

Risk of hepatitis C in patients who received blood from donors subsequently shown to be carriers of hepatitis C virus

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SUMMARY. A retrospective study was undertaken to identify recipients of blood from donors subsequently shown to be positive for hepatitis C virus using second-generation tests and polymerase chain reaction. The main aims were to determine the numbers of such recipients who were still alive and traceable, and to determine the risk of infection in this group. The feasibility and workload of this procedure, which is currently not practised in the U.K. or U.S.A., was also assessed.

In the first six months of routine testing 42,697 donors were tested. Of 20 confirmed to be HCV-positive, 15 were regular donors. Eighty-three com-

ponents were prepared from 63 anti-HCV positive previous donations from these donors. In all, nine recipients were found to be alive. All were positive for anti-HCV. We conclude that although this retrospective procedure is time-consuming and difficult, substantial numbers of infected recipients can be identified. The availability of treatment for chronic hepatitis C for such patients should encourage transfusion services to reassess current policies on the hepatitis C retrospective.

Key words: blood donor, blood transfusion, hepatitis C.

The introduction by the U.K. transfusion services of routine tests for antibodies to hepatitis C virus (anti-HCV) in September 1991 has led to the identification of blood donors who are now known to be anti-HCV positive, and who had donated prior to the commencement of testing. The retrospective procedure (look-back) consists of tracing the recipients of these donations in order to determine whether or not they have been infected. This procedure is standard practice in the case of HIV and hepatitis B-infected donors, but most Western countries have resisted the introduction of HCV lookbacks on the grounds that the benefits to patients would be small in relation to the workload engendered by the procedures. In the U.S.A., the FDA recommends against HCV-related lookbacks, and a similar policy is in place in the U.K. We undertook a comprehensive retrospective study based on the donors found to be HCV positive during the first 6 months of testing, with the aim to quantify the outcome (patients

infected/donor) in relation to the workload and resource requirements of the procedure.

METHODS

Routine screening of blood donors for anti-HCV began in September 1991. Blood packs whose samples were repeatedly anti-HCV reactive by second-generation enzyme-linked immunosorbent assay (ELISA) (Abbott Laboratories) were further tested with the second-generation Ortho recombinant immunoblot assay (RIBA 2). The presence of viral RNA was confirmed using polymerase chain reaction (PCR), the method for which has been published previously (McOmish *et al.*, 1993). A sample was considered to be confirmed HCV-positive if two or more bands were positive by the manufacturer's criteria on RIBA-2, regardless of PCR result, or if RIBA-2 was indeterminate (one band only positive) with a positive PCR result.

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Donor call-up/counselling

All donors confirmed to be HCV-positive were notified and an early appointment made. The initial counsel-

ling and assessment were carried out by a medical officer experienced in donor counselling. Apart from being counselled, the donors were questioned concerning their health, risk behaviours and the possibility of parenteral routes of infection. The virological findings were confirmed on a second sample to rule out mistaken identity.

Recipient identification

We identified from blood bank records the fate of all blood components from the previous donations of donors shown to be HCV-positive as defined above. Where possible, retained frozen samples from each of these previous donations were tested for anti-HCV by Abbott ELISA.

The recipients' hospital records were obtained and scrutinized (except in cases where the notes were not traceable). Unless it was clear that the recipient had subsequently died, the consultant responsible for the patient at the time of transfusion was notified of the fact that the donation was now known to have been anti-HCV positive. A sample of the recipient's blood was requested, and when obtained was tested for anti-HCV using ELISA and RIBA-3. PCR was carried out on samples that were suitable for analysis.

The plan of investigation is shown in Figure 1.

RESULTS

Between 1 September 1991 and 29 February 1992, 42,697 donors were screened routinely. Twenty donors were confirmed positive as defined above. Fifteen had previously donated in South East Scotland (Figure 2). Seven of these donors reported previous intravenous drug use (IVDU), and two were sexual partners of IVDU. Eight gave a history of tattooing or ear-piercing but in only one case was this the sole risk factor (tattoo). One each reported male homosexuality, multiple sexual partners, previous transfusion and vaccination with reusable needles. One donor gave no history of risk behaviour.

In total these 15 donors had given 70 previous donations, of which 65 had frozen aliquots available for testing. All but two of these stored samples were anti-HCV-positive by ELISA. The two negative samples were from a donor who reported that these two donations predated the risk behaviour leading to seroconversion. No attempt was made to trace the recipients of these units. No samples were available from five donations taken prior to 1984, and the recipients of these units have not been traced.

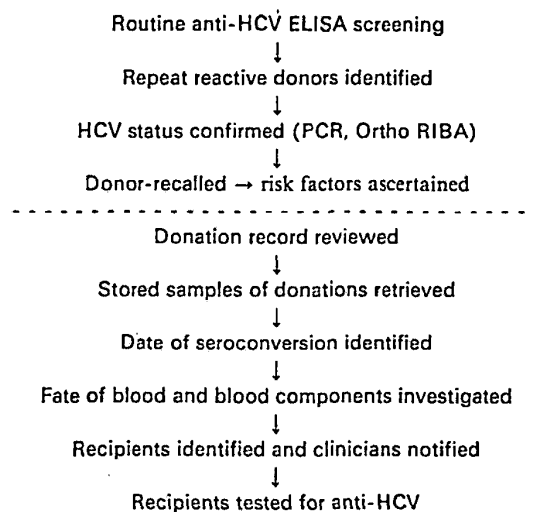


Fig. 1. Plan of investigation.

Eighty-three components were made from 63 HCV positive blood donations (excluding plasma sent for fractionation). The fate of these components is shown in Figure 2. Of the 35 components not available for transfusion, 17 were outdated, five were short packs, seven were destroyed and six were used for QA, research or reagents. Nine recipients could not be identified because of incomplete blood bank records. Of the 39 recipients identified 27 had died and no further information could be obtained for three. Two of the 27 dead recipients are known to have been HCV-positive as a result of testing frozen samples. One was positive before transfusion and the other represented transfusion-transmission.

Samples were received from the nine living, traceable recipients. All were positive on HCV-ELISA, and further results, where available, are shown in Table 1. One of the donors was found to be negative on PCR on the index sample. Of this donor's three previous donations, only one was PCR positive. The recipient was HCV-positive on ELISA, but the sample was unsuitable for further analysis. There were no traceable, living recipients of the two PCR-negative donations. Table 2 shows the likelihood of survival by year of transfusion. No recipient was alive and traceable more than 5 years after transfusion.

The workload was assessed as approximately 60 h each of secretarial time and medical time. In addition to this, microbiology staff were required to retrieve frozen samples and carry out approximately 70 additional EIA tests. A small amount of consultant time was required for liaison and recipient counselling, as well as for supervision of the project.

