TABLE 2. Multivariate analysis of the association of receiving blood transfusion before and after screening with HBV and HCV prevalence in endoscopy patients after controlling for other risk factors

	Hepatitis B infection*		Hepatitis C infection*	
	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Ever received blood transfusion				
Before screening	0.97 (0.51-1.86)	1.17 (0.57-2.39)	2.97 (1.74-5.06)	4.60 (2.26-9.34)
After screening	1.28 (0.93-1.76)	1.32 (0.92-1.89)	2.77 (1.68-4.58)	2.99 (1.44-6.22)
Never	1	1	1	1
P value	*0.30*	*0.32*	*0.0001*	*<0.0001*
Ever been diagnosed with hepatitis				
No	1	1	1	1
Yes	4.61 (3.38-6.28)	4.91 (3.37-7.15)	4.60 (3.37-6.28)	30.64 (16.41-57.21)
P value	0.0001	<0.0001	0.0001	<0.0001
Ever injected nonmedicinal drugs				
No	1	1	1	1
Yes	2.51 (1.45-4.33)	2.00 (1.04-3.85)	32.4 (19.27-40.55)	24.6 (11.00-55.12)
P value	0.0006	0.04	<0.0001	<0.0001
Sex				
Males	1	1		
Females	*0.49 (0.37-0.65)*	*0.57 (0.42-0.79)*		
P value < 0001	<0.0004			
Age group				
Less than 40 years	1	1		
40 and over	1.55 (1.09-2.20)	1.48 (1.00-2.25)		
P value	0.01	0.05		
Places of birth				
Asia/Pacific (NZ)	6.58 (4.52-9.59)	9.1 (5.90-13.97)		
North Africa/Middle East/Mediterranean	3.73 (2.60-5.35)	5.00 (3.33-7.52)		
Rest of the world	1.84 (1.20-2.82)	2.27 (1.43-3.61)		
Australia	1	1		
P value	0.0001	<0.0001		
Ever been diagnosed with HIV				
Yes	21.56 (5.18-89.64)	21.18 (5.09-88.10)		
No	1	1		
P value	0.0001	0.0001		
Ever been vaccinated for hepatitis B				
Yes	1	1		
No	2.67 (1.71-4.18)	2.36 (1.45-3.83)		
Unsure if ever did	2.49 (1.42-4.36)	2.13 (1.16-3.91)		
P value	0.0001	0.001		
Ever lived with someone with HIV				
No			1	1
Yes			3.21 (1.48-6.94)	0.28 (0.08-0.91)
P value			0.007	0.02
Ever received a blood product type				
Clotting factors/growth hormone			11.86 (4.93-28.52)	4.69 (1.48-14.79)
Plasma/PLTs/others			1.76 (0.41-7.52)	0.56 (0.10-3.17)
Never had			1	1
P value			0.0001	0.02

* P of GENMOD chi-square.

the risk of exposure to hepatitis C compared with non-transfused patients (Fig. 2).

Further, in the multivariate analysis for hepatitis B and C, the risk factors significantly associated with both infections were ever having injected nonmedicinal drugs ($p = 0.04$ and $p < 0.0001$, respectively) and ever having been diagnosed with hepatitis ($p < 0.0001$). In addition, sex ($p < 0.0004$), age group ($p = 0.05$), place of birth ($p < 0.0001$), having ever been diagnosed with HIV ($p = 0.0001$), and being vaccinated for hepatitis B ($p = 0.001$) were independently associated with hepatitis B infection, whereas ever having lived with someone with HIV ($p = 0.02$) and ever having received any blood products other than RBCs ($p = 0.02$) were associated with hepatitis C infection (Table 2).

DISCUSSION

In this study more than 2000 Australian endoscopy patients were tested for blood-borne viruses and admin-

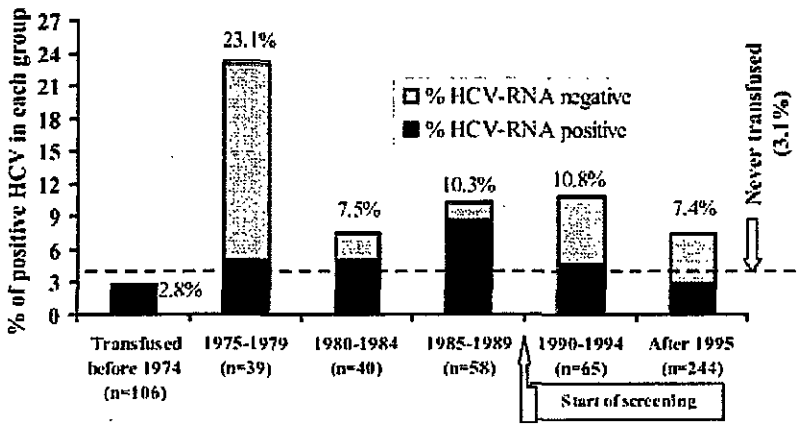

Fig. 2. The prevalence of current and/or past hepatitis C infection in patients transfused during different 5-year time intervals since 1975.

istered a comprehensive risk factor questionnaire. As in most other published surveys, we relied on patients' recall and reporting of risk factors for viral transmission. The prevalence of current and past hepatitis B and C infection was related to past history of transfusion and other risk factors for exposure. An intrinsic limitation of using data obtained from hospital patients is to determine how representative they are of the wider community. Hospital patients are more likely to have been exposed to hepatitis B and C than the general population both in the course of management of their underlying disease and because their longer average life span encompasses an era where there was less appreciation of the risk of transmitting blood-borne viruses by injections and other minor invasive procedures. Nevertheless, they are probably more representative of the general community than blood donors in whom recognized risk factors have been rigorously excluded.

