# LETTERS TO THE EDITOR

## Antenatal screening for hepatitis B

The recent review by Jordan and Law[1] aimed at assessing different policies of antenatal screening for hepatitis B carriers to prevent chronic infection and its complications in the offspring. It considered a wide range of issues affecting effectiveness and costs, but there is a striking absence of any mention of the pregnant women who will be identified as hepatitis B carriers in such a screening programme.

Although there is no compelling evidence that the natural history of their own disorder can be altered favourably by offering such women treatment for liver disease, or screening for hepatocellular carcinoma, they, at the least, need the implications of a positive test explained to them.[2] One small study of hepatitis B carriers showed a wide range of reactions to receiving a positive test result, from overreaction and self imposed social isolation to denial of the possibility of disease transmission, and a high degree of depression and anxiety on psychological tests. After counselling, all carriers were more appropriately aware of the risks of transmission.[3] In addition, hepatitis B vaccine should be considered for close family members.

Possibly, measured benefits and costs associated with the identification of carrier mothers are negligible in comparison with the costs and benefits to children, but ignoring women altogether has the unfortunate effect of making it seem as if only babies count. Could it also lead policy makers and clinicians to forget the importance of appropriate follow up of women?

Women are also invisible in the recent screening brief on AIDS from maternally transmitted HIV infection.[4] Elsewhere in your journal it has been recommended that analysis of costs and effects of such antenatal screening programmes should include the consequences of a positive test for women, not only for obstetric management but also in a wider psychological and social context.[5]

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1 Jordan R, Law M. An appraisal of the efficacy and cost effectiveness of antenatal screening for hepatitis B. *J Med Screen* 1997;**4**:117–27.
2 Paul C, Thomas M. Screening for hepatitis B carriers: perspectives from New Zealand. *Aust NZ J Med* 1997;**27**:698–705.
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4 Anonymous. AIDS from maternally transmitted HIV infection [screening brief]. *J Med Screen* 1997;**4**:177.
5 Dunn DT, Nicoll A, Holland FJ, *et al*. How much paediatric HIV infection could be prevented by antenatal HIV testing? *J Med Screen* 1995;**2**:35–40.

Jordan and Law present a detailed and thorough analysis of the efficacy and cost effectiveness of antenatal screening for hepatitis B.[1] However, their suggestion that horizontal transmission between children in Britain is responsible for the majority of carriers is based on the unjustified assumption that the current prevalence of carriage is sustained by transmission in Britain.

Clearly, perinatal transmission alone cannot maintain the prevalence of carriage in any population, as transmission of carriage from mother to infant is not 100% efficient. In countries highly endemic for the disease the prevalence of carriage is maintained largely through horizontal transmission between children. However, we are not aware of any data to suggest that such transmission is common in Britain. The most likely explanation of the prevalence of carriage in Britain's antenatal population is that most carriers are immigrants from highly endemic countries, who acquired their carriage through perinatal transmission or horizontal transmission in childhood in their country of birth. In 1991 more than 6% of births in Britain were to women born in Africa and Asia,[2] who may have been at high risk of hepatitis B infection in childhood. An overall prevalence of carriage of 2% in these women would account for a rate of 120 carriers per 100 000 women in the antenatal population, approximately the rate attributed to horizontal transmission by Jordan and Law. Data from antenatal screening in the West Midlands support our explanation: in all ethnic groups, hepatitis B carriage was four to five times higher in those born abroad than in those born in the United Kingdom.[3]

A comprehensive antenatal screening programme in Britain would prevent many perinatal infections, but there is no evidence of widespread horizontal transmission in children.

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1 Jordan R, Law M. An appraisal of the efficacy and cost effectiveness of antenatal screening for hepatitis B. *J Med Screen* 1997;**4**:117–27.
2 Office of Population Censuses and Surveys. *Birth statistics 1991*. London: HMSO, 1993. (Series FM1 No 22.)
3 Boxall E, Skidmore S, Evans C, *et al*. The prevalence of hepatitis B and C in an antenatal population of various ethnic origins. *Epidemiol Infect* 1994;**113**:523–8.

