The prevalence of three risk factors that have been identified as important predictors of more progressive forms of chronic hepatitis C viral (HCV) infections (male gender, transfusion recipients and age greater than 50 years at the onset of infection) were documented by a retrospective chart review of 337 HCV-infected patients attending an urban, hospital-based, viral hepatitis clinic. One hundred and ninety-five patients (58%) were male. One hundred and eighteen (35%) had received blood or blood product transfusions in the past, 33% of whom also gave a history of intravenous drug use. Approximately 5% of patients were over the age of 50 years at the estimated time of infection. Twenty percent of patients had two and 4% had all three risk factors. In conclusion, intrinsic host risk factors associated with progressive HCV infection were common in this patient population. If confirmed in other centres, these results suggest that the medical and financial demand on the health care system is likely to be appreciable unless effective and safe therapies for HCV are identified and implemented in the near future.

La prévalence de trois facteurs de risque identifiés comme d’importants prédicteurs de formes plus progressives d’infection chronique par le virus de l’hépatite C (VHC) (homme, transfusion et plus de 50 ans à l’apparition de l’infection) a été documentée à l’aide d’un examen rétrospectif des dossiers médicaux de 337 patients infectés par le VHC qui ont fait appel aux services d’une consultation externe pour l’hépatite virale, située dans un hôpital urbain. Cent quatre-vingt-quinze patients (58%) étaient de sexe masculin. Cent dix-huit (35%) avaient eu par le passé une transfusion de sang ou de produit du sang, 33 % d’entre eux ayant aussi des antécédents d’usage de drogues injectables. Environ 5 % des patients étaient âgés de plus de 50 ans au moment présumé de l’infection. Vingt pour cent des patients avaient deux des trois facteurs, et 4% avaient les trois. En conclusion, les facteurs de risque intrinsèques chez l’hôte associés à une infection progressive par le VHC sont apparus courants au sein de ce segment de la population. S’ils sont confirmés par d’autres centres, ces résultats indiqueront que les demandes financières et médicales qui vont être faites au système de soins de santé risquent d’être importantes, à moins que des thérapies anti-VHC efficaces et sans danger soient découvertes et mises en œuvre dans un avenir proche.

**ABSTRACT**

The prevalences of three risk factors that have been identified as important predictors of more progressive chronic hepatitis C viral (HCV) infections. These factors include male gender, acquisition of HCV by blood or blood product transfusions, and age >50 years at the time of infection. What percent of the current HCV patient population possess one, two or all of these risk factors has yet to be reported. In addition to patient counselling, such information is also important in predicting the health care needs of HCV patients and the financial burden those needs will place on the health care system. Thus, the purpose of the present study was to document the prevalence of these host factors in HCV patients attending an urban, outpatient viral hepatitis clinic.

Because various governments and health care providers are contemplating whether to offer compensation to patients who may have acquired their HCV infections from blood or blood product transfusions during the 1986–90 period when surrogate screening of blood donors for HCV was available but not employed, we also endeavored to determine what percent of the total HCV population these individuals constituted and what percent had blood or blood product transfusions as their sole risk factor for viral acquisition.

**MATERIALS AND METHODS**

**Study population**

The charts of 398 patients seen at the Liver Diseases Unit, Health Sciences Centre, Winnipeg, Manitoba between January 1, 1991 and January 1, 1998 with a diagnosis of HCV infection were retrospectively reviewed for: 1) accuracy of diagnosis, and 2) the patients’ responses to a questionnaire posed by a physician during one-on-one interviews at the initial evaluation visit. Only patients who were anti-HCV positive by second or third generation screening (enzyme-linked immunosassays) and supplemental (recombinant immunoblotting or HCV-RNA by polymerase chain reaction) assays were included in the study. All serologic testing was performed by the Cadham Provincial Laboratory (Winnipeg, Manitoba) using commercially available kits. Questions asked with respect to risk factors for HCV transmission included: have you ever received a blood or blood product transfusion and if so in what year(s)? have you ever used (even on only one occasion) non-prescribed "street drugs" that require needles for administration and if so, when was the first such use of these drugs? have you ever had a sexually transmitted disease or have you had more than five sexual partners during the course of one year? (positive responses defined as sexual promiscuity); and if you have had your body pierced or tattooed, was the procedure performed by an individual with a licence to perform these procedures?

