Prevalence and epidemiological characteristics of hepatitis C in Scottish blood donors

R. J. Crawford,* J. Gillon,† P. L. Yap,‡ E. Brookes,‡ F. McOmish,§ P. Simmonds,§ B. C. Dow,§ and E. A. C. Follett†

*Glasgow and West of Scotland Blood Transfusion Service, Law Hospital, Carluke ML8 3ES, †Edinburgh and South East Scotland Blood Transfusion Service, 41 Lauriston Place, Edinburgh EH3 9HB, ‡East of Scotland Blood Transfusion Service, Ninewells Hospital, Dundee DD1 9SY, §Department of Medical Microbiology, University Medical School, Teviot Place, Edinburgh EH8 9AG, and †Scottish National Blood Transfusion Service Microbiology Reference Unit, Regional Virus Laboratory, Ruchill Hospital, Glasgow G20 9NB, U.K.

SUMMARY. All blood donors in Scotland who were found to be infected with hepatitis C virus (HCV) in the first 6 months of routine testing of all donations for anti-HCV were contacted. Those who attended were counselled, a history of exposure to risk was sought, and blood was taken for alanine aminotransferase (ALT) level as a measure of liver function. The epidemiological features were then correlated with the virological findings and ALT.

In the period under study between September 1991 and February 1992, 180658 blood donors attended. The prevalence of HCV infection was 0.088%. Of the 151 donors who attended for counselling, 101 (68%) were male. Intravenous drug use was the most common risk activity (39%), followed by previous blood transfusion (15.2%), other parenteral exposure (11.2%) and heterosexual contact with a parenterally infected partner (8.6%); 29.1% of donors gave no history of possible exposure.

Elevated ALT levels were found in 59%. ALT levels were higher in donors with HCV types 1 and 3 than in HCV type 2 or non-viraemic donors.

The prevalence of HCV in Scottish blood donors is thus relatively low. This may relate to the effectiveness of donor selection procedures, but donors with risk activities which should debar them continue to donate. The combination of ALT and PCR appears to be useful in counselling and assessing infected donors.

Since September 1991, every donation of blood or plasma in the United Kingdom has been tested for antibodies to hepatitis C virus (HCV). The lack of data on the incidence of post-transfusion hepatitis (PTH) in the U.K. made prediction of the prevalence of hepatitis C in blood donors impossible, though a study carried out in North London suggested a rate of PTH much lower than those reported in other parts of the world (Contreras et al., 1991), and indicated that transmission occurred at a true rate of 1 in 1300 donors.

Most published reports of the prevalence of HCV in blood donor populations relate to initial experience with the 'first-generation' enzyme-linked immunosorbent assay (ELISA) (Stevens et al., 1990; Richards et al., 1991). The introduction of a second-generation ELISA incorporating antigens from the core and NS3 regions of HCV as well as from the NS4 region has led to increased sensitivity without a loss of specificity (Kolho, 1992), while the use of recombinant immunoblot (RIBA) and the polymerase chain reaction (PCR), as 'supplemental' assays to help define true positivity, have shown that most 'positive' results on ELISA are false positives (Brestersef et al., 1992; Garson et al., 1992; Kolho, 1992). PCR is crucially important, in that a proportion of samples deemed indeterminate on RIBA are found to be positive by PCR (Garson et al., 1990; McOmish et al., 1993).

When routine screening of blood donations for anti-HCV was introduced, the Scottish National Blood Transfusion Service (SNBTS) opted for a second-generation ELISA as the initial screening test, with repeatedly reactive samples being subjected to RIBA and PCR in order to identify donors infected with HCV. Using methods developed in this laboratory, PCR in

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Correspondence: Dr J. Gillon, Edinburgh & SE Scotland Blood Transfusion Service, 41 Lauriston Place, Edinburgh EH3 9HB, U.K.
combination with restriction fragment length polymorphism (RFLP) was also used to define whether the HCV infection was due to HCV types 1, 2 or 3 (McOmish et al., 1993). All donors shown by this combination of tests to have evidence of previous or current infection with HCV were invited to attend for counselling and further assessment. We present the epidemiological and clinical data obtained from those donors identified in the first 6 months of routine testing of 180,658 donations in Scotland.

METHODS

Samples repeatably reactive on the second-generation screening ELISA for anti-HCV (Abbott or Ortho) were referred to the SNBTS Microbiology Reference Unit for confirmation. A donor was confirmed to be infected with HCV if two or more bands were present on Ortho RIBA-2 using the manufacturer's criteria (c-100 and c 5-1-1 were regarded as one band), or if there was one band on RIBA-2 (RIBA 'indeterminate') and a positive result on HCV PCR. On receipt of a result confirming HCV infection, each transfusion centre recalled the relevant donor for counselling and further assessment. A history of risk behaviour was sought. A further sample was taken from the donor and sent for ALT testing by the routine methods currently in use in the respective departments of clinical chemistry. Since the various laboratories used different assay methods, statistical analysis of ALT levels in relation to HCV type was restricted to West of Scotland donors.

