# Clinical and epidemiologic characteristics of hepatitis C in a gastroenterology/hepatology practice in Ottawa

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**Objective:** To examine the clinical and epidemiologic features of hepatitis C virus (HCV) infection in a gastroenterology/hepatology practice in Ottawa.
**Design:** Retrospective chart review.
**Patients:** Sixty-three consecutive patients found to be anti-HCV positive. Their charts were analysed with respect to risk factors, history of hepatitis, serum aspartate aminotransferase (AST) levels and the presence of hepatitis B markers. The long-term sexual partners of 29 patients agreed to undergo HCV antibody testing.
**Results:** Of the patients 48 (76%) had been exposed to HCV parenterally: 27 used intravenous drugs, and 21 had received blood or blood products. Eleven patients did not have any known risk factor (sporadic infection), but eight of them had lived in countries where hepatitis C may be more prevalent; the other three had locally acquired infection. The mean serum AST level at the first visit was 140 (normally less than 40) IU/L. At least one hepatitis B marker was identified in 33% of the patients. None of the sexual partners who were tested were anti-HCV positive.
**Conclusion:** Most cases of hepatitis C in Ottawa are acquired through parenteral exposure; sexual transmission is rare. Sporadic infection in the Ottawa region is rare but may be more common in people from countries with a higher prevalence rate of hepatitis C. Most cases of hepatitis C are asymptomatic.

**Objectif :** Examiner les caractéristiques cliniques et épidémiologiques de l'infection à virus de l'hépatite C (VHC) dans un cabinet de gastro-entérologie et d'hépatologie d'Ottawa.
**Conception :** Examen rétrospectif des dossiers.
**Patients :** Soixante-trois patients consécutifs diagnostiqués comme anti-VHC positifs. Leurs dossiers ont été analysés en ce qui concerne les facteurs de risque, les antécédents d'hépatite, les taux sériques d'aspartate aminotransférase (AST) et la présence de marqueurs de l'hépatite B. Les partenaires sexuels à long terme de 29 patients ont accepté de subir le dépistage de l'anticorps du VHC.
**Résultats :** Quarante-huit (76 %) des patients avaient été exposés au VHC par voie parentérale : 27 ont utilisé des drogues injectables et 21 ont reçu du sang ou des dérivés sanguins. Onze patients ne présentaient aucun facteur de risque connu (infection sporadique), mais huit d'entre eux avaient habité des pays où l'hépatite C peut être plus fréquente; les trois autres ont contracté l'infection localement. Le taux sérique moyen

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d'AST à la première visite était de 140 (normalement moins de 40) UI/L. Chez 33 % des patients, on a identifié au moins un marqueur de l'hépatite B. Aucun des partenaires sexuels contrôlés n'était anti-VHC positif.

**Conclusion :** À Ottawa, la plupart des patients atteints d'hépatite C ont contracté la maladie par voie parentérale; la transmission sexuelle est rare. Dans la région d'Ottawa, l'infection sporadique est rare, mais elle peut être plus fréquente chez les personnes originaires de pays où le taux de prévalence de l'hépatite C est plus élevé. La plupart des cas d'hépatite C sont asymptomatiques.

The hepatitis C virus (HCV), recently identified by Choo and associates,[1] is responsible for most cases of non-A, non-B hepatitis.[2] This virus is spread predominantly through parenteral exposure to blood and blood products. However, some patients have no known risk factors for HCV transmission ("sporadic" infection).[3] Chronic hepatitis C develops in almost 50% of people with acute infection.[4]

HCV is an RNA virus with some characteristics similar to those of flaviviruses such as the yellow fever virus. A recombinant protein-based enzyme-linked immunosorbent assay (ELISA) has been developed to detect antibodies to a nonstructural region of the HCV.[5] The prevalence rate of HCV antibody in blood donors varies from country to country, and the predominant mode of transmission may depend on local geographic or sociologic factors. In Japan and Italy the test detected HCV antibodies in 80% of patients with chronic post-transfusion hepatitis.[5] In Spain studies of high-risk patient populations showed that 70% of those who used intravenous drugs, 64% of those with hemophilia and 20% of those who underwent hemodialysis were found to be anti-HCV positive.[6] In contrast, only 0.52% of Canadian blood donors have detectable anti-HCV levels.[7] A confirmatory radioimmunoblot assay (RIBA) has been developed that incorporates a second HCV antigen. It is of value in low-risk populations such as blood donors, in which there is a high false-positive rate (up to 50%) with the ELISA.[8]

The HCV antibody can appear from 4 to 52 (mean 21) weeks after transfusion but persists for several years if chronic infection develops.[2] Retrospective studies of transfusion-related hepatitis have shown that most patients with HCV antibodies are infectious.[9] In addition, their infectivity is demonