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The prevalence of hepatitis B infection in adults in England and Wales

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SUMMARY

Cost effectiveness analyses of alternative hepatitis B vaccination programmes in England and Wales require a robust estimate of the lifetime risk of carriage. To this end, we report the prevalence of infection in 3781 anonymized individuals aged 15–44 years whose sera were submitted in 1996 to 16 microbiology laboratories in England and Wales. One hundred and forty-six individuals (3·9%) were confirmed as anti HBc positive, including 14 chronic carriers (0·37%). The prevalence of infection and carriage was higher in samples collected in London and increased with age. No increased risk of infection was seen in sera from genito-urinary (GUM) clinics. Only 15 sera positive for hepatitis B were also positive for hepatitis C. Our results confirm the low prevalence of hepatitis B in England and Wales, are consistent with previous estimates of carriage and suggest that many infections were acquired while resident outside the UK. Future prevalence studies should determine the country of birth and other risk factors for each individual in order to confirm these findings.

INTRODUCTION

The most appropriate strategy for hepatitis B vaccination in England and Wales is the subject of much debate [1, 2]. Currently, immunization is recommended only in individuals at increased risk of infection because of their lifestyle, occupation or other factors [3]. The WHO recommends that all countries should implement universal immunization, but it is not clear that the burden of disease in England and Wales justifies the high cost that would be entailed. Previous studies have found a high prevalence of past infection, typically 15–40%, in intravenous drug users and homosexual men [4–7], but the low prevalence of carriage in antenatal women [8] and new blood donors [9] suggests that infection may be confined largely to these high risk groups. Better information on the incidence and prevalence of hepatitis B infection in the general population is needed to inform cost effectiveness analyses of the vaccination programme options.

Most of the morbidity attributable to hepatitis B infection is due to the sequelae of chronic carriage, which include cirrhosis and hepatocellular carcinoma. The prevalence of hepatitis B carriage varies considerably around the world and is used to classify countries as having high ($\geqslant 8\%$ carriage), intermediate (2–7%) or low ($< 2\%$) endemicity [10]. In countries with high endemicity, most infections are acquired perinatally or in childhood [10]. England and Wales has low endemicity; the prevalence of carriage

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Table 1. *Criteria used to classify hepatitis B infection from the results of serological tests*

Anti HBc	HBsAg	IgM	Categorization	No. samples (%)
Negative	—	—	Not infected	3635 (96·1%)
Positive	Negative	Negative	Resolved infection	128 (3·4%)
Positive	Positive	Strong positive	Acute infection	4 (0·1%)
Positive	Positive	Negative/weak positive	Chronic carrier	14* (0·4%)

* One carrier was positive for HBe antigen.

has been estimated as 0·3% [11], based on data from antenatal screening programmes. The incidence of acute infection is also low – approximately 600 acute infections are reported annually (a rate of 1 per 100000 population) – with most cases occurring in intravenous drug users (IDUs) and sexual high risk groups [12]. Infection in childhood is rare [13]. A full appraisal of the potential impact of different vaccination strategies would require a detailed knowledge of the epidemiology of hepatitis B infection. A more limited exploratory analysis of the cost effectiveness of universal infant immunization could be based on an estimate of the risk that an infant will become a carrier in its lifetime.

The lifetime risk of an infant becoming a carrier will depend on future trends in the incidence of infection, which may be inflenced by unpredictable changes in the behaviour of high risk groups. An estimate of lifetime risk could be based on the current age-specific incidence of acute infection, by adjusting reports of laboratory confirmed acute infection for asymptomatic infection and underreporting [14], or on the prevalence of markers of past infection. Although seroprevalence is an indicator of the past incidence in a population, it is also affected by migration and death. Immigration from countries where hepatitis B is highly endemic may be an important influence on the prevalence of past infection in England and Wales. We report the results of a large cross-sectional study of the prevalence of hepatitis B infection in the population of England and Wales, and assess the contributions of infections acquired while resident in England and Wales and those acquired while resident overseas.

METHODS

In 1996, 3781 residual diagnostic sera from adults aged 15–44 years were collected in 16 laboratories in England and Wales as part of the PHLS serological surveillance programme. Sera submitted for testing for hepatitis B infection were not excluded. Each serum was unlinked from patient identifiers and tested anonymously; the only information retained was age, sex, collection laboratory and, where available, whether or not the serum was submitted from a GUM clinic.

