

Can the United Kingdom control viral hepatitis?

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Part I Can the United Kingdom control viral hepatitis?

– bibliography (in alphabetical order) –

Atkins M, Nolan M. Sexual transmission of hepatitis B. *Curr Opin Infect Dis* 2005; 18:67-72.

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Hepatitis B virus infection is prevalent worldwide and is a significant cause of morbidity and mortality particularly in Asia. Adults chronically infected with hepatitis B virus remain a significant potential source of sexually transmitted hepatitis B. The purpose of this article is to review the recent literature relating to hepatitis B virus transmission with particular emphasis on sexual transmission and efforts to prevent spread. The introduction of hepatitis B virus vaccine and the implementation of universal childhood vaccination for hepatitis B in some countries have led to a dramatic reduction in the number of children with chronic hepatitis B. However, recent reports suggest that we are not as successful in preventing infection by sexual transmission. It is clear that sexual transmission of hepatitis B virus is still widespread and is a major problem in certain high-risk groups such as men who have sex with men, intravenous drug users, prisoners and sex workers. Significant problems remain with respect to education and vaccination within these groups. Hepatitis B virus remains a major health burden but it is preventable by education and vaccination. Greater resources are required to expand vaccination to the at-risk, sexually active adult populations if the World Health Organization ideal of hepatitis B virus eradication is to be realized and the burden of hepatitis B virus-related morbidity and mortality contained.

Balogun MA, Ramsay ME, Hesketh LM, Andrews N, Osborne KP, Gay NJ, Morgan-Capner P. The prevalence of hepatitis C in England and Wales. *J Infect* 2002; 45:219-226.

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The objectives were to estimate the background population prevalence of hepatitis C in England and Wales, observe the prevalence over time and assess the extent of infection outside of known risk groups. Sera from residual specimens from adult patients submitted to laboratories in England and Wales were tested for anti-HCV. Testing was carried out using a cost-effective pooling strategy. Although the prevalence of anti-HCV was highest in 1986 (1.07%), in the multivariable analysis, prevalence did not vary significantly between the 3 periods 1986, 1991 and 1996 ($P = 0.14$). The prevalence of infection was higher in males than in females ($P = 0.0013$). An age-period-cohort analysis revealed a cohort effect due to a lower HCV prevalence in the most recent birth cohorts, that is, those born between the calendar years 1971-1975 and 1976-1980. The majority of HCV infections in England and Wales were probably acquired before 1986. Infections in younger males identified in 1996 may signify more recent acquisition by injecting drug use.

Balogun MA, Ramsay ME, Parry JV, Donovan L, Andrews NJ, Newham JA, Cliffe S, Harris KA, Teo CG. The prevalence and genetic diversity of hepatitis C infection in antenatal clinic attenders in two regions of England. *Epidemiol Infect* 2000; 125:705-712.

Hepatitis and Retrovirus Laboratory, PHLS Central Public Health Laboratory, London.

The prevalence and genetic diversity of hepatitis C infection in women attending antenatal clinics

in two regions of England was investigated to inform future surveillance and control measures. Women booking into antenatal care are routinely offered a test for immunity to rubella. Serum residues from these tests were unlinked, anonymized and archived as part of the Unlinked Anonymous Prevalence Monitoring Programme (UAPMP). The serum specimens were tested for anti-HCV using a cost-effective pooling strategy. After taking into account differential sampling from the UAPMP serum archive, the adjusted overall prevalence of anti-HCV was 0.43% (95% CI: 0.32-0.53) in London and 0.21% (95% CI: 0.14-0.28) in the Northern and Yorkshire region. Restriction fragment length polymorphism of amplified HCV RNA identified type 3a as the most common HCV genotype in these antenatal women. The prevalence of anti-HCV in antenatal women in the UK is low and consistent with that expected from injecting drug use.

Balogun MA, Ramsay ME, Parry JV, Donovan L, Andrews NJ, Newham JA, McGarrigle C, Harris KA, Teo CG. A national survey of genitourinary medicine clinic attenders provides little evidence of sexual transmission of hepatitis C virus infection. *Sex Transm Infect* 2003; 79:301-306.

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The objectives were to determine the prevalence and genetic diversity of hepatitis C virus in genitourinary medicine clinic attenders and to assess the extent of sexual transmission of the virus. A cross sectional, unlinked, anonymous survey in 14 genitourinary medicine clinics situated in England, Wales, and Northern Ireland. Serum specimens from genitourinary medicine clinic attenders, retained as part of the Unlinked Anonymous Prevalence Monitoring Programme (UAPMP) serum archive, were tested in small pools, for the presence of antibody to hepatitis C virus (anti-HCV). The main outcome measures were prevalence of antibodies to hepatitis C virus and identification of hepatitis C virus genotypes. Testing of 17,586 specimens from 1995 showed an adjusted prevalence of anti-HCV in genitourinary medicine clinic attenders of 1.03% (95% CI: 0.89 to 1.16) overall and 0.65% (95% CI: 0.51 to 0.78) among those who did not report injecting drug use. Prevalence in injecting drug users attending genitourinary medicine clinics was 36.9% in both 1995 and 1996. Heterosexual injecting drug users had a higher prevalence of anti-HCV than homosexual / bisexual injectors. The most common hepatitis C genotypes were types 3a and 1a. There was a high degree of concordance between genotype and serotype. The low prevalence of anti-HCV in genitourinary medicine clinic attenders who deny injecting drugs suggests that the majority of hepatitis C infections have been acquired in adult life, mostly by injecting drug use, and that the hepatitis C virus is rarely transmitted sexually. The use of needle exchanges may explain the relatively low prevalence observed in the injecting drug users.

Bath GE, Scott TG, Sibbald CJ, Upton PA, Ramsay CN, Willocks LJ. Acute hepatitis B in Edinburgh 1975-92: a retrospective study in a population where human immunodeficiency virus is highly prevalent. *Epidemiol Infect* 1997; 119:85-89.

Lothian Health, Edinburgh, UK.

A retrospective study of notified hepatitis B virus (HBV) infection in Edinburgh during 1975-92 identified 525 acute cases. For 343 where a probable transmission route could be determined, 215 were due to shared equipment by injection drug users (IDUs), 29 to homosexual intercourse, 25 to heterosexual or household contact with IDUs, 21 to heterosexual contact with infected non-IDU partners and 53 to various other or multiple routes. Cases were unevenly distributed geographically, particularly those among IDUs. The highest incidence within a post code district was approximately 2.5 times that for all Edinburgh. Annual cases peaked in 1984 then declined to low levels in the early 1990s. This reduction was most marked among IDUs, and may be ascribed both to changed injecting behaviour and decreased susceptibility within this group. The latter

factor implies that HBV infections may be an unreliable guide to human immunodeficiency virus (HIV) infection in populations where HBV is highly prevalent.

Bell A, Ncube F, Hansell A, Davison KL, Young Y, Gilson R, Macdonald N, Heathcock R, Warburton F, Maguire H. An outbreak of hepatitis A among young men associated with having sex in public venues. *Commun Dis Public Health* 2001; 4:163-170.

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An increase in hepatitis A virus (HAV) infection was noted among young men in the former Thames regions during 1997. A retrospective case-control study, using a standardised questionnaire at interview, was conducted in the area most affected (London and East Sussex) to investigate the hypothesis that this increase was mainly among homosexual men and to establish the risk factors associated with transmission. Forty-eight cases and 161 controls completed questionnaires. Forty-one cases (85%) described their sexuality as homosexual ($p < 0.0001$). Cases were more likely than controls to have eaten shellfish (Odds Ratio (OR) 2.4; 95% Confidence Interval (CI) 1.16, 5.04) during the two months before onset of illness. Cases had more sexual partners ($p = 0.015$), and more casual sexual partners ($p = 0.007$) than controls. Cases were more likely to have had sex in a gay sauna (OR 3.5; 95% CI 1.53, 8.30), or in a gay club, pub or disco (OR 2.9; 95 CI 1.29, 6.63) than controls. After adjusting for confounding factors, cases were more likely to have eaten shellfish (adjusted [adj] OR 3.0; 95% CI 1.33, 6.59) and to have had sex in a gay sauna (adj OR 3.9; 95% CI 1.42, 10.59). Public health messages need to inform homosexual men about recognised risk factors such as eating shellfish and travel abroad to endemic areas, as well as sexual risks. Homosexual men can benefit from hepatitis A vaccine. We would suggest that in an outbreak situation men who have multiple anonymous partners and have sex in public venues should be targeted as a priority for health education and immunisation.

Beutels P, Edmunds WJ, Antoñanzas F, De Wit GA, Evans D, Feilden R, Fendrick AM, Ginsberg GM, Glick HA, Mast E, Pechevis M, Van Doorslaer EK, van Hout BA, on behalf of the Viral Hepatitis Prevention Board. Economic evaluation of vaccination programmes: a consensus statement focusing on viral hepatitis. *Pharmacoeconomics* 2002; 20:1-7.

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The methods that have been used to estimate the clinical and economic impact of vaccination programmes are not always uniform, which makes it difficult to compare results between economic analyses. Furthermore, the relative efficiency of vaccination programmes can be sensitive to some of the more controversial aspects covered by general guidelines for the economic evaluation of healthcare programmes, such as discounting of health gains and the treatment of future unrelated costs. In view of this, we interpret some aspects of these guidelines with respect to vaccination and offer recommendations for future analyses. These recommendations include more transparency and validation, more careful choice of models (tailored to the infection and the target groups), more extensive sensitivity analyses, and for all economic evaluations (also nonvaccine related) to be in better accordance with general guidelines. We use these recommendations to interpret the evidence provided by economic evaluation applied to viral hepatitis vaccination. We conclude that universal hepatitis B vaccination (of neonates, infants or adolescents) seems to be the most optimal strategy worldwide, except in the few areas of very low endemicity, where the evidence to enable a choice between selective and universal vaccination remains inconclusive. While targeted hepatitis A vaccination seems economically unattractive, universal hepatitis A vaccination strategies have not yet been sufficiently investigated to draw general conclusions.

Bird SM, Goldberg DJ, Hutchinson SJ. Projecting severe sequelae of injection-related hepatitis C virus epidemic in the UK. Part 1: Critical hepatitis C and injector data. *J Epidemiol Biostat* 2001; 6:243-265.

MRC Biostatistics Unit, Institute of Public Health, Cambridge, UK.

Hepatitis C is transmitted by transfusion of unscreened blood, through injecting drugs, from mother-to-child and, on occasion, sexually. Transmission generally requires that the infector is hepatitis C virus (HCV) RNA positive, a 'carrier'. About three-quarters of injectors who are hepatitis C antibody positive are HCV-RNA positive and so infectious to others. Incubation periods from HCV infection to cirrhosis and hepatocellular carcinoma are even longer than from HIV infection to AIDS, being counted in decades; they depend on age, gender, alcohol consumption and co-infection with other viruses. We identify 25 data sources that are available, or required, for projecting the severe sequelae of the injection-related hepatitis C epidemic. Three data sources relate to hepatitis C diagnosis: register of confirmed HCV infections (with initial of first name + soundex of surname + date of birth + gender = master index, exposure category, year of starting to inject, and region); surveys of HCV test-uptake by injectors and others; documentation of pregnancy and its outcome in HCV-infected women (injectors and others). Four data sources relate to HCV prevalence and incidence among injectors and others: anonymous testing for HCV antibodies in blood or saliva (for sentinel groups ranging from new blood donors, pregnant women, patients awaiting kidney transplantation, non-injector prisoners, health-care workers, non-injector heterosexuals attending genitourinary medicine clinics; to injectors in the community, at drug treatment centres or in prison); historical data on HCV prevalence in injectors; HCV incidence studies in injectors; and uptake of harm reduction measures – frequency of sharing and methadone substitution – by injectors. Key reporting problems in HCV incidence studies, which inhibit checks on the convenient exponential assumption for time from start of injecting to hepatitis C infection, are discussed. Nine critical data sources are identified for monitoring the late sequelae of hepatitis C carriage, its investigation and treatment: linkage surveillance, for example by master index, to identify deaths, hospitalisations or cancer registrations among confirmed HCV infections; surveys of HCV status among patients who undergo liver biopsy, are newly diagnosed with cirrhosis or are newly diagnosed with liver cancer; surveys of liver-biopsy rate in HCV-infected injectors and others; uptake and outcome of interferon + ribavirin in the treatment of hepatitis C carriers; cohort studies of HCV progression; sample surveys of genotype in HCV-infected injectors, and others; acute hepatitis B infections and uptake of hepatitis B immunisation by injectors; liver transplantation in HCV-infected patients; and hepatitis C-status and other risk factors in deaths from cirrhosis or liver cancer, to determine whether they are HCV and injector-related. Finally, nine critical data sources are identified for quantitative understanding of the underlying injector epidemic: drug misuse databases plus capture-recapture methods to assess number of injectors, drug-related deaths by region to assess injector numbers; number of HIV-infected injectors; HIV progression in injectors; overdose and other causes of death in injectors; expert opinion on injector incidence historically, plus survey information on age-distribution at initiation and duration of injector careers; injector incidence historically inferred from hepatitis C infected blood donors; age-distribution of current injectors and at initiation, as a check on the assumptions made in stochastic simulation about injector incidence and 'outcidence' from injecting historically; mortality of former injectors; and general population or other survey ratios of surviving ever-injectors to injectors in the last 5 years, last year and currently, as a check on simulations. We recommend a common HCV diagnosis report form to improve ascertainment of risk-factor information, especially year of starting to inject – which is a key date epidemiologically. We also recommend updated surveys of current and former injectors' HCV-test uptake, or a denominator study that registers master index and risk factor information for all HCV testees. We recommend that injector surveys ask about typical frequency of needle sharing per 4 weeks in three distinct periods this year, last year and in the first year of injecting. We also recommend the location of stored historical samples from injectors to be tested retrospectively and anonymously for HCV antibodies. We recommend immediate attention to the uptake of, and response to, combination treatment by hepatitis C carriers who are former or recovering injectors.

Bird SM, Goldberg DJ, Hutchinson SJ. Projecting severe sequelae of injection-related hepatitis C virus epidemic in the UK. Part 2: Preliminary UK estimates of prevalent injection-related hepatitis C carriers, and derivation of progression rates to liver cirrhosis by gender and age at hepatitis C virus infection. *J Epidemiol Biostat* 2001; 6:267-277.

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In Part 2, we illustrate how available data can be used to obtain preliminary estimates for Scotland of prevalent injection-related hepatitis C carriers and of maternally hepatitis C virus (HCV)-infected infants. Novel approaches to reducing uncertainty about the number of Scotland's HCV infected children of injector parents are discussed in brief. Three approaches, one direct and two indirect, to estimating the number of current and ever-injectors are presented for England and Wales. Diagnosed HCV infections in injectors and HCV test uptake by current injectors are combined with survey estimates for the ratio of ever-injectors to current injectors to estimate prevalent injection-related hepatitis C carriers. Household surveys give direct but potentially biased estimates of the number of current and ever-injectors. Indirect estimates make use of hepatitis C diagnoses in injectors, HCV prevalence and test-uptake by injectors, or exploit international comparisons. We comment on key reporting problems that inhibit synthesis of HCV progression studies; and suggest how to derive preliminary gender-and-age specific progression rates to liver cirrhosis for use in projections. Preliminary estimates for Scotland of prevalent injection-related hepatitis C carriers are: central estimate 39,000, inner uncertainty 16,000-59,000; of maternally hepatitis C virus (HCV)-infected infants central estimate 260, uncertainty 110-1100; and for England and Wales estimates of the number of prevalent ever-injectors are central estimate 360,000, uncertainty 240,000-835,000. Both hepatitis C prevalence in injectors and estimated numbers of current injectors are similar in Australia, and England and Wales (but not so for Scotland), Australian work on projections of severe HCV sequelae from hepatitis C infections may therefore be a suitable starting point for projections for England and Wales. Australia anticipates a doubling in the number of persons living with hepatitis C cirrhosis from 8500 in 1997 to over 17,000 in 2010. Australian projections of severe HCV sequelae used progression rates that, for simplicity, were independent of gender and of age at HCV infection. Faster HCV progression for males, and their higher injector prevalence, means that the impact of HCV infection on, for example, liver cancer may be evident to a greater extent and earlier in males.

Boxall EH, A Sira J, El-Shuhkri N, Kelly DA. Long-term persistence of immunity to hepatitis B after vaccination during infancy in a country where endemicity is low. *J Infect Dis* 2004; 190:1264-1269.

Health Protection Agency, West Midlands Public Health Laboratory, Heartlands Hospital, Birmingham, United Kingdom. elizabeth.boxall@heartsol.wmids.nhs.uk.

The long-term response to hepatitis B vaccination during infancy has not been fully evaluated in countries where endemicity is low. The present study was a serological investigation of immunity to hepatitis B during adolescence. In a cohort of children who were born to hepatitis B virus carrier mothers and who were vaccinated during infancy, evidence of past or current infection and the response to a single booster dose of vaccine were analyzed. Sixty-four children whose antibody levels were measured after immunization (group 1) and 52 younger siblings who did not undergo postvaccination antibody tests (group 2) were studied. One child in each group showed evidence of natural infection. In group 1, 32 children (50%) had undetectable antibody to hepatitis B surface antigen (anti-HBs), and only 8 (13%) had levels >100 mIU/ml. After a booster dose of vaccine, only 7 (11%) still had undetectable anti-HBs, 3 (5%) showed a primary response, and 50 (78%) had levels >100 mIU/ml. Five of the 7 vaccine nonresponders and all of the primary responders had also received hepatitis B-specific immunoglobulin (HBIG) at birth. The children in group 2 showed a similar response to the vaccine, but with slightly higher levels of anti-HBs. Most children vaccinated at birth retain immunological memory to hepatitis B vaccine for 15 years, but

those who did not were more likely to have received HBIg at birth, suggesting that passive antibody may interfere with the induction of immunological memory.

Bramley JC, Wallace LA, Ahmed S, Duff R, Carman WF, Cameron SO, Kitchin NR, Watson MW, Goldberg DJ. Universal hepatitis B vaccination of UK adolescents: a feasibility and acceptability study. *Commun Dis Public Health* 2002; 5:318-320.

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The feasibility of introducing universal hepatitis B immunisation was assessed by offering the vaccine to all 11-12 year old pupils in Greater Glasgow (approximately 10,800). Consent was received from 92% of the school roll, and 91.3%, 89.2% and 80.3% received at least 1, at least 2, and 3 doses respectively. The findings of this study constitute key evidence for the ongoing debate in the UK on hepatitis B vaccination.

Brant L, Harris HE, Ramsay ME, Grieve R, Roberts J, on behalf of the HCV National Register Steering Group. Pathways of care and resource utilization in a national cohort of patients with transfusion-acquired hepatitis C. *J Viral Hepat* 2005; 12:618-626.

Health Protection Agency, Communicable Disease Surveillance Centre, London, UK.

The Hepatitis C Strategy and Action Plan for England recommend that all individuals testing positive for hepatitis C virus (HCV) should be referred to a specialist centre for assessment and care. One key aim is to reduce the number of people progressing to liver disease and therefore reduce the associated costs. The aims of this paper are to describe the care pathways and evaluate resource utilization in a cohort of 826 patients with transfusion-acquired hepatitis C enrolled in the HCV national register. We reviewed data extracted from patient notes to establish pathways of care since HCV-positive diagnosis through to May 2002, and to document all treatment, liver biopsy and hospital usage for each patient. Type of care was classified into specialist-interest in HCV-related care, other-hospital care or general practitioner (GP)-led care. Over 70% of patients were referred to specialist care following HCV diagnosis. Patients who were older or who had normal liver function were less likely to be referred to specialist-care. Between first diagnosis and May 2002, no patients were referred from GP to specialist-care. Less than half of this cohort had undergone liver biopsy and only 18% had been treated. Younger patients and those with abnormal liver function were more likely to have undergone liver biopsy and to have received treatment. Analysis of care histories of patients with transfusion-acquired hepatitis C suggest that changes are needed in the care and management of patients with HCV infection, if the recommendations of the HCV strategy and action plan are to be fully implemented.

Brown RE, De Cock E, Colin X, Antoñanzas F, Iloeje UH. Hepatitis B management costs in France, Italy, Spain, and the United Kingdom. *J Clin Gastroenterol* 2004; 38(10 Suppl):S169-S174.

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The goal was to estimate the costs associated with the management of chronic hepatitis B (CHB) and its sequelae in France, Italy, Spain, and the United Kingdom from the perspective of the healthcare payer. The World Health Organization estimates that the disease sequelae related to hepatitis B account for 1 million deaths annually worldwide. Northern Europe is a low endemic area, while Mediterranean regions are classified as intermediate endemic areas. The introduction of vaccination programs in France, Italy, and Spain in recent years has lowered the hepatitis B

incidence rates. The purpose of this study was to identify the medical management patterns of CHB patients in France, Italy, Spain, and the United Kingdom and estimate the economic burdens of CHB-related disease states for each country. A central questionnaire was used to collect data from specialist physicians in four countries, and responses were collated into management patterns for chronic active hepatitis, compensated and decompensated cirrhosis, and hepatocellular carcinoma. The average cost by disease state for each European country was found to increase across the identified disease states reflecting disease progression. Year-2001 average annual disease state costs per patient were estimated to be as follows: CHB, 1,093 euro-3,396 euro; compensated cirrhosis, 1,134 euro-3,997 euro; decompensated cirrhosis, 5,292 euro-8,842 euro; hepatocellular carcinoma, 3,731 euro-9,352 euro; and, from published sources, liver transplant surgery, 25,165 euro-84,568 euro. The cost of CHB is variable both within and between European countries. The association of disease progression with increased cost of disease management suggests that measures to prevent or delay its progression would be economically beneficial.

