factor (RF) using different commercial kits by latex agglutination and a modified Waaler-Rose procedure (Searle, Hyland and Denver) in the two laboratories and discrepant results were re-tested. HBsAg subtyping was performed using solid phase radioimmunoassay and by radioimmunoprecipitation using monospecific antisera. Glm(a) and Glm(f) allotyping was performed by a passive haemagglutination inhibition technique (Vyas et al., 1968) using red cells coated with anti-Rh of appropriate Glm allotype. The screening for anti-Gm was carried out using a panel of cells coated with various anti-Rh sera known to detect most anti-Gm antibodies (M. M. Izatt, personal communication).

Results

HBeAg was found in 9 (8.6%) sera and anti-HBe in 38 (36.2%), while 58 (55.2%) sera showed neither reaction. Blood group A was less common (p < 0.05) in HBeAg positive donors than in the total carrier population, which itself showed ABO and Rhesus(D) blood group frequencies similar to those of the overall regional population (Table 1).

<table>
<thead>
<tr>
<th>Group</th>
<th>HBeAg</th>
<th>anti-HBe</th>
<th>Neither</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>O</td>
<td>8</td>
<td>19</td>
<td>31</td>
<td>58</td>
</tr>
<tr>
<td>A</td>
<td>10</td>
<td>14</td>
<td>20</td>
<td>34</td>
</tr>
<tr>
<td>B</td>
<td>1</td>
<td>2</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td>AB</td>
<td>0</td>
<td>3</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Rh(D) positive</td>
<td>9</td>
<td>31</td>
<td>52</td>
<td>92</td>
</tr>
<tr>
<td>Rh(D) negative</td>
<td>0</td>
<td>7</td>
<td>6</td>
<td>13</td>
</tr>
<tr>
<td>Total</td>
<td>9</td>
<td>38</td>
<td>58</td>
<td>105</td>
</tr>
</tbody>
</table>

The Glm allotype frequencies among all HBsAg carriers were similar to those for the region as a whole, and no relationship was seen between Glm allotype and HBeAg/anti-HBe status or the presence of RF (Table 3). Similarly, the presence of anti-Gm or red cell antibodies was not correlated with HBeAg/anti-HBe status.

The HBsAg subtype composition of the sera is also shown in Table 3. No association existed between either major subtype and the presence of RF or HBeAg/anti-HBe status of the donors. In a further analysis, no effect of age was found on the prevalence of HBsAg subtype.

Finally, as only seven of the 105 HBsAg carriers were female it was not possible to correlate the above information in relation to the sexes.

Discussion

Radioimmunoassay increased the anti-HBe rate from 35.9% (by gel diffusion) to 88.5% in a study of
156 HBsAg carriers in West Germany (Biswas et al., 1978), whereas the HBeAg rate was increased only from 2-6% to 3-6% with the more sensitive assay. It is therefore possible that the nine HBeAg positive donors detected by gel diffusion in our study represent nearly all those who would be detectable by a more sensitive assay, and that the majority of donors above with neither HBeAg nor anti-HBe detectable would prove to have low levels of anti-HBe.

In Japanese HBsAg carriers, the HBeAg rate declined with age from 76-9% in those aged 0-9 years to 9-5% in those aged 50 or above, while a reciprocal increase in anti-HBe rate with age was seen (Miyakawa and Mayumi, 1978). However, vertical transmission appears to play a much greater role in maintaining infection in Japan than in western Europe, introducing additional age-related factors. In a French study of 329 HBsAg carriers, no effect of age on the HBeAg rate was seen, while the anti-HBe rate declined with age (Courouce-Pauty and Plancon, 1978). As factors such as age of acquisition of infection, prevalence of various subtypes, varying transmission routes, and possible differences in life expectancy for those carriers who are HBeAg positive could conceivably influence HBeAg/anti-HBe prevalence data, we cannot conclude from our age-related data that seroconversion from HBeAg to anti-HBe over a number of years commonly occurs in the natural history of the carrier state. In contrast, several workers have described seroconversion from HBeAg to anti-HBe positivity during most acute HBV infections (Frösner et al., 1978; Miyakawa and Mayumi, 1978).

An association between blood group A and a lack of an HBeAg response has not to our knowledge been previously reported. We found no association be-
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We are grateful to Dr J. Wallace for advice and encouragement during the course of this work, and to Miss M. M. Izatt for providing Gm reagents.

References


Requests for reprints to: Dr C. J. Burrell, Hepatitis Reference Laboratory, Department of Bacteriology, Edinburgh University Medical School, Teviot Place, Edinburgh EH8 9AG, UK.
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A Barr, S H Black, C J Burrell, B Dow and I Macvarish

doi: 10.1136/jcp.32.2.132