All sera were tested at Preston Public Health Laboratory for total hepatitis B core antibody (anti HBc) by enzyme immunoassay (Ortho, UK). Reactive sera were tested by another anti HBc enzyme immunoassay (Johnson and Johnson UK Ltd). Sera confirmed as positive for anti HBc were tested for other markers of hepatitis B infection using commercial enzyme immunoassays. The status of hepatitis B infection in each individual was categorized according to these results (Table 1). Sera from individuals with confirmed hepatitis B infection were also tested for antibody to hepatitis A and hepatitis C. Testing for hepatitis A antibody was extended to a representative sample of negative sera; 1785 sera (47%) were tested in all.

It was not possible to ascertain the country of birth of the individuals from whom the sera were taken. Population data were used to investigate the relationship between the prevalence of hepatitis B infection and the extent of immigration from countries with much higher endemicity. For this analysis it was assumed that the samples were representative of the catchment population in terms of continent of birth. For each laboratory the expected proportion of samples in each age group from individuals born in Africa and Asia, the continents with the highest prevalence of hepatitis B infection, was calculated from population data for the approximate catchment area [15].

RESULTS

One hundred and forty-six sera (3·9%) were confirmed as anti HBc positive (Table 1). The prevalence of both infection and carriage was higher in samples collected

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Table 2. *Prevalence of hepatitis B infection by sex in samples collected in and outside London: number of samples tested, number (%) infected (i.e. positive for anti HBc) and number (%) of chronic carriers*

	Males			Females		
Region	Tested	Infected	Carriers	Tested	Infected	Carriers
Outside London	1384	46 (3·3%)	4 (0·3%)	1655	29 (1·8%)	2 (0·1%)
London	366	36 (9·8%)	7 (1·9%)	376	35 (9·3%)	1 (0·3%)

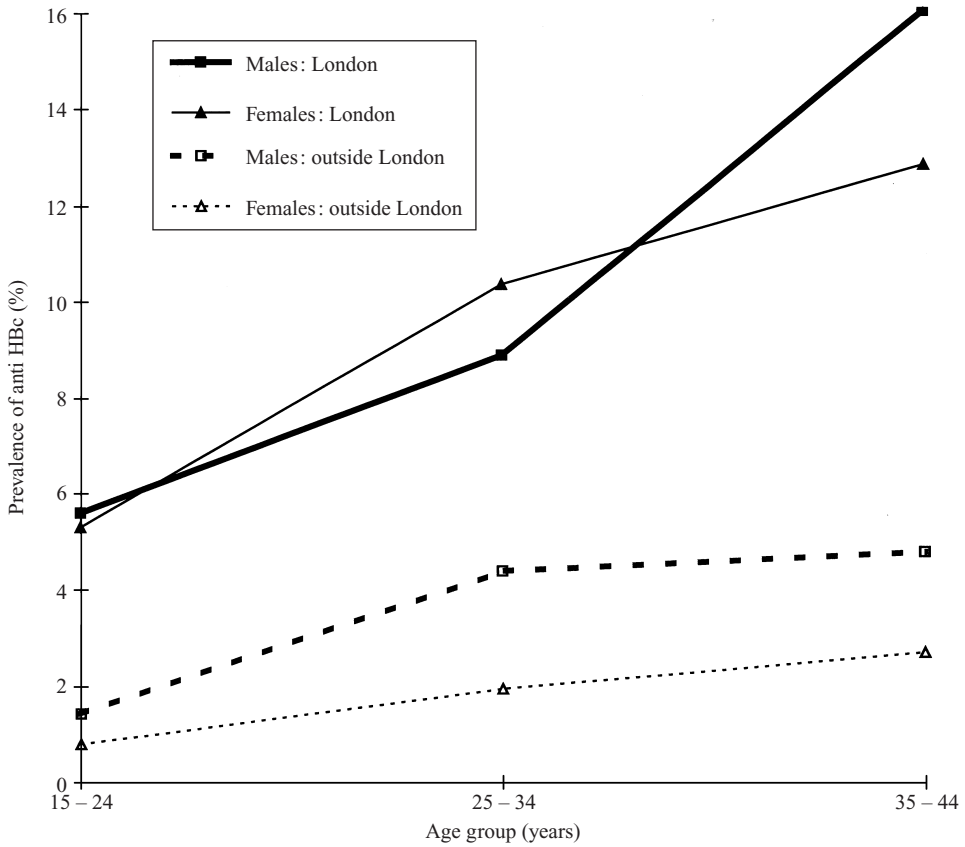

Fig. 1. Age specific prevalence of anti HBc in serum samples stratified by sex and region.