Budd J, Robertson R, Elton R. Hepatitis B vaccination and injecting drug users. *Br J Gen Pract* 2004; 54:444-447.

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This study seeks to test the feasibility of vaccinating injecting drug users for hepatitis B in primary care and to identify predictors of poor immune response. Two hundred and seventy-five injecting drug users were identified from the case notes of a large general practice in an area of high multiple deprivation in northwest Edinburgh and, where appropriate, offered hepatitis B vaccination followed by a post-vaccination serological test. We concluded that hepatitis B vaccination of drug users in primary care is both feasible and effective. This study was unable to identify a group at risk of vaccine failure, however, it found post-vaccination serological testing to be problematic and potentially misleading. Therefore, we would not recommend its routine use in a primary care setting. Significantly, prolonged primary courses were not associated with reduced efficacy. The findings indicate that an appropriate vaccination schedule for primary care should be flexible to maximise compliance.

Champion JK, Taylor A, Hutchinson S, Cameron S, McMenamin J, Mitchell A, Goldberg D. Incidence of hepatitis C virus infection and associated risk factors among Scottish prison inmates: a cohort study. *Am J Epidemiol* 2004; 159:514-519.

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To gauge the incidence of hepatitis C virus (HCV) infection and associated risk factors among inmates during their imprisonment, the authors recruited adult males in a long-stay Scottish prison into a cohort study between April 1999 and October 2000. On two occasions (at 0 and 6 months), saliva was collected for anonymous HCV antibody testing and risk behavior data were obtained through a self-administered questionnaire. The participation rate was 85% at both initial recruitment (612/719) and follow-up (375/441; 171 men were ineligible for follow-up). For inmates who reported never having injected drugs, ever having injected drugs, having injected drugs during follow-up, and having shared needles/syringes during follow-up, HCV incidences per 100 person-years of incarceration risk were 1, 12, 19, and 27, respectively. Ever having injected drugs (relative risk = 13.0, 95% confidence interval: 1.5, 114.3) and having shared needles/syringes during follow-up (relative risk = 9.0, 95% confidence interval: 1.1, 71.7) were significantly associated with HCV seroconversion. The effectiveness of existing interventions, including the provision of bleach tablets for sterilizing injection equipment, was suboptimal. The development of methadone maintenance programs in prisons and the creation of drug courts to keep offending drug injectors out of prison might help to reduce transmission in this setting.

Chatzipantazi P, Roy KM, Cameron SO, Goldberg D, Welbury R, Bagg J. The feasibility and acceptability of collecting oral fluid from healthy children for anti-HCV testing. *Arch Dis Child* 2004; 89:185-187.

Department of Public Health, University of Glasgow, UK.

This pilot study investigated the feasibility of surveying, anonymously, HCV infection among healthy children using an oral fluid specimen. Seventy seven per cent of children provided their assent, or where appropriate, consent to participate; 2.8% were anti-HCV positive. Oral fluid collection is acceptable to children and more extensive studies are indicated.

Crook PD, Jones ME, Hall AJ. Mortality of hepatitis B surface antigen-positive blood donors in England and Wales. *Int J Epidemiol* 2003; 32:118-124.

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Large population-based cohort studies in areas of high hepatitis B virus (HBV) prevalence have provided the evidence establishing hepatitis B surface antigen (HBsAg) carriage as a risk factor for hepatocellular carcinoma (HCC) and liver disease. Fewer studies have examined this in Western countries, where both HBV infection and carriage are less common and transmission patterns differ. This is the only prospective population-based study to examine this relationship in Europe. In all, 2681 male and 977 female blood donors in England and Wales, found to be HBsAg positive during routine blood-donation screening, were followed up from recruitment in 1970-1982 to December 1999 and their cause-specific mortality was analysed. This was compared with that of the general population of England and Wales. During a mean of 22 years of follow-up, 17.4% of the 420 deaths were due to HCC or liver disease. There were 20 deaths from HCC in male HBsAg carriers, representing a significantly high standardized mortality ratio (SMR) compared to the male population of England and Wales of 26 (SMR = 26.26; 95% CI: 16.04- 40.54). The HCC incidence rate in males was 33.5 per 100 000 person years and 4.4 per 100 000 person years in females. Men had 8.5 (SMR = 8.50; 95% CI: 6.25- 11.31) and women had 3.9 times the risk of death from liver disease (SMR = 3.89; 95% CI: 1.26-9.09). The risk of circulatory disease deaths was reduced in both males and females. There was a significant increased risk of non-Hodgkins lymphoma that was not apparent in the first decade of follow-up. The increased risk of HCC and liver disease in men fell with follow-up. Hepatitis B surface antigen carriage is a significant risk factor in England and Wales for both liver disease and HCC mortality. However, this risk has declined with duration of follow-up. This could be due to natural reversion to HBsAg negativity or as a result of treatment and avoidance of other risk factors. The increased risk of non-Hodgkins lymphoma seen in longer follow-up is likely to be related to HIV infection acquired subsequent to recruitment.

Crowcroft NS, Walsh B, Davison KL, Gungabissoon U, on behalf of the PHLS Advisory Committee on Vaccination and Immunisation. Guidelines for the control of hepatitis A virus infection. *Commun Dis Public Health* 2001; 4:213-227.

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The PHLS Advisory Committee on Vaccination and Immunisation, following a review of the evidence on control measures for preventing hepatitis A virus (HAV) infection and widespread consultation, has prepared the following guidelines. They include a description of the current epidemiology of HAV infection in England and Wales, where most individuals are now susceptible to HAV. HAV infection is uncommon, with around 1000 infections notified per year in England and Wales. Clusters occur in families and in settings where potential for faecal/oral

spread is high, e.g. day care centres, nurseries, primary schools. Larger outbreaks have been recorded in men who have sex with men and injecting drug users. Personal hygiene remains the cornerstone of measures for preventing HAV infection and its spread. Those with haemophilia, hepatitis B or C virus infection or liver cirrhosis, intravenous drug users and men who have sex with men should be offered HAV vaccination as a preventive measure. HAV vaccine should be used for preventing secondary cases and outbreaks provided that patients are informed that the latest date the vaccine is most likely to be effective in preventing disease in contacts is probably 7 days from onset of illness in the primary case. Human normal immunoglobulin (HNIG) should be offered in addition or in preference to vaccine for contacts who are more than 7 days from onset of illness in the primary case, and for those at risk of adverse outcome of HAV infection. Individuals at particular risk of an adverse outcome to infection include those more than 50 years old, with liver cirrhosis of any cause, or with pre-existing hepatitis B or C virus infection. HAV vaccine should be used to prevent infection for travellers to countries where HAV infection is a risk. HNIG is no longer indicated for travellers. Children travelling to such countries should be offered vaccine from 5 years and consideration should be given to vaccinating those aged 1-4 years.

Davidson F, Lycett C, Sablon E, Petrik J, Dow BC. Hepatitis B virus genotypes and precore mutations in Scottish blood donors. *Vox Sang* 2005; 88:87-92.

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This study was carried out to determine the frequency of hepatitis B virus (HBV) core promoter variants (nucleotide positions 1762, 1764) and precore variants (nucleotide position 1896) in hepatitis B surface antigen (HBsAg)-positive Scottish blood donors. HBV genotypes present in this population were also identified. A total of 85 HBsAg-positive blood donor samples were included in the study. Of these, 79 were polymerase chain reaction (PCR) positive and had sequence and mutation information. They were divided into two groups: group 1 (23 individuals) were hepatitis B e antigen (HBeAg)-positive and negative for antibody to HBe (anti-HBe); and group 2 (56 individuals) were HBeAg negative and positive for anti-HBe. A line probe assay was used to detect mutations, and a comparison was made by using direct sequence analysis. A different line probe assay was used to identify HBV genotype. The frequencies of mutations in group 1 were 22% each for mutations 1762, 1764 and 1896, increasing to 26%, 35% and 55% in group 2, respectively. By contrast, direct sequence analysis failed to identify 70% of wild-type/mutant mixes. The prevalence of viral genotypes was 41% for genotype A, 12% for genotype B, 5% for genotype C, 30% for genotype D and 12% for mixed-genotype infections. Precore mutations were seen in 10%, 88%, 25% and 74% of genotypes A, B, C and D, respectively. The results indicate that core promoter and/or precore mutants may be under-reported. The combination of HBV PCR and line probe assays is useful for supplementing HBV serological tests. Non-Caucasian genotypes are present in the UK blood-donating population and will therefore affect the demographics of HBV infection.

Davis M, Rhodes T, Martin A. Preventing hepatitis C: 'common sense', 'the bug' and other perspectives from the risk narratives of people who inject drugs. *Soc Sci Med* 2004; 59:1807-1818.

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There is little published research about how people who inject drugs are responding to the hepatitis C epidemic. This study seeks to address the prevention of hepatitis C using qualitative interviews with people who inject drugs in London. We explored narratives about risk reduction and hepatitis C in the social and historical context of other risks such as HIV, vein damage and overdose. Themes of the narratives included: the importance of autonomy in the acquisition of safer injecting

skills; that safer injection was regarded as 'common sense', normalised and predicated on the risk of HIV; that hepatitis C risk was relativised with HIV risk and thereby seen as less important; and that hepatitis C infection was also seen as unavoidable. These narrative forms represent significant challenges for the management of the hepatitis C epidemic, both in terms of the existing risk reduction efforts designed for HIV and in terms of the articulation of risk reduction for injectors with general public health policy.

Dawson AJ. An ethical argument in favour of routine hepatitis B vaccination in very low-incidence countries. *Lancet Infect Dis* 2005; 5:120-125.

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Hepatitis B is a potentially life-threatening viral infection that can be prevented through safe vaccination. This article argues that, firstly, there are important reasons to question the common policy of focusing on at-risk populations, and secondly, that there are positive reasons for very low-incidence countries such as the UK to consider implementing a programme of routine vaccination for hepatitis B. These conclusions can be supported by the strong ethical presumption that where a potentially devastating disease is easily preventable, those at potential risk should be protected. Even in very low-incidence countries such as the UK a policy based upon routine vaccination for hepatitis B may be an efficient and ethical way to reduce the burden of this disease.

Dike AE, Christie JM, Kurtz JB, Teo CG. Hepatitis C in blood transfusion recipients identified at the Oxford Blood Centre in the national HCV look-back programme. *Transfus Med* 1998; 8:87-95.

NBS Oxford Blood Centre, John Radcliffe Hospital, UK.

After the introduction in September 1991 of donor screening for hepatitis C, 95 potentially infectious blood donors who had given blood before this date were identified at the Oxford blood centre. Three hundred and ninety-nine blood components issued previously from these donors were identified in the course of the national HCV look-back programme. Of 399 questionnaires sent to hospital blood banks 392 were returned, identifying 290 recipients of whom 177 (61%) had died, and 113 (39%) were still alive 4-13 years after transfusion. One hundred and four recipients were traced and tested. Forty-nine recipients were not HCV infected. Forty-four of 58 (76%) recipients who received blood from donors found to be HCV RNA positive after September 1991 gave positive test results for HCV RNA. Eleven of 58 showed only antibody (anti-HCV), and 3/58 who had apparently received infectious blood showed no sign of past infection. The 11 who showed anti-HCV only, together with the three who showed no sign of past infection despite strong evidence of receiving HCV RNA-positive blood, had a mean age at transfusion of 27 years, compared with mean age at transfusion of 46 years in the 44 recipients with persistent HCV infection. Virus genotyping in 33/44 HCV RNA-positive recipients revealed five different genotypes. These did not seem to influence the outcome. Virus genotypes in 31 donor-recipient pairs showed complete concordance. Liver biopsies in 23/44 RNA-positive recipients showed minimal inflammation in four, mild in eight and moderate in 11. Liver fibrosis, Ishak grades 1-3, was present in 16/23 recipients. One other male recipient, not subjected to a liver biopsy, developed a hepatocellular carcinoma which caused his death at the age of 71, 8 years after transfusion.

Dillon JF. Hepatitis C: What is the best treatment? *J Viral Hepat* 2004; 11(Suppl 1):23-27.

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The treatment of hepatitis C is expensive, difficult and arduous from the patient's perspective. It is similarly difficult for the clinician to decide who and when to treat. If hepatitis C is viewed from the liver's perspective we need only treat those patients who will develop the complications of chronic liver disease within their lifetimes. If we take a more holistic approach, then we have to consider the implications of being a carrier of a potentially transmissible blood borne virus on the patient themselves, their relationships, their families and their sense of wellbeing. There is now evidence of the large impact HCV has on quality of life and we have to consider extra hepatic manifestations of hepatitis C infection, possibly including the syndrome of 'brain fog' recently described. An additional factor that has to be considered in the decision to treat is whether patients perceive hepatitis C as a significant problem for themselves. For some patients, who have chaotic live styles, it is extremely difficult to get them to access healthcare. To then undergo the rigors and tribulations of hepatitis C therapy that is posing no current problem is unlikely to succeed. However, failure to engage these patients with therapy will lead to a significant proportion of them presenting with serious complications of chronic liver disease, with its attendant mortality, morbidity and cost. Underlying all these considerations is the tension between the costs of therapy and the benefits of therapy. Good arguments can be made in terms of cost-effectiveness for treating patients with a high likelihood of progressing to chronic liver disease and its complications. These arguments become much less persuasive when all patients are concerned.

Edmunds WJ. Universal or selective immunisation against hepatitis B virus in the United Kingdom? A review of recent cost-effectiveness studies. *Commun Dis Public Health* 1998; 1:221-228.

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There is still no consensus on which hepatitis B virus (HBV) immunisation option should be adopted in the United Kingdom (UK). This review considers why three recent UK studies on the subject reached different conclusions, and whether they provide sufficient information to base an informed decision on cost-effectiveness grounds. The studies differed in methodology, particularly in the models used to estimate the effectiveness of the competing programmes. This led the authors to draw very different conclusions as to the relative cost-effectiveness of universal infant and selective immunisation, probably because the study that favoured infant immunisation omitted an allowance for the indirect protection afforded to others by immunisation of a proportion of the population. This would lead to the underestimation of the relative effectiveness of a programme targeted at high-risk individuals. Selective vaccination is probably more cost-effective than mass immunisation, but universal immunisation may still be considered a cost-effective option (in addition to selective immunisation) if future health benefits are not discounted (i.e., given a lower value than present ones). If future health benefits are discounted then mass infant immunisation is almost certainly not cost-effective. If selective immunisation is to be adopted, then the current (selective) strategy should be properly implemented, as it appears to have had little impact on HBV infection and disease.

Edmunds WJ, Medley GF, Nokes DJ, Hall AJ, Whittle HC. The influence of age on the development of the hepatitis B carrier state. *Proc R Soc Med* 1993; 253:197-201.

Department of Biology, Imperial College of Science, Technology and Medicine, London, U.K.

The relation between the age at infection with hepatitis B virus (HBV) and the development of the carrier state is examined by using data from a number of published and unpublished surveys. A remarkably consistent relation was found. Infants infected perinatally (within the first 6 months of life) were found to have a high probability of becoming carriers (0.885; 95% C.L. 0.84-0.93). Over the infant and early childhood age classes there was found to be a sharp decrease in the proportion

of infections which lead to the carrier state. By adulthood (over 15 years) the probability of developing the carrier status was found to be about 0.1. A model was fitted to the data by using maximum likelihood, which provides a good empirical description of the observed data and can be used to predict the expected probability of developing the carrier state given the age at infection. It is postulated that, as a result of this rapid decline in the probability of becoming a carrier during early childhood, a mass childhood immunization campaign, which will tend to postpone the average age at infection in the unvaccinated community, will have a disproportionately large impact on the rate of generation of new carriers.

Gibb DM, Neave PE, Tookey PA, Ramsay M, Harris H, Balogun K, Goldberg D, Mieli-Vergani G, Kelly D. Active surveillance of hepatitis C infection in the UK and Ireland. *Arch Dis Child* 2000; 82:286-291.

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The aim was to investigate the prevalence, distribution, and clinical details of paediatric hepatitis C virus (HCV) infection in the UK and Ireland. Active monthly surveillance questionnaire study coordinated through the British Paediatric Surveillance Unit, to all consultant paediatricians in 1997 and 1998. A total of 182 HCV infected children were reported from 54 centres and by paediatricians from eight different specialties. In 40 children HCV was acquired through mother to child transmission (MTC children); 142 were infected by contaminated blood products (n = 134), organ transplantation (n = 2), needles (n = 4), or unknown risk factor (n = 2). Intravenous drug use was the risk factor for 35 mothers of MTC children. Twelve children were coinfecting with HIV and four with HBV. Recent serum aspartate aminotransferase or alanine aminotransferase values were at least twofold greater than the upper limit of normal in 24 of 152 children; this occurred in five of 11 HIV coinfecting children. Liver histology, available in 53 children, showed normal (7%), mild (74%), moderate (17%), or severe (2%) hepatitis. Twenty eight children had received therapy with interferon alfa. Most current paediatric HCV infection in UK and Ireland has been acquired from contaminated blood products, and most children are asymptomatic. There is a need for multicentre trials to inform clinical practice and development of good practice guidelines in this area. Long term follow up of this cohort of HCV infected children is planned to help determine the natural history over the long term of HCV acquired during infancy and childhood.

Gilbert RL, Costella A, Piper M, Gill ON. Increasing hepatitis B vaccine coverage in prisons in England and Wales. *Commun Dis Public Health* 2004; 7:306-311.

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The most frequently reported risk factor for hepatitis B infection in England and Wales is injecting drug use (38%). Since approximately 61% of injecting drug users (IDUs) had been imprisoned and less than 40% had received hepatitis B vaccine, a prison based hepatitis B vaccination programme was set up in 2001. At the 42 establishments participating in this study, all prisoners were offered vaccine at reception. Prisoners over 18 years were vaccinated using the 0, 7 and 21 days schedule and those under 18 years, using the 0, 1 and 2 months schedule. As far as possible a fourth dose was given to all after 12 months. In 2003, 14,163 prisoners received at least one dose of vaccine and altogether 26,265 doses were administered. A further 1111 prisoners reported they had already been vaccinated against hepatitis B. The median vaccine coverage rate was 17% (range 0-94%). Despite low coverage levels, the vaccination programme in prisons can be said to have vaccinated a sizable number of young, male prisoners, a group that have previously been shown to be at high risk of infection. The prisons which achieved vaccine coverage levels over 50% had designated nursing staff who ran the vaccination clinics.

Gilbert RL, O'Connor T, Mathew S, Allen K, Piper M, Gill ON. Hepatitis A vaccination – a prison-based solution for a community-based outbreak? *Commun Dis Public Health* 2004; 7:289-293.

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In December 2001, an increase in cases of hepatitis A was observed in South Yorkshire. Cases were predominantly young males who reported injecting drug use. A community-based vaccination programme was introduced in November 2002, but new cases continued to occur. In March 2003, a vaccination campaign was implemented in the local prison for a four-week period. One thousand two hundred and thirty-six (91%) prisoners were vaccinated. Two thirds (895/1,363) of the prisoners came from the area affected by the outbreak and 52% (465/895) reported injecting drugs. The median age of injectors was 25 years. Notifications of cases of hepatitis A from South Yorkshire ceased in August 2003. Although on this occasion the prison vaccination campaign was probably implemented too late to have had a significant impact on the local outbreak, a large number of young male injectors from the local area were successfully vaccinated. This suggests that a prison-based intervention offers a potentially effective way of immunising the IDU population and interrupting a community-based outbreak.

Gilson RJ, de Ruiter A, Waite J, Ross E, Loveday C, Howell DR, Tedder RS, Weller IV. Hepatitis B virus infection in patients attending a genitourinary medicine clinic: risk factors and vaccine coverage. *Sex Transm Infect* 1998; 74:110-115.

Department of Sexually Transmitted Diseases, University College London Medical School.

