Prevalence of Immunity to Hepatitis A in Recruits to the British Army and Royal Air Force

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SUMMARY: Between 1989 and 1992, 92% of a sample of 2790 Service recruits aged between 17 and 35 years (mean age 19 years 7 months) were found not to be immune to infection by hepatitis A virus. The proportion of males with immunity was consistently greater than that for females. There was a significantly increased probability of immunity if individuals originated from Northern England, the Midlands and Scotland, in particular the suburbs.

Among male recruits there were significantly increased probabilities of immunity associated with travel to Southern and Eastern Europe or to the Tropics, and for females with travel to North West Europe or to Southern and Eastern Europe.

Introduction:

An inactivated hepatitis A vaccine has become available at a time when the prevalence of antibodies to hepatitis A virus (anti-HAV) is low in the young people resident in the United Kingdom (UK), and when the UK has seen a steady rise in reported cases of hepatitis A infection (1-4). This may reflect acquisition during travel outside the UK and community outbreaks in densely populated urban areas of Britain (2,3,4).

Previous studies of the prevalence of immunity to hepatitis A have mostly concentrated on individual populations (e.g. blood donors, travellers), age groups, different geographical areas and each during differing years. However, all of these studies suggest that the prevalence of immunity in those below 30 years of age in the UK generally has been falling during the last 15 years (4-10).

Nevertheless, there have been exceptions to this trend in certain populations: blood donors from West Scotland (11) and from North East Thames (12); and further regular serological surveys in different regions of the UK have been called for (8,12).

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In this study we present the prevalence of immunity to hepatitis A in recruits to the Army and Royal Air Force, from all regions of the UK between 1989 and 1992.

Subjects and Methods:

The prevalence of antibody (IgG) to hepatitis A virus was determined in the serum of 2790 healthy recruits to the British Army and Royal Air Force presenting to three UK Service recruiting centres between July 1989 and March 1992.

The Army samples were obtained predominantly from recruits to the Women's Royal Army Corps, and the remainder from a male recruiting centre. The Royal Air Force recruits also were predominantly female. Overall, the age range was between 17 and 35 years, with a mean age of 19 years 7 months; (median age 18 years 3 months, median ages: males, 18 years 5 months; females, 18 years 3 months).

During the first medical examination, each recruit completed a questionnaire which included the area of recruitment within the UK, and the areas where each recruit spent most of his/her life (suburbs, inner city or countryside).

Travel histories were obtained and categorised into four groups according to the estimated risk of exposure to hepatitis A infection: (a) no travel outside the UK; (b) travel only to North West Europe, North America/Canada or Australia - low risk; (c) travel to Southern and Eastern Europe, Mediterranean countries and Hong Kong - medium risk; (d) travel to Tropical countries of Africa, South America and South East Asia, the Middle and Far East and Indian sub-continent - high risk. Individuals were categorised according to the highest risk areas, and the lengths of stay in areas outside the UK were recorded.

Hepatitis A IgG antibodies were measured in serum by enzyme immunoassays; HAVAB EIA (Abbott Laboratories, Chicago, Illinois) at the Royal Army Medical College, and Hepanostika Anti-HAV (Organon Technika) at Royal Air Force Institute of Pathology and Tropical Medicine.

The relationships between the factors: gender, areas from which recruits were drawn, foreign travel history and the prevalence of hepatitis A antibodies were examined using multiple logistic regression on the GLIM software programme (13). The results are presented as odds ratios (with their associated confidence intervals and significance levels testing the null hypothesis of no association between the factors and antibody response), which estimate the ratio of the probabilities of immunity in going from one level of a factor to another (14).

Table 1
Prevalence of Hepatitis A Antibodies in Service Recruits

Year	Male (27.3%)	(%)	Female (72.7%)	(%)	Total (100.0%) (%)
1989 second half	37/299	(12.4)	12/117	(10.3)	49/416 (11.8)
1990	22/179	(12.3)	55/821	(6.7)	77/1000 (7.7)
1991	19/169	(11.2)	50/837	(6.0)	69/1006 (6.9)
1992 first quarter	14/115	(12.2)	15/253	(5.9)	29/368 (7.9)
Total	92/762	(12.2)	132/2028	(6.5)	224/2790 (8.0)

Results

The overall prevalence of immunity to hepatitis A in Service recruits between July 1989 and April 1992 was 8.0% (Table 1). The immunity among females (who formed 73% of the sample) was 6.5%, significantly lower than the 12.1% among males ($p < 0.00001$, Chi-squared with Yates' continuity correction, 95% Confidence Interval (CI) for the difference: male percentage minus female percentage = 3.0% to 8.1%)

Immunity to hepatitis A, determined on an annual basis, fell from 11.8% in the second half of 1989, to 7.7% in 1990, 6.9% in 1991 and 7.9% in the first quarter of 1992, (the relatively high level in 1989 is partly attributable to the disproportionately high number of males sampled in this year). However, the decrease in

immunity was only noticeable in female recruits (10.3% in 1989 to 5.9% in 1992), who, since they form the majority of the study sample, influence the overall figures. The prevalence of immunity in male recruits has been consistently higher than that in females, (about two-fold) since January 1990. The mean age for males with immunity was 21 years (range 17 to 28 years) compared to 19 years 8 months (range 17 to 26 years) for non-immune males. The corresponding ages for females were 21 years 2 months (range 17 to 35 years), and 19 years 6 months (range 17 to 35 years) respectively.

Table 2
Immunity to Hepatitis A by Area of Recruitment

Area	Number of recruits	% of Total recruits	Immune recruits number	(%)	% of total immune	% of total non immune
Total UK	2758	98.9	217	(7.9)	96.9	99.1
N. England Midlands & Scotland	1775	63.6	169	(9.5)	75.4	62.6
NW England	487	17.5	45	(9.2)	20.1	17.2
NE England	588	21.1	63	(10.7)	28.1	20.5
Midlands	420	15.1	36	(8.6)	16.1	15.0
Scotland	280	10.0	25	(8.9)	11.2	9.9
S England Wales & Ireland	983	35.2	48	(4.9)	21.4	36.4
SW England	276	9.9	11	(4.0)	4.9	10.3
SE England	435	15.6	24	(5.5)	10.7	16.0
Wales	228	8.2	11	(4.8)	4.9	8.5
Ireland	44	1.6	2	(4.5)	0.9	1.6
Overseas	32	1.1	7	(21.9)	3.1	1.0

The geographical locations from which the recruits were drawn and the corresponding prevalences of immunity are shown in Table 2. Overall, 64% of all recruits in the sample were drawn from Northern England (North East and North West), the Midlands and Scotland. From these four areas originated 75% of immune and 63% of non-immune recruits. The thirty-two recruits from outside the UK demonstrated a high prevalence of immunity to hepatitis A (21.9%) and these individuals were omitted from the subsequent analysis. The effect of area of recruitment was independent of the effects of gender and origin; 9.5% of recruits drawn from the Northern areas were immune, compared to the 4.9% of recruits from Southern England, Wales and Ireland (the odds ratio, estimating the increased probability of being immune if from the North = 1.94, $p = 0.0001$, 95% CI = 1.38 to 2.73). The origins of recruits with anti-HAV within the areas from which they were drawn indicated that 60.8% spent most of their life in the suburbs, 24.4% in the inner city areas and 14.8% in the countryside, compared to 44.4%, 28.1% and 27.6% respectively for recruits without the antibody.

Table 3 shows the prevalence of hepatitis A immunity by the interacting factors of gender and origin. Only among those recruits who originated from the suburbs is there a significantly increased probability of immunity if male (stratified by area of recruitment), the odds ratio being 3.24 ($p < 0.00001$, 95% CI = 2.23 to 4.73). The effect of origin was greater among the male recruits, with life in the suburbs being associated with significantly higher probabilities of immunity than in the inner city (odds ratio = 3.88, $p < 0.00001$, 95% CI = 2.30 to 6.56) or the country (odds ratio = 3.42, $p = 0.001$, CI = 1.63 to 7.20). For females, the only significant result was an odds ratio of 1.87 ($p = 0.01$, 95% CI = 1.16 to 3.02), when immunity in recruits originating from the suburbs was compared to that from the country.

Table 3
Prevalence of Hepatitis A Immunity by Gender and Origin*

Origin	Number immune/Total recruits (%)				
	Male		Female		Total
Suburbs	58/274	(21.2)	74/985	(7.5)	132/1259 (10.5)
Inner City	22/323	(6.8)	31/444	(7.0)	53/767 (6.9)
Country	9/151	(6.0)	23/581	(4.0)	32/732 (4.4)
Total	89/748	(11.9)	128/2010	(6.4)	217/2758 (7.9)

*Excluding recruits drawn from countries outside the United Kingdom.

Travel histories were available for 2712 (97.2%) recruits, and the observed prevalence of hepatitis A immunity by gender and travel history is shown in Table 4. Overall, 41.7% of males and 35.4% of females had not travelled outside the UK. Travel solely to countries within North West Europe, North America and Australia was recorded by 19.5% of males and 4.8% of females. None of the recruits recorded travel to South America. A large proportion of males (32.8%) and females (52.7%) had visited countries within Southern and Eastern Europe (Spain, Portugal, Italy, Greece, Turkey, former Yugoslavia and the Mediterranean countries). Over two-thirds of recruits with immunity (68%) and 46% of those without immunity had spent one month or less in any one of these Southern or Eastern European countries. Tropical countries of Africa and Asia had been visited by 6.0% of males and 7.1% of females. More immune males (10%) than females (7%) had travelled to the Tropics, and whereas 75% of those with immunity had spent more than one year in these areas, only 26% of those without immunity had stayed for this period. Among male recruits, the increased probabilities of immunity associated with travel to Southern and Eastern Europe or the Tropics compared to travel only to North West Europe or to no travel outside the UK, were statistically significant: (for South East Europe compared to North West Europe, the odds ratio = 2.31, $p = 0.01$, 95% CI = 1.20 to 4.45; for the Tropics compared to North West Europe, the odds ratio = 2.61, $p = 0.04$, 95% CI 1.03 to 6.61; for South East Europe compared to no foreign travel, the odds ratio = 2.83, $p = 0.0001$, 95% CI = 1.66 to

4.84; and for the Tropics compared to no foreign travel, the odds ratio = 3.20, $p = 0.007$, 95% CI = 1.37 to 7.48). For females, the situation was less clear, travel to some of the more endemic areas being associated with significantly lower prevalences of immunity than travel to less endemic areas. However, the increased probabilities of immunity associated with travel to North West Europe or to Southern and Eastern Europe compared to no travel outside the UK were significant; (for North West Europe compared to no foreign travel the odds ratio = 6.09, $p = 0.00001$, 95% CI = 3.33 to 11.12 and for South East Europe compared to no foreign travel, the odds ratio = 1.58, $p = 0.04$, 95% CI = 1.02 to 2.44).

Discussion

This study shows that nearly 90% of males and 95% of females recruited to the British Army and Royal Air Force between 1989 and 1992, aged between 17 and 35 years (mean age 19 years 7 months), and drawn from all areas of the UK, did not have immunity to hepatitis A. To some extent, this may reflect the present situation within this age group in the general population; however, due to the distribution of age and the bias towards females (73% of the sample) and certain geographical locations, this study group is not fully representative of the whole UK population.

Table 4
Observed Prevalence of Hepatitis A Immunity by Gender and Foreign Travel History

	Number immune		Total recruits (%)		Total	
	Male		Female			
Area of travel outside UK						
Nil	23/301	(7.6)	31/705	(4.4)	54/1006	(5.4)
North Western Europe	13/141	(9.2)	21/96	(21.9)	34/237	(14.3)
Southern & Eastern Europe	45/237	(19.0)	71/1048	(6.8)	116/2185	(9.0)
Tropics & Asia	9/43	(20.9)	9/141	(6.4)	18/184	(9.8)
Total	90/722	(12.5)	132/1990	(6.6)	222/2712	(8.2)

A decreasing trend in prevalence of immunity to hepatitis A between 1989 and 1992 was noticeable only among female recruits, who formed the majority of the study sample and thus influenced the overall figures. As the majority of Service recruits are male there is little evidence to indicate an appreciable decrease in immunity over this period in the total recruit population. Nevertheless, the results from this survey are in marked contrast to those in two reviews in 1986, the first of 467 male recruits aged between 17 and 20 years, in which 49.8% were found to be immune to hepatitis A (Menzies

RC, unpublished report), and the second of 296 recruits of whom 49% were immune (15). Also, we found lower percentile levels of immunity than those of 13 to 20% in 16 to 30 year old male Service personnel reported in 1984-1986 (5).

Opinions have differed as to the validity of the association between travel to areas endemic for hepatitis A and the acquisition of infection and immunity. Whereas no apparent increase in the level of hepatitis A immunity was shown for individuals travelling abroad (12,15), the majority view is that international travel by civilian populations and British soldiers is associated with infection and immunity to hepatitis A (3,11,16-20).