The strengths of this study include the large sample size and the diversity of risk factors, demographic, and social information that was collected and analyzed. A limitation of this study was the superficial enquiry regarding sexual risk factors.

Blood transfusion is a relatively common procedure so that even a low rate of transmission of blood-borne infection will have a significant impact on the prevalence in the community. Just over one-fourth of our entire study cohort of patients attending a central Sydney hospital endoscopy unit had been transfused at some time in the past. The median age at which transfusion occurred was 52 years, and the mean time that had elapsed between transfusion and enrollment in our study was 8.8 years. The incubation period from infection with hepatitis C and the development of cirrhosis is at least 20 years so will not become clinically significant during the remaining natural life span of many transfused individuals.

For hepatitis B the situation is more complex. Most transfusion transmissions result in acute hepatitis followed by clearance and do not lead to chronic liver disease. Some subclinical cases do occur and may become persistent, but patients may also spontaneously recover over time. Chronic liver disease as a consequence of transfusion in adult life is therefore very uncommon, and the original justification for screening of donations was primarily the frequency and severity of acute posttransfusion hepatitis B.

Univariate analysis showed no significant difference in hepatitis B prevalence among nontransfused patients and recipients of screened or unscreened blood, whereas the prevalence of HCV in those transfused before and after screening was significantly different from those never transfused.

Almost all (98%) of our transfused patients also reported other risk factors for hepatitis exposure. Multivariate analysis to consider the adjustment for the effects of these risk factors did not change the conclusion based on univariate analysis for hepatitis B. For hepatitis C, it strengthened the effect of receiving a transfusion with increased ORs for receiving both screened and unscreened blood. The prevalence in the screened cohort was reduced to almost half the prescreening rate, although this was still more than double that of nontransfused controls. The difference in ORs between recipients of screened and unscreened blood was not significant.

In prospective studies of posttransfusion hepatitis, a low rate of unexplained hepatitis C infection has been observed in nontransfused controls,[4-7] and this may be attributable to other nosocomial risks related to surgery or other hospital treatment. A similar conclusion has been drawn from intensive investigation of putative posttransfusion cases.[5,8,9] Screening tests for HCV have been subjected to exhaustive scrutiny and the chance of an infective donation escaping detection are now very remote indeed.[3]

The prevalence of HCV in recipients was higher than we anticipated from earlier prospective studies of posttransfusion hepatitis in Australia. In a prospective study of cardiac surgery patients in Australia that we conducted in 1988 to 1999,[10] only 1.1 percent of 736 transfusion recipients, given a mean of 4 units, were infected with HCV, compared with none of the 514 nontransfused controls operated on during the same period. In this study, the number of units received was not recorded, and the indications for transfusion and the circumstances under which they were administered were very diverse, so it was not possible to examine whether the condition treated or

the number of units transfused were related to increased risk.

Multivariate analysis showed an increased risk of HCV in those who had received blood products other than RBCs compared with those never transfused (Table 2), attributable mainly to the use of clotting factors and growth factors, which increased the risk 4.7-fold. The prevalence of markers in the 31 individuals who had received both blood products and blood (12.9% were HBV-positive and 16.1 percent were HCV-positive) was close to the HBV prevalence (10.6%) but almost 5-fold higher than the hepatitis C prevalence (3.1%) in those never transfused. The difference between those receiving blood products as well as transfusion and recipients of blood only was not significant

It is not surprising that we could not demonstrate a beneficial effect of HBV screening in this study. We could not control for the confounding effects of some potential risk factors for hepatitis B transmission like perinatal exposure or sexual risks, which are likely to account for the high background prevalence of current and past hepatitis B among the nontransfused population (10.6% [162/1525]). In addition, a low rate of detection of hepatitis B–positive units in Australia was reported at the time of the introduction of screening (0.1%).[11] Not all HBsAg-positive donors are infective,[12] so even if the average number of units received was high (say 6 units), transfusion could only be responsible for a very few cases of hepatitis B infection. In contrast, sexual and perinatal risk factors are not as important for hepatitis C transmission, the background prevalence of HCV is much lower (3.1% [47/1517]), and the detection rate of anti-HCV at the introduction of screening was substantially higher (0.5%)[13] than that for HBV.

The risk of acquiring transfusion transmitted hepatitis C was not constant throughout the prescreening period (Fig. 2). The increase during the late 1970s is consistent with an increase in the prevalence of hepatitis C in the community associated with an increase in injecting drug use, whereas the subsequent sharp decline may be attributable to the introduction of stringent donor selection procedures to combat the threat of HIV contamination of the blood supply.

In conclusion, transfusion is only a minor risk for acquisition of hepatitis B in the community, but has played a more significant role in transmission of hepatitis C both before and after the introduction of screening. The continuing association of hepatitis C with transfusion requires critical investigation because there is very convincing evidence that HCV has been almost completely eradicated from the blood supply by the combination of donor evaluation and screening of donations. Our findings strongly imply that other nosocomial risks are associated with the clinical situations where patients require blood transfusion.

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