The hepatitis B virus (HBV) immunisation policy in the United Kingdom includes offering vaccines selectively to those at risk by sexual contact. Among genitourinary medicine (GUM) clinic attenders, homosexual men are offered vaccine, but estimates of the vaccine uptake are required to monitor policy and estimate the possible impact on transmission; heterosexuals are not routinely offered vaccine, but this policy might change if the prevalence was found to be high. The objective was to determine the prevalence of HBV infection and vaccine uptake among patients attending a GUM clinic. HBV seroprevalence determined by unlinked anonymous testing of consecutive blood samples sent for syphilis serology. Demographic and risk factor data and history of HBV immunization extracted from clinic notes before unlinking. Prevalence data were compared with a population of first time blood donors from the same area. Open access GUM clinic in central London. Samples were obtained and tested from 441 homosexual and 527 heterosexual men and from 821 women over a 4 month period in 1990. After exclusion of injecting drug users and their sexual partners ($n = 30$) and HBV carriers attending for follow up ($n = 12$), the prevalence of antibody to HBV core (anti-HBc) was 38.7% in homosexual men, 5.9% in heterosexual men, and 3.5% in women (50.0%, 6.0%, 3.7% respectively if previous vaccinees were also excluded). The prevalence of HBV surface antigen positivity was 4.2%, 0.60%, and 0.39% respectively after exclusion of vaccinees (χ^2 $p < 0.001$ for homosexual men versus others). The prevalence of the anti-HBc in first time blood donors was 1.1% (8/749). Among male GUM clinic attenders, the prevalence of anti-HBc was higher in those of non-UK origin or place of birth and/or non-white ethnicity (odds ratios 2.87, 95% CI 1.57-5.24 and 8.06, CI 3.39-19.1, in homosexuals and heterosexuals respectively). In homosexual men anti-HBc prevalence increased with age (OR 1.05, CI 1.02-1.07 for each year) and lifetime number of STDs (OR 6.36, CI 3.77-10.8 for $> \text{ or } = 2$ versus < 2) and in clinic reattenders compared with new patients (OR 5.42, 95% CI 3.32-9.16). Among heterosexuals, age was associated with anti-HBc prevalence in women (OR 1.09, CI 1.04-1.12) but not men (OR 0.99, 95% CI 0.95-1.02). There were no other associations in heterosexuals. A history of HBV immunisation in homosexual men was recorded in 13/131 (9.9%) of new patients and 103/305 (33.8%; OR 4.63, CI 2.49-8.60) clinic reattenders. Although higher than a sample of blood donors, the prevalence of serological markers of HBV infection among

heterosexuals was low, providing little support for extending HBV immunisation to all heterosexuals attending GUM clinics as a targeted strategy for control of HBV infection. Homosexual men remain at high risk of infection, but many are now being immunised. Efforts to improve compliance with existing vaccine policies in GUM clinics should be encouraged.

Goldberg D, Anderson E. Hepatitis C: who is at risk and how do we identify them? *J Viral Hepat* 2004; 11(Suppl 1):12-18.

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The transmission of, and screening for, HCV infection varies considerably throughout the world; differences between resource-poor and resource-rich countries are particularly pronounced. The perspective of this review, principally, is that of resource-rich countries. The UK, particularly Scotland, experience is drawn on.

Goldberg D, Burns S, Taylor A, Cameron S, Hargreaves D, Hutchinson S. Trends in HCV prevalence among injecting drug users in Glasgow and Edinburgh during the era of needle/syringe exchange. *Scand J Infect Dis* 2001; 33:457-461.

Department of Public Health, University of Glasgow, UK.

In 1998, we reported that anti-HCV prevalence among injectors from Glasgow had declined between 1990 and 1995. We set out to ascertain if the anti-HCV prevalence among injectors from Edinburgh had declined similarly during this period and if there had been any trend in prevalence among injectors from both cities since 1995. Residual sera from both cities' injecting drug users who had undergone named HIV testing were identified, linked to age band and gender information and tested anonymously for anti-HCV. Among Edinburgh's injectors, significant ($p < 0.0001$) decreases in anti-HCV prevalence from 69% (1989/90) to 13% (1997) and from 80% (1989/90) to 54% (1997) were seen in those aged < 25 y and ≥ 25 y, respectively. Among Glasgow's injectors, a significant ($p < 0.0001$) decrease in prevalence from 91% (1990) to 43% (1997) was seen only among those aged < 25 y. Of both cities' 15-19 y olds, sampled during 1995-97, 17% (24/139) were anti-HCV-positive. The findings suggest that the incidence of HCV among young injectors continued to decrease during the 1990s – the era of needle / syringe exchange and other interventions--but is still too high. Further investigative and preventive work is required.

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; 1:95-97.

Scottish Centre for Infection and Environmental Health, Glasgow.

Few data have been published on the prevalence of hepatitis C virus (HCV) among injecting drug users (IDUs) in the United Kingdom. This study compares the prevalence of antibody against HCV (anti-HCV) among IDUs in Glasgow in 1990 (when Glasgow's needle / syringe exchange programme had become established) with that in 1995. Serum left over from specimens taken for named HIV antibody testing was tested anonymously for anti-HCV. The prevalence of anti-HCV fell significantly between 1990 and 1995 among IDUs of all ages (90% to 77%), IDUs aged 15 to 19 years (92% to 29%), and IDUs aged 20 to 24 years (91% to 65%). This study suggests that the incidence of HCV infection among young IDUs fell in the early to mid 1990s, after the establishment of Glasgow's needle/syringe exchange scheme between 1988 and 1990. Since almost a third of injectors under 20 years of age when tested in 1995 had been infected with HCV, however, other interventions may be needed to prevent the spread of HCV in this high risk group.

Goldberg D, Cameron S, Sharp G, Burns S, Scott G, Molyneaux P, Scoular A, Downie A, Taylor A. Hepatitis C virus among genitourinary clinic attenders in Scotland: unlinked anonymous testing. *Int J STD AIDS* 2001; 12:17-21.

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Our objective is to gauge the prevalence of hepatitis C virus (HCV) antibodies among a population at risk of contracting sexually transmitted infections (STIs) and, thus, the efficiency with which the virus is transmitted sexually. The investigators undertook an unlinked anonymous HCV antibody testing study of residual syphilis serology specimens taken from attenders of genitourinary clinics in Glasgow, Edinburgh and Aberdeen during 1996/97. The results were linked to non-identifying risk information. Anti-HCV prevalences among non-injecting heterosexual men and women, and non-injecting homosexual/bisexual males ranged between 0 and 1.2%; the only exception to this was a 7.7% (4/52) prevalence among homosexual/bisexual males in Aberdeen. The overall anti-HCV prevalence for homosexual/bisexual males was 0.6% (4/668), for heterosexual males 0.8% (32/4135), for heterosexual females 0.3% (10/3035) and for injecting drug users 49% (72/148). Only 3 (all female) of the 46 non-injectors who were antibody positive were non-UK nationals or had lived abroad. HCV antibody positive injectors were less likely to have an acute STI and more likely to know their HCV status than non-injectors; no differences in these parameters were found between positive and negative non-injectors on anonymous HCV antibody testing. Our findings are in keeping with the prevailing view that HCV can be acquired through sexual intercourse but, for most people, the probability of this occurring is extremely low. Interventions to prevent the spread of HCV should be targeted mainly at injecting drug user (IDU) populations.

Goldberg D, McIntyre PG, Smith R, Appleyard K, Dunlop J, Taylor A, Hutchinson S. Hepatitis C virus among high and low risk pregnant women in Dundee: unlinked anonymous testing. *BJOG* 2001; 108:365-370.

Glasgow University Department of Public Health, Scottish Centre for Infection and Environmental Health, UK.

The objective was to determine the prevalence of the hepatitis C virus among pregnant women, to gauge the non-injecting, particularly sexual, risk of them being hepatitis C virus infected and to assess the potential impact of selective antenatal screening. Population: antenatal clinic attenders and women undergoing termination of pregnancy in 1997. Setting: Ninewells Hospital, Dundee. Design: unlinked anonymous hepatitis C virus antibody testing of residual sera from specimens sent to the virus laboratory for routine serological testing. The results were linked to non-identifying risk information. Overall anti-hepatitis C virus prevalence was 0.6% (23/3,548). Prevalences among injecting drug users, non-injectors who had a sexual partner who injected, and those with neither risk respectively were 41% (7/17), 15% (5/33) and 0.3% (11/3,498). Relative risks for being an injector and a sexual partner of an injector respectively were 131 (95% CI 58-297) and 48 (95% CI 5-32). It is estimated that one of the 18 antenatal clinic attenders gave birth to an infected child. Findings suggest that non-injecting partners of injectors may be at considerable risk of acquiring hepatitis C virus sexually. Efforts to promote the use of condoms among injectors and their sexual partners should be increased. Selective anti-hepatitis C virus screening of women who reported high risk behaviour would have failed to detect half the cases. Research to gauge the views of women of childbearing age on anti-hepatitis C virus testing is required.

Goldberg D, McMenamin J. The United Kingdom's hepatitis B immunisation strategy – where now? *Commun Dis Public Health* 1998; 1:79-83.

Scottish Centre for Infection and Environmental Health, Glasgow.

The World Health Organization recommended in 1992 that all countries should introduce universal hepatitis B vaccination into their immunisation schedules by December 1997. Over 80 countries, many of them in western Europe, have complied with the recommendation, but, in the United Kingdom (UK), hepatitis B vaccine is offered to selected high risk population groups only. Vaccination uptake in many of these groups is poor and transmission of hepatitis B remains a problem. The current incidence of hepatitis B is lower in the UK than in countries that have adopted a universal approach. It is impossible, however, to predict the number of acute infections that might occur in an unvaccinated teenage population in the year 2015 if the UK's current strategy remains unaltered. Universal immunisation would guarantee that hundreds, if not thousands, of acute illnesses and an appreciable number of severe outcomes would be prevented each year. The authors believe that funding this intervention would be money well spent.

Gore SM, Bird AG, Cameron SO, Hutchinson SJ, Burns SM, Goldberg DJ. Prevalence of hepatitis C in prisons: WASH-C surveillance linked to self-reported risk behaviours. *QJM* 1999; 92:25-32.

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We used cross-sectional willing anonymous salivary hepatitis C (WASH-C) surveillance linked to self-completed risk-factor questionnaires to estimate the prevalence of salivary hepatitis C antibodies (HepCAbS) in five Scottish prisons from 1994 to 1996. Of 2121 available inmates, 1864 (88%) participated and 1532/1864 (82%) stored samples were suitable for testing. Overall 311/1532 (20.3%, prevalence 95% CI 18.3-22.3%) were HepCAbS-positive: 265/536 (49%, 95% CI 45-54%) injector-inmates but only 27/899 (3%, 95% CI 2-4%) non-injector-inmates. Among injectors, HepCAbS positivity was only slightly higher ($p = 0.03$) in those who had injected inside prison (53%, 162/305) than in those who had not (44%, 98/224). Those who began injecting in 1992-96 were much less likely to be HepCAbS-positive than those who started pre-1992 (31%, 35/114 vs. 55%, 230/422; $p < 0.001$). Even with injectors who began in 1992-96 but had never injected inside prison, the prevalence of hepatitis C carriage was 17/63 (95% CI 16-38%). The prevalence and potential transmissibility of hepatitis C in injector-inmates are both high. Promoting 'off injecting' before 'off drugs' (both inside and outside prison), methadone prescription during short incarcerations, alternatives to prison, and support of HepCAbS-positive inmates in becoming eligible for treatment, all warrant urgent consideration.

Gore SM, Hutchinson SJ, Cassidy J, Bird AG, Biswas S. How many drug rehabilitation places are needed in prisons to reduce the risk of bloodborne virus infection? *Commun Dis Public Health* 1999; 2:193-195.

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Transmission of HIV and hepatitis B virus infection has been recognised in prisons, and injecting drug use is a major route of infection. Combined results of two pilot health care surveys showed that 47% of prisoners with a history of injecting drug use wanted help to give up class A drugs but only 11% of non-injecting drug users expressed a similar wish. It would therefore seem appropriate for prisons to estimate the number of inmates with a history of injecting drug use and provide drug rehabilitation places for half that number (47% rounded up). Data from three prisons in England and Scotland for which the numbers of drug rehabilitation places were known showed that they provided less than quarter of the minimum requirement based on this formula. The proportion of inmates with a history of injecting or of non-injecting drug use who want help to give up class A drugs requires further investigation in order to refine the needs formula.

Green ST, Mohsen AH, McKendrick MW, Dawes Y, Prakasam SF, Walberg R, Schmid ML. Potential for hepatitis C transmission among non-needle/syringe sharing Sheffield drug injectors through the sharing of drug preparation paraphernalia. *Commun Dis Public Health* 2001; 4:38-41.

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This study aimed to investigate possible means by which hepatitis C virus (HCV) might be transmitted between drug injecting individuals without the sharing of needles and syringes. A questionnaire-based survey of 143 (out of 287) attendees was conducted at an Infectious Diseases Unit-based HCV clinic. Those patients (all of whom were positive for antibodies to HCV) who asked about risk activities and those that admitted to a history of recreational drug injecting were questioned in detail about their past and current drug preparation practices. Ten per cent denied any history of needle and/or syringe sharing and had no other apparent source of their HCV infection, but instead admitted to having shared drug preparation equipment. The existence among drug injectors of such practices with the potential to transmit blood-borne viruses is important as it may explain how HCV, which is capable of being spread via very small quantities of blood, can be passed between drug injecting individuals who might otherwise never come into contact with another drug injector's blood. Clinical and public health messages regarding the prevention of the spread of HCV may need to be revised and strengthened.

Grieve R, Roberts J. Economic evaluation for hepatitis C. *Acta Gastroenterol Belg* 2002; 65:104-109.

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This paper describes the methods used in economic evaluation and illustrates the challenges of assessing the cost-effectiveness of new interventions in Hepatitis C (HCV), where the impact of interventions needs to be assessed over the patient's lifetime. This paper provides an example of an economic evaluation in HCV using a model estimating the cost-effectiveness of combination therapy (CMB) for patients with mild HCV. The preliminary results from the model suggested that for 1000 cases with mild disease CMB lead to 55 fewer deaths from liver disease compared to no treatment, an average gain of 1.2 life years. Although CMB lead to additional costs of 14,882 EUROS, the cost-effectiveness ratio was 8,490 EUROS per Quality Adjusted Life Year (QALY), which suggests the intervention is relatively cost-effective. The sensitivity analysis showed that the cost-effectiveness ratio was sensitive to the effectiveness of the intervention, and the progression rates between mild disease and cirrhosis. A large UK study is collecting data on the effectiveness of CMB for patients with mild disease, and the costs and quality of life for patients at different stages of HCV. These data will be used to improve the projections of the model. In general, economic evaluations can provide information to help decide where priorities lie both in HCV, and other disease areas.

Grieve R, Roberts J, Wright M, Sweeting M, Deangelis D, Rosenberg W, Bassendine M, Main J, Thomas H. Cost-effectiveness of interferon α or peginterferon α with ribavirin for histologically mild chronic hepatitis C. *Gut* 2005; [Epub ahead of print].

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For patients with mild chronic hepatitis C the cost-effectiveness of antiviral therapy is unknown. The aim was to assess whether anti-viral therapy (either interferon alpha or peginterferon alpha combined with ribavirin) is cost-effective at a mild stage compared to waiting and only treating those cases who progress to moderate disease. Patients: Cases with mild chronic hepatitis C. A

cost-effectiveness model estimates long-term costs and outcomes for patients with mild chronic hepatitis C. The model uses effectiveness and cost data from the UK mild hepatitis C RCT, combined with estimates of disease progression and cost from observational studies. For patients with genotype non-1 antiviral treatment at a mild rather than a moderate stage improved outcomes measured by Quality Adjusted Life Years (QALYs) gained. The mean cost per QALY gained from antiviral treatment with interferon alpha-2b and ribavirin, compared to no treatment, was pound5,285 (\$8,284). For these patients treatment at a mild stage with peginterferon alpha-2b and ribavirin rather than interferon alpha-2b and ribavirin, led to further additional QALYs; the average cost per QALY gained was pound21,155 (\$33,158). For patients with genotype 1, interferon alpha-2b and ribavirin treatment for mild disease only led to a sustained virological response (SVR) for 18% of cases and was not cost-effective. For patients with chronic hepatitis C and genotype non-1, antiviral treatment compared to no treatment at a mild stage, is cost-effective. For patients with genotype 1, antiviral therapy at a mild disease stage is not cost-effective.

Gyawali P, Rice PS, Tilzey AJ. Exposure to blood borne viruses and the hepatitis B vaccination status among healthcare workers in inner London. *Occup Environ Med* 1998; 55:570-572.

Department of Virology, Guy's NHS Trust, St Thomas' Hospital, London, UK.

Occupational exposure to blood borne viruses was examined during one year at a London teaching hospital. A total of 236 incidents occurred of which 83% were related to sharps, 32% were clearly avoidable, and 7% involved an infected source patient. Overall uptake of hepatitis B vaccine was 78% but it was particularly low in paramedical (70%) and domestic staff (45%). Continued effort needs to be applied to improve uptake of hepatitis B vaccine and to maintain high standards of control of infection.

Hahne S, Ramsay M, Balogun K, Edmunds WJ, Mortimer P. Incidence and routes of transmission of hepatitis B virus in England and Wales, 1995-2000: implications for immunisation policy. *J Clin Virol* 2004; 29:211-220.

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The incidence of hepatitis B virus (HBV) infection in the UK is low. Since the infection can have serious sequelae, there is a continuing need to examine its epidemiology so as to inform control measures. We aimed to describe the current HBV incidence and patterns of transmission in the UK, to estimate the rate of new carrier infections, and to discuss implications for the control of HBV through immunisation. We analysed routine England and Wales laboratory surveillance data of acute HBV infection (1995-2000) and data on migration and global HBsAg prevalence. The estimated annual incidence of HBV infection in England and Wales was 7.4 per 100,000. Injecting drug use was the most frequently reported route of transmission. The number of cases attributed to heterosexual contact was fairly stable, whereas the number of cases in men having sex with men decreased. These observations continue trends reported for the early 1990s. Transmission during childhood was rarely reported, but was more frequent among South Asians. The incidence in South Asians is relatively high, and their main risk factors are medical treatment overseas and heterosexual contact. For about a third of cases of acute HBV infection no route of transmission is reported, but analysis of secular trends and age distribution suggest that many of these may be related to injecting drug use. Endemic transmission gives rise to only a small proportion of all new chronic infections, with the vast majority arising from immigration of established HBV carriers. The incidence of acute HBV infection in England and Wales has remained low, with a similar pattern of reported routes of transmission compared to the early 1990s. The UK prevalence of HBV infection is dependant on global rather than national immunisation policy. Endemic transmission may be reduced by improving immunisation coverage among injecting drug users,

which is expected to also reduce the number of cases without a risk factor reported. In addition, immunisation options that better suit the needs of ethnic minorities need to be explored.

Hahne S, Ramsay M, Soldan K, Balogun K, Mortimer P. Hepatitis B incidence among South Asian children in England and Wales: implications for immunisation policy. *Arch Dis Child* 2003; 88:1082-1083.

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The incidence of acute hepatitis B virus (HBV) infection is higher among South Asian than among non-South Asian UK residents, and infections in South Asians occur more often during childhood. The UK's immunisation policy should be changed to protect ethnic minority children against HBV infection.

Hallett RL, Ngui SL, Meigh RE, Mutton KJ, Boxall EH, Teo CG. Widespread dissemination in England of a stable and persistent hepatitis B virus variant. *Clin Infect Dis* 2004; 39:945-952.

Sexually Transmitted and Blood Borne Virus Laboratory, Health Protection Agency Colindale, London, United Kingdom. Rachel.Hallett@lshtm.ac.uk

Outbreaks of acute hepatitis B among inmates of six prisons in three regions of northern England occurring from 1992 through 1994 were found to be associated with a single hepatitis B virus (HBV) variant, which was carried by 20 of the 24 case patients. We instigated a study of cases of acute hepatitis B to trace the spread and prevalence of this variant. A denaturing gradient gel electrophoresis assay was optimized to detect the HBV variant, and cases of acute HBV infection in 3 regions in England occurring from 1990 through 1996 were screened for its presence. Samples from HBV-transmission incidents that were received for molecular investigation were also tested. The variant was identified in 117 (41%) of the 266 cases of acute hepatitis examined in representative regions in England. In North Humberside, but not in southeast England or the West Midlands, a trend toward an increase in the prevalence of the variant was observed. Furthermore, the same variant was identified in the case patients or the individuals implicated in transmission in 11 (22%) of 51 transmission incidents occurring in England from 1997 through 2002. The spread of the variant was primarily associated with injection drug use. The finding of a single, genetically identical variant (over the 600 bp sequenced) occupying a large niche among the circulating viruses was unexpected. This finding has major implications for the use of DNA sequencing analysis in the investigation of chains of transmission. The study also highlights the need for better protection of at-risk groups through vaccination against HBV, a strategy that currently achieves poor coverage.

Harris HE, Ramsay ME, Andrews NJ. Survival of a national cohort of hepatitis C virus infected patients, 16 years after exposure. *Epidemiol Infect* 2005; 1-6.

Immunisation Department, Health Protection Agency, Centre for Infections, London, UK.

The aim of this study was to describe the natural history of HCV after 16 years of infection, in a cohort of individuals who acquired their infections on a known date in the United Kingdom. A total of 924 HCV-infected transfusion recipients (cases) and 475 anti-HCV negative transfusion recipients (controls) were eligible for inclusion in the study. Survival was compared between cases and controls to see if there was any excess mortality attributable to HCV. The results show that all-cause mortality was not significantly different between cases and controls (hazard ratio 1.17, 95% CI 0.92-1.49, P = 0.21). However, the risk of death directly from liver disease was higher in cases

than controls (hazard ratio 2.71, 95% CI 1.09-6.75, P = 0.03). Nearly 30% of those HCV-infected cases who died directly from liver disease were known to have consumed excess alcohol.

