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(Accepted 17 February 1994)

## Follow up of blood donors positive for antibodies to hepatitis C virus

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BMJ 1994;308:696-7

The hepatitis C virus has been identified as the main cause of post-transfusion hepatitis.<sup>1</sup> Mandatory screening of blood donations for antibodies to hepatitis C virus was introduced by the National Blood Transfusion Service on 1 September 1991. Donors confirmed to be positive for antibodies to hepatitis C virus at the North London Blood Transfusion Centre are offered counselling by medical staff at the centre, who explain the relevance of the test results. They are then referred to their general practitioner.

Current evidence suggests that many of the asymptomatic donors positive for antibodies to hepatitis C virus are chronic carriers, in whom the virus replicates.<sup>2</sup> Probably some asymptomatic donors will progress to clinically significant, and possibly severe, liver disease in the future. Follow up of the donor by the general practitioner or hospital clinic, or both, will be influenced by information and advice given as a result of the initial counselling. To date there has been

no information on the effectiveness of the counselling procedure and the fate of donors after leaving the transfusion centre. We carried out a postal survey on the follow up arrangements for blood donors positive for antibodies to hepatitis C virus.

### Subjects, methods, and results

A postal questionnaire was sent to 83 of 107 blood donors positive for antibodies to hepatitis C virus who had been identified and counselled at the North London Blood Transfusion Centre until the end of June 1992. The remaining donors were excluded either because they had failed to attend for counselling (16 donors) or because they were uncontactable (eight donors). A questionnaire was then sent to the doctors of 80 of these donors (two donors withheld consent and in one case the general practitioner was unknown). Replies were received from 50 donors and 61 general practitioners (response rates 60% and 76% respectively). Taken together, the questionnaire responses gave information on 70 donors. Presentation of the donor to the general practitioner and subsequent management by the general practitioner are shown in the flow chart. The demographic details and possible sources of infection of these donors have been analysed separately.<sup>3</sup>

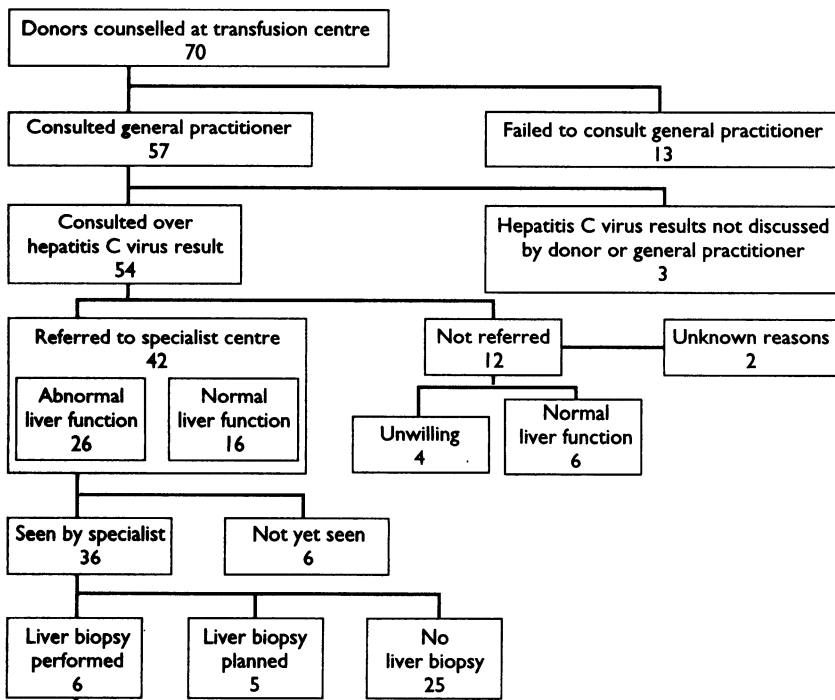
Most of the donors positive for antibodies to hepatitis C virus were referred for specialist opinion irrespective of whether their liver function was reported as abnormal by the transfusion centre. Of the 12 donors not referred, four either refused or failed to attend follow up appointments with the general practitioner and six had normal liver function values; lack of referral was in accordance with the centre's guidelines at the time. Liver biopsy was performed or pending in 11 cases. One donor had been considered for treatment with interferon alfa after the biopsy result.

The partners (all heterosexual) of 27 donors were tested. None of 14 male partners and one of 13 female partners was found to be infected, but details of possible shared risk factors for this partner were not available. Overall, general practitioners and donors indicated satisfaction with the counselling service at the transfusion centre. The main concerns expressed by donors were implications for sexual partners and for future offspring.

### Comment

The positivity rate positive for antibodies to hepatitis C virus among first time donors at the North London Blood Transfusion Centre is one in 1400. Based on these figures, we should anticipate that 30 such asymptomatic subjects would be identified annually at the centre once the established donor panel had been screened.