in London than elsewhere ($P < 0{\cdot}0001$) (Table 2) and increased with age ($P < 0{\cdot}0001$) (Fig. 1). In samples collected outside London, the prevalence was higher in males than females ($P = 0{\cdot}004$), but this difference was not significant in London ($P = 0{\cdot}82$). The prevalence of infection in sera from GUM clinics (11/425, 2·6%) was not significantly different from the prevalence in sera known to be taken elsewhere (86/2538, 3·4%) ($P = 0{\cdot}33$, adjusted for age, sex and region). For 818 sera it was not known whether they were submitted from GUM clinics.

The prevalence of antibody to hepatitis A in sera positive for anti HBc was 68% (76/112, 34 insufficient), significantly higher than in sera negative for anti HBc (491/1673, 29%) ($P < 0{\cdot}0001$, adjusted for age, sex and region). The prevalence of antibody to hepatitis C in anti HBc positives was 10% (15/145, 1 insufficient), with no significant regional variation.

The proportion of the population of England and Wales born in Africa and Asia increases with age and is considerably higher in London than outside [15]. Assuming that the samples from each laboratory are representative of the catchment population in terms of continent of birth, the prevalence of hepatitis B infection (stratified by 10 year age group, sex and London versus outside London) is plotted against the expected proportion of samples from individuals born in Africa and Asia (Fig. 2). The apparent linear

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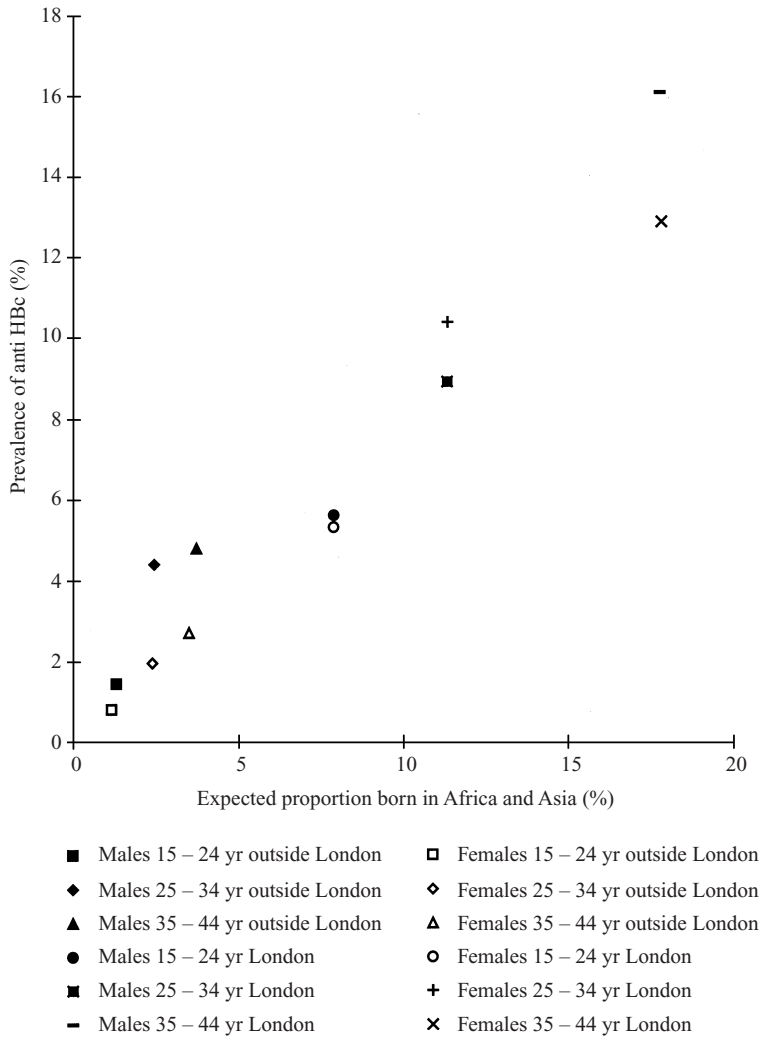

Fig. 2. Relationship between prevalence of anti HBc and expected proportion of samples from individuals born in Africa and Asia. The data are stratified by sex, region and by three age groups.

relationship suggests that the proportion born in Africa and Asia may be an important influence on the prevalence of hepatitis B infection.