Harris HE, Ramsay ME, Heptonstall J, Soldan K, Eldridge KP, on behalf of the HCV National Register Steering Group. The HCV National Register: towards informing the natural history of hepatitis C infection in the UK. *J Viral Hepat* 2000; 7:420-427.

Immunization Division, Communicable Disease Surveillance Centre, London, UK.
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The aim of this paper is to describe the development of a national hepatitis C register and the completeness of the data it contains. This is a descriptive report of the structure and function of the register, including case definitions, registration and follow-up procedures, and methods used to maximize data quality and to obtain comparative data sources. The register contains data on HCV-infected individuals who acquired their infections on a known date and by a known route; to date all are transfusion recipients identified during the UK lookback exercise, who tested positive or indeterminate for anti-HCV after receiving 'infected' blood issued before the introduction of routine testing of the blood supply for anti-HCV. By 31 December 1999, 871 (87%) of 996 eligible transfusion recipients had been registered, and 984 (99%) flagged in the NHS Central Registers. Registered patients had been infected for an average of 11.1 years (SEM 0.1); around half were being cared for by clinicians with a specialist interest in liver disease. Except for the information on tobacco use, current alcohol use, and hepatitis B status, data were more than 80% complete, and for most variables, more than 90% complete. The consistency of data abstraction was found to be 98% (SEM 0.5). In conclusion, the Register contains high quality anonymised data on one of the largest cohorts of individuals with HCV infections acquired on a known date and by a known route. It could serve as a model for other chronic disease registers; developers may find the structure, design, and methodological issues addressed useful.

Hinds A, Cameron JC. Acceptability of universal hepatitis B vaccination among school pupils and parents. *Commun Dis Public Health* 2004; 7:278-282.

Centre for Health and Social Research, Fife.

The World Health Organisation (WHO) recommends universal hepatitis B (hepB) vaccination for all countries, but this policy has not been adopted in the UK and its acceptability there is unknown. We investigated the attitudes of secondary one (S1) school pupils aged 12-13 years (n = 50) and parents (n = 39) using semi-structured focus group discussions. There was a lack of awareness of hepB among most participants prior to the study. Parents sought further information, including the risks of infection and vaccine side effects. No participants identified cultural or socioeconomic barriers to being vaccinated against hepB. The majority of pupils and nearly all parents were in favour of universal hepB vaccination. Offering hepB vaccination to all S1 pupils, in school, should therefore be highly acceptable, providing that sufficient information on the risk of hepB infection and vaccine safety is provided. A facility for answering questions and a forum for pupil education

Hope VD, Judd A, Hickman M, Lamagni T, Hunter G, Stimson GV, Jones S, Donovan L, Parry JV, Gill ON. Prevalence of hepatitis C among injection drug users in England and Wales: is harm reduction working? *Am J Public Health* 2001; 91:38-42.

Public Health Laboratory Service, Communicable Disease Surveillance Centre, 61 Colindale Ave, London NW9 5EQ, United Kingdom. vhope@phls.org.uk

This study sought to establish the prevalence of hepatitis C antibodies (anti-HCV) and hepatitis B

antibodies (anti-HBc) among injection drug users in England and Wales. A voluntary cross-sectional survey collected oral fluid samples and behavioral information; 2203 injectors were recruited through drug agencies, and 758 were recruited in the community. Prevalence was 30% for anti-HCV, 21% for anti-HBc, and 0.9% for HIV antibodies. Anti-HCV prevalence rates were significantly greater among those with longer injecting careers, those in older age groups, those residing in London, those recruited in drug agencies, those positive for anti-HBc, and those with a previous voluntary HIV test. Anti-HCV prevalence rates among injectors in England and Wales, where comprehensive harm reduction programs exist, are lower than rates in other industrialized countries.

Hutchinson SJ, Bird SM, Goldberg DJ. Modeling the current and future disease burden of hepatitis C among injection drug users in Scotland. *Hepatology* 2005; 42:711-723.

Health Protection Scotland, Glasgow, UK.

Quantitative estimates of the current and future burden of hepatitis C virus (HCV) disease are required to plan a public health response to the HCV epidemic with regard to both prevention and treatment. A forward projection model was used to estimate the numbers of both current and former injecting drug users (IDUs) who acquired HCV and progressed to moderate and severe disease in Glasgow and Scotland during 1960-2030. The model was designed to synthesize information on the incidence and cessation of injecting drug use, the incidence of HCV infection among IDUs, the rate of HCV disease progression, and the annual number of IDUs developing HCV-related decompensated cirrhosis. During 2003, a total of 17,400 and 42,900 HCV-infected IDUs were estimated in Glasgow and Scotland, respectively; this compares with approximately 5,000 and 13,900 diagnosed, respectively, and 13,200 and 32,200 with chronic HCV, respectively. The number of IDUs developing HCV-related decompensated cirrhosis in Scotland is estimated to double between 2000 and 2020. As many as 16% and 27% of former IDUs in 2005 aged 30-39 and 40-49 years, respectively, were estimated to have moderate disease, which highlights the potential benefit of targeting HCV testing at former IDUs who belong to these age groups. In conclusion, the identification and treatment of a larger proportion of former IDUs with HCV disease and education about the importance of minimal alcohol consumption are needed to help achieve a greater impact on the future morbidity and mortality of this disease.

Hutchinson SJ, Goldberg DJ, Gore SM, Cameron S, McGregor J, McMenamin J, McGavigan J. Hepatitis B outbreak at Glenochil prison during January to June 1993. *Epidemiol Infect* 1998; 121:185-191.

MRC Biostatistics Initiative for AIDS and HIV in Scotland, Centre for HIV Research, Edinburgh.

This data linkage study examined the extent of hepatitis B transmission and co-infection with HIV among 636 former inmates of Glenochil prison, Scotland, during an outbreak of bloodborne diseases in 1993 which was related to needle sharing. Eleven inmates imprisoned during the first half of 1993 presented with hepatitis B infection, of whom co-infection with HIV was detected in six. Based on dates of test results in relation to time of imprisonment, seven definitely acquired their hepatitis B infection within the prison. Only two infections were reported to Scotland's hepatitis B register and neither could be prison-linked. This outbreak of hepatitis B is the first of its kind to be reported but not the first to have occurred. It not only highlights the urgency for measures to prevent further spread of infection among prisoners but also illustrates the need for comprehensive surveillance of hepatitis B infection, and the need for a protocol on how to manage such outbreaks and on how to establish the extent of transmissions when acute hepatitis B occurs in prison.

Hutchinson SJ, Goldberg DJ, King M, Cameron SO, Shaw LE, Brown A, MacKenzie J, Wilson K, MacDonald L. Hepatitis C virus among childbearing women in Scotland: prevalence, deprivation, and diagnosis. *Gut* 2004; 53:593-598.

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The objectives were: (a) To examine the prevalence and demographic characteristics of hepatitis C virus (HCV) infection among childbearing women in Scotland; and (a) to determine the extent of maternal HCV infection diagnosed prior to birth. Methods: (a) Residual dried blood spot samples from routine neonatal screening, collected throughout Scotland during March-October 2000, were unlinked from identifiers and tested anonymously for HCV antibodies; and (b) electronic record linkage of Scotland's databases of births and diagnosed HCV infections was performed. Results: (a) Of 30,259 samples, 121 were enzyme linked immunosorbent assay repeat reactive and 88 of these were confirmed as anti-HCV positive in the recombinant immunoblot assay, representing a seroprevalence of 0.29-0.40%. HCV seroprevalence was high among 25-29 year olds (0.4-0.57%), in high deprivation areas (0.92-1.07%), and in Greater Glasgow (0.83-0.96%) and Grampian (0.38-0.62%). Adjusted relative risk for HCV infection was highest among residents in high deprivation areas of Glasgow (7.2 (95% confidence interval 2.0-25.5)). (b) Of 121 HCV infections found among women at delivery, 24% and 46% were estimated to have been diagnosed prior to pregnancy and birth, respectively. HCV prevalence among Scottish childbearing women is consistent with that expected from injecting drug use. Based on reported rates of mother to child transmission, 8-11 paediatric infections are expected per annum. Diagnosis in only 24% of infected women prior to pregnancy indicates the extent to which HCV goes unrecognised in the injecting community. The current HCV screening approach-to test only those with a history of injecting drug use (or other risk factors for infection)-identifies approximately a quarter of previously undetected infections among pregnant women.

Hutchinson SJ, McIntyre PG, Molyneaux P, Cameron S, Burns S, Taylor A, Goldberg DJ. Prevalence of hepatitis C among injectors in Scotland 1989-2000: declining trends among young injectors halt in the late 1990s. *Epidemiol Infect* 2002; 128:473-477.

Scottish Centre for Infection and Environmental Health, Glasgow, UK.

We previously reported a continual decline in anti-HCV prevalence among young injectors from Glasgow and Lothian between 1990 and 1997. The original study was extended to ascertain if the anti-HCV prevalence among injectors from Glasgow, Lothian, Tayside and Grampian had changed since 1997. Residual sera from injectors who had undergone attributable anti-HIV testing were tested anonymously for anti-HCV. In all four regions, no significant changes in prevalence were found among those aged < 25 years during the late 1990s (Glasgow 1997-9/00: 43%-41%; Lothian 1997-9: 13%-17%; Tayside 1997-9: 45%-35%; Grampian 1996-9: 28%-29%). Among those aged > or = 25 years, significant decreases in prevalence were only observed in Glasgow (1997-9/00: 79%-72%, P = 0.03) and Lothian (1997-9: 54%-45%, P = 0.05). The findings highlight that existing harm reduction measures, acknowledged as having helped to reduce the spread of HCV, are not sufficient to bring this epidemic under control and reduce transmission to sporadic levels.

Hutchinson SJ, Taylor A, Goldberg DJ, Gruer L. Factors associated with injecting risk behaviour among serial community-wide samples of injecting drug users in Glasgow 1990-94: implications for control and prevention of blood-borne viruses. *Addiction* 2000; 95:931-940.

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The aims were to examine the association between recipient-sharing of needles and syringes and demographic characteristics, injecting behaviour and needle and syringe exchange utilisation. Design: self-report data from serial cross-sectional surveys. Setting: multiple street, needle and syringe exchange and drug treatment sites throughout Glasgow. Participants: 2576 current injecting drug users (IDUs) recruited during 1990-94. In the multiple logistic regression analysis, a significantly lower level of recipient-sharing was associated with respondents who resided within 1 mile of a needle and syringe exchange compared to those who lived further away (adjusted OR 1.3; 95% CI 1.0-1.6), and by IDUs who reported obtaining either 6-15, 16-30, or > 30 sterile needles and syringes in an average week from a needle exchange and/or pharmacist (adjusted ORs 0.55, 0.34, 0.25; 95% CIs 0.3-0.9, 0.2-0.6 and 0.2-0.4, respectively) compared to those who obtained no sterile equipment from these sources. Recipient-sharing of needles and syringes in the previous 6 months reduced significantly between 1990 (43%) and 1991-94 (27-33%) ($p < 0.0001$); this decline was not explained by needle and syringe exchange utilization, suggesting that additional factors were influencing behavioural change at that time. Our data indicate that improving injectors' convenience of access to exchange facilities and increasing the numbers of sterile needles and syringes available to them is likely to result in further reductions in recipient-sharing, and thus the potential for blood-borne virus transmission, among IDUs.

Hutchinson SJ, Wadd S, Taylor A, Bird SM, Mitchell A, Morrison DS, Ahmed S, Goldberg DJ. Sudden rise in uptake of hepatitis B vaccination among injecting drug users associated with a universal vaccine programme in prisons. *Vaccine* 2004; 23:210-214.

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Hitherto, services have failed to deliver the UK Government's 1988 recommendation to vaccinate injecting drug users (IDUs) against hepatitis B virus (HBV). In April 1999, the Scottish Prison Service implemented an initiative to offer HBV vaccination to all inmates; we sought to determine the impact of this initiative on the IDU population. Among community-recruited IDUs (who had injected for ≤ 5 years) in Glasgow, vaccine uptake was significantly higher among those surveyed in 2001-2002 (52% of 387) than in 1993 (16% of 166), 1994 (19% of 138) or January-March 1999 (15% of 128); of the 2001-2002 vaccinees, 56% had been vaccinated in prison. Our results indicate that the universal offer of vaccination to all prisoners, within two years of the initiative's implementation, has had a dramatic impact on uptake among IDUs.

Ijaz S, Arnold E, Banks M, Bendall RP, Cramp ME, Cunningham R, Dalton HR, Harrison TJ, Hill SF, Macfarlane L, Meigh RE, Shafi S, Sheppard MJ, Smithson J, Wilson MP, Teo CG. Non-travel-associated hepatitis E in England and Wales: demographic, clinical, and molecular epidemiological characteristics. *J Infect Dis* 2005; 192:1166-1172.

Virus Reference Division, Centre for Infections, Health Protection Agency, University College London, London, United Kingdom.

Between 1996 and 2003, 186 cases of hepatitis E were serologically diagnosed. Of these, 17 (9%) were not associated with recent travel abroad. Patients were >55 years old (range, 56-82 years old) and tended to be male (76%). Two patients presented with fulminant hepatitis. A total of 129 (69%) cases were associated with recent travel to countries where hepatitis E virus (HEV) is hyperendemic. Compared with patients with travel-associated disease, patients with non-travel-associated disease were more likely to be older, living in coastal or estuarine areas, not of South Asian ethnicity, and infected by genotype 3 strains of HEV. The genotype 3 subgenomic nucleotide sequences were unique and closely related to those from British pigs. Patients infected by HEV indigenous to England and Wales tended to belong to a distinct demographic group, there were multiple sources of infection, and pigs might have been a viral reservoir.

Jaleel H, Allan PS, Huengsberg M, Natin D, on behalf of the West Midlands Regional Audit Committee. Offering the vaccine and accepting it: an audit of hepatitis B vaccination in West Midlands region. *Int J STD AIDS* 2003; 14:632-635.

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The practice of hepatitis B screening and vaccination in genitourinary medicine clinics in the West Midlands Region is audited against the standards set by 1999 Medical Society for the Study of Venereal Disease National Guidelines.

Jarvis LM, Dow BC, Cleland A, Davidson F, Lycett C, Morris K, Webb B, Jordan A, Petrik J. Detection of HCV and HIV-1 antibody negative infections in Scottish and Northern Ireland blood donations by nucleic acid amplification testing. *Vox Sang* 2005; 89:128-134.

Scottish National Blood Transfusion Service, Transfusion Transmissible Infections Group, University of Edinburgh, Edinburgh, Scotland, UK. ljarvis@ed.ac.uk

To reduce the risk of transfusion-transmissible viruses entering the blood supply, the nucleic acid amplification testing (NAT) was implemented to screen Scottish and Northern Irish blood donations in minipools. After 5 years of NAT for hepatitis C virus (HCV) and 2 years for human immunodeficiency virus-1 (HIV-1), the yield of serologically negative, nucleic acid positive 'window donations' and cost-benefit of NAT is under review. When the Scottish National Blood Transfusion Service (SNBTS) implemented NAT in 1999, a fully automated 'black box' system was not available. Therefore, an 'in-house' assimilated NAT assay was developed, validated and implemented. The system is flexible and allows testing for additional viral markers to be introduced with relative ease. The HCV and HIV NAT assays have 95% detection levels of 7.25 IU/ml and 39.8 IU/ml, respectively, as determined by probit analysis. One HCV (1 in 1.9 million) and one HIV (1 in 0.77 million) window donation have been detected in 5 and 2 years, respectively, of NAT. The SNBTS NAT assays are robust and have performed consistently over the last 5 years. The design of the in-house system allowed HIV NAT to be added in 2003 at a relatively small additional cost per sample, although for both assays, the royalty fee far exceeds the cost of the test itself. Clearly NAT has a benefit in improving the safety of the blood supply although the risks of transfusion-transmitted viral infections, as reported in the Serious Hazards of Transfusion (SHOT) report, are extremely low. Also, in UK the yield of HCV antibody negative, NAT positive donations is far lower than predicted although the early detection of an HIV window period donation and the increase of HIV in the blood donor and general populations may provide a stronger case for HIV NAT. The yield of HCV and HIV NAT in UK is significantly less than that anticipated from statistical models.

Jazayeri M, Basuni AA, Sran N, Gish R, Cooksley G, Locarnini S, Carman WF. HBV core sequence: definition of genotype-specific variability and correlation with geographical origin. *J Viral Hepat* 2004; 11:488-501.

Division of Virology, Institute of Biomedical and Life Science, University of Glasgow, Glasgow, UK.

There are eight genotypes and nine subtypes of HBV. Small differences in geographical origin are associated with sequence changes in the surface gene. Here, we compared core gene sequences from different genotypes and geographical regions. Specific combinations of 24 amino acid substitutions at nine residues allowed allocation of a sequence to a subtype. Six of these nine residues were located in different T cell epitopes depending on HBV geographical area and/or genotype. Thirty-seven nucleotide changes were associated uniquely with specific genotypes and

subtypes. Unique amino acid and nucleotide variants were found in a majority of sequences from specific countries as well as within subtype ayw2 and adr. Specific nucleotide motifs were defined for Korean, Indian, Chinese, Italian and Pacific region isolates. Finally, we observed amino acid motifs that were common to either South-east Asian or Western populations, irrespective of subtype. We believe that HBV strains spread within constrained ethnic groups, result in selection pressures that define sequence variability within each subtype. It suggests that particular T cell epitopes are specific for geographical regions, and thus ethnic groups; this may affect the design of immunomodulatory therapies.

Judd A, Hutchinson S, Wadd S, Hickman M, Taylor A, Jones S, Parry JV, Cameron S, Rhodes T, Ahmed S, Bird S, Fox R, Renton A, Stimson GV, Goldberg D. Prevalence of, and risk factors for, hepatitis C virus infection among recent initiates to injecting in London and Glasgow: cross sectional analysis. *J Viral Hepat* 2005; 12:655-662.

Department of Primary Care and Social Medicine, Centre for Research on Drugs and Health Behaviour, Imperial College London, London.

Our aim was to compare the prevalence of antibody to hepatitis C virus (anti-HCV) among recently initiated injecting drug users (IDUs) in London and Glasgow, and to identify risk factors which could explain differences in prevalence between the cities. Complementary studies of community recruited IDUs who had initiated injection drug use since 1996 were conducted during 2001-2002. Data on HCV risk behaviours were gathered using structured questionnaires with identical core questions and respondents were asked to provide an oral fluid specimen which was tested anonymously for anti-HCV but was linked to the questionnaire. Sensitivities of the anti-HCV assays for oral fluid were 92-96%. Prevalence of anti-HCV was 35% (122/354) in London and 57% (207/366) in Glasgow ($P < 0.001$). Multifactorially, factors significantly associated with raised odds of anti-HCV positivity were increasing length of injecting career, daily injection, polydrug use, having had a needlestick injury, and having served a prison sentence. In addition lower odds of anti-HCV positivity were associated with non-injection use of crack cocaine and recruitment from drug agencies. After adjustment for these factors, the increased odds of anti-HCV associated with being a Glasgow IDU were diminished but remained significant. HCV continues to be transmitted among the IDU population of both cities at high rates despite the availability of syringe exchange and methadone maintenance. Effectiveness of harm reduction interventions may be compromised by inadequate coverage and failure to reduce sufficiently the frequency of sharing different types of injecting equipment, as well as the high background prevalence of HCV, and its high infectivity. Comprehensive action is urgently required to reduce the incidence of HCV among injectors.

Kawsar M, Goh BT. Hepatitis B virus infection among Chinese residents in the United Kingdom. *Sex Transm Infect* 2002; 78:166-168.

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The objective was to determine prevalence of hepatitis B virus (HBV) serological markers in Chinese residents in the United Kingdom. Retrospective case-controlled study between January 1997 and June 2000 in two genitourinary medicine (GUM) clinics. 117 Chinese and 234 non-Chinese controls were studied. Baseline characteristics except marital status showed no difference. Overall prevalence of HBV serological markers was 35.8% in Chinese, controls 5.5% ($p < 0.001$). Hepatitis B surface antigen (HBsAg) positive carrier rate was 12.8% in Chinese, controls 0.4% ($p < 0.001$); 1.7% of Chinese patients were also hepatitis B e antigen (HBeAg) positive, none in controls. Natural immunity was acquired in 23.0% of Chinese, controls 5.1% ($p < 0.001$). Prevalence of HBV serological markers in UK born Chinese was 6.7%, non-UK born Chinese 40.1% ($p < 0.011$). Only 7.6% of Chinese had a history of previous HBV vaccination. Prevalence

of HBV serological markers among Chinese patients attending two GUM clinics in London was high and only a minority of Chinese had immunisation against HBV. Although the prevalence of HBV markers in UK born Chinese was lower than non-UK born Chinese, they may be at continuous risk of HBV infection. Non-UK born Chinese patients attending GUM services in the United Kingdom should be targeted for screening and vaccination to reduce HBV transmission.

