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Hepatitis A antibody in blood donors in North East Thames region: implications to prevention policies

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SUMMARY

A total of 1786 blood donors were screened for the presence of anti-hepatitis A antibody (anti HAV). 64·5% of the donors were found to be positive. The prevalence of the antibody was found to be age-related, 55% at 18 years and 75% at 65 years. No relationship was noted between the presence of antibody, foreign travel or a specific destination. Assay of antibody levels in selected seropositive individuals gave a mean level of 5·0 IU/ml.

The prevalence of infection in this selected population is important in the context of passive immunization with normal human immunoglobulin and for defining a policy of immunization with hepatitis A vaccines, which are currently undergoing clinical trials.

INTRODUCTION

Immunoglobulin prophylaxis is given to individuals travelling to areas where hepatitis A is endemic, since the risk of infection is well recognized (1). Evidence from the West of Scotland suggests that 20% of acute cases of hepatitis A are found in returning travellers (2). Recent reports indicate that the number of individuals immune to HAV in the UK is decreasing (2–4). The apparent decrease in immunity to HAV should be reflected in the titre of the immunoglobulin manufactured in the UK and also in the effectiveness of this product. Other studies indicate that the prevalence of anti-HAV in young British subjects is high (5), hence there is a clear need to establish the prevalence of this infection when defining a policy for passive immunization with recently developed vaccines which are undergoing clinical trial. A further consideration is the increasing severity of hepatitis A and mortality from the infection with increasing age in the general population, which was recently confirmed in a highly selected group of patients presenting with fulminant hepatic failure in London (6).

MATERIALS AND METHODS

Individuals were selected at random during blood donor sessions. With their consent, donors were questioned as to whether they had a history of jaundice, if they had received immunoglobulin, if they had been in contact with anyone with a history of jaundice, and finally about their foreign travel. Of necessity the individuals selected for this study were between 18 years and 65 years, being the age group accepted for blood donation.

Total anti-HAV was assayed in serum samples by an ELISA inhibition technique (Hepanostika anti-HAV, Organon International). Controls consisted of dilutions of the WHO International Standard for Anti-HAV (100 IU/ml), obtained from the Dutch Red Cross, Amsterdam. Dilutions which gave a final concentration of 0·5 IU/ml and 1·0 IU/ml of the control were used as positive controls for each test strip. A negative control of known anti-HAV negative serum was used. Titrations of positive sera were made using dilutions of 0·5 IU/ml, 1·0 IU/ml, 5·0 IU/ml, 10 IU/ml and 20 IU/ml of the International Standard as controls.

Aliquots of 5 ml from two batches of normal human immunoglobulin prepared from pooled plasma by the Blood Products Laboratory, Elstree (Batch no. GG 97) and by the Institute Merieux, France (Batch no. M1 4197) were titrated for their content of total anti-HAV, and the results expressed in international units (IU).

RESULTS

The total number of samples tested was 1786, of which 1153 (64·5%) were found to be positive for anti-HAV. The distribution of seropositive donors by age group is shown in Table 1. A higher frequency of seropositive individuals was observed in age groups over 50 years, 73% to 75% compared to 57% for the 18 to 30 years age group. The results clearly show an increase in the frequency of seropositive individuals from 18 to 65 years. No apparent variation was found between males and females.

Although donors were not questioned specifically to determine their social class, certain assumptions could be made based on the area in which the particular blood donor sessions were held. Comparison of two distinct districts, Dagenham and Brentwood, revealed that 71·2% of donors (313 individuals) attending the Dagenham sessions were seropositive whilst 57·3% (129 individuals) attending the Brentwood sessions were found to be seropositive.

All the donors who reported a history of jaundice were found to be seropositive for HAV (45 donors). Of those donors who had received immunoglobulin prophylaxis, 46% were found to be seropositive (18 of 39 individuals).

It has been suggested that the risk of contracting HAV as a result of foreign travel is increased and that Southern Europe, Asia and N. Africa pose the highest risk. On examination of the data it was found that 132 individuals had never been abroad. This effectively formed a control group; of this group 60% were found to be positive for anti-HAV, which was similar to the overall frequency of 64·6%. Conversely, of those individuals who had been to N. Africa (256 individuals) 54%

Table 1. *Variation with age of percentage of seropositive individuals*

Age group	Total	Positive	Negative	% Positive
18–29	614	350	264	57
30–39	436	288	148	66
40–49	465	316	149	68
50–59	218	159	59	73
60–65	53	40	13	75
Total	1786	1153	633	

Table 2. *Antibody levels in seropositive individuals*

IU/ml anti-HAV	0·5	0·5–1·0	1–5	10–20	> 20
Percentage of anti-HAV positives (n = 112)	22	28	23	14	13
History of jaundice	26	31	28	15	0

Table 3. *Frequencies of anti-HAV in donor groups investigated*

	% Anti-HAV positive	Total in group
Overall frequency:	64·4	1786
at 18 yrs	55·5	126
at 65 yrs	75·0	98
History of jaundice	100·0	46
Family contact	67·3	120
Immunoglobulin prophylaxis	46·2	39
Travel to N. Africa	54·4	256
Never travelled abroad	60·2	132

Table 4. *Content of anti-HAV (IU/ml) in immunoglobulin*

Blood Products Laboratory, Elstree	Institut Merieux, France
295	520
345	472
310	460
390	579
410	440

were found to be seropositive, which suggested that the risk of contracting HAV while vacationing abroad is not significantly different from the risk in the UK.