This survey shows that, after counselling, 13 of 70 donors did not consult their general practitioner about their hepatitis C virus result. Of those who do, however, most are being referred to a specialist clinic



Histological picture

- Mild inflammatory change 2
- Chronic active hepatitis (mild) 1
- Chronic persistent hepatitis 1
- Results not available 2

Flow chart showing management of anti-HCV positive blood donors

and numbers are likely to increase given that the current advice from the centre to general practitioners is to refer all donors irrespective of liver function values. All donors seen at hospital will need long term surveillance and many will have liver biopsies. The implications of hospital follow up should be considered. The donor becomes a "patient," subject to a burden of anxiety owing to the possibility of morbidity disclosed by screening for antibodies to hepatitis C virus and the inconvenience of regular hospital visits.<sup>4</sup> The financial burden of repeated attendance and monitoring should also be borne in mind. Conversely, screening may offer donors a beneficial service in terms of the early detection of possible clinically significant liver disease that might be ameliorated by treatment. Both financial and psychosocial factors need to be taken into account

when assessing the cost effectiveness of the screening of blood donations and in planning resources for long term follow up of people identified as anti-HCV positive.

We thank Mrs C Mooring and Mrs E Dukes for clerical support and Miss M Mobed for secretarial support.

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(Accepted 21 December 1993)

## Normal aminotransferase concentrations in patients with antibodies to hepatitis C virus

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BMJ 1994;308:697

Two studies have recently reported normal aminotransferase concentrations in patients with antibodies to hepatitis C virus and histologically proved chronic liver disease.<sup>1,2</sup> These studies, however, disagreed about the predictive values of concentrations of hepatitis C virus RNA in detecting liver disease.

Tests for hepatitis C virus are now included in screening tests for blood donors and in health check ups in Italy, and the number of patients with antibodies to hepatitis C virus and normal aminotransferase concentrations referred to outpatient clinics is rising sharply. We conducted a study to determine the prevalence of histological liver disease in these patients and its relation to serum hepatitis C virus RNA.

### Patients, methods, and results

During April 1991 to March 1992, 22 patients presented to our liver clinic with antibodies to hepatitis C virus (detected by enzyme linked immunoassay (ELISA 2)), normal aminotransferase concentrations, and no biochemical or ultrasonographic evidence of liver disease. Of these patients, eight had relatives with chronic liver disease due to hepatitis C virus, three were blood donors, one was a nurse in a dialysis unit, and 10 had had a test for hepatitis C virus as part of general health screening. Nineteen patients (eight men, median age 55 (range 22 to 69) years) agreed to participate in the study.

We measured patients' serum alanine aminotransferase concentrations monthly for at least six months (median 12 (range 7-28) months). The records of five patients showed that they had previously had aminotransferase concentrations above the upper limit of normal (45 IU/l) and they were excluded. A further six patients were excluded because of indeterminate results in the second generation recombinant immunoblot assay (RIBA-2, Ortho, Raritan, New Jersey). In the remaining eight patients we tested for hepatitis C virus RNA by the polymerase chain reaction using primers from the 5' UT region.

After a median follow up of 14 (range 7-28) months the eight patients had persistently normal aminotransferase concentrations. All gave informed consent for a percutaneous liver biopsy and the biopsy specimens were blindly evaluated by a pathologist. Chronic liver disease was found in seven patients (table). A test for serum hepatitis C virus RNA done at the time of the biopsy gave positive results in all patients.

Test results in patients with antibodies to hepatitis C virus

Case No	Age (years)	Mean (SD) alanine aminotransferase (IU/l)	Hepatitis C virus RNA	Histology
1	57	30 (4)	Positive	Normal
2	47	32 (7)	Positive	Chronic lobular hepatitis
3	56	24 (4)	Positive	Chronic lobular hepatitis
4	58	11 (2)	Positive	Chronic persistent hepatitis
5	37	34 (10)	Positive	Chronic persistent hepatitis
6	64	23 (3)	Positive	Chronic active hepatitis
7	57	24 (3)	Positive	Chronic active hepatitis
8	22	34 (10)	Positive	Chronic active hepatitis

### Comment

Patients with hepatocellular damage have been thought always to have raised serum aminotransferase concentrations. Our results show, however, that chronic liver disease is also likely in patients with antibodies to hepatitis C virus who have normal aminotransferase concentrations and no biochemical or ultrasonographic signs of liver disease.

Unlike an earlier study,<sup>1</sup> we found that tests for hepatitis C virus RNA in the serum were no better than cheaper conventional tests in identifying patients with liver disease. Monthly measurement of serum aminotransferase concentrations to detect flare ups of disease was also unhelpful. Thus liver disease can be diagnosed only by biopsy.

None of our patients had advanced disease and since the risk of complications is low in patients without cirrhosis<sup>3</sup> we believe that at present liver biopsy is justified for diagnosis alone. Large scale prospective studies are needed to determine the rate of progression of liver disease in these patients.

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(Accepted 8 November 1993)