Lamagni TL, Hope VD, Davison KL, Parry JV, Gill ON. Failure to vaccinate current injecting drug users against hepatitis B in England and Wales. *Commun Dis Public Health* 2001; 4:71-72.

HIV and STD Division, Communicable Disease Surveillance Centre, Public Health Laboratory Service, 61 Colindale Avenue, London NW9 5EQ. tlamagni@phls.org.uk

In most industrialised countries the elimination of hepatitis B infection is highly reliant on effective vaccine delivery to injecting drug users. This paper highlights the very poor vaccine coverage achieved in England and Wales in the ten years since this problem was officially recognised and targeted. This is despite the existence of a comprehensive and well-utilised network of specialist services for injecting drug users.

Lamden KH, Kennedy N, Beeching NJ, Lowe D, Morrison CL, Mallinson H, Mutton KJ, Syed Q. Hepatitis B and hepatitis C virus infections: risk factors among drug users in Northwest England. *J Infect* 1998; 37:260-269.

Regional Infectious Disease Unit, Fazakerley Hospital, Liverpool, UK.

The objectives were to identify the risk factors for hepatitis B (HBV) and hepatitis C (HCV) virus infections in drug users attending two drug treatment centres in Northwest England, and to evaluate the effect of both needle exchange and hepatitis B vaccination on the prevalence of hepatitis B and hepatitis C infections. A retrospective, cross-sectional study performed at the Regional Infectious Disease Unit and a Primary Care Centre for drug users in Liverpool. The study population included 773 drug users who had hepatitis serology performed between January 1992 and April 1996. Information on risk factors was obtained from clinical records; hepatitis serology data were obtained from the Liverpool Public Health Laboratory database. The overall seroprevalences of exposure markers for HBV (anti-HBc antibody) and HCV (anti-HCV antibody) were 48% and 67%, respectively. Duration of injecting drug use was the strongest predictor of HCV infection, with a crude odds ratio of 8.9 (95% confidence interval (CI): 4.5-17) for >10 compared to < 3 years of injecting, and was also a strong predictor of HBV infection, with an adjusted odds ratio (controlled for the effects of HBV vaccination) of 5.7 (95% CI: 3.2-10) for >10 compared to < 3 years' injecting. Vaccination against HBV was associated with greatly reduced HBV seroprevalence (crude odds ratio 0.11, 95% CI: 0.06-0.18). Overall, HCV was acquired earlier in the injecting career than HBV, but drug users who were not vaccinated against HBV acquired markers for HBV even more rapidly than for HCV. We found no independent protective effect for either anti-HBc or anti-HCV acquisition after the introduction of a needle-exchange scheme. Hepatitis C is highly prevalent among Merseyside drug users and is likely to prove difficult to control because of rapid acquisition early in the injecting career. Vaccination against hepatitis B is the best means of protecting drug users from hepatitis B, and should be offered before injecting is commenced.

Larcher VF, Bourne J, Aitken C, Jeffries D, Hodes D. Overcoming barriers to hepatitis B immunisation by a dedicated hepatitis B immunisation service. *Arch Dis Child* 2001; 84:114-119.

Department of Queen Elizabeth Children's Services, 3rd Floor, Fielden House, The Royal London Hospital, Whitechapel, London E1 1BB, UK.

The aims were to determine the effectiveness of a selective hospital based hepatitis B immunisation programme and the barriers to be overcome in obtaining a successful outcome. Retrospective case note review of 265 infants born over a five year period to hepatitis B carrier mothers at a university affiliated hospital in Hackney, London. A total of 242 infants (91%) were fully vaccinated; 217 (82%) had serology; 31 required booster doses. Percentages failing to reach second, third vaccinations, and serology on schedule rose exponentially (7%, 18%, 33% respectively). Mobility was high (25%) and significantly affected outcome. A total of 95% Hackney resident babies were fully vaccinated compared with 78% non-residents. Uptake of routine immunisations was higher in Hackney residents than non-residents and greater in those who were eligible for hepatitis B vaccine. Name changes occurred in 35%. Translation requirements were high (85% for Turkish, Vietnamese, and Asian families). Requirements for specific postnatal counselling of mothers and hepatology referral fell significantly during the course of the study. Only seven of 22 babies born in 1995 in Tower Hamlets compared with 53 of 58 Hackney babies received a full vaccination course in non-hospital based primary care. In inner city areas with high prevalence of hepatitis B carriage, mobility, and diverse ethnicity, a dedicated centralised immunisation service can be highly effective, provided that adequate support services (translation, counselling, and parental referral) are available.

Leal P, Stein K, Rosenberg W. What is the cost utility of screening for hepatitis C virus (HCV) in intravenous drug users? *J Med Screen* 1999; 6:124-131.

Wessex Institute for Health Research and Development, University of Southampton, UK.

The objective was to model the likely cost utility of the prevalence round of a screening programme for hepatitis C (HCV) in intravenous drug users (IVDUs) in contact with services in the South and West health region of the UK. Information on the prevalence of HCV, performance of diagnostic tests, and effectiveness of interferon alpha (IFN alpha) for treatment of chronic hepatitis were brought together with estimates of the costs of service provision. A simple spreadsheet model was used to estimate cost utility (cost/quality adjusted life year (QALY)). Assumptions (including use of ribavirin plus IFN alpha combination therapy) were tested by a one way sensitivity analysis. About 5600 IVDUs live in the region. A combination of enzyme linked immunosorbent assay (ELISA) and polymerase chain reaction (PCR) testing has high sensitivity and specificity for detecting HCV. There is excellent evidence that IFN alpha is effective in producing sustained normalisation of liver function and, by inference, eradicating HCV. Evidence for long term benefits comes from modelling studies based on progression of HBV or non-A, non-B hepatitis and is considerably less robust. The cost of the prevalence round of screening in IVDUs would be about 700,000 Pounds and is likely to identify about 1400 people, of whom about 270 would be eligible for treatment and 20 would respond to IFN alpha. This gives a cost/QALY of 9300 Pounds for the screening programme. However, much uncertainty around the estimates used to inform the cost utility calculation limits confidence in the value of screening IVDUs for HCV. Sensitivity analysis shows a range of possible cost utility from 3333 Pounds to 81,438 Pounds. Estimates are particularly sensitive to adherence to liver biopsy and treatment and to discounting of benefits. Although potentially cost effective, many important uncertainties surround the assumptions used to estimate the long term effectiveness of screening and treatment. There is insufficient evidence to inform policy development and further research is required in this rapidly changing field.

Mackenzie AR, Molyneaux PJ, Cadwgan AM, Laing RB, Douglas JG, Smith CC. Increasing incidence of acute hepatitis B virus infection referrals to the Aberdeen Infection Unit: a matter for concern. *Scott Med J* 2003; 48:73-75.

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The objectives were to assess the epidemiology and clinical outcomes of acute hepatitis B virus (HBV) infections presenting to a regional Infection Unit over a ten year period – with reference to the issues of injection drug use and strategies aimed at reducing transmission, notably needle exchange and immunisation programmes. A retrospective casenote review of all patients with acute HBV managed at the Infection Unit in Aberdeen between 1991-2000. One hundred and nineteen (119) patients with acute HBV infection were managed during the period of review. The annual number of patients increased from a mean of 3.3/year during the years 1991-96 to 46 in 2000. The risk factors associated with HBV infection were being an injection drug user (IDU) in 57 (47.9%), heterosexual sex in 22 (18.5%), sex with an IDU in 4 (3.4%), men who had sex with men in 10 (8.4%), tattooing in 1 (0.8%), a needle stick injury in 1 (0.8%), trauma 1 (0.8%) and unknown in 23 (19.3%). Many of these patients had ‘dabbled’ in drug use. Thirty-one (54.4%) of the IDU patients had previously been hospitalised with drug-related medical problems. Eighteen (31.6%) of the IDUs were receiving methadone at the time of presentation. There is an epidemic of HBV infection in the Grampian region of Scotland currently. Forty-six (65.7%) of the 70 infected patients diagnosed during 2000 were seen at the Infection Unit. The remainder had mild or asymptomatic disease and were managed in the community. This epidemic has occurred despite extensive use of local needle exchange facilities and might reflect missed opportunities to immunise IDUs against HBV infection. A co-ordinated approach is now in place to immunise IDUs and other high-risk groups, but the use of universal immunisation demands consideration.

Main J, Thomas H. Hepatitis C: How should we manage the patient? *J Viral Hepat* 2004; 11(Suppl 1):19-22.

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The patient with HCV infection may present with a variety of problems and range from the asymptomatic patient with mild liver damage to a patient presenting with complications of cirrhosis or hepatocellular carcinoma. The diagnosis of hepatitis C may be a complete surprise to the patient or be an expected diagnosis in someone with known risk factors. Similarly the physician may be faced with a patient who knows very little about hepatitis C or someone who has read extensively on the subject. The initial consultation is useful for gaining information on the patient's background, physical examination may give useful clinical clues on the stage of the liver disease. The consultation gives the physician a chance to educate the patient on the current thinking on hepatitis C and to organize confirmatory and other investigations that will help decide on the next line of management, i.e. whether the patient is a candidate for combination therapy of interferon and ribavirin.

Mangtani P, Hall AJ, Normand CE. Hepatitis B vaccination: the cost effectiveness of alternative strategies in England and Wales. *J Epidemiol Community Health* 1995; 49:238-244.

Department of Epidemiology and Population Studies, London School of Hygiene and Tropical Medicines.

The objective was to assess the cost effectiveness of adding universal hepatitis B vaccination in infancy or pre-adolescence to a policy of selective vaccination of at risk groups. Costs of a selective policy and additional costs of universal vaccination policies were estimated from costs of vaccine delivery and published data on target populations. Additional years of life gained were calculated for each policy by applying life tables to estimates of mortality attributable to hepatitis B. Setting: England and Wales. Compared with no vaccination, vaccination in infancy was the most cost effective followed by vaccination in preadolescence. Selective vaccination was the least effective (cost per year of life gained 2568 pounds, 2824 pounds, and 8564 pounds respectively). Adding vaccination in infancy or at pre-adolescence to a selective policy cost 1537 pounds or 1658

pounds per year of life gained. Discounting years gained in the future at 6% per annum, however, made pre-adolescent vaccination more cost effective than infant or selective vaccination (51,817 pounds, 94,821 pounds, and 124,779 pounds per discounted year of life gained). Adding pre-adolescent vaccination to a selective policy cost 32,125 pounds per discounted year of life gained and infant vaccination, 77,085 pounds. Universal vaccination against hepatitis B was more cost effective than selective vaccination in a low prevalence country. Discounting future health gain, however, made universal infant vaccination less cost effective than universal pre-adolescent vaccination. If future health gained is as important as present gain the addition of universal vaccination to a selective policy is equivalent to the cost per quality adjusted year of life from renal transplantation or breast cancer screening.

Mangtani P, Heptonstall J, Hall AJ. Enhanced surveillance of acute symptomatic hepatitis B in England and Wales. *Commun Dis Public Health* 1998; 1:114-120.

Department of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine.

A prospective incidence study was used to estimate the effect on transmission of hepatitis B virus (HBV) in England and Wales of maximising uptake of HBV vaccination in patients at risk attending genitourinary medicine (GUM) clinics or any medical services. Laboratory based surveillance in 1993 gave an incidence of acute symptomatic hepatitis B of 1 case per 100,000 population. Transmission through sexual intercourse was twice as common as through injecting drug use. Less than 20% of patients with acute HBV infection had attended a GUM clinic before their illness, but 42% had had access to other medical services where vaccination could have been offered routinely. Sixty per cent of patients' sexual partners and 37% of other members of their household had been offered vaccination. Compared with universal infant or pre-adolescent vaccination, extending the current selective policy to all who attend GUM clinics or any medical services would have a limited impact on the incidence of HBV, particularly as uptake of three doses of vaccine in adults is likely to be low.

McCarron B, Fox R, Wilson K, Cameron S, McMenamin J, McGregor G, Pithie A, Goldberg D. Hepatitis C antibody detection in dried blood spots. *J Viral Hepat* 1999; 6:453-456.

Department of Infectious Diseases and Tropical Medicine, Brownlee Centre, Gartnavel General Hospital, Glasgow, UK.

In the UK, there have been few studies of the seroprevalence of antibodies to hepatitis C virus (anti-HCV). As part of an ongoing prevalence study of HCV in injecting drug users, we have developed a technique for detecting anti-HCV in blood spots dried on filter paper using a commercially available assay. Subjects with and without serum anti-HCV were studied. The manufacturer's recommended cut-off (CO) for a positive anti-HCV result is kit-dependent, and therefore a ratio of test result (T) to kit CO was used to standardize results. T/CO values greater than 0.99 had a sensitivity of 100% and a specificity of 87.5% for anti-HCV detection. T/CO values greater than 1.99 had a sensitivity of 97.2% and a specificity of 100%. Hence, testing dried blood spots may be useful for detecting anti-HCV in epidemiological studies and as a diagnostic test in patients with poor peripheral venous access.

McIntyre PG, Hill DA, Appleyard K, Taylor A, Hutchinson S, Goldberg DJ. Prevalence of antibodies to hepatitis C virus, HIV and human T-cell leukaemia/lymphoma viruses in injecting drug users in Tayside, Scotland, 1993-7. *Epidemiol Infect* 2001; 126:97-101.

Department of Medical Microbiology, Ninewells Hospital & Medical School, Dundee, UK.

The prevalence of blood-borne viruses in injecting drug users (IDUs) in Tayside, Scotland was determined by testing serum samples from IDUs who underwent attributable HIV antibody testing during 1993-7. The prevalence of antibodies to HIV was 29/802, (3.6%); to hepatitis C virus (HCV) 451/691, (65.3%); and to human T-cell leukaemia/lymphoma viruses type 1 and 2 (HTLV) 0/679, (0.0%). The prevalence of HIV and HCV antibodies were higher in subjects over the age of 25 ($P = 0.03$ and $P = 0.001$, respectively). During 1993-7 the prevalence of HCV fell only in younger female IDUs ($P < 0.01$). HIV prevalence has declined dramatically since 1985, when a rate of 40% was recorded in similar populations. Harm reduction measures have failed to control HCV the spread of infection among IDUs in Tayside, as indicated by the high proportion of antibody positive IDUs, particularly males under the age of 25. Future studies should address the nature and effective reduction of continuing risk taking among IDUs in Tayside.

Medley GF, Lindop NA, Edmunds WJ, Nokes DJ. Hepatitis-B virus endemicity: heterogeneity, catastrophic dynamics and control. *Nat Med* 2001; 7:619-624.

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Hepatitis B virus infection is globally ubiquitous, but its distribution is very heterogeneous, with prevalence of serological markers in various nations ranging from less than 1% to more than 90%. We propose an explanation for this diversity using a mathematical model of hepatitis B virus transmission dynamics that shows, for the first time, 'catastrophic' behavior using realistic epidemiological processes and parameters. Our major conclusion is that the prevalence of infection is largely determined by a feedback mechanism that relates the rate of transmission, average age at infection and age-related probability of developing carriage following infection. Using the model we identify possible, highly non-linear, consequences of chemotherapy and immunization interventions, for which the starting prevalence of carriers is the most influential, predictive quantity. Taken together, our results demand a re-evaluation of public health policy towards hepatitis B.

Mohsen AH, Murad S, Easterbrook PJ. Prevalence of hepatitis C in an ethnically diverse HIV-1-infected cohort in south London. *HIV Med* 2005; 6:206-215.

Department of HIV/GU Medicine, The Guys Kings' and St Thomas School of Medicine, Kings' College Hospital, London, UK.

There is limited information on the prevalence of and risk factors for hepatitis C virus (HCV) infection among HIV-1-infected patients in the UK. Our objective was to determine the prevalence of HCV infection among an ethnically diverse cohort of HIV-infected patients in south London, and to extrapolate from these data the number of co-infected patients in the UK. A total of 1017 HIV-1-infected patients who had attended King's College Hospital HIV clinic between September 2000 and August 2002 were screened for HCV antibody using a commercial enzyme-linked immunosorbent assay (ELISA). Positive results were confirmed by polymerase chain reaction (PCR) or recombinant immunoblot assay. Demographic, clinical and laboratory data were obtained from the local computerized database and medical records. We applied our HCV prevalence rates in the different HIV transmission groups to the estimated number of HIV-infected persons in these groups in the UK, to obtain a national estimate of the level of HIV-HCV co-infection. Of the 1017 HIV-1-infected patients, 407 (40%) were white men, 158 (15.5%) were black African men, 268 (26.3%) were black African women, and 61 (6%) and 26 (2.6%) were black Caribbean men and women, respectively. Heterosexual exposure was the most common route of HIV acquisition (53.5%), followed by men having sex with men (36.9%), and current or previous injecting drug

use (IDU) (7.2%). The overall prevalence of HCV co-infection was 90/1017 (8.9%), but this varied substantially according to route of transmission, from 82.2% among those with a history of IDU (which accounted for 67% of all HCV infections), to 31.8% in those who had received blood products, to 3.5% and 1.8% in those with homosexually and heterosexually acquired infection, respectively. Multivariate logistic regression analysis identified several independent risk factors for HCV infection: a history of IDU [odds ratio (OR) = 107.2; 95% confidence interval (CI) = 38.5-298.4], having received blood products (OR = 16.5; 95% CI = 5.1-53.7), and either being from a white ethnic group (OR = 4.3; 95% CI = 1.5-12.0) or being born in Southern Europe (OR = 6.7; 95% CI = 1.5-30.7). Based on the 35,473 known HIV-1-infected persons in the UK and the 10 997 estimated to be unaware of their status, we projected that there are at least 4136 HIV-HCV co-infected individuals in the UK and 979 who are unaware of their status. Overall, 9% of our cohort was HIV-HCV co-infected. The prevalence was highest among intravenous drug users (82%), who accounted for most of our HCV cases, and lowest among heterosexual men and women from sub-Saharan Africa and the Caribbean [$< 2\%$]. Our estimate that a significant number of co-infected persons may be unaware of their HIV and HCV status, highlights an urgent need to increase the uptake of HCV and HIV testing, particularly among injecting drug users, to reduce the risk of onward transmission.

Moore MA, Macpherson LM, Kennedy C, Bagg J. Provision of hepatitis B vaccination for primary care dental staff in Scotland. *J Infect* 2003; 47:322-327.

Community Dental Service, NHS Lanarkshire, Coathill Hospital, Coatbridge, UK.

All dental surgeons should be protected from hepatitis B virus (HBV) infection by immunisation, ideally administered and monitored via occupational health services (OHS). This study examined relevant OHS systems in place for dental primary care healthcare workers (DHCW) across all Health Board Areas (HBAs) in Scotland. It also explored the DHCWs' knowledge of, and access to, these systems in three HBAs. Data from senior staff in all Scottish Health Boards and Primary Care Trusts were collected by self-completing questionnaires. Information from DHCWs was collected via telephone interviews with General Dental Practitioners (GDPs) and Community Dental Officers (CDOs) in each of Ayrshire and Arran, Highland and Lothian Health Boards. Thirteen of the 15 HBAs had robust HBV vaccination and monitoring systems. However, only 7/15 (47%) of these covered all DHCWs. Seven HBAs provided vaccination and monitoring for CDOs only, leaving GDPs to undertake these responsibilities for themselves. Of the 105 DHCWs approached, 82 gave an interview. These interviews highlighted major differences between HBAs in relation to access of DHCWs to OHS and indicated that CDOs had greater access than GDPs to OHS. Overall, 31% of DHCWs were not satisfied with the OHS available. In order to safeguard both staff and patients, significant further work is required to ensure that all DHCWs have access to appropriate OHS support for provision and monitoring of immunisation procedures and related functions such as management of sharps injuries.

Morris K, Bharucha C. Completed hepatitis C lookback in Northern Ireland. *Transfus Med* 1997; 7:269-275.

NIBTS, Belfast, UK.

Hepatitis C virus screening of blood donors was introduced in September 1991 using a second-generation enzyme-linked immunoassay (ELISA) and subsequent confirmatory testing with immunoblot (RIBA) and polymerase chain reaction (PCR). In April 1995 a lookback exercise was announced by the Department of Health, the purpose of which was to trace, counsel, investigate and, if necessary, treat individuals who may have been infected with HCV through blood and blood products prior to screening. A total of 231,321 donations have been screened, of which 553 were found to be reactive. Subsequent confirmatory tests identified 24 HCV-positive donors; 13

were repeat donors who had given a total of 164 units. Ninety-three units were traced and 117 components were identified as having been issued to hospitals. Twenty-five recipients requiring follow-up were identified, of which three were assessed by their GPs as not requiring counselling. Of 22 recipients of potentially infectious units 12 showed no evidence of exposure to HCV. We discuss these results in detail.

Morris-Cunnington M, Edmunds WJ, Miller E. Immunity and exposure to hepatitis A virus in pre-adolescent children from a multi-ethnic inner city area. *Commun Dis Public Health* 2004; 7:134-137.