DISCUSSION

The sera used in this study were not sampled randomly from the population, but were the residues of sera submitted to laboratories for microbiological or biochemical investigation. The sera are broadly geographically representative having been collected in 16 microbiology laboratories across England and Wales. Sources of sera include general practitioners, antenatal and GUM clinics and hospitals. Although similar studies of more common infections suggest no major bias in sampling [16–18], it is possible that the risk groups for acute hepatitis B infection in England and Wales may be over or under represented. Sera submitted for testing for hepatitis B infection were not excluded, causing acute and recent infections to be overrepresented. Alternative sampling methods might not produce a more representative sample, given the potential for selection and non-compliance biases.

Our results confirm the low prevalence of hepatitis B in England and Wales and are consistent with previous estimates of carriage based on data from antenatal screening [8]. The high prevalence of past infection and carriage in London has been observed in previous studies [19, 20].

Most acute hepatitis B infections reported in England and Wales occur in IDUs and sexual high risk groups [12]. To investigate the contribution of infections in IDUs to the hepatitis B infections detected in our study, we tested these sera for hepatitis C infection, a relatively sensitive marker for a history of intravenous drug use (the prevalence of hepatitis C

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infection in intravenous drug users is approximately 70% [21–23]). Only 10% were positive. To investigate the contribution of sexual high risk groups, we compared the prevalence of hepatitis B infection in samples taken from GUM clinics with the prevalence in samples taken elsewhere. There was no increased risk in GUM clinic attenders. These results suggest that the risk groups for reported acute infection contributed little to the prevalence of past hepatitis B infection observed in our study. So how and where did these individuals acquire their infection? One possible explanation is that they were infected whilst resident in England and Wales but that the infections were not reported. This might be the case if they were infected in childhood, when a high proportion of infections are asymptomatic. However, a seroprevalence study of more than 2000 children aged 13–14 years from outside London found that only 15 (0·7%) had any evidence of hepatitis B infection [13]. The most likely explanation is that many infections were acquired while resident outside England and Wales, by persons born in countries with a higher endemicity of hepatitis B. This would also account for the strong association we observed between the age specific prevalence of hepatitis B infection and the proportion of the denominator population born in Africa and Asia (Fig. 2). The higher prevalence of hepatitis A antibody in anti HBc positives could also be explained by their exposure to a high endemic level of hepatitis A overseas.

This study does not demonstrate explicitly that many hepatitis B infections were acquired while resident overseas, but such a scenario does provide a consistent explanation for all our observations. Infections acquired while resident overseas may even account for the majority of past hepatitis B infections in residents of England and Wales. This should be confirmed by studies that determine the country of birth and other risk factors of each individual. A study of heterosexual GUM clinic attenders in the West Midlands found a prevalence of past infection of 1·9%, with most (15/28) positives born outside the UK [24]. Similar studies elsewhere would provide an upper limit on the risk of heterosexual infection in England and Wales.

Better data on transmission within communities with a higher prevalence of carriage are also needed. A well-implemented universal antenatal screening programme with appropriate immunization of infants of carrier mothers should prevent most perinatal transmission, but horizontal transmission within families is not well studied. Data from antenatal screening in the West Midlands suggest that, for all ethnic groups, the prevalence of carriage is 4–5 times lower in persons born in the UK than those born overseas [8]. This reinforces the suggestion that horizontal transmission is not common, but further studies are warranted.

The overall prevalence of carriage in this study was 0·37%. However, if many of these infections were acquired overseas before migration to England and Wales, they could not have been prevented by a vaccination programme in England and Wales. The prevalence of carriage preventable by universal vaccination in England and Wales, determined by the lifetime risk of hepatitis B carriage in an infant born in England and Wales, may be considerably lower. The published cost-effectiveness analyses of hepatitis B immunization have used estimates of the lifetime risk of carriage in the range 0·1–0·5% [14, 25, 26]. Our results suggest that the true risk lies towards or below the bottom of this range; further studies would refine this estimate. The lower this risk, the less attractive universal vaccination becomes.

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REFERENCES

1. van Damme P, Kane M, Meheus A. Integration of hepatitis B vaccination into national immunisation programmes. BMJ 1997; **314**: 1033–6.
2. Mortimer PP, Miller E. Commentary: antenatal screening and targeting should be sufficient in some countries. BMJ 1997; **314**: 1036–7.
3. Department of Health. Immunisation against infectious disease. London: HMSO, 1996.
4. Gilson RJC, de Ruiter A, Waite J, et al. Hepatitis B virus infection in patients attending a genitourinary medicine clinic: risk factors and vaccine coverage. Sex Trans Inf 1998; **74**: 110–5.
5. Unlinked Anonymous Surveys Steering Group. Unlinked anonymous HIV prevalence monitoring programme England and Wales. Data to the end of 1995. London: Department of Health, 1996.

6. Bhatti N, Gilson RJC, Beecham M, et al. Failure to deliver hepatitis B vaccine: confessions from a genitourinary medicine clinic. BMJ 1991; **303**: 97–101.
7. Hart GJ, Dawson J, Fitzpatrick RM, et al. Risk behaviour, anti-HIV and anti-hepatitis B core prevalence in clinic and non-clinic samples of gay men in England, 1991–1992. AIDS 1993; **7**: 863–9.
8. Boxall E, Skidmore S, Evans C, Nightingale S. The prevalence of hepatitis B and C in an antenatal population of various ethnic origins. Epidemiol Infect 1994; **113**: 523–8.
9. CDSC. Surveillance of viral infection in donated blood: England and Wales, 1996. CDR 1997; **7**: 258.
10. Grosheide P, van Damme P. Prevention and control of hepatitis B in the community. Antwerp: Viral Hepatitis Prevention Board Secretariat, 1996.
11. Boxall EH, Flewett TH. Prevalence of HBsAg in UK population. BMJ 1987; **294**: 57.
12. Balogun MA, Ramsay ME, Fairley CK, Collins M, Heptonstall J. Acute hepatitis B infection in England and Wales: 1985–96. Epidemiol Infect 1999; **122**: 125–131.
13. Hesketh LM, Rowlatt JD, Gay NJ, Morgan-Capner P, Miller E. Childhood infection with hepatitis A and B viruses in England and Wales. CDR 1997; **7**: R60–3.
14. Fenn P, Gray A, McGuire A. An economic evaluation of universal vaccination against hepatitis B virus. J Infect 1996; **32**: 197–204.
15. Office of Population Censuses and Surveys and General Register Office for Scotland. 1991 Census: ethnic group and country of birth, Great Britain. London: HMSO, 1993.
16. Gay NJ, Ramsay ME, Cohen BJ, et al. The epidemiology of measles in England and Wales since the 1994 vaccination campaign. CDR 1997; **7**: R17–21.
17. Gay NJ, Miller E, Hesketh LM, et al. Mumps surveillance in England and Wales supports the introduction of two dose vaccination schedule. CDR 1997; **7**: R21–6.
18. Miller E, Tookey PA, Morgan-Capner, P, et al. Rubella surveillance to June 1994: third joint report from the PHLS and the National Congenital Rubella Surveillance Programme. CDR 1994; **4**: 146–52.
19. King R, Johnson PJ, White YS, Smith HM, Williams R. Frequency of asymptomatic hepatitis types B and C in an inner city community and relation to possible risk factors. Quart J Med 1991; **80**: 641–9.
20. Brook MG, Lever AML, Kelly D, et al. Antenatal screening for hepatitis B is medically and economically effective in the prevention of vertical transmission: three years experience in a London hospital. Quart J Med 1989; **71**: 313–7.
21. Ramsay ME, Balogun MA, Collins M, Balraj V. Laboratory surveillance of hepatitis C infection in England and Wales: 1992 to 1996. Commun Dis Public Health 1998; **1**: 89–94.
22. Goldberg D, Cameron S, McMenamin J. Hepatitis C virus antibody prevalence among injecting drug users in Glasgow has fallen but remains high. Commun Dis Public Health 1998; **1**: 95–7.
23. Majid A, Holmes R, Desselburger U, Simmonds P, McKee A. Molecular epidemiology of hepatitis C infection amongst intravenous drug users in rural communities. J Med Viron 1995; **46**: 48–51.
24. El-Dalil AA, Jayaweera DT, Walzman M, et al. Hepatitis B markers in heterosexual patients attending two genitourinary medicine clinics in the West Midlands. Genitourin Med 1997; **73**: 127–30.
25. Mangtani P, Hall AJ, Normand CEM. Hepatitis B vaccination: the cost effectiveness of alternative strategies in England and Wales. J Epidemiol Comm Hlth 1995; **49**: 238–44.
26. Williams JR, Nokes DJ, Anderson RM. Targeted hepatitis B vaccination – a cost effective strategy for the UK? J Epidemiol Comm Hlth 1996; **50**: 667–73.