Titration of sera containing anti-HAV revealed that 30% of those tested had levels below 0·5 IU/ml and 87% of those tested had levels below 20 IU/ml. Of the 13% who had levels of anti-HAV in excess of 20 IU/ml, one individual was found with levels of anti-HAV in excess of 40 IU/ml. Table 2 shows the levels of immunoglobulin detected in the individuals tested. Comparison of the antibody titres of those who reported a history of jaundice with those who did not, showed no significant difference in antibody levels (Table 2).

There was no clear evidence from this survey to suggest that there was a significantly higher frequency of seropositive individuals as a result of close contact with a member of the family with a history of jaundice. Sixty-seven per

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cent of this group were found to be positive compared to the overall frequency of 64·5%. Table 3 summarizes the data obtained for this survey.

The titre of total antibodies to hepatitis A in two batches of immunoglobulin is shown in Table 4, with an average of 250 IU/ml of anti-HAV in the immunoglobulin prepared from donated plasma in the UK and 482 IU/ml in the immunoglobulin fractionated in France.

DISCUSSION

The results in Table 1 show that the frequency of seropositive donors within the population investigated was 64·5%, which was identical to the frequency of 64% reported from the West of Scotland, and in British army personnel and recruits (1, 5, 7). However, the results show a marked difference from other published data (3, 4), where a lower frequency of the antibody in the population studied was reported. This included members of the Royal Air Force.

The results in Table 1 also show an increase in the frequency of immune individuals relative to age; 55% at 18 years rising to 75% at 65 years, which is again in broad agreement with the incidence previously reported. The inference from these results (Table 1), and others (5–7) is that the overall level of infection is declining, reflected by the lower incidence of immunity in individuals under 30 years old, but it is still relatively high. However, this interpretation should be made with care and further, more extensive, serological surveys should be undertaken in different regions of the UK.

All the donors who reported a history of jaundice were found to be seropositive. It should be noted, however, that some potential donors exclude themselves from blood donation if they have had a history of jaundice, so that the prevalence of anti-HAV seropositivity in the general population may be even higher than that in blood donors.

The data obtained for those people travelling abroad showed no apparent difference in terms of risk of infection, to that for people who remained in the UK. However, one difficulty in examining the results of any group having visited a specified region is that the farther away the country visited then the greater the possibility that those individuals have travelled extensively, making it difficult to draw any conclusions about those having visited a specified area. Furthermore, the more widely travelled individuals tended to be from the higher social classes.

It has been reported (5), that the prevalence of anti-HAV among 296 army recruits in a British Army Battle Group prior to deployment on exercise abroad, was found to 49%, which was similar to that found in the 17–20 year age group (56%, Table 1). In addition, of the 170 men who were anti-HAV negative prior to the battle exercise in a country in Africa, only one man seroconverted within 2 months of return and there were no reported cases of clinical hepatitis during the exercise or in the follow-up period.

Although only limited interpretation of the data relating to the differences in the frequency of seropositive individuals and social class was performed, there were indications that there are differences in communities within N.E. Thames Region. Two contrasting areas, in terms of social class, Brentwood and Dagenham, were compared. Brentwood is an affluent area with high cost housing and a much

larger percentage of residents in the upper social classes than are likely to live in Dagenham. Comparison of these two groups showed a significant difference in the frequency of seropositive individuals, 57·3% in Brentwood as opposed to 71·2% in Dagenham. The results indicted that the risk of hepatitis A infection is greater relative to social class and environmental conditions than travel.

Perhaps the most important point is to estimate the true clinical risk of hepatitis A, the value of immunoglobulin prophylaxis, and the requirement to protect individuals travelling to HAV endemic areas by prophylaxis with immunoglobulin and in due course by active immunization. The level of subclinical to clinical infection is known to be high and varies markedly with age at infection, with asymptomatic and anicteric infections occurring in early life. Furthermore, the finding that 64% of the surveyed population possessed antibody, suggests that there is a value in screening individuals for anti-HAV, which would avoid unnecessary administration of immunoglobulin to more than half the individuals requesting prophylaxis, as has previously been suggested (2). In this context it is reassuring to note that the context of total anti-HAV antibody in normal human immunoglobulin manufactured in the UK is in excess of the minimum titre of 100 IU of anti-HAV/ml recommended by a group of the World Health Organisation (8). The dosage for prophylaxis should be 2 IU anti-HAV/kg body weight and, in special cases such as pregnant women and patients with liver diseases, doubling of the dose may be considered.

Finally, killed and live attenuated hepatitis A vaccines are undergoing clinical trial. Infection with hepatitis A virus continues to be endemic in developing countries and, like other enterically transmitted viruses, in some counties infects 90% or more of the population by the age of 5–10 years, the infection often being mild and unrecognized. However, as socio-economic and sanitary conditions improve in such countries and the average age of exposure to hepatitis A virus increases, a paradoxical increase in clinical hepatitis and its severity is usually observed. For these reasons there will be a need for active prophylaxis against hepatitis A with vaccines which induce life long immunity, if the age of infection is not to rise any further. The policy in the UK will have to be defined according to the risk of infection in selected groups, such as military personnel and travellers to endemic areas, after laboratory screening for anti-HAV.

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