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Seroprevalence data among ethnic minority groups within England and Wales are rare. An opportunistic approach was taken to test residual oral fluid, collected from pre-adolescent school children from an ethnically diverse region of northwest England, for anti-hepatitis A virus (HAV) IgG. Individual data on ethnicity and country of birth were also available. Of the 257 children who consented to participate, 62% were of South Asian ethnic origin. The overall seroprevalence was 18.8%, higher than 13.1% reported from a recent population-based survey in England and Wales among a mainly Caucasian population of the same age. The only factor significantly associated with HAV seropositivity in a multivariable logistic regression model was birth of the child abroad. Association with the place of birth of the child, but not that of the parent indicates that infection within this group occurs mainly abroad. Larger studies among ethnic minority groups are needed to investigate this claim further.

Morris-Cunnington MC, Edmunds WJ, Miller E, Brown DW. A population-based seroprevalence study of hepatitis A virus using oral fluid in England and Wales. *Am J Epidemiol* 2004; 159:786-794.

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Population-based seroprevalence studies provide important data on susceptible groups and the potential for future outbreaks. However, the invasive nature of serum collection has limited studies. This paper describes the first postal population-based survey using noninvasive oral fluid technology to collect antibody prevalence data in conjunction with extensive risk factor data to assess the distribution of immunity to common viral infections in England and Wales. These results pertain to hepatitis A virus (HAV). Approximately 5,500 oral fluid samples were collected between August 2001 and May 2002, as well as individual risk factor data through a questionnaire, from persons aged less than 45 years randomly sampled from general practices countrywide. Samples were tested for immunoglobulin G-specific antibody marking a past infection or immunity to HAV using an antibody-capture enzyme-linked immunosorbent assay. The age-specific HAV seroprevalences indicated a low incidence of infection (overall seroprevalence of 18.9% (95% confidence interval: 17.0, 20.9) and of 9.2% (95% confidence interval: 7.1, 11.3) after the exclusion of vaccinees). Vaccination proved the most important determinant of seropositivity. Ethnic minority groups were underrepresented, and adjustment increased the overall prevalence to 20.1% and to 12.1% in unvaccinated individuals. The availability of comprehensive risk factor data allowed the description of two risk profiles related to natural infection and vaccination.

Perrett K, Granerod J, Crowcroft N, Carlisle R. Changing epidemiology of hepatitis A: should we be doing more to vaccinate injecting drug users? *Commun Dis Public Health* 2003; 6:97-100.

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Since 2001 there have been significant outbreaks of hepatitis A virus (HAV) across South Yorkshire, largely in intravenous drug users, and HAV infection has been reported to be an increasing problem in England and Scotland during this time. This paper reports a brief investigation to clarify current HAV epidemiology in England and Wales. The epidemiology of HAV in England, but not yet Wales, has recently changed. Laboratory reports now show that most cases are occurring in young adults, mainly young men, and that the commonest reported risk group is injecting drug users. That cases may now be concentrated in injecting drug users is supported by reports from consultants in communicable disease control (CsCDC). These detail fourteen outbreaks in England in 2002 alone, all involving injecting drug users. Links to prisons and to the homeless, usually those in hostels, were also common. A combined Hepatitis A/B vaccine is readily available and we recommend that this now be used to extend the national immunisation programme against Hepatitis B in injecting drug users to include HAV.

Ramsay ME, Balogun MA, Collins M, Balraj V. Laboratory surveillance of hepatitis C virus infection in England and Wales: 1992 to 1996. *Commun Dis Public Health* 1998; 1:89-94.

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Screening assay for antibody to hepatitis C virus (HCV) became available late in 1990 and their use has subsequently become widespread. Laboratories in England and Wales reported 5232 confirmed HCV infections to the PHLS Communicable Disease Surveillance Centre (CDSC) between 1992 and 1996. Fifty-seven per cent (2976) of reports included risk factor information, 80% of which (2382) identified injecting drug use as the main route of transmission. Thirty-one per cent of reports (1640) included clinical information: 41% (665) were asymptomatic, 57% (938) had symptoms, signs, or biochemical abnormalities of hepatic origin, and 2.2% (37) had non-hepatic conditions. To enhance these data two additional surveys have been undertaken to collect data on all anti-HCV tests performed in public health laboratories. In 1993, a retrospective survey of people tested between 1990 and 1993 revealed that the prevalence of antibody was highest (222/331 [67%]) among injecting drug users and recipients of blood or blood products (189/548 [34%]) and lower among other groups. In a prospective survey of HCV tests performed in transfusion recipients in early 1995, the prevalence of antibody was higher in those transfused before 1985 (11/418 [2.6%]) than in those transfused after 1985 (14/1441 [1.0%]). Reports of confirmed infections are a useful method of monitoring hepatitis C infection but additional data on testing are needed to interpret trends overall and in specific risk groups.

Ramsay M, Gay N, Balogun K, Collins M. Control of hepatitis B in the United Kingdom. *Vaccine* 1998; 16(Suppl):S52-S55.

Immunization Division, PHLS Communicable Disease Surveillance Centre, London, UK.

Control of hepatitis B in the UK is based upon selective vaccination of persons in high-risk groups. To assess the likely cost-effectiveness of changes to this policy, information on the current burden of HBV infection in the UK is required. Laboratory reports of acute hepatitis B suggest that the vast majority of new hepatitis B infections acquired in the UK occur in adults, even after adjustment for unapparent infection. In childhood, perinatal transmission remains the most significant known risk factor. Universal antenatal screening has the potential to prevent perinatal infections in UK births and a substantial proportion of those UK acquired infections which lead to carriage. In addition, to antenatal screening, universal infant vaccination (at 2, 3 and 4 months)

can, in the short term, only prevent the small number of infections acquired in childhood. Economic analysis using current surveillance data is required to assess the possible cost-benefit of universal vaccination. Regardless of this, there is an urgent need to improve selective vaccination and to ensure that a high proportion of antenatal carriers is identified.

Ramsay ME, Rushdy AA, Harris HE. Surveillance of hepatitis B: an example of a vaccine preventable disease. *Vaccine* 1998; 16(Suppl):S76-S80.

Immunisation Division, PHLS Communicable Disease Surveillance Centre, London, UK.

The objectives of surveillance for vaccine preventable disease vary with the stage of the vaccination programme. Pre-implementation data is required to estimate the burden of disease and to decide on the appropriate vaccination strategy. Post-implementation data is required to monitor effectiveness but when high coverage is achieved surveillance must be able to accurately identify remaining pockets of susceptible persons. Sources of data include clinical and laboratory reporting. In most countries, all vaccine preventable diseases (including acute viral hepatitis) are notifiable by law. Such systems are prone to under-reporting but are usually satisfactory for monitoring trends. To encourage the rapid tracing and vaccination of contacts of acute hepatitis B, a sensitive case definition and timely reporting system are required. A clinical definition (e.g. for viral hepatitis) may be too broad, however, to assess the impact of vaccination and additional laboratory criteria may be necessary. As a country nears elimination, the predictive value of any case definition will fall and laboratory confirmation will always be required to target policy appropriately. Serological surveillance is another method for estimating disease incidence. This may be useful for hepatitis B as tests can distinguish vaccine induced immunity from natural infection and acute from prevalent cases. To monitor vaccine impact, age-coded specimens can be collected on an intermittent basis. Where the incidence is low, however, this approach, will be very expensive. Surveillance of vaccine preventable disease therefore requires flexible surveillance systems which are able to adapt to changes in incidence of infection and in control policy. The use of multiple data sources and supportive information from special studies is essential for the valid interpretation of routine data.

Rhodes T, Davis M, Judd A. Hepatitis C and its risk management among drug injectors in London: renewing harm reduction in the context of uncertainty. *Addiction* 2004; 99:621-633.

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The aim was recognizing the dearth of qualitative research on hepatitis C virus (HCV) infection associated with injecting drug use in the UK, this paper summarizes qualitative insights from a study exploring the social relations of HCV risk management among drug injectors in London. Method: adopting an inductive approach to data collection and analysis, 59 depth tape-recorded qualitative interviews were undertaken in 2001 with drug injectors recruited via drug user networks. While access to injecting equipment was reportedly good, needle and syringe sharing continued in exceptional circumstances and in the context of 'trust relationships'. Analyses of drug injectors' accounts of variations of 'I never share' showed that this construction denoted less a descriptor of actual risk behaviour than presentation of perceived risk status. Paraphernalia sharing, including spoons and filters, was common. There was much confusion and uncertainty concerning HCV knowledge, including its medical and transmission risks. Injectors were aware of the provisionality and partiality of their HCV knowledge. Confusion also surrounded the meaning of HCV antibody test results, with some feeling that their positive diagnosis had been 'trivialized' by their experiences of HCV testing. Injectors tended to make sense of HCV risk in relation to HIV. With most viewing HCV prevalence as high and HCV transmission as an inevitable consequence of injecting, HCV risk was perceived as ubiquitous and unavoidable. There is an

urgent need to renew UK policies of harm reduction in order to support perceptions that HCV is avoidable and preventable.

Roy KM, Ahmed S, Cameron SO, Shaw L, Yirrell D, Goldberg D, on behalf of the Incident Control Team. Patient notification exercise following a dentist's admission of the periodic use of unsterilized equipment. *J Hosp Infect* 2005; 60:163-168.

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During 2001, Greater Glasgow National Health Service (NHS) Board undertook a patient notification exercise in a Glasgow dental practice following the admission, by the dentist, of the use of unsterilized dental equipment on patients. Four thousand and eighty-nine exposed patients were identified; of these, 1696 contacted the NHS helpline and 1005 were counselled and screened for hepatitis C virus (HCV), hepatitis B virus (HBV) and human immunodeficiency virus. One patient showed evidence of previous HBV infection and 13 had antibodies to HCV. Molecular investigation of the HCV isolates indicated no significant associations. The investigation found no evidence of patient-to-patient transmission of HCV among patients attending the practice of a dentist who admitted periodically using unsterilized equipment.

Roy KM, Goldberg DJ, Hutchinson S, Cameron SO, Wilson K, MacDonald L. Hepatitis C virus among self declared non-injecting sexual partners of injecting drug users. *J Med Virol* 2004; 74:62-66.

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While much is known about hepatitis C virus (HCV) among injecting drug users (IDUs), there is scant information about the risk of HCV infection to non-injecting sexual partners of injecting drug users; it is possible that such individuals may have a greater risk of acquiring HCV than any other group barring injecting drug users. This study examines the prevalence of HCV among a population of non-injecting sexual partners of injecting drug users. Unlinked anonymous testing for anti-HCV of residual sera stored following the named HIV testing of specimens originally from persons who had indicated to their attending clinicians that they were non-injecting sexual partners of injecting drug users. The prevalence of anti-HCV among the sexual partners was 4.1% (25/611) overall, 6.4% (13/202) among heterosexual male and 3.0% (12/397) among the heterosexual female partners. None of the homosexual/bisexual partners were HCV antibody positive (0/12). Although we cannot be sure how non-injecting partners of injecting drug users acquire their HCV infection, having a relationship with someone who injects drugs may place an individual at appreciable risk of being infected; such individuals should consider being tested for HCV.

Roy KM, Goldberg D, Taylor A, Hutchinson S, MacDonald L, Wilson KS, Cameron SO. A method to detect the incidence of hepatitis C infection among injecting drug users in Glasgow 1993-98. *J Infect* 2001; 43:200-205.

The objective was to determine the incidence of HCV infection in a selected population of Glasgow injectors during the mid-1990s, using a retrospective cohort design. Unlinked anonymous anti-HCV testing was undertaken on serum residues collected from injecting drug users (IDUs) having two or more voluntary named HIV tests between 1993 and 1998. Seventy-seven percent (164/212) of IDUs had detectable HCV antibody in their first specimen collected. Of the 44 IDUs who were initially HCV seronegative and had a subsequent specimen available for testing, 11

(25%) seroconverted, giving an estimated incidence of 28.4 per 100 person-years (95% CI 15.7-51.2); the incidence of infection was greatest amongst older males. This study provides evidence of continuing transmission of HCV among Glasgow IDUs during an era of interventions to prevent the spread of bloodborne infections in this population and demonstrates the application of the unlinked anonymous testing approach to gauge incidence rather than prevalence of infection.

Roy KM, Goldberg D, Taylor A, Mills P. Investigating the source of hepatitis C virus infection among individuals whose route of infection is undefined: a study of ten cases. *Scand J Infect Dis* 2003; 35:326-328.

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Hepatitis C virus (HCV) transmission is predominantly parenteral via infected blood products or shared injecting equipment. Many infected individuals, however, deny these risk factors. This study set out to determine whether an in-depth interview would determine the likely source of infection for those whose route of infection was undefined. Between May 1999 and July 1999, risk factor information was sought, through in-depth interview, from 10 patients whose source of hepatitis C infection was undefined. The clinical notes of the patients were scrutinized to complement the information provided through the questionnaire. Despite undertaking an in-depth interview, it was not possible to establish the likely route of infection for 9 of the 10 individuals studied as they reported several risk events. There is little benefit to interviewing routinely those HCV-infected people who have no history of injecting drugs or having received a contaminated blood/blood product transfusion, to ascertain their likely source or time of infection; at best, such effort might only increase one's confidence that infection was acquired through means other than these 2 routes.

Roy K, Hay G, Andragetti R, Taylor A, Goldberg D, Wiessing L. Monitoring hepatitis C virus infection among injecting drug users in the European Union: a review of the literature. *Epidemiol Infect* 2002; 129:577-585.

Scottish Centre for Infection and Environmental Health, Clifton House, Clifton Place, Glasgow G3 7PN, UK.

Hepatitis C virus (HCV) among injecting drug users (IDUs) is one of the European Union's (EU) major public health problems. This review examines the current state of knowledge regarding HCV among IDUs in EU countries. Studies published between January 1990 and December 2000, were identified through a computerised search (MEDLINE and EMBASE). Ninety-eight studies have reported prevalence for HCV among groups of IDUs in all EU countries except Luxembourg. The prevalence of anti-HCV ranged from 30 to 98%. Incidence rates ranged from 6.2 to 39.3 per 100 person years. This review provides a comprehensive examination of HCV infection among IDUs in the countries of the EU, and quite clearly demonstrates that the quality and epidemiological relevance of the studies published varies widely. Thus, the reported data may not reflect accurately the current or recent past prevalence of HCV among IDUs in the EU. A strategic approach to the surveillance of HCV among IDUs in the EU, utilising robust and consistent methods, is required urgently.

Roy K, Howie H, Sweeney C, Parry J, Molyneaux P, Goldberg D, Taylor A. Hepatitis A virus and injecting drug misuse in Aberdeen, Scotland: a case-control study. *J Viral Hepat* 2004; 11:277-282.

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To describe an epidemiological investigation of an outbreak of hepatitis A virus (HAV) infection among injecting drug users in Aberdeen, Scotland. A case-control study to determine whether transmission was facilitated by poor personal hygiene or through sharing injecting equipment. Cases were more likely to report not washing their hands after using the toilet [odds ratio (OR) = 12.9, 95% confidence interval (CI) = 1.58-105.89] or before preparing food (OR = 4.0, 95% CI = 1.01-15.8), and less likely to have washed their hands prior to preparing drugs (OR = 10.67, 95% CI = 2.14-53.07). Cases were also more likely to report recipient sharing of needles/syringes (OR = 8.27, 95% CI = 1.68-40.57), and to have had injecting contact with someone who was jaundiced (OR = 29.4, 95% CI = 3.18-271.44). The results indicate that the lack of hygiene within the context of individuals gathering to prepare and inject drugs provides ample opportunity for the transmission of HAV. Although the promotion of good hygiene and the avoidance of sharing injecting equipment are important measures in preventing HAV transmission, they are unlikely to effect major behavioural change. Such measures should, therefore, be reinforced by routinely offering HAV vaccine to injectors.

Roy K, Kennedy C, Bagg J, Cameron S, Hunter I, Taylor M. Hepatitis C infection among dental personnel in the West of Scotland, UK. *J Hosp Infect* 2003; 55:73-76.

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Hepatitis C virus (HCV) is considered a serious occupational hazard for healthcare workers, particularly those performing exposure-prone procedures. In the UK, the majority of dental procedures are classified as exposure prone. In order to gauge the prevalence and determinants of infection among dental healthcare workers, a voluntary anonymous survey of HCV infection among primary care dental workers employed in the West of Scotland was undertaken, in which occupational and personal risk data were collected in parallel with a blood specimen. The overall prevalence of HCV antibodies was 0.1% (1/880, 95% CI 0-0.6); this is no greater than the estimated prevalence of HCV infection in the local population. Personal risk data collected suggested that the single infection identified was acquired through a non-occupational route. These results suggest that HCV infection is not a major occupational risk for dental healthcare workers.

Shaw L, Taylor A, Roy KM, Cameron SO, Burns S, Molyneaux P, McIntyre P, Codere G, Goldberg D. Establishment of a database of diagnosed HCV-infected persons in Scotland. *Commun Dis Public Health* 2003; 6:305-310.

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To provide a comprehensive understanding of the epidemiology of hepatitis C virus (HCV) infection in Scotland, a database of all persons known to have been infected with HCV in Scotland was established. Non-identifying data, held on the computers and requests forms in Scotland's principal and confirmatory HCV testing laboratories, were entered onto a National Database at the Scottish Centre for Infection and Environmental Health. As at December 2001, records from 13,519 persons in Scotland known to have been infected with HCV had been entered on to the database (one in 378 of Scotland's population). Of the 13,519, 69% were male and 90% of the 9,092 for whom risk factor information was available had injected drugs; 37% were from Greater Glasgow. Fifty-six per cent of the 13,519 were diagnosed between 1998 and 2001; 1,727 (23%) of the new diagnoses from 1998 to 2001 were aged under 25 years. The data provide an insight into the epidemiology of HCV infection in Scotland. They support other data, which indicate that the current major risk factor for HCV in the country is injecting drug use.

Skidmore S, Parry JV, Nottage P. An investigation of the potential risk of an HAV outbreak in a prison population following the introduction of cases from a community outbreak. *Commun Dis Public Health* 2001; 4:133-135.

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Increasing Hepatitis A (HAV) infection has been reported in communities in which there is a high level of intravenous drug use. Several cases were identified in a local prison and since the risk of transmission within the prison was felt to be high, it was decided to determine the prevalence of HAV antibodies in the prison population and therefore the number of susceptible inmates. Oral fluid was collected from 269 prisoners for testing for antibodies to HAV. Both IgM and IgG anti-HAV were assessed so that the percentage susceptible and the number recently infected could be ascertained. Eight inmates had evidence of a recent infection. Of the remaining 261, only 56 (21%) were immune to HAV. Therefore vaccination against HAV in addition to HBV should be considered for intravenous drug users and for prisoners remanded from a community where infection is known to be occurring.

Skipper C, Guy JM, Parkes J, Roderick P, Rosenberg WM. Evaluation of a prison outreach clinic for the diagnosis and prevention of hepatitis C: implications for the national strategy. *Gut* 2003; 52:1500-1504.

HMP Parkhurst, Isle of Wight, UK.

Hepatitis C virus (HCV) infection is a major public health problem recognised by the UK National Strategy that proposes that a care pathway for assessment, diagnosis, and treatment be established in all prisons, integrated within managed clinical networks. A prison sentence provides the opportunity to focus on traditionally hard to reach patients. The aims were to evaluate the prevalence of HCV infection in a UK prison cluster and to assess the effectiveness of a prison outreach service for hepatitis C. Subjects: male prisoners. A nurse specialist led clinic within a cluster of adult prisons was established, offering health education on hepatitis C, advice on harm minimisation, and HCV testing. Infected prisoners were offered access to a care pathway leading to treatment. Outcome measures were uptake of the service, and diagnosis and treatment of hepatitis C. A total of 8.5% of 1618 prisoners accepted testing: 30% had active infection with HCV. Most were ineligible for treatment due to psychiatric illness or did not receive treatment for logistic reasons. Injecting drug use was the major risk factor in all cases. Only 7% of HCV polymerase chain amplification positive inmates received treatment in prison. There is a large pool of HCV infected prisoners at risk of complications, constituting a source of infection during their sentence and after discharge. A prison outreach clinic and care pathway was perceived as effective in delivering health education, reducing the burden on prison and hospital services. It provided an opportunity for intervention but had a limited effect in eradicating HCV in prisoners and it remains unclear how this might be achieved.

Soldan K, Barbara JA, Ramsay ME, Hall AJ. Estimation of the risk of hepatitis B virus, hepatitis C virus and human immunodeficiency virus infectious donations entering the blood supply in England, 1993-2001. *Vox Sang* 2003; 84:274-286.

