Hepatitis B antigen (HBAg) and its antibody (HBAb) in hospital patients

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SYNOPSIS  Sera from 5171 inpatients have been tested for HBAg and HBAb during the 18-month period ending in December 1972. The incidence of HBAg (0.116%) was similar to that in blood donors (0.119%) in the same area, being tested for the first time by the same technique. By contrast the incidence of HBAb in patients (0.271%) was significantly higher than in donors (0.103%). A possible mode of infection was identified in three of six HBAg-positive patients and in seven of 12 HBAb patients. None of the positive patients was regarded as 'high risk' when admitted to hospital. The study thus emphasizes the need to regard all specimens as potentially infective.

The hepatitis-associated antigen (HAA), formerly known as Australia antigen, appears to be a specific marker for 'serum' or viral hepatitis type B (Blumberg, Sutnick, and London, 1968; Prince, 1968). A recent World Health Organization report (1973) proposes that HAA or Australia antigen should be referred to as hepatitis B antigen (HBAg) and the corresponding antibody as hepatitis B antibody (HBAb). Although this antigen may not itself be the actual infective agent, any individuals found to be HBAg positive must be regarded as potentially infectious. There is little published information regarding the prevalence of HBAg in hospital patients, and indeed most of the available figures refer to prevalence rates in healthy blood donors. There is, however, no reason to suppose that patients referred to hospital are in this respect atypical and hospitals must constantly be treating unknown carriers of HBAg (Department of Health and Social Security, 1972a).

This study was primarily undertaken to determine the prevalence of HBAg and HBAb among selected inpatients in a general hospital group and among healthy blood donors in the same region over the same period of time; and secondarily to investigate implications of the findings.

Materials and Methods

Patients
An aliquot of serum was obtained from each inpatient in whom blood grouping was performed in the Haematology Department of the Victoria

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Infirmary. The serum samples were stored at −20°C and subsequently transferred at weekly intervals to the Glasgow and West of Scotland Regional Transfusion Centre for HBAg and HBAb testing. Sera from 5171 individual patients were tested between June 1971 and December 1972. These 5171 patients represented 29% of the patients admitted to hospital during the same period of time: 83% were admitted to surgical and 17% to medical wards.

A detailed medical history was obtained from those patients in whom HBAg or HBAb was detected; in addition biochemical tests of liver function were performed.

Blood Donors
Since October 1970, the sera of all blood donors in the west of Scotland have been routinely tested for the presence of HBAg and HBAb; 86 182 donors were tested for the first time between June 1971 and December 1972.

Laboratory Methods
All sera were tested for HBAg and HBAb by immunoelectroosmophoresis (IEOP). The screening procedure and confirmatory techniques have already been described (Wallace, Milne, and Barr, 1972). Repeat specimens for confirmatory tests were obtained from patients and donors found positive on preliminary testing.

Results

Prevalence of HBAg
The sera of six out of a total of 5171 patients were
HBAg positive (0·116%), while 103 out of a total of 86,182 blood donors were HBAb positive (0·119%) (table I). The difference is not statistically significant.

Table I  HBAg and HBAb results in hospital inpatients and in blood donors

<table>
<thead>
<tr>
<th></th>
<th>Hospital Inpatients</th>
<th>Blood Donors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number tested</td>
<td>5171</td>
<td>86,182</td>
</tr>
<tr>
<td>HBAg positive</td>
<td>6 (0·116%)</td>
<td>103 (0·119%)</td>
</tr>
<tr>
<td>HBAb positive</td>
<td>14 (0·271%)</td>
<td>89 (0·103%)</td>
</tr>
</tbody>
</table>

Table I  HBAg and HBAb results in hospital inpatients and in blood donors

PREVALENCE OF HBAB
The sera of 14 out of a total of 5171 patients were HBAb positive (0·271%), whereas 89 out of a total of 86,182 blood donors were HBAb positive (0·103%) (table I). This difference is statistically highly significant ($\chi^2 = 12·149; P < 0·001$).

HBAG AND HBAB-POSITIVE PATIENTS

Diagnosis, age, and sex
The principal diagnosis, age and sex of the six HBAg and of the 14 HBAb-positive patients are given in table II. It should be noted that none of these patients was icteric nor regarded as a 'high-risk' case in relation to transmission of hepatitis (Department of Health and Social Security, 1972b).

Possible modes of infection
The six HBAg patients and 12 of the 14 HBAb patients were closely questioned concerning their previous medical history; in two HBAb patients this was not practicable. Particular attention was paid to a history of previous transfusion of blood or blood products; of jaundice occurring within six months of transfusion; of jaundice or hepatitis of unknown type or close contact with a jaundiced individual within the previous six months; of any injection within the previous six months and of previous pulmonary tuberculosis treated with chemotherapy. These findings are summarized in table III.

A history of blood transfusion before the screening of donations for HBAg was obtained from one of six HBAg patients and from six of 12 HBAb patients; two of those HBAb patients had developed jaundice within six months of transfusion. None of the HBAg patients admitted to any episode of jaundice, but one admitted to close contact with a jaundiced individual during the previous six months. One of the HBAb patients admitted to an episode of jaundice some 30 years earlier, while, as noted above, two other patients had in the past had posttransfusion jaundice. Histories of injection within the previous six months were obtained from one HBAg patient and three HBAb patients. One HBAg patient and three HBAb patients gave histories of pulmonary tuberculosis treated with chemotherapy during the previous 10 years. Thus, in summary, a possible mode of infection was identified in three of six HBAg patients and in seven of 12 HBAb patients.
Liver function tests

Conventional biochemical tests of liver function were performed in the six HBAg patients and in 12 HBAb patients; all results were within normal ranges.