**Authors' reply**

Globally the horizontal transmission of hepatitis B infection between children is the most important factor in maintaining the prevalence of carriers. Gay and Miller suggest that such horizontal transmission is important only in areas where hepatitis B is already endemic (carrier prevalence about 15%) and not in Britain, where many of the carriers in the antenatal population acquired the infection from childhood transmission in other countries (before immigration).

There is insufficient direct evidence to judge the extent to which the carrier children of these women will transmit their infection horizontally. In the study in the Birmingham antenatal clinic that Gay and Miller cite the prevalence of hepatitis B carriage in women born abroad and in Britain was 12/946 (1.3%) and 1/328 (0.3%) respectively among women of Asian origin, and 2/78 (2.6%) and 2/423 (0.5%) respectively among women of West Indian origin. The numbers of carriers are small and even with both sets combined the difference is of marginal statistical significance (p=0.07). We agree, therefore, that the rate of horizontal transmission is likely to be lower in Britain, but it is not possible to specify whether it is much lower or a little lower. We recognised that the extent of horizontal transmission in Western countries is uncertain, and it was for this reason that we reported the cost estimates that take this into account as a subsidiary analysis rather than as our main result.

Since horizontal transmission is so widespread in other countries it might be considered surprising if it did not take place at all in Britain. The mechanism whereby hepatitis B infection is horizontally transmitted in early childhood is poorly understood, but the diversity of the populations in which hepatitis B is endemic (rural Africa, urban Taiwan, and Inuit (Eskimo) communities in Alaska) tends to rule out a mode of transmission (such as an insect vector) that is specific to a locality and not maintained at all when people migrate.

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# MEETINGS IN 1998

**Screening for Down's syndrome**

20–22 May

An intensive theoretical and practical course for staff directly involved in screening programmes. The core teaching staff will be from the screening team at the Wolfson Institute of Preventive Medicine with outside experts from the USA. Course fee £400 includes course materials and lunch each day. CME accredited.
*Further details:* Joan Noble, course organiser, Wolfson Institute of Preventive Medicine, St Bartholomew's and the Royal London School of Medicine and Dentistry, Charterhouse Square, London EC1M 6BQ. Tel: 0171 982 6263. Fax: 0171 982 6270. Email: j.m.noble@mds.qmw.ac.uk

**18th Conference of the International Health Evaluation Association**

28–30 September, The Royal College of Physicians, London

This IHEA conference entitled "New opportunities for prevention: developing practical approaches" will consider the following topics:

- Advances in screening
- Developing informatics
- Pharmaceutical interventions
- Target setting
- Health in the workplace
- Behavioural interventions

*Further details:* Profile Productions, Northumberland House, 11 The Pavement, Popes Lane, London W5 4NG. Tel: +44 (0) 181 566 1902. Fax: +44 (0) 181 579 9258. Email: profilep@dial.pipex.com

# *Screening brief*

## Hepatoma and chronic liver disease from maternally transmitted hepatitis B infection

*Natural history*

- In carriers of the hepatitis B virus (defined as persistence of hepatitis B surface antigen (HBsAg) for > 6 months after infection) the lifetime risk of death from hepatoma or chronic liver disease in carriers is about 17%. On average seven years of life are lost from hepatoma, 14 years lost from chronic liver disease[1 2]
- After hepatitis B infection in neonates the risk of becoming a carrier is high (90%); in adults it is low (<10%)[3]
- 25% of infants born to carrier mothers in Britain become carriers (285 per year)[1]
- If the mother is e antigen positive (about 20% of all carriers) about 80% of infants become carriers; if e antigen negative, 10%[1]
- For each perinatally infected carrier three other children are carriers; horizontal transmission from perinatally infected carriers is likely to be important[1 4]