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The frequency of hepatitis B virus (HBV), hepatitis C virus (HCV) or human immunodeficiency virus (HIV) infectious donations entering the blood supply in England is too low to monitor using observational studies. The expected frequency of infectious donations can be estimated and these estimates may be used to contribute to monitoring of blood safety and used in the design of

strategies to decrease the risk of transfusion-transmitted infections. The prevalence and incidence of hepatitis B surface antigen (HBsAg), and antibodies to HCV and HIV (anti-HCV and anti-HIV, respectively) in donors in England, between 1993 and 2001, were used together with data about the length of negative 'window-periods' of current assays for each of these markers and data about test performance, to estimate the number of infectious donations that enter the blood supply. The risks were calculated separately for donations from new donors and from repeat donors, and for the three time periods 1993-95, 1996-98 and 1999-01. The estimated frequency of infectious donations entering the blood supply in England, between 1993 and 2001 was 1 in 260,000 for HBV and 1 in 8 million for HIV. For HCV, the frequency of infectious donations was 1 in 520,000 during 1993-98 and fell to 1 in 30 million during 1999-2001 when all donations were tested for HCV RNA. The frequency of HBV- and HCV-infectious donations entering the blood supply fell over these 9 years: the frequency of HIV-infectious donations remained essentially unchanged. The risk from donations from new donors was found to be approximately sevenfold higher than the risk from donations from repeat donors. The risks of HBV-, HCV- or HIV-infectious donations entering the blood supply in England are very low, and have decreased since 1993. Although the accuracy of these estimates is imperfect, mainly owing to uncertainty in some assumptions and to small numbers of infections, they provide some quantification of the risk of HBV, HCV or HIV transmission by transfusion, and allow comparison of the magnitude of these risks for each infection and over time. The methods we have used have been developed and improved from previously published methods.

Soldan K, Davison K, Dow B. Estimates of the frequency of HBV, HCV, and HIV infectious donations entering the blood supply in the United Kingdom, 1996 to 2003. *Euro Surveill* 2005; 10:17-19.

Health Protection Agency Centre for Infections, Colindale, London, United Kingdom.

Several new tests have been recently introduced by the United Kingdom Blood Services to improve safety. The frequency (or risk) of hepatitis B virus (HBV), hepatitis C virus (HCV) and HIV infectious donations entering the UK blood supply during 1996-2003 has been estimated. These years span the introduction of nucleic acid testing (NAT) for HCV, HIV combination antigen and antibody test and NAT for HIV. The frequency of an infectious donation entering the blood supply due to i) the window period, ii) assay failures and iii) human and technical errors in testing and processing, was estimated. The window period risk was estimated using the incidence of infection in donors and the length of the window period for tests in use, with an adjustment for atypical inter-donation intervals in seroconverting donors. The estimated frequency of infectious donations entering the blood supply during 1996-2003 was 1.66, 0.80 and 0.14 per million for HBV, HCV and HIV respectively. HCV NAT resulted in an over 95% fall in the risk of HCV. Current usage of HIV combined antibody-antigen tests and of HIV NAT reduced the estimated risk of HIV by 10%. Since 1996, the risk of transfusion-transmitted HBV, HCV and HIV infection in the UK has been lowered by several improvements to donation testing, although the absolute reduction in risk has been small. Vigilance for errors and the affects of donor selection may be as or more important than further reductions to window periods of tests for improving blood safety with respect to HBV, HCV and HIV.

Soldan K, Ramsay M, Robinson A, Harris H, Anderson N, Caffrey E, Chapman C, Dike A, Gabra G, Gorman A, Herborn A, Hewitt P, Hewson N, Jones DA, Llewelyn C, Love E, Muddu V, Martlew V, Townley A. The contribution of transfusion to HCV infection in England. *Epidemiol Infect* 2002; 129:587-591.

National Blood Service, Oak House, Reeds Crescent, Watford WD24 4QN, UK.

The English HCV lookback programme has identified some individuals with transfusion-

transmitted HCV infection. The path from the collection of donations from HCV-infected donors to the identification of infected recipients was constructed. The probability of different outcomes at each branch was derived from data collected during this programme. This path of probabilities was then used to produce a complete estimate of the number of recipients infected by blood transfusions (dead and alive at the end of 1995) by re-entry of blood components that fell out of the lookback at various steps prior to recipient testing, and entry of components from HCV-infected donations that were never identified for lookback. Less than 14,000 recipients were estimated to have been infected with HCV during the decade prior to the start of donation testing. Over 60% of these were expected to have died by the end of 1995. Transfusion has infected a large group of individuals. However, this group constitutes a very small, and declining, proportion of all HCV infections in the population.

Stein K, Dalziel K, Walker A, Jenkins B, Round A, Royle P. Screening for hepatitis C in genito-urinary medicine clinics: a cost utility analysis. *J Hepatol* 2003; 39:814-825.

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The aim of this study was to estimate the cost utility (cost per QALY) of screening for hepatitis C (HCV) infection in people attending genito-urinary medicine clinics in England. An epidemiological model of screening and diagnosis was combined with a Markov chain model of treatment with combination therapy to estimate cost utility. Parameters for the model were informed by literature review, expert opinion and a survey of current screening practice. The base case estimate was about pound 85,000 per QALY. Selective screening is more cost effective. If screening is restricted to only 20% or 10% of attenders, cost utility is estimated as pound 39,647 and pound 34,288 per QALY. If screening is restricted only to those with a history of injecting drug use, cost utility would be pound 27,138 per QALY. Estimates are particularly sensitive to acceptance rates for screening and treatment. Universal screening for HCV in GUM clinics is unlikely to be cost effective. There is limited evidence to support screening of people other than those with a history of injecting drug use and even this policy should be considered with some care and in the context of further research.

Stein K, Dalziel K, Walker A, Jenkins B, Round A, Royle P. Screening for hepatitis C in injecting drug users: a cost utility analysis. *J Public Health (Oxf)* 2004; 26:61-71.

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Hepatitis C is a major public health problem of increasing importance among injecting drug users, among whom screening has been proposed. We therefore estimated the cost utility of screening for hepatitis C infection among people with a history of injecting drug use in contact with drug misuse services. A spreadsheet-based model of screening using ELISA followed by polymerase chain reaction tests and treatment using combination therapy with interferon alpha and ribavirin was developed. Parameters were informed by literature review, expert opinion and a survey of current screening practice in England. A range of one-way sensitivity analyses were carried out to explore uncertainty in the results for cost effectiveness. Screening for HCV is likely to yield benefits in the population concerned at around 28,000 pounds per quality adjusted life year. This estimate is reasonably stable when explored in extensive one-way sensitivity analysis but appeared sensitive to the proportion of HCV positive people who accept biopsy or treatment and the utility gains associated with successful drug treatment. Important other areas of uncertainty include the effects of mortality from other causes on the cost effectiveness of screening in this population and the time at which symptoms would have led to presentation in the absence of a screening programme. Screening for HCV in this population is moderately cost effective, although some caution must

remain in accepting this estimate given the current uncertainties in this field, and further research is required.

Stein K, Dalziel K, Walker A, McIntyre L, Jenkins B, Horne J, Royle P, Round A. Screening for hepatitis C among injecting drug users and in genitourinary medicine clinics: systematic reviews of effectiveness, modelling study and national survey of current practice. *Health Technology Assessment* 2002, Vol. 6, No. 31. 122 pages.

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The objectives of screening for HCV should be clarified. Policy makers might wish to elucidate whether the primary purpose of screening is to: identify infected individuals for treatment, enable monitoring of infected individuals regardless of eligibility for treatment, achieve harm reduction in relation to the progression of HCV disease through reducing alcohol consumption or influence behaviour in relation to the spread of HCV. Evidence in support of objectives other than the treatment of infected individuals appears to be limited. Screening for HCV in IDUs in contact with services is moderately cost-effective (about £30,000/QALY) and reasonably stable when explored in extensive one-way sensitivity analyses. Uncertainty around acceptability of screening and adherence to treatment and the simple nature of our model leads us to recommend caution in accepting this estimate. Universal screening in GUM clinics is less cost-effective and subject to greater uncertainty than screening IDUs in contact with services. Assessment of selective screening policies in the GUM clinic setting is restrained by scarcity of information on the epidemiology of HCV in groups other than IDUs. While selective screening may be more cost-effective and affordable than universal screening, we believe that it remains open to question whether seeking people other than IDUs for screening represents a cost-effective use of NHS resources.

Stein K, Rosenberg W, Wong J. Cost effectiveness of combination therapy for hepatitis C: a decision analytic model. *Gut* 2002; 50:253-258.

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The objective was to estimate the cost utility of treatment with combination therapy (ribavirin and interferon alpha) for hepatitis C compared with no treatment or monotherapy (interferon alpha) based on UK costs and clinical management. Design: decision analysis model using a Markov approach to simulate disease progression. Setting: UK secondary care. Participants: hypothetical cohort of patients with hepatitis C. Main outcome measures: cost per quality adjusted life year (QALY) gained. Discounted cost per QALY for combination therapy over no treatment was 3791 pounds. Cost per QALY varied between 1646 pounds and 9170 pounds according to subgroup, with the lowest ratios being for genotype 2 or 3, women, those aged less than 40 years, and those with moderate hepatitis. The discounted cost per QALY of the combination over monotherapy was 3485 pounds. Similar findings were shown for subgroups as for the comparison with no treatment. One way sensitivity analysis showed that while drug costs were more important in the analysis than assumptions about disease progression or costs of treating hepatitis C disease, the results were robust to large changes in underlying assumptions. It was concluded that combination therapy for hepatitis C is a cost effective treatment option and is superior to monotherapy. Considerable uncertainties remain over the appropriate management strategies in the populations excluded from randomised controlled trials and in whom treatment is currently being considered in the UK.

Steinke DT, Weston TL, Morris AD, MacDonald TM, Dillon JF. Epidemiology and economic burden of viral hepatitis: an observational population based study. *Gut* 2002; 50:100-105.

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The objective of this study was to describe the epidemiology and estimate the health resource use of patients with viral hepatitis in Tayside, Scotland, using record linkage techniques. Design: a retrospective observational study. Setting: Liver disease database, Tayside, Scotland. Patients: all subjects resident in Tayside in the study period 1989-1999 and registered on the Epidemiology of Liver Disease in Tayside (ELDIT) database. Main outcome measures: incidence and prevalence of known viral hepatitis in Tayside, survival of subjects diagnosed with viral hepatitis, and the health resource use with respect to hospital admissions compared with the general population. There were 4992 patients identified with viral hepatitis in the study period 1989-1999; 86 were IgM positive anti-hepatitis A, 187 patients were hepatitis B surface antigen (HBsAg) positive, and 469 were anti-hepatitis C (HCV) positive. HCV and HBsAg seropositive patients were more likely to be hospitalised and stay in hospital longer, less likely to survive after six years, and used more drugs of potential abuse than the general population. There was an increase in cost per admission and per patient as a consequence of liver disease. A record linkage population based study of viral hepatitis allows outcomes to be identified and costed. Those at risk of viral hepatitis infection in the Tayside population should be informed about the future implication to their health and costs to society. The health service should investigate the cost effectiveness of vaccination and opportunity costs to the health service of viral hepatitis taking into consideration the increasing incidence and prevalence of disease.

Stevenson J, Tannahill M, Biggs V. An outbreak of acute hepatitis B infection among injecting drug users in Inverclyde, Scotland. *Commun Dis Public Health* 2001; 4:60-63.

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This large outbreak of acute hepatitis B infection among injecting drug users (IDUs) was precipitated by an increase in injecting heroin use in Inverclyde in the West of Scotland, between 1997 and 1999. Ninety-two cases of hepatitis B infection in residents of Inverclyde were reported to Argyll and Clyde Health Board from January 1996 to December 1999. An investigation of risk factors found 87% (80/92) of the cases were IDUs, of whom four-fifths were men. Fifty six per cent of cases were aged 20-29 years old and 12% were aged 16-19 years old. Further investigations among this close community of young and relatively inexperienced IDUs revealed that many admitted to sharing injecting equipment particularly spoons, water and filters. Only a minority had been using local needle exchange facilities in the area. After public consultation a second needle exchange was opened in 1998 staffed by a dedicated needle exchange development worker who has continued to develop harm reduction services locally.

Sundkvist T, Smith A, Mahgoub H, Kirkby A, Kent R, Wreghitt T, Davidkin I. Outbreak of hepatitis A infection among intravenous drug users in Suffolk and suspected risk factors. *Commun Dis Public Health* 2003; 6:101-105.

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A prolonged outbreak of hepatitis A infection amongst drug users in Suffolk prompted a study of the natural immunity against hepatitis A in this population, and a retrospective analysis of the relationship between specific drug-taking behaviours and the risk of hepatitis A infection. Prior to the outbreak, age-specific seroprevalence of hepatitis A IgG in drug users was similar to that amongst blood donors in the region. Of those without effective immunity, intravenous drug users, multiple drug users and those injecting frequently were more likely to have developed hepatitis.

The reported frequency of equipment sharing and the number of injecting partners were not related to the risk of infection. The potential for blood-to-blood, and a suggested faecal-blood transmission were considered to be important in propagating the outbreak in this population. We suggest that a single dose of hepatitis A vaccine administered opportunistically should be used in outbreaks involving drug users.

Syed NA, Hearing SD, Shaw IS, Probert CS, Brooklyn TN, Caul EO, Barry RE, Sarangi J. Outbreak of hepatitis A in the injecting drug user and homeless populations in Bristol: control by a targeted vaccination programme and possible parenteral transmission. *Eur J Gastroenterol Hepatol* 2003; 15:901-906.

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The objective was to study the use of hepatitis A virus (HAV) vaccination in controlling an outbreak of HAV in inner-city Bristol among injecting drug users (IDUs). To study whether hepatitis C virus (HCV) and hepatitis B virus (HBV) co-infection increases morbidity. Design: community-based cohort study. Setting: Avon Health Authority area, UK. Participants: all laboratory-confirmed cases of HAV infection notified in 2000. Intervention: administration of a targeted vaccination, education and liaison programme. Main outcome measures: number of cases of HAV before and after introduction of HAV vaccination programme. Mortality and number of patients requiring hospital admission. Association of HCV and HBV co-infection with hospital admission. Ninety cases of HAV were reported in the first 6 months of 2000, of whom a substantial number were IDUs and/or inner-city hostel residents. In the second 6 months of 2000, following the introduction of a vaccination programme among homeless people, hostel residents, and IDUs, the number of HAV cases fell to 33. Sixteen patients had evidence of HCV co-infection. No patient had chronic HBV infection. Two patients died as a result of HAV, and two subsequently died from drug misuse. Fifty-six per cent of HCV-co-infected patients required admission to hospital compared with 28% non-HCV-co-infected patients. This is the first reported successful use of vaccination to control an outbreak of HAV in a population of IDUs and to prevent transmission to the wider population. HCV co-infection appears to increase the severity of HAV illness, as demonstrated by increased incidence of hospital admission.

Taylor A, Goldberg D, Hutchinson S, Cameron S, Gore SM, McMenamin J, Green S, Pithie A, Fox R. Prevalence of hepatitis C virus infection among injecting drug users in Glasgow 1990-1996: are current harm reduction strategies working? *J Infect* 2000; 40:176-183.

Scottish Centre for Infection and Environmental Health, Glasgow, UK.

The objectives were to determine the prevalence of HCV antibodies among injecting drug users and to gauge the effectiveness of needle/syringe exchange in preventing the transmission of HCV infection. Between 1990-1994 and in 1996, annual cross-sectional surveys of injecting drug users in Glasgow were conducted. In order to ensure as representative a sample as possible, the 1949 respondents were recruited from both 'in-treatment' and 'out-of treatment' settings. Injectors were interviewed about their risk behaviours for blood-borne viruses and provided a saliva sample which was initially tested, anonymously, for HIV antibodies, and subsequently tested for hepatitis C infection. Among 1949 injectors, the prevalence of salivary antibodies, indicative of hepatitis C viraemia, was 61%(95% confidence interval (CI) 59%-63%): the estimated prevalence of serum antibody positivity was 72%. Length of injecting, year of commencing drug injecting and the number of times in prison were predictive of antibody positivity. Thirty-one per cent of injectors who commenced their injecting after 1992, following the full establishment of needle/syringe exchange in the city, were salivary antibody positive, and the majority of their infections were acquired outside the prison setting. Respondents who began injecting after the introduction of needle/syringe exchange in the city were significantly less likely to test HCV antibody positive

than those who commenced injecting prior to the advent of needle/syringe exchange, after adjusting for length of injecting career. The prevalence of HCV among injectors in Glasgow has decreased during the era of needle / syringe exchange. However, there is evidence to suggest that the incidence of infection remains high. Since the prevalence of hepatitis C viraemia among the city's injecting population is extremely high, ongoing transmission is inevitable unless more effective interventions are identified and implemented urgently.

Thomas SL, Newell ML, Peckham CS, Ades AE, Hall AJ. A review of hepatitis C virus (HCV) vertical transmission: risks of transmission to infants born to mothers with and without HCV viraemia or human immunodeficiency virus infection. *Int J Epidemiol* 1998; 27:108-117.

Department of Epidemiology & Biostatistics, Institute of Child Health, London, UK.

Hepatitis C virus (HCV) vertical transmission studies have reported conflicting findings, possibly due to differences in HCV transmission risk factors among maternal populations, or to methodological differences. Methods: systematic review of worldwide published and unpublished HCV vertical transmission studies. Standardised diagnostic criteria were applied to minimise methodological differences, and transmission rates recalculated according to maternal HCV viraemic and human immunodeficiency virus (HIV) infection status. In all, 976 eligible infants from 28 studies were followed up sufficiently for recalculation of transmission rates. Overall transmission rates were less than 10% in 8/12 studies of HIV negative mothers, compared with 2/7 studies comprising at least 50% HIV-coinfected mothers. Rates from 409 viraemic mothers in 15 studies ranged from 0% to 41%, being less than 10% from HIV negative mothers in 6/13 studies and from HIV positive mothers in 1/6 studies. Nine studies measured maternal viraemia levels, with only 2/30 transmitting mothers having $< 10^6$ copies/ml of HCV RNA. Eight transmissions were identified overall from non-viraemic mothers. Significant transmission rate variation remained after accounting for maternal viraemia and HIV coinfection, possibly due to differences in other vertical transmission risk factors, in frequencies of postnatal transmission, or residual differences in study methodologies. Overall, HCV transmission is largely restricted to infants born to HCV viraemic mothers, and low risks among most HIV negative mothers may be due to lower HCV viraemia levels. International agreement on standardized diagnostic criteria for HCV vertical transmission would facilitate pooling of individual findings, to allow more precise transmission estimates and further investigation of risk factors.

Thomson BJ, Finch RG. Hepatitis C virus infection. *Clin Microbiol Infect* 2005; 11:86-94.

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Hepatitis C virus (HCV) infection is a major public health problem. Up to 3% of the world's population is infected with HCV, and at least 200 000 adults in the UK carry the virus. Of those exposed to HCV, 80% become chronically infected, and at least 30% of carriers develop chronic liver disease, including cirrhosis and hepatocellular carcinoma. This review provides an overview of selected features of the molecular biology and pathogenesis of HCV infection, and thereafter discusses in detail the epidemiology of HCV, the hepatic and extra-hepatic diseases caused by the virus, and the current treatment options for both acute and chronic virus infection. The special cases of healthcare workers, prison inmates and individuals coinfecting with human immunodeficiency virus and HCV are considered in detail.

Thorburn D, Dundas D, McCrudden EA, Cameron SO, Goldberg DJ, Symington IS, Kirk A, Mills PR. A study of hepatitis C prevalence in healthcare workers in the West of Scotland. *Gut* 2001; 48:116-120.

Whether healthcare workers have an increased prevalence of hepatitis C virus infection as a result of exposure to patient's blood and body fluids is controversial. This study assesses the prevalence of hepatitis C virus infection in healthcare workers, and its relation to the performance of exposure prone procedures and duration of occupational exposure, allowing an estimate to be made of the incidence of occupationally acquired hepatitis C infection among medical staff. In this anonymous retrospective cohort study, we estimated the prevalence of hepatitis C infection in 10 654 healthcare workers. ELISA-3 testing was performed on pools of five sera collected during immunisation against hepatitis B. Healthcare workers were arranged into five occupational groups, according to the degree of patient exposure, and three age bands (< 30 years, 30-39 years, > 40 years). Prevalence of antibodies to hepatitis C was 0.28% (30/10 654), comparable in all occupational groups ($p = 0.34$) and unrelated to duration of potential exposure. Assuming that all detected infections had been occupationally acquired, the maximum estimated risk of hepatitis C infection in exposure prone medical staff was low: 1.4% for surgeons and 1.0% for physicians over a 35 year professional career. Hepatitis C infection is infrequent in healthcare workers in Glasgow. Those conducting exposure prone procedures do not seem to be at higher risk than other healthcare staff.

Thorburn D, Roy K, Cameron SO, Johnston J, Hutchinson S, McCrudden EA, Mills PR, Goldberg DJ. Risk of hepatitis C virus transmission from patients to surgeons: model based on an unlinked anonymous study of hepatitis C virus prevalence in hospital patients in Glasgow. *Gut* 2003; 52:1333-1338.

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The risk of a surgeon acquiring the hepatitis C virus (HCV) through occupational exposure is dependent on the prevalence of HCV infection in the patient population, the probability of a percutaneous injury transmitting HCV, and the incidence of percutaneous injury during surgery. The aims were to estimate the prevalence of HCV infection in the adult surgical patient population in North Glasgow and thereafter estimate the risk of HCV transmission to surgeons through occupational exposure. The prevalence of HCV infection was estimated through the unlinked anonymous testing of samples from male surgical patients, aged 16-49 years, in two North Glasgow hospitals from 1996 to 1997, and adjusting these data for age and sex. Using published estimates of the incidence of percutaneous injury during surgery and percutaneous injury transmitting HCV, the risk of occupational transmission of HCV to surgeons was then derived. The estimated prevalence of anti-HCV infection for all adult patients in the two hospitals combined was 1.4% (cardiothoracic/cardiology 0.8%, orthopaedics/rheumatology 1.4%, general surgery/ENT 2.0%). The estimated probability of HCV transmission from an HCV infected patient to an uninfected surgeon was 0.001-0.032% per annum (0.035-1.12% risk over a 35 year professional career). The risk of an individual surgeon acquiring HCV through occupational exposure is low, even in an area with an extremely high prevalence of HCV among its injecting drug using population. Surgeons however should be encouraged to observe universal precautions and present for assessment after needlestick injuries to protect themselves and their patients from this insidious infection.

