Letters to the Editor

NON-A, NON-B HEPATITIS SURROGATE TESTING OF BLOOD DONATIONS

SIR,—Surrogate testing of blood donations has been introduced in the USA as a means of reducing post-transfusion non-A, non-B (NANB) hepatitis. This policy is based on the principle that it is safer not to use an acceptable proportion of the blood supply found to contain non-specific marker(s) of NANB hepatitis—namely, anti-HBc or raised alanine aminotransferase (ALT) levels.

Like Dr Anderson and colleagues (April 18, p 912) we have found a very low incidence of reported cases of post-transfusion NANB hepatitis in West Scotland, with only 23 cases in the past 8 years, a period when over 800 000 units of blood have been transfused. 3 cases were excluded because of a high probability that the toxic effects of therapeutic drugs were the cause. A further 5 cases occurred in recipients of commercial and/or Scottish factor concentrates. The remaining 15 cases (mean incubation period 7 weeks) involved 51 blood donors, none of whom were involved more than once. Samples from the implicated donations together with subsequent donations from these donors were examined for anti-HBc and ALT levels. 3 donors had anti-HBc (and anti-HBs) and 2 donors had raised ALT levels at subsequent donations. All 5 donors were involved in separate cases. Thus if ALT and anti-HBc tests had been done routinely for the past 8 years, at an estimated cost of more than £1 million and with a loss of around 4% of the blood supply, only 5 of the reported cases might have been prevented. This presupposes that the donors with surrogate markers were indeed the source of NANB infection.

Before the introduction of surrogate testing, the incidence of post-transfusion NANB hepatitis as reported to volunteer blood collection agencies in the USA was 0·1–0·2 cases per 1000 units.[1] The US studies[2,3] which used abnormal ALT levels to diagnose post-transfusion NANB hepatitis found significantly higher incidences of 10 and 28 cases per 1000 units. Thus when ALT follow-up studies are not done in transfusion recipients only 1% hepatitis cases are reported. Conversely, 99% of hepatitis cases are never brought to the attention of transfusion centres or are not considered to be hepatitis by clinicians or are not even thought to be serious enough for the patients themselves to seek medical attention.

It would be prudent to do a UK study to assess the real incidence of acute post-transfusion NANB hepatitis and to assess the proportion of those chronically affected, before considering following the American surrogate testing policy.

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SIR,—The advent of serological tests for hepatitis A and B has focused attention on non-A non-B (NANB) hepatitis, for which no specific virus markers are known. Studies in the United States,[1-4] however, have suggested that screening blood donors for alanine aminotransferase (ALT) and antibody to hepatitis B core antigen (anti-HBc) might reduce the incidence of post-transfusion NANB hepatitis by up to 60% at a cost of around 7% of donated blood. In 1986 the US Food and Drug Administration recommended that both these "surrogate" tests for NANB hepatitis agent be done by all blood-collecting agencies. However, the clinical value of such a policy has not been proved by prospective controlled trials and it is not known whether donors identified by such screening have clinical or epidemiological features suggesting chronic NANB hepatitis.

Between April and November, 1986, ALT activity was measured in 1742 regular blood donors. They consented to the additional tests and agreed to recall if necessary. The assays were done on a 'Cobas-FARA' centrifugal analyser (Roche Diagnostics) with kit reagents from Boehringer Mannheim Diagnostics. The upper limit of normal was set at 45 U/l. Donors with an ALT of 45 U/l or more were asked to attend for further clinical evaluation and tests. All donors were also tested for anti-HBc by an enzyme-linked immunoassay (Wellcome Diagnostics). Donors who were positive were not recalled, but stored samples were then retested for anti-HBc and were tested for anti-HBs and anti-HBe. We also examined the records of 708 plasmapheresis donors; liver function tests are done routinely every 6 months in these donors.