*Prevalence of hepatitis B carriers in the antenatal population*

- About 0.15% in Britain (usually <1% in Western countries)[1 5]
- Higher in ethnic groups from countries where the disease is endemic—Africans 3%, Chinese 6%, Indian subcontinent 1%, Caribbeans 0.5%, but white Europeans 0.04%[1 5 6]
- In Britain 67% of carriers are African, Chinese, or South Asian, 25% are white[1]

*Screening test for hepatitis B carriers in the antenatal population*

- ELISA serum test for hepatitis B surface antigen
- Detection rate 100%; false positive rate (after confirmatory tests) 0

*Intervention*

- Recombinant vaccine (three to four doses) to children of carrier mothers; also hepatitis B immunoglobin (200 IU) given at birth except when mother known to have antibodies to the e antigen
- 90% effective in preventing carrier state[1 7]

*Screening options*

- Test all women, or
- Test only women in high risk ethnic groups

*Costs per year of life saved (testing at first pregnancy only)*

- All women (in Britain) £1300. Prevents 90% of deaths (eventually 45 per year in Britain in those perinatally infected and, possibly, additional deaths if horizontal transmission in childhood occurs)[1]
- Varies with ethnic group—Chinese £180, Africans £360, Indian subcontinent £430, Caribbeans £630, white Europeans £4500[1]
- Above costs reduced if horizontal transmission occurs
- Costs increased by 2.3-fold with testing at each pregnancy

*Overall assessment*

- Screening all pregnant women is equitable and affordable and should be implemented[1]

1 Jordan RE, Law MR. An appraisal of the efficacy and cost effectiveness of antenatal screening for hepatitis B. *J Med Screen* 1997;**4**:117–27.
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# *Screening clips*

**Gestational diabetes**

No consensus exists as to whether all pregnant women should be screened for gestational diabetes. Many obstetricians screen all pregnant women by measuring their plasma glucose after a 50 g glucose challenge, but others use clinical criteria to select women at higher risk. Now a study in Canada (*New England Journal of Medicine* 1997;**337**:1591–6) has used data on 3131 pregnant women to develop criteria for a scoring system for the identification of those at low risk who need not be tested. The women at lowest risk of having abnormal test results were those aged 30 or under, with a body mass index of 22 or lower, and of white or black race. Older women, those with higher body mass indices, and those of Asian or other race scored higher. A lower glucose threshold was used for women with high scores on the risk assessment scale. Use of this test would reduce the number of women being tested in the second trimester by around one third, but a leading article in the same issue of the *NEJM* suggests that "the criteria for excluding women from screening are so hard to discern that universal screening will probably be used as a matter of practical convenience"...even though the value of screening has yet to be determined.

***PET screening for cancer***

*Most cancer cells have abnormally high rates of glycolysis, and this observation has been used as the basis of a novel screening test for cancer. Whole body positron emission tomography (PET) using radioactive labelled fluorodeoxyglucose seems to be able to detect a high proportion of cancers in the major organs at a single examination. A brief report in the* Lancet *(1997;**350**:1819) from Japan describes the results of using this test to screen 1872 people who were members of a medical health club and were enrolled in a continuing programme using clinical, imaging, and immunochemical methods for the early detection of cancers. Over 21 months 26 cancers were detected in this population; 15 of these were detected by the PET screening method. Six of the 11 false negative results were cancers of the prostate or kidney and three were lung cancers. PET screening also detected a "substantial number" of benign lesions, such as chronic thyroiditis and sarcoidosis, but the authors argue that these should not be classed as false positives because the lesions warranted further investigation. Again, whether this would be the basis of a worthwhile screening programme is uncertain.*

**Detecting coeliac disease**

Adult coeliac disease often goes unrecognised because people with the disease may have few or even no symptoms or their symptoms may be atypical. Nevertheless, identifying preclinical cases may be worthwhile because treatment is usually straightforward and effective. Serological screening using tests for reticulin or endomysium antibodies is unsuitable for the whole population, but several risk factors have been identified. A recent report from Finland (*Scandinavian Journal of Gastroenterology* 1997;**32**:1129–33) gives the results of using antibody tests on individuals at high risk: these included first degree relatives of patients with coeliac disease, people with connective tissue diseases, people with diabetes, people with memory disturbances or peripheral neuropathy, and women with infertility. Tests on 720 men and women identified 54 new cases of coeliac disease. Investigation using endoscopy and biopsy of people with atypical or minor symptoms or with dermatitis herpetiformis yielded a further 344 cases, raising the prevalence of coeliac disease in the population to 270 per 100 000. This is in line with the results of similar programmes in Sweden, Italy, and other European countries and substantially higher than the figures quoted 10 years ago.

***Screening of children***

*The Royal College of Paediatrics and Child Health recently joined with the National Screening Committee to organise a meeting on screening of children, and a report in the* British Medical Journal *(1998;**316**:1–2) makes gloomy reading. The meeting was unconvinced of the value of preschool vision testing or of tests in current use for the diagnosis of congenital dislocation of the hip. It heard clear evidence that the traditional distraction test of hearing at eight months was failing to detect even severe deafness. The answer lay in providing universal electronic screening of newborn, which was said to more reliable and cheaper and which led to hearing aids being fitted at a mean age of below four months. Expanding testing for inborn errors of metabolism was feasible technically, but its introduction would require the replacement of the established programme for screening for phenylketonuria, which is working well.*

**Ultrasound and chromosomal defects**

Controversy continues as to whether ultrasound examination of the fetus at 10–15 weeks provides a useful means of screening for chromosomal abnormalities, including Down's syndrome and other trisomies and Turner's syndrome. Critics say that when ultrasound screening is used in low risk populations its detection rate is too low to be useful, but a study from Finland has now claimed that it can be done earlier than serum screening and gives comparable results. The report in the *New England Journal of Medicine* (1997;**337**:1654–8) gives the results of transvaginal ultrasound examinations of 10 010 women aged less than 40 with singleton fetuses at 10–16 weeks' gestation. The tests used were increased nuchal translucency (at least 3 mm in width) or the presence of a cystic hygroma. Women found to have fetuses with these abnormalities were offered karyotyping. One or other ultrasound abnormality was found in 76 fetuses, and 18 of these had an abnormal karyotype. The test detected seven of 13 fetuses with trisomy 21 and 18 of 26 fetuses with any type of aneuploidy.

The Finnish authors claim that ultrasound provides an effective and sensitive screening test for aneuploidy, but an editorial in the same issue of the *NEJM* (1689–90) refers to other studies with lower rates of detection and concludes that at present there is insufficient experience with screening for increased fetal nuchal translucency in low risk women to justify the adoption of this technique.

***Breast cancer genes***

*The identification of the two breast cancer genes BRCA1 and BRCA2 has been given a lot of publicity and many women who suspect that they may have inherited one of the genes are coming forward for testing or being offered it. A study from Italy (*Journal of Medical Genetics *1997;**34**:990–5) has shown that few turn out to have either of the genes. Patients were tested if they fulfilled any of the following criteria: women under 40 years with breast cancer but no affected relatives; women under 50 years with a first degree relative under 50 years with breast*

*cancer; women under 50 years with breast cancer and a first degree relative with ovarian cancer at any age; women with ovarian cancer with a first degree relative with ovarian cancer; women with bilateral breast cancer diagnosed before the age of 60; and women with both breast and ovarian cancer. In all, 86 women with these criteria were tested and six were found to have mutations in BRCA1 and three in BRCA2. The authors conclude that other genes are probably responsible for most familial breast and ovarian cancer.*

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# *Acknowledgments*

Professor Wald would like to thank the following who have generously given their time to help with the assessment of manuscripts during 1997, and particularly those who have collaborated on the screening briefs.

## Referees

Dr Freda Alexander
Dr Bruce Armstrong
Dr Wendy Atkin
Dr Harland Austin
Ms Joan Austoker
Dr Beaman
Dr Michal Berkenstadt
Dr Roger Black
Dr Roger Blanks
Professor Martin Bobrow
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