Thursz MR. Host genetic factors influencing the outcome of hepatitis. *J Viral Hepat* 1997; 4:215-220.

Imperial College School of Medicine at St Mary's, London, UK.

A strong genetic component determining the outcome of hepatitis B virus (HBV) infection has been established through twin studies. The immunopathogenesis of HBV infection is well described and it has therefore been possible to predict some gene loci, exhibiting polymorphism, may influence the outcome of HBV infection. As expected, the immune response genes in the

major histocompatibility complex (MHC) on the short arm of chromosome 6 have provided confirmed susceptibility genes. In hepatitis C virus (HCV) infection the picture is not so clear although comparison of the known immunological phenomena with those of HBV suggest that polymorphisms in the MHC may also influence disease outcome. Identification of susceptibility genes, which modify disease phenotype, may assist in predicting natural outcome of infection or response to therapy.

Thursz M. Genetic susceptibility in chronic viral hepatitis. *Antiviral Res* 2001; 52:113-116.

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Infection with hepatitis B virus (HBV) or hepatitis C virus (HCV) may result in a number of different clinical outcomes. There is strong evidence in HBV infection that host genetic factors play a major role in determining the outcome of infection. A number of approaches may be used to determine the specific genetic factors involved but the principal method which has been used to date is the disease association study. Disease association studies have a number of drawbacks but trials with well-constructed designs and large numbers of cases have recently produced compelling and reproducible results. In particular alleles in the MHC class II loci and interleukin 10 promoter have been demonstrated to influence the outcome of these infections.

Tompkins CN, Wright NM, Jones L. Impact of a positive hepatitis C diagnosis on homeless injecting drug users: a qualitative study. *Br J Gen Pract* 2005; 55:263-268.

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Increasing numbers of injecting drug users are presenting to primary care and a growing number of general practices are specifically providing care for homeless people. Injecting drug users are at the greatest risk of hepatitis C infection and homeless drug misusers, because of their drug-taking behaviour and patterns, have been identified as being at greater risk of harm of blood-borne diseases than the general population. However, little work has been conducted with injecting drug users or homeless people who have hepatitis C and little is known about how the virus may affect them. The aim was to explore the impact of a positive hepatitis C diagnosis on homeless injecting drug users. Design of study: This study employed qualitative research. In-depth interviews allowed the exploration of the impact of a potentially life-threatening diagnosis within the context of a person's expressed hierarchy of needs. Setting: a primary care centre for homeless people in the north of England. In-depth interviews about the impact of a positive hepatitis C diagnosis on their lives were conducted with 17 homeless injecting drug users who had received a positive hepatitis C diagnosis. The interviews were audiotaped, transcribed, and analysed using the framework approach. Receiving a positive diagnosis for hepatitis C resulted in feelings of shock, devastation, disbelief, anger, and questioning. A positive diagnosis had lasting social, emotional, psychological, behavioural, and physical effects on homeless injecting drug users, even years after the initial diagnosis. Most responders were diagnosed by a doctor in primary care or by hospital staff; however, not all had sought testing and a number were tested while inpatients and were unaware that blood had been taken for hepatitis C virus serology. The implications for clinical policy and primary care practice are discussed, including the issues of patient choice, confidentiality, and pre- and post-test discussions. Posttest discussions should be followed up with additional social, psychological, and medical support and counselling.

Wallace LA, Bramley JC, Ahmed S, Duff R, Hutchinson SJ, Carman WF, Kitchin NR, Goldberg DJ. Determinants of universal adolescent hepatitis B vaccine uptake. *Arch Dis Child* 2004; 89:1041-1042.

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The UK is currently considering the introduction of universal hepatitis B vaccination. This study of determinants of vaccine uptake among school based adolescents shows that living in areas of high deprivation, commonly associated with injecting drug risk behaviours, was the most important factor, with statistically significant lower odds of receiving three doses. This was less pronounced for receipt of two doses. Thus, there are implications for future policy; if universal vaccination is approved, a licensed two dose schedule would be most appropriate in this setting.

Wallace LA, Young D, Brown A, Cameron JC, Ahmed S, Duff R, Carman WF, Kitchin NR, Nguyen Van Tam JS, Goldberg DJ. Costs of running a universal adolescent hepatitis B vaccination programme. *Vaccine* 2005; [Epub ahead of print].

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In the first UK study to examine feasibility and acceptability of universal adolescent hepatitis B vaccination, the costs associated with the administration and uptake (80.2 and 89.3% for three doses and at least two doses, respectively), of a three-dose regimen in pupils in Glasgow schools (2001/2002) were measured. These data were used to estimate the economic outlay for the delivery of a routine, ongoing three-dose and two-dose hepatitis B vaccine programme in schools. Vaccine, accounting for almost 70% of the overall costs, was the largest cost item for both the pilot and routine programmes, using either regimen. However, the ongoing, two-dose regimen was the cheapest option in this analysis, irrespective of vaccine price. Cost data from this study may be useful for other countries wishing to implement a similar programme.

Walsh B, Maguire H, Carrington D. Outbreak of hepatitis B in an acupuncture clinic. *Commun Dis Public Health* 1999; 2:137-140.

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A retrospective cohort serological study identified five confirmed cases of acute hepatitis B virus (HBV) infection in three and a half years at an acupuncture clinic in London. These cases made up 1.7% of those treated by an acupuncturist who was a hepatitis B 'e' antigen (HBeAg) carrier. Virus subtyping and polymerase chain reaction – single strand conformation polymorphism assay (PCR-SSCPA) showed that strains of virus from the acupuncturist and two of the five patients for whom it was possible to perform the test were indistinguishable. Nine other patients who attended the same acupuncturist had antibody to the hepatitis B core antigen but had other risk factors for HBV infection. No obvious mode of transmission was identified but cross contamination of needles could not be ruled out in two cases. The fifth case was exposed to HBV after disposable needles were introduced. Routine immunisation of acupuncturists against HBV is recommended.

Weightman R, Walton R, Bury J. Audit of bloodborne virus prevention activity with drug users seen in primary care. *Commun Dis Public Health* 2004; 7:301-305.

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Drug misuse is increasingly being managed in general practice. It has been proposed that better use could be made of this contact to identify people with bloodborne virus (BBV) morbidity and to deliver prevention strategies. The Hepatitis B and C Prevention Project was designed to enhance the work of primary healthcare teams in preventing transmission of BBVs in people known to have

a history of problem drug use. As part of this work a baseline audit of current provision was undertaken and the results are reported here. Primary care records of 1278 people with a history of illicit drug use were audited to establish the levels of hepatitis B immunisation and testing for BBVs and to determine whether there was a record of any professional discussion of BBV issues with the patient. Records were drawn from rural and city-based general practices. Audit feedback, training, and advice were offered to raise awareness and discussion of how this work was currently being undertaken, and how it might be improved. This baseline audit showed that 90% (n = 1153) of the patients had been questioned about injecting drug use and of these 50% (579/1153) reported injecting at some point in the past. Only 4% (54/1278) had completed a course of hepatitis B immunisation and of these three quarters gave a history of injecting drug use. Another 6% (74/1278) of patients tested for hepatitis B virus (HBV) showed markers of natural immunity. Up to 90% of this group therefore remained vulnerable to this preventable disease. A discussion of BBV issues with a professional was recorded in 41% (523/1278) of cases, and was more likely to have occurred in those with a known history of injecting. Individuals were less likely to have been tested for hepatitis C virus (HCV) than for HIV or HBV despite its high prevalence in this group. Only 28% (354/1278) were tested for HCV compared with 33% (416/1278) tested for HBV and 36% (454/1278) tested for HIV. Prevalence of anti-HCV for people with a history of injecting was 51% (137/268) compared to 11% (9/83) in those with no history of injecting. Prevalence of anti-HIV in those with a history of injecting was 10% (29/294) compared 0.7% (1/137) in those with no history of injecting. Prevalence of HBV markers in those with a history of injecting was 23% (65/279) compared with 7% (8/114) in those with no history of injecting. Of the 530 patients with test results, only 52% (275/530) had been tested for all three viruses despite the common transmission routes.

Williams JR, Nokes DJ, Anderson RM. Targeted hepatitis B vaccination – a cost effective immunisation strategy for the UK? *J Epidemiol Community Health* 1996; 50:667-673.

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The objective was to compare the potential cost effectiveness of vaccination against hepatitis B virus (HBV) targeted at genitourinary clinic (GU) attendees with that of universal infant vaccination. A mathematical model of sexual and perinatal transmission of HBV was used to compare the effectiveness among heterosexual and homosexual populations of programmes of mass infant vaccination and targeted immunisation of genitourinary medicine (GU) clinic attendees. Each was applied to 90% of the eligible population with differing assumptions about rates of compliance and seroconversion – problems of delivery (obtaining high compliance) was considered a significant drawback of targeted vaccination. Observed relationships between GU clinic attendance and sex partner change rates for heterosexuals and for homosexuals were used to define the rates of vaccination uptake within sexual activity risk groups. Setting: England and Wales. Model results showed that for heterosexuals universal infant vaccination became more effective than clinic based vaccination only approximately 40 years after the start of the programme and that the predicted cost effectiveness of GU clinic vaccination was greater at all times. For homosexuals, clinic vaccination was always more effective over the time frame considered, but by 50 years if it were carried out without prior screening it had become appreciably less cost effective than a mass infant programme. With prior screening in GU clinics this cost effectiveness deficit was only marginal. Targeted vaccination might have a much greater potential than is realised at present, particularly if it were possible to improve compliance of clinic attendees. A fuller comparison between mass infant and targeted vaccination must await the specific inclusion in the model of other risk groups such as intravenous drug users. An important determinant of the relative merits of the two approaches is the relationship between rates of attendance and of changing sexual partners. Further research on this is required.

Williams JR, Nokes DJ, Medley GF, Anderson RM. The transmission dynamics of hepatitis B in the UK: a mathematical model for evaluating costs and effectiveness of immunization programmes. *Epidemiol Infect* 1996; 116:71-89.

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Complex hepatitis B (HBV) epidemiology makes it difficult to evaluate and compare effectiveness of different immunization policies. A method for doing so is presented using a mathematical model of HBV transmission dynamics which can represent universal infant and adolescent vaccination strategies and those targeted at genito-urinary (GU) clinic attenders and infants born to infectious mothers. Model structure, epidemiological underpinning, and parameterization, are described. Data from the UK National Survey of Sexual Attitudes and Lifestyles is used to define patterns of sexual activity and GU clinic attendance; data deficiencies are discussed, in particular that of UK seroprevalence of HBV markers stratified by age, sex, and risk factors. General model predictions of endemic HBV marker prevalence in homosexual and heterosexual populations seem consistent with published UK data. The simulations exhibit non-linearities in the impact of different vaccination strategies. Estimated number of carriers prevented per vaccine dose for each strategy provides a measure of costs and benefits, varying temporally over the course of a programme, and with level of vaccine coverage. Screening before vaccination markedly increases payback per dose in homosexuals but not in heterosexuals; mass infant vaccination gives the poorest effectiveness ratio and vaccination of infants after antenatal screening the best; in general, increasing vaccine coverage yields lower pay-back per dose. The model provides a useful framework for evaluating costs and benefits of immunization programmes, but for precise quantitative comparison more UK epidemiological data is urgently needed.

Winstock AR, Sheridan J, Lovell S, Farrell M, Strang J. National survey of hepatitis testing and vaccination services provided by drug services in England and Wales. *Eur J Clin Microbiol Infect Dis* 2000; 19:823-828.

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Since viral hepatitis among intravenous drug users continues to be a major cause of morbidity and mortality, the present study was conducted to survey drug agencies in England and Wales in order to identify the prevalence of hepatitis B and C testing and vaccination being provided. A postal survey of all 539 drug agencies in England and Wales was thus conducted to assess their current treatment provisions and practices. An analysis of the responses provided by the 373 agencies that returned usable data (69.2% response rate) revealed that only one-quarter (26.6%) of the drug agencies conducted routine hepatitis B testing, and 26.9% did not offer it at all. Just over half (55.7%) of the agencies provided hepatitis B vaccination, but only 21.7% did so routinely. Seventy percent provided hepatitis C testing, but only 24% did so routinely. Nevertheless, the majority of respondents, of whom 40.3% were nurses and 25.1% drug workers, believed that clients and their partners should be offered hepatitis B and C screening. The paucity of hepatitis testing and vaccination services being offered to injecting drug users is unacceptable, with users, their partners and children being needlessly exposed to continued risk. The disparity between recommended policy and current practice needs to be urgently addressed.

Wright M, Forton D, Main J, Goldin R, Torok E, Tedder R, Grant P, Thursz M, Naoumov N, Millson C, Mills PR, Bassendine M, Thomas HC, on behalf of the UK Mild HCV Trial investigators. Treatment of histologically mild hepatitis C virus infection with interferon and ribavirin: a multicentre randomized controlled trial. *J Viral Hepat* 2005; 12:58-66.

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Current guidelines advocate no treatment for patients with histologically mild hepatitis C virus (HCV) infection. This was a UK multicentre randomized controlled trial comparing alpha-interferon (3 MU thrice weekly) + ribavirin (1000-1200 mg/day) for 48 weeks with no treatment in treatment naive, adult patients with histologically mild chronic HCV infection. The aim was to compare benefits, safety and efficacy of combination therapy with alpha-interferon 2b and ribavirin for 48 weeks with no treatment (current standard management) in this patient group. In the treatment group 32 of 98 (33%) patients achieved a sustained virological response (SVR). Patients infected with genotype 1 had a lower SVR than those infected with genotype non-1 (18% vs 49% $P = 0.02$). No patients who failed to achieve a 2-log drop in viral load at 12 weeks achieved SVR. Improvements in quality of life 24 weeks postcessation of therapy compared with baseline using the SF-36 questionnaire measures were observed in the treated group. For patients with mild HCV infection with viral genotype non-1, the results are sufficiently good to suggest that therapeutic decisions should no longer be biopsy-driven. For patients infected with genotype 1, a liver biopsy is still indicated as the low chance of SVR is outweighed by an unacceptable burden of side-effects. Patients who fail to respond by 12 weeks of therapy should have their treatment curtailed early.

Wright M, Goldin R, Fabre A, Lloyd J, Thomas H, Trépo C, Pradat P, Thursz M, on behalf of the HENCORE collaboration. Measurement and determinants of the natural history of liver fibrosis in hepatitis C virus infection: a cross sectional and longitudinal study. *Gut* 2003; 52:574-579.

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The rate of development of liver fibrosis in hepatitis C virus (HCV) infection varies between individuals. This accounts for the variation in duration of progression to cirrhosis. The aims of this study were: (1) to determine whether fibrosis progresses linearly through the grading scales and (2) to identify factors which influence the rate of fibrosis. HCV-infected patients who had undergone at least one liver biopsy were identified. Biopsies were scored using the modified HAI (Ishak) and METAVIR systems, which were compared. Patients were treatment naive at first biopsy. Demographic features were examined for their relationship to fibrosis rate (defined as fibrosis stage / infection duration) using univariate and multivariate analysis. A subgroup of patients with two biopsies was examined to test the assumption that fibrosis progresses in a linear fashion. A total of 917 patients were included. Male sex ($p < 0.00001$), older age at infection ($p \leq 0.00001$), and viral genotype non-1 ($p = 0.005$) were all associated with a rapid rate of fibrosis. On multiple linear regression they accounted for 29.5% of the variability in fibrosis rate ($r^2 = 0.295$). METAVIR and Ishak scores were highly correlated ($r = 0.935$, $p < 0.0001$). In 137 patients who had two biopsies, the predicted probability for an increase of 1 on the fibrosis score was too low to assess linearity. Demographic features account for a minority of fibrosis rate variability. The Ishak and METAVIR scoring systems are equivalent. Linearity of fibrosis progression cannot be assessed in biopsies only a few years apart.

Wright NM, Tompkins CN, Jones L. Exploring risk perception and behaviour of homeless injecting drug users diagnosed with hepatitis C. *Health Soc Care Community* 2005; 13:75-83.

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Injecting drug users (IDUs) are at the greatest risk of hepatitis C infection by using any item of injecting equipment that has come into contact with contaminated blood. Alongside this, homeless

IDUs have been identified as being at increased risk of harm in their illicit drug taking behaviour. This study interviewed 17 hepatitis C positive homeless IDUs about their injecting practices. In-depth interviews explored the impact of a positive hepatitis C diagnosis on their injecting and identified their risk behaviours and perceptions. The interviews were tape-recorded, transcribed and analysed using the framework approach. Homeless IDUs engaged in both high risk and unhygienic injecting practices, such as using drugs outside and in public places, sharing injecting equipment and re-using cleaned needles. Excessive needle reuse whilst in prison was also identified. However, the findings were not universally bleak as a positive diagnosis of hepatitis C did lead to some behaviour change towards safer injecting and some adopted other lifestyle and behaviour changes. It was, however, common for homeless people to devolve responsibility for preventing hepatitis C transmission to their peers, especially when injecting with others. Knowledge regarding possible transmission through injecting paraphernalia appeared to make users more careful to reduce it through these routes. Placing a continuous emphasis on health promotion is therefore important in educating IDUs about the hepatitis C transmission risks associated with injecting drug use. Information regarding safer and hygienic use, including accurate information regarding the most effective methods to clean used equipment, must be re-enforced by people working with homeless injecting drug users.

Yee LJ, Rhodes SD. Understanding correlates of hepatitis B virus vaccination in men who have sex with men: what have we learned? *Sex Transm Infect* 2002; 78:374-377.

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Hepatitis B infection (HBV) is prevalent among men who have sex with men (MSM) and may lead to significant morbidity and death. Although an effective vaccine exists vaccination rates among MSM are low. We conducted a systematic review to synthesise the various findings from empirical correlational studies to understand HBV vaccination and series completion among MSM. We systematically searched the Medline, PubMed, EMBASE, CINAHL, ERIC, and Web of Science databases to identify the breadth of published studies pertaining to HBV vaccination among MSM and to synthesise findings from these studies to better identify common themes that may direct future research and intervention approaches. Eight papers specifically addressed correlates of HBV vaccination among MSM. Six domains were identified as predictors of vaccination: (1) demographic variables such as younger age and higher education level; (2) knowledge of the vaccine; (3) access to health care; (4) level of "outness" regarding one's same sex sexual orientation; (5) behavioural factors including sexual and drug use behaviour; and (6) psychosocial variables. Three papers addressed predictors of vaccine series completion among MSM, observing two main domains: (1) demographic variables such as younger age and higher income level; and, (2) behavioural factors including sexual and health promotion behaviours. Continued educational efforts, creation of environments that facilitate proper risk factor evaluation, and access to low cost vaccine may facilitate vaccine uptake. Although we observed important trends in the studies we reviewed, there is a lack of empirical research regarding this important public health issue.

Zuckerman J, Langer B. Hepatitis B vaccination in a school age population: a feasibility study. *J Med Virol* 2005; 76:47-54.

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There remains no consensus on whether to adopt a universal hepatitis B vaccination strategy in the

United Kingdom, where the endemicity of hepatitis B virus (HBV) is considered to be very low in the general population. To assess the feasibility and acceptance of a school-based adolescent vaccination approach, 11-13 years old pupils in local secondary schools in the London Borough of Camden and Islington were contacted and offered a three-dose hepatitis B vaccination course using a 0, 1, and 12 months schedule. The adult dose of hepatitis B vaccine (Engerix B GlaxoSmithKline) containing 20 mug recombinant hepatitis B surface antigen (HBsAg) in 1 ml suspension was administered. This dosage is normally intended for adults and children older than 15 years of age, but can be administered in 10-15 years old children when compliance may be low, since a higher proportion of those vaccinated develop protective antibody levels following administration of only two doses of vaccine. Overall, a total of 528 pupils were contacted, with 122 (23%) consenting to be vaccinated. Of these, 117 (96%) received the complete three-dose regimen according to the schedule (four did not receive vaccine: three were non-attendees and one was previously vaccinated; one withdrew following a flu-like adverse event). The results of this study show that it is feasible and practical to administer hepatitis B vaccination to adolescents in a school setting, and that it is possible to achieve high rates of uptake for the complete three-dose course among adolescents. However, in order to attain and sustain high coverage rates among pupils, this would require additional general health promotion, including health education and provision of information, targeting of teachers, pupils, and parents in order to increase participation in a school-based hepatitis B vaccination programme. A further requirement includes the availability of good local health support within schools so as to allow for an efficient vaccine delivery system to maximize vaccination in this setting.

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