Three hundred and thirty-seven patients were confirmed anti-HCV positive and had responded to all of the above questions. Limited findings in 89 of these patients were reported in a previous publication.4
Study site and patient accrual
The Liver Diseases Unit is located within the Health Sciences Centre, a tertiary care centre in the core area of Winnipeg (population: 680,000). The Unit is the principal referral centre for patients with liver disease within the province. It was established in 1987, four years prior to the availability of specific serologic testing for HCV infections. All serologic testing for HCV infection within the province is performed at the Cadham Provincial Laboratory. Positive results are mailed to the physician of record with the suggestion that the patient be referred to the Liver Diseases Unit for further evaluation. Thus, although precise figures are not available, the HCV patient population evaluated in the Liver Diseases Unit is thought to be representative of the majority of HCV cases within the province.

STATISTICAL ANALYSES
The following statistical analyses were performed where appropriate: t tests for parametric data and Chi-square test ($\chi^2$) with Yates correction for non-parametric data. $p$ values <0.05 were considered significant.

RESULTS

Study population
As shown in Table I, of the 337 patients, 195 (58%) were males and 142 (42%) females ($p<0.001$). The mean (±SD) age of the study population was 42.5 ± 12.9 years (range 7-79 years) with males being older (44.1 ± 12.1 years) than females (39.9 ± 9.2 years) ($p<0.001$). Aside from the group of patients aged 21-30 years in which females were more common than males (20.4% versus 7.7% respectively, $p<0.001$), there were no significant gender differences in the various age populations.

Risk factors for HCV acquisition
The most common risk factor for viral acquisition (Table II) was a history of intravenous drug use (56.4%) followed by a history of body piercing/tattoos using non-sterile techniques (52.2%) which often serves as a surrogate marker for other high-risk activities. Third most common was a history of blood or blood product transfusions (35%). Sexual promiscuity was a risk factor in 22.6% of the patient population. No identifiable risk factor could be found in 7.7% of individuals. The difference between the percentage of patients with the two most clearly established risk factors for HCV transmission – those with a history of intravenous drug use and those who had received blood or blood product transfusion.
sions — was significant (p<0.001). When analyzed by gender, males were more commonly represented in the blood or blood product transfusion (males: 57.6% vs. females: 42.4%, p<0.05) and sexual promiscuity (males: 60.5% vs. females: 39.5%) groups (p<0.01 respectively).

Of the 118 patients with a history of blood or blood product transfusions, 79 (67%) had transfusion as their only risk factor, 39 (33%) also had a history of intravenous drug use (Table III). Of these 39 individuals with both risk factors, 28 (72%) also had a history of either sexual promiscuity and/or body piercing/tattoos. The high rate of additional risk factors appears to have been related to a history of intravenous drug use as 110 of the 151 patients (73%) with a history of intravenous drug use also had a history of sexual promiscuity and/or body piercing/tattoos. There were no gender differences amongst patients with histories of blood transfusions alone, blood transfusions plus intravenous drug use, blood transfusions plus intravenous drug use plus other risk factors, intravenous drug use alone, or intravenous drug use plus other risk factors.

**Intrinsic host factors**

As stated above and shown in Figure 1, males constituted 58% of the study population, 35% of all HCV patients had received blood or blood product transfusions in the past, and 12 of the 261 (4.5%) patients in whom a date of first blood transfusion or intravenous drug use was provided were above the age of 50 at the estimated time of HCV infection (Tables IV and V). Ten of those 261 (3.8%) patients were both male and over the age of 50 at the estimated time of infection (Figure 2). Sixty-eight of the 337 (20.2%) patients were both male and had a history of blood or blood product transfusions. Eleven of 118 (9.3%) blood or blood product transfusion recipients in whom the date of their first transfusion was provided, were over the age of 50 at the time of infection. Finally, 9 patients (3.5%) had all three host factors present.

**Symptoms**

Because the presence or absence of symptoms has been suggested as a possible factor determining whether and/or to what extent compensation might be offered to blood or blood product transfusion recipients, we also analyzed what percent of patients on presentation complained of fatigue, right upper quadrant discomfort or both symptoms (Table VI). Fatigue was present in 18.1%, right upper quadrant discomfort in 7.4% and both symptoms in 3.9% of patients. There were no age or gender differences with respect to the presence or absence of these symptoms. When the analysis was limited to patients with a history of blood or blood product transfusions, similar results were obtained with 17% of these patients being fatigued, 10.2% complaining of right upper quadrant discomfort and 3.4% with both symptoms. Once again, there were no differences in age or gender distribution within these subpopulations.

**1986-1990 Subpopulation**

Approximately one half (54.8%) of patients with a history of previous blood or
blood product transfusions received transfusions between the years 1986-1990, 38% of these individuals also had a history of intravenous drug use. Although these individuals tended to be younger, more often male and slightly more commonly symptomatic, these differences were not statistically significant (Table VII).