The results were analysed for statistical significance using the SPSS statistical package (Mann-Whitney U-test and Wilcoxon rank sum test).

RESULTS

Between September 1991 and February 1992, 180,658 blood donations were screened: 609 samples were repeatably reactive. Of these, 148 were positive on RIBA-2, 237 were 'indeterminate' and 224 were negative. Of the RIBA-2 positives, 85.1% were positive on PCR, compared with 4.6% of indeterminates.

One hundred and fifty-nine donors were found to be infected with HCV: 151 (95%) of these donors responded to the invitation to attend for further counselling and follow-up. One hundred and one (68%) were male. The analysis of risk behaviours that might have been relevant to transmission of HCV infection is shown in Table 1. The most significant risk activity was previous intravenous drug use (39%).

A history of previous transfusion was present in 15.2% and sexual contact with an intravenous drug user in 8.6%. Homosexuality was reported by only one donor. Other possible sources of parenteral transmission (tattoos, ear-piercing and needlestick injuries) were the only reported possible routes of infection in 11.2%. A history of jaundice was infrequent (5.9%), as was a non-U.K. origin (1.9%). There was no history of risk activity in 29.1% of donors.

Of the 151 donors 89 (59%) had ALT levels above the upper limit of normal. Comparison of ALT levels with HCV type showed that RIBA positive donors with a negative PCR result (H=21) had lower ALT levels than all PCR positive donors combined (P<0.001), and that donors infected with HCV type 2 (n=12) had lower ALT levels than those with HCV type 1 (P<0.05) or HCV type 3 (P<0.01). There was no statistical difference in ALT level between HCV type 1 (n=43) and HCV type 3 (n=28).

Donors infected with HCV type 2 were older than those with HCV 1 and 3 (mean age of 36.3 vs. 32.0 years, P<0.05), and were less likely to report intravenous drug use (13 vs. 39% for the whole group). 'Other' parenteral exposures were reported by 26% of HCV type 2 donors, versus 11.2% overall.

DISCUSSION

The prevalence of hepatitis C in Scottish blood donors was 0.088% for the period studied. As suggested by several other preliminary reports (Gesinde et al., 1992; Goodrick et al., 1992; MacLennan et al., 1992) intravenous drug use was the most commonly reported route of exposure, in spite of this being a reason for lifetime exclusion as a blood donor. This finding has important implications for the methods used to screen...
potential donors, since current methods are clearly not completely effective in excluding such donors. Better methods are therefore required to identify donors with a history of intravenous drug use, since these donors may harbour other, as yet unidentified transmissible agents.

Heterosexual infection (i.e. contact with a parenterally infected partner) was reported in 8.5%, a level consistent with other studies (Esteban et al., 1991; Osmond et al., 1993), and this is a further cause for concern since these donors also should be excluded. Improved selection procedures will not, however, eliminate potential HCV carriers entirely, since those with a history of transfusion and other parenteral routes of inoculation, such as tattooing, are only excluded for 1 year. Furthermore, a disturbingly large proportion of the seropositive donors reported no identifiable risk behaviour. Since no attempt was made to determine the prevalence of risk factors in the seronegative donor population we cannot assume that anti-HCV testing will eliminate all, or even the majority, of donors who should be deferred according to current selection criteria.

A single ALT level is not an adequate assessment of liver function, but the relationship between ALT levels and HCV type is of great interest. We found that donors with antibodies to HCV but negative on PCR have lower ALT levels than those who are PCR positive. The degree of liver damage on biopsy has been shown to correlate with ALT level and with PCR status (Esteban et al., 1991; Alberti et al., 1991, 1992), and it is possible that PCR may have a role in the evaluation of HCV-infected donors.

In a previous study we reported that ALT levels were higher in HCV type 3 than in types 1 and 2 (McOmish et al., 1993). The present study extends this observation using larger numbers, and indicates that higher ALT levels occur in donors with HCV types 1 and 3 than in HCV type 2 or PCR negatives. This suggests that more serious liver damage occurs in types 1 and 3 than in type 2. Donors with HCV type 2 were epidemiologically different from types 1 and 3, being older and less likely to report intravenous drug use. Determination of the HCV type by RFLP may therefore potentially be of importance in the assessment of individuals with antibodies to HCV and in seroepidemiological studies of the disease.

The prevalence of infection in this previously unscreened blood donor population is relatively low by international standards (Stevens et al., 1990; Alberti et al., 1991; Richards et al., 1991), though few data are available for comparison in which equally rigorous screening methods were used. Many of those donors shown to be infected had been donating regularly, and the prevalence can be expected to fall as they are excluded from further donation. Nevertheless, extrapolation of these figures to the whole of the U.K. would suggest that around 3000 infected donors will have been identified in the first year of testing. No systematic attempt is being made to trace recipients of previous donations from these donors, and the numbers of infected recipients still alive and potentially in need of assessment or treatment cannot yet be estimated. Further work is required to define the scale of this problem and to develop strategies for identifying such patients.

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REFERENCES