42 (2·4%) of 1742 donors had a raised ALT and 33 of them attended for further evaluation. Most of them expressed anxiety at the request to attend the donor centre. 26 of these 33 recalled donors were more than 10% above ideal body weight, including 15 who were more than 20%. On clinical assessment (usually about 1 month after donation) 5 of the 26 had normal ALT levels. 10 of the 26 obese donors admitted to a daily alcohol intake of more than 40 g, and a 21-year-old non-obese female donor admitted to drinking over 40 g daily. The other 6 donors were neither obese nor heavy drinkers and had no clinical abnormality to account for their raised ALT. At the time of clinical assessment 4 of them had normal ALT levels. Significant abnormalities of liver function other than raised ALT were found in only 3 of the 33 donors. 1 of these was due to alcohol abuse, another to the contraceptive pill, and the third to chronic active hepatitis proven by biopsy.

Of the plasmapheresis donors 26 (3·7%) had a raised ALT initially. ALT activity returned to normal in 5 of them while 41 (6%) of those with normal ALT levels to start with subsequently became abnormal.

2086 donors were screened for anti-HBc (the above 1742 plus all first-time donors attending the same sessions). 42 (2·0%) were positive, including 38 of the regular donors. None had a raised ALT. 27 of the 42 were positive for anti-HBs and 11 had anti-HBe.

Our findings confirm the doubts expressed by Dr Contreras and her colleagues on the wisdom of introducing surrogate testing for NANB hepatitis into blood transfusion practice in the UK. We found a strong association between a raised ALT and both obesity and alcohol ingestion, and these two factors alone might account for 82% of the abnormal ALT values found. Alter[5] concluded that 45% of his donors with raised ALT could be carriers of NANB hepatitis, but he noted that many of the donors had been selected as having been implicated in cases of post-transfusion NANB hepatitis. 4 of the 6 raised ALTs not explained by obesity, alcohol, or other clinical abnormality had normal ALT levels at follow-up, a higher proportion than Alter's series (17%). Those who support ALT testing should recognise the tendency (seen in our plasmapheresis donors) of ALT levels to fluctuate: the loss of donated blood would be far in excess of that suggested by published studies, and most of the excluded donors would not be NANB hepatitis carriers.

If the degree of benefit claimed from the retrospective American studies were to hold for the UK, the blood transfusion services would have to spend well over £5 million more every year (2½ million donations at £2–3 per donation). Account must also be taken of the consequences of identifying up to 5% of the donor population as being potential carriers—not just the costs of further laboratory tests, clinical assessments, and counselling but also the anxiety raised in the donors themselves.

The Americans have concluded that a large, prospective, randomised trial to test the hypothesis that surrogate testing carries clinical benefit will never be done.[4] Of the four small prospective studies, two using ALT screening and two using anti-HBc, three failed to demonstrate any reduction in post-transfusion NANB hepatitis as a result of donor screening[5-7] and one found an apparent association between anti-HBc in donor units and recipient hepatitis.[8]

We conclude that the introduction of ALT/anti-HBc screening tests as an indicator of NANB hepatitis carrier status in blood donors cannot at present be justified.

We thank Wellcome Diagnostics for anti-HBc kits and our virological colleagues for the additional tests. Supported by a grant from the Scottish Home and Health Department. Further details of the clinical findings in this study and of the calculations will be published elsewhere.

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CIPROFLOXACIN FOR CHOLANGITIS AFTER HEPATIC PORTOENTEROSTOMY

SIR,—Extrahepatic biliary atresia, a disorder confined to early infancy, is characterised by a total obliteration of the bileducts outside the liver. In up to 80% of cases bile drainage can be reconstituted by hepatic portoenterostomy.[1] However, ascending cholangitis will develop in more than 50% of patients after successful restoration of bile flow, and this is an important cause of death in children with corrected extrahepatic biliary atresia.[2] Cholangitis leads to deterioration in liver function and prolonged hospital admission. The standard therapy is an intravenous cephalosporin and aminoglycoside for at least 6 weeks but this is often insufficient and longer treatment with other combinations is necessary. Even then the treatment failure rate is high, and many patients die.

Ciprofloxacin, a quinolone derivative introduced for the oral treatment of infections with gram-positive and gram-negative rods,[3] provides selective decontamination of the gastrointestinal tract,[4] and high bile concentrations[5] make it an ideal candidate for the treatment and prevention of cholangitis after hepatic portoenterostomy. We have treated three such cases.