Individuals aged between 17 and 35 years often travel to countries with a moderate to high endemicity for hepatitis A, either for recreation (particularly trekking and back-packing), or as members of the Armed Services. Three studies have illustrated that the development of immunity to hepatitis A in British soldiers has been associated with time spent in such areas. During 1986, a study of 519 males from an infantry battalion showed that between 56% and 73% of those aged 17 to 30 years were immune to hepatitis A (the mean age was 24 years with a range of 17 to 47 years; mean length of Service 6.5 years with a range of 1 to 26 years), (20). In the same year, 67% of 334 male personnel aged between 25 and 35 years, in a Specialist Army Unit which had travelled frequently to highly endemic areas were immune (Worsely S, unpublished report). In contrast, only 26% of 394 male personnel from an infantry battalion with less frequent foreign travel possessed immunity. Although the overall age was 18 to 45 years, 290 soldiers of this battalion were in their first 3 years of service and were aged 18 to 24 years (mean age 20 years) (Cumberland N, 1990. Unpublished data). These, and other studies have indicated that the prevalence of immunity in the UK population increases with age (5,8-11,20.).

The present study provides evidence of significant increases in the prevalence of antibodies to hepatitis A in males who have travelled to Southern and Eastern Europe or to Tropical Africa and Asia when compared to those who have not visited these areas. The increased relative risks of infection after travel to these areas reported here are similar to those reported for similar areas in a recent large Italian study (16). Increases in the prevalence of immunity were also seen in females who had travelled to Southern and Eastern Europe or to North West Europe, when compared to those who had not travelled outside the UK.

For cost-efficiency and for minimising the unnecessary use of Human Normal Immunoglobulin (HNIG) or of vaccine, the determination of immune status before passive immunisation or vaccination against hepatitis A is considered desirable (3). Whilst some authors have recommended screening all adults before immunisation (5), others have indicated that the need for screening depends upon factors such as age, socio-economic

background, traveller's place of residence in UK, travel to and length of stay in endemic areas, a past history of jaundice and local prevalence of immunity in regions of the UK (5,8,10,12,15,21). More specifically, authors recommend that for those normally resident in UK and aged below thirty to fifty years of age, screening would not be worthwhile (2,5,10,11,22). The prevalence of immunity found in this study population also would confirm that screening those under 30 years of age before immunisation would not be cost effective.

Following screening for antibody to hepatitis A, the Royal Air Force immunise personnel with HNIG prior to travel to endemic areas. In contrast, with the exception of individuals and small units, the Army has not used HNIG prophylaxis routinely to protect personnel against hepatitis A infection. Reliance has been placed on strict personal and food hygiene and minimal contact with the local population. This policy proved effective for British troops in the Gulf (October 1989 to March 1991), from which only 9 presumed cases of hepatitis A in Army personnel were evacuated to the UK, three of which were confirmed serologically (23).

Concern has been expressed that falling levels of immunity in UK blood donors, with the concomitant reduction in anti-HAV titres, will compromise the potency of donated pooled HNIG (1,3,24). The failure of passive immunisation to protect fully against infection may occur; indeed, two cases, one fatal, of hepatitis A infection despite HNIG have recently been reported (24). Our evidence would support this concern, that the present trend in low levels of immunity may continue in the young population of the UK.

The higher prevalence of immunity in recruits from the north of England, the Midlands and Scotland reflects the higher levels of reported cases of hepatitis A among the general population in these regions (3,11,25), and the lower prevalence in the south west of England reflects that reported in Avon between 1985 and 1987 (8). Likewise, the consistently higher prevalence of anti-HAV in males in this study reflects the higher proportion of males in both notified and laboratory reports of hepatitis A infection (3).

Hepatitis A vaccine may be used as an alternative to HNIG prophylaxis (1), for frequent travellers to areas of moderate to high endemicity or for visits of longer than 3 months. The target groups for vaccination have been reviewed: it should be considered for travellers from developed countries making frequent or long term visits to Greece, Turkey and countries outside North West Europe, North America and Australia, and for members of the Armed Services going abroad (2,3,4,22). Moreover, Service personnel may be required frequently, and at short notice, to operate in countries located in sub-Saharan Africa, Central America, South East Asia and recently the Middle East and republics of former Yugoslavia, where the endemicity of hepatitis A infection is higher than that in the UK (18,26,27). This study provides a further

indication that immunity to hepatitis A in the UK population (with a few exceptions (25)), aged between 17 and 35 years has fallen during the last 10 to 15 years, and that today, Service recruits drawn from this age range are largely unprotected.

Taken together with previous reports, the present study provides information upon which to construct a policy for the active immunisation with hepatitis A vaccine of Service personnel and others in the same age group who are at risk of infection during travel, or by occupation (1,2,3,22). In addition, the study documents levels of immunity observed during 1989-92 in this age-group which can be compared to future serological surveys. Finally, these data could be used as a basis for constructing policies, applicable to the 17 to 35 year age group, for the need to screen for hepatitis A immunity and for immunisation, both of which could be tailored to the underlying regional prevalence of immunity.

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