Laboratory specimens

During the interval between the patients’ admission and the availability of HBAg results, specimens were examined in a routine manner in various individual laboratories. The distribution of the specimens is given in table IV.

Table IV  Nature and distribution of laboratory specimens from six HBAg inpatients

<table>
<thead>
<tr>
<th>Laboratory Department</th>
<th>No. of Patients Investigated</th>
<th>No. and Nature of Specimens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical chemistry</td>
<td>3</td>
<td>3 Blood</td>
</tr>
<tr>
<td>Haematology</td>
<td>6</td>
<td>6 Blood</td>
</tr>
<tr>
<td>Histopathology</td>
<td>5</td>
<td>2 'Unfixed' tissue</td>
</tr>
<tr>
<td>Medical microbiology</td>
<td>2</td>
<td>1 Urine</td>
</tr>
</tbody>
</table>

Discussion

The hepatitis B antigen (HBAg) appears to be a specific marker for the viraemic phase of so-called ‘serum’ hepatitis (Blumberg et al., 1968; Prince, 1968), although there is no direct evidence that it is the infectious agent of the disease (Taylor, 1972). The significance of the corresponding antibody (HBAb) is less certain, but it probably represents evidence of earlier infection (Department of Health and Social Security, 1972a). Heathcote and Sherlock (1973) studied the spread of acute viral hepatitis type B, and found that non-parenteral spread was more common than parenteral. Close contact with HBAg carriers now appears to be the single most important factor in the spread of type B hepatitis in a large, urban, cosmopolitan community.

Reports of the prevalence of HBAg and HBAb among healthy blood donors have been summarized (Maycock, 1972). The prevalence of the antigen appears to be higher in paid than in unpaid donors and also to show considerable geographical variation, the lowest rates quoted being in the United Kingdom (0·07% in Sheffield) and the highest in Kenya (6·0%). Less information regarding the prevalence of the antibody is available; a rate of 0·03% in Sheffield can be compared with a rate of 0·4% in France.

Little information is available regarding the prevalence of HBAg in general hospital patients. Cossart has reviewed the prevalence of HBAg in various groups of patients at special risk (Cossart, 1972), and a prevalence rate of 0·34% for hospital admissions in Denmark has been reported (Cherubin...
and Prince, 1971). An overall prevalence rate of 1.34% for HBAg has recently been reported in patients attending a venereal disease clinic in London (Jeffries, James, Jefferiss, MacLeod, and Willcox, 1973). Fulford, Dane, Catterall, Woof, and Denning (1973) also found a high frequency of HBAg and of HBAb in patients attending a clinic for sexually transmitted diseases. In both these studies it was shown that there were distinct populations, the highest rates of exposure to type B hepatitis virus being found in homosexual patients. Heathcote and Sherlock (1973) have also emphasized the importance of close sexual contact in the transmission of type B hepatitis.

Many different methods of testing for HBAg and HBAb have been described, and these vary considerably in their sensitivity (Department of Health and Social Security, 1972b; Taylor, 1972). It is therefore quite possible that some of the differences in reported prevalence are due to variations in the sensitivity of methods of testing used. The World Health Organization Report (1973) states that the successful detection of HBAg and HBAb depends as much on the meticulous performance of the chosen test as on its relative sensitivity. For these reasons comparison and interpretation of reported prevalence in different studies require considerable caution. In the present study both hospital patients and blood donors were tested in one centre using the same technique (IEOP). Bloomfield (1973) has challenged the validity of using blood donors in comparative studies, because in some countries potential donors with a history of jaundice or of contact in the past six months with a case of jaundice are rejected. Cossart (1972) also considers that the exclusion of volunteers with a past history of jaundice makes a population of blood donors unrepresentative of the community as a whole. The World Health Organization (1973), however, suggests that individuals with a history of overt hepatitis may not have a high incidence of HBAg, and evidence supporting this contentions has recently appeared (Wallace, 1973).

Clearly, however, both hospital inpatients and blood donors form highly selected groups of the general population, and within these groups of patients and of donors there are subpopulations according to age, sex, race, and social class. The patients studied showed considerable 'surgical' bias and formed a further selected group within the general hospital population. It is interesting nevertheless that the prevalence of HBAg was found to be very similar in both the patients and donors (0.12%), whereas the prevalence of HBAb was considerably greater in the patients (0.27%) than in the donors (0.10%). That this difference is due to the exclusion of some potential blood donors because of their previous medical history seems unlikely (Wallace, 1973).

Potential modes of infection were identified in just over half the HBAg or HBAb hospital patients. Conversely and perhaps more importantly no such episode was identified in nearly half of these patients. These findings not only confirm the importance of blood donations unscreened for HBAg and the parenteral route of infection, but also lend support to the suggestion of a natural circulation of the virus in the community (Cossart, 1972). In their study of the spread of acute type B hepatitis, Heathcote and Sherlock (1973) found no definite source of infection in 24 out of 67 patients.

Although the possibility of subclinical hepatitis cannot be absolutely excluded, it seems more likely that the HBAg-positive hospital patients were 'healthy carriers' of the virus, since biochemical liver function tests were all normal. Similarly liver function tests were also normal in the HBAb-positive patients, in whom this finding was probably evidence of earlier infection. Hospitals must constantly be treating unknown carriers of HBAg.

The risks of handling specimens of unfixed tissues, blood, and body fluids from 'high-risk' patients have been emphasized recently (Department of Health and Social Security, 1972c). None of the patients in this study subsequently found to be HBAg or HBAb positive was regarded as a 'high-risk' patient when admitted to hospital. However, one of 862 (0.12%) specimens submitted for routine blood grouping was found to contain HBAg in retrospect; in addition specimens had been examined in other laboratories for routine diagnostic purposes before this information became available. This study again emphasizes the importance of regarding all specimens as highly infective and of handling all specimens with great care.

References

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