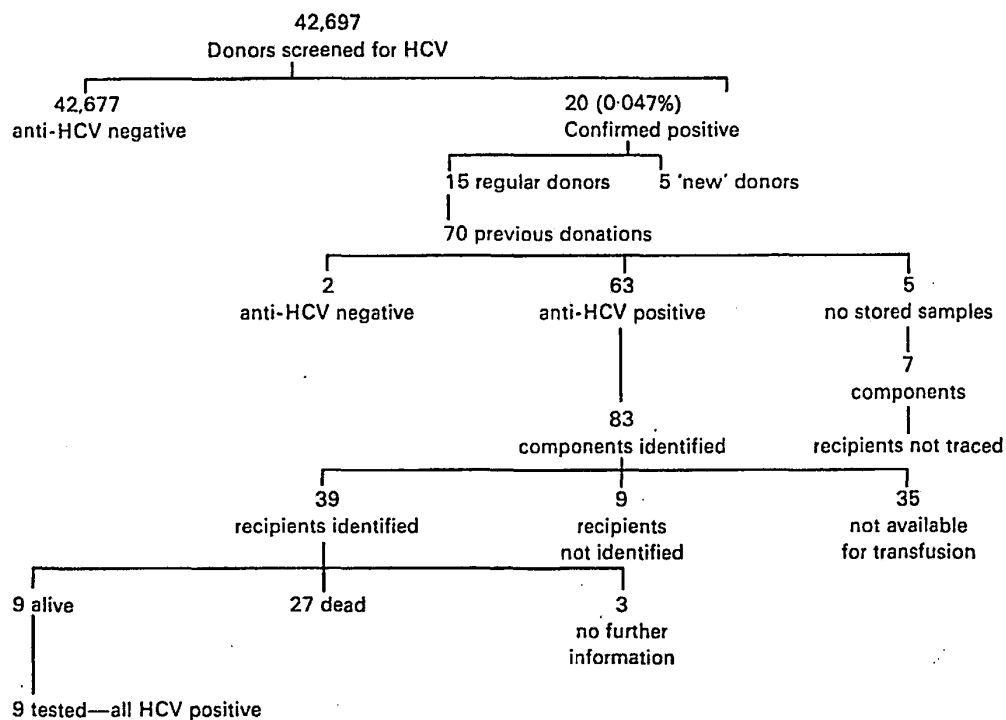


Fig. 2. HCV lookback results.

Table 1. HCV markers in donors and their recipients

Donor							Recipient					
RIBA-2				PCR	Duration (years)*		HCV-EIA	RIBA-3			PCR	
1	-	c100	c33c	c22	-	15	+	NA			NA	
2	-	-	-	c22	+	11	+	-	-	c22	-	
3	5-1-1	c100	c33c	c22	+	12		+	c100	c33	c22	NS5
4	5-1-1	c100	c33c	c22	+	22	+	NA	c33c	c22	NS5	
5	5-1-1	c100	c33c	c22	+	16	+	NA			NA	
6	-	c100	c33c	c22	+	17	+	-	c33c	c22	-	
7	5-1-1	c100	c33c	c22	+	no risk	+	-	c33c	-	-	
								+	c100	c33c	c22	NS5

* Time since last reported risk behaviour.

NA = not available.

Table 2. Likelihood of survival by year of transfusion

	Total recipients	Dead	Alive
1991	4	2	2
1990	13	9	4
1989	3	2	1
1988	3	3	0
1987	6	5	1
1986	2	1	1
1985	4	4	0
1984	1	1	0

DISCUSSION

In a comprehensive survey of 92 HIV-infected donors who had donated during the preceding 8 years, Perkins *et al.* (1987) found that, of the 406 recipients, 55% had died, 17.2% could not be traced and 27.8% were alive and traceable. Approximately, one living, infected recipient was found for each donor. Although the current study is smaller in scale and the two viruses cannot be assumed to be equally infectious, the results are broadly similar. Nine living, traceable recipients were found from a starting point of 15 donors, and all of those tested were shown to have been infected. The relatively small number of infected recipients is a reflection of the high proportion of components (42%) which were not made available for transfusion. In an earlier lookback study in the USA only 17.3% of components remained unused (Bove *et al.*, 1987).

In this study, all of the traceable recipients of blood positive by RIBA 2 or PCR were found to have been infected with HCV. This contrasts with earlier studies using the first generation EIA and less rigorous confirmation methods, in which 40–93% of recipients were shown to have seroconverted (van der Poel *et al.*, 1990; Kolho *et al.*, 1992; Aoki *et al.*, 1993). Our results suggest that virtually all recipients of blood shown to be HCV-positive by currently available immunoblot and PCR techniques will have seroconverted.

The requirement to carry out a retrospective study when an HIV-infected donor is identified has not been questioned, but the greater numbers involved in the case of HCV and doubts about the efficacy of the procedure have, until now, inhibited blood transfusion centres from applying the same standards (Busch, 1991). It is the policy of the U.K. transfusion services not to carry out HCV lookbacks. If we assume approximately one infected recipient per donor, we estimate that around 3,000 patients may be alive and infected with HCV as a result of transfusion in the

U.K., based on the prevalence of HCV in Scottish blood donors and excluding haemophiliacs. Our experience confirms that the identification of these patients is a daunting task, but the availability of potentially efficacious treatment for chronic hepatitis C, in the form of α -interferon, compels us to suggest that we have a clear ethical responsibility to these patients to identify them and offer counselling, testing and, if necessary, treatment (Kolins, 1990). Many of these patients will be old and most will have only mild liver disease, but it is our view that this problem should not be ignored on logistical grounds when, in each case, there is an overwhelming responsibility to the individual patient.

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