**DISCUSSION**

The results of this study indicate that at this centre, a significant proportion of patients with chronic HCV infections have host factors that have been associated with an increased risk of progression to cirrhosis. Specifically, 58% of the patient population were male, 35% had acquired their infection from a previous blood or blood product transfusion, and 4.5% were over the age of 50 years at the estimated time of infection. The results also indicate that 33% of transfused patients have a history of previous intravenous drug use. Finally, less than 20% of patients with chronic HCV are symptomatic and the presence or absence of symptoms appears to be unrelated to the route of transmission, age or gender of the patient.

To date, the largest studies designed to identify host factors associated with an increased risk of chronic HCV progressing to cirrhosis were two European multi-centre studies reported by Rudolph-Thoraval et al. and Poynard et al. In the former, acquisition of viral infection by blood transfusion was identified as the variable most strongly associated with the presence of cirrhosis. In the Poynard study, rates of fibrosis were highest in males and those estimated to be over the age of 40 years at the time of infection. Whether the presence of two or more host factors increases the likelihood of disease progression and whether that increase is additive or synergistic remains to be determined. If additive or synergistic effects do occur, approximately 1 in 5 patients with chronic HCV infections are at a further increased risk of disease progression and 1 in 20 would be considered at high risk of progressive disease. These ratios would almost certainly be higher were the effects of ethanol and perhaps other intrinsic and extrinsic host factors to be incorporated into the analyses.

The results of this study provided a somewhat different patient profile than had been described by ourselves in a previous study of 89 HCV patients at the same centre in 1994. While in both studies, intravenous drug use was the most common risk factor identified, there has been a clear increase in the percent of patients with this risk factor (present study: 56%, previous study: 34%). The percent of patients with a history of blood or blood product transfusions has also increased when compared to the previous study (35% versus 25%, respectively). Presumably these increases reflect targeted efforts to identify and manage the segments of the general population with those risk factors in place. A history of sexual promiscuity was somewhat less common in the present study population (22.6%) compared to that obtained in the previous study (35%). The results of this study provided a somewhat different patient profile than had been described by ourselves in a previous study of 89 HCV patients at the same centre in 1994. While in both studies, intravenous drug use was the most common risk factor identified, there has been a clear increase in the percent of patients with this risk factor (present study: 56%, previous study: 34%). The percent of patients with a history of blood or blood product transfusions has also increased when compared to the previous study (35% versus 25%, respectively). Presumably these increases reflect targeted efforts to identify and manage the segments of the general population with those risk factors in place. A history of sexual promiscuity was somewhat less common in the present study population (22.6%) compared to that obtained in the previous study (32%). Finally, for unknown reasons, body piercing/tattoos was more than twice as common in the present population (52.2%) when compared to the previous study (19%).
Compensation for patients who have received blood or blood product transfusions between the years 1986-90 when surrogate testing for HCV in the blood donor population was available but not employed is a difficult and contentious issue. In the present study, approximately 50% of our blood or blood product recipient population and 14% of the overall HCV patient population received their transfusions during those years. One of the arguments against providing compensation for all such patients has been that other routes of transmission might have been responsible for their HCV infections. Indeed, our data indicate that 38% of patients who had received blood or blood product transfusions between the years 1986-1990 also had a history of intravenous drug use. This figure was similar to the 33% figure obtained in all blood or blood product transfusion recipients irrespective of the year(s) of transfusions.

A smaller percent of patients complained of fatigue and right upper quadrant discomfort than would have been predicted based on the results of previous studies. Perhaps the explanation for this finding relates to the method whereby the presence or absence of symptoms was ascertained. In our study, patients were asked an open-ended question regarding how they were feeling at the time of their initial office visit. Only 20% of patients volunteered they were fatigued and 10% complained of right upper quadrant discomfort. Patients who did not volunteer these symptoms but only responded positively to the physicians’ direct questioning regarding fatigue and right upper quadrant discomfort were not included in the symptomatic group. More sensitive testing with visual analogue scales and quality-of-life questionnaires were not employed in this patient population.

In conclusion, in this retrospective chart review we have found that as many as 58% of patients with chronic HCV infections possess at least one host factor that has been associated with an increased risk of progression to cirrhosis. Twenty percent of patients have two and 4% have all three host risk factors. If these findings are confirmed in other Canadian centres, the results would suggest that the medical and financial demand on the health care system are likely to be appreciable in the near future unless effective and safe therapies for this condition are identified and implemented.

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