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.⁴ 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.

- 1 Aach RD, Stevens CE, Hollinger FB, Mosley JW, Peterson DA, Taylor PE, *et al.* Hepatitis C virus infection in post-transfusion hepatitis. *N Engl J Med* 1991;325:1325-9.
- 2 Esteban JI, Gonzales A, Hernandez JM, Viladomiu L, Sanchez C, Juan C, *et al.* Evaluation of antibodies to hepatitis C virus in a study of transfusion-associated hepatitis. *N Engl J Med* 1990;323:1107-12.
- 3 MacLennan S, Moore C, Barbara JAJ, Hewitt PE. Risk factors in HCV infected blood donors. *Transfusion Medicine* (in press).
- 4 Managing patients with hepatitis C. *Drug Ther Bull* 1993;31:61-2.

(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.^{1,2} 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,¹ 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 cirrhosis³ 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.

- 1 Alberti A, Morsica G, Chemello L, Cavalletto D, Noventa F, Pontisso P, *et al.* Hepatitis C viraemia and liver disease in symptom-free individuals with anti-HCV. *Lancet* 1992;340:697-8.
- 2 Brilanti S, Folli M, Gaiani S, Masci C, Miglioli M, Barbara L. Persistent hepatitis C viraemia without liver disease. *Lancet* 1993;341:464-5.
- 3 Piccinino F, Sagnelli E, Pasquale G, Giusti G. Complications following percutaneous liver biopsy. A multicentre retrospective study. *J Hepatol* 1986;2:165-73.

(Accepted 8 November 1993)