A 10-week-old girl with extrahepatic biliary atresia underwent a succesful hepatic portoenterostomy. A few weeks later she deteriorated and biopsy revealed cholangitis. Blood cultures yielded *Klebsiella* and, later on, *Escherichia coli*. The antibiotic regimen was adjusted several times according to the susceptibility pattern of these species. Treatment was continued for 5 months with no effect. As a last resort ciprofloxacin 25 mg twice daily was given. No more cholangitis episodes were recorded, and the serum bilirubin returned to normal. After 6 months of treatment ciprofloxacin was discontinued by the parents, and cholangitis recurred almost immediately.

A boy, treated by portoenterostomy at age 8 weeks, attained only partial reconstitution of bile drainage. In the first year after surgery he was repeatedly admitted to hospital for treatment of cholangitis. Ciprofloxacin 50 mg twice daily was then prescribed and in two years of this treatment cholangitis has not recurred. Faecal cultures, done every 6 weeks, have demonstrated selective decontamination of the bowel, with absence of gram-negative rods, yeasts, and fungi.

A girl was operated on when she was 2 months old because of extrahepatic biliary atresia. Portoenterostomy restored bile flow. At age 4 months she had a persistent fever with a rising serum bilirubin and raised erythrocyte sedimentation rate. Cholangitis was diagnosed and ciprofloxacin was given for 3 months. With the administration of this oral antibiotic hospital admission was avoided. *Klebsiella* and *E Coli*, present in the faeces at the beginning of treatment, were eliminated, and within 6 weeks the child's serum bilirubin and sedimentation rate were normal. This girl is now 1 year old and cholangitis has not recurred.

The first two patients had therapy-resistant cholangitis, successfully treated with ciprofloxacin. As a consequence of this favourable experience we then gave ciprofloxacin to a patient with uncomplicated cholangitis. These three cases suggest that ciprofloxacin has a place in the treatment of cholangitis.

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^{14}C-UREA BREATH ANALYSIS, A NON-INVASIVE TEST FOR CAMPYLOBACTER PYLORI IN THE STOMACH

SIR,—The only generally available methods for detecting colonisation of the stomach by *Campylobacter pylori* are histological examination and bacterial culture of biopsy material. Serological tests will not show whether gastric colonisation is still present. *C pylori* contains a powerful urease and gastric urea hydrolysis has provided the basis for diagnostic tests for *C pylori* in gastric mucosal biopsy samples. Dr Graham and colleagues (May 23, p 1174) describe a breath test, based on ^{13}C-urea. ^{13}C is not radioactive but the mass spectrometer required to measure recovery of $^{13}CO_2$ is not available to district general hospitals. In contrast, the ^{14}C-urea breath test we have been evaluating requires a scintillation counter, which is inexpensive and readily available.

We have studied three groups of patients already investigated[1] for *C pylori* colonisation of the antral region of the stomach. 24 *C pylori* positive patients (17 duodenal ulcer, 3 gastric ulcer, 4 gastritis alone) were not taking and had not recently received antibiotics or any bismuth-containing substance, all but 6 of them being on drugs (cimetidine, ranitidine, sucralfate) that do not affect *C pylori*. 9 patients (2 duodenal ulcer, 2 gastritis alone, 4 functional bowel disease, 1 previous partial gastrectomy) were *C pylori* negative. 12 patients (8 duodenal ulcer, 1 gastric ulcer, 2 gastritis alone, and 1 duodenitis) who were *C pylori* positive were studied while taking tripotassium dicitrato bismuth (TDB; liquid 'DeNol'); 9 of them had had a ^{14}C-urea breath test before starting TDB.

Full details of the test can be had from G. H., department of medical physics, Ipswich Hospital (Anglesea Road Wing), Ipswich IP1 3PY. In brief, after an overnight fast the patient was given a 350 ml liquid meal followed by 0·4 MBq ^{14}C-urea (Amersham International) in 20 ml water. Breath samples were collected periodically for up to 2 h and ^{14}C in the exhaled CO_2 was measured in a liquid scintillation counter. The area under the curve was computed and this was used as an expression of the cumulative excretion of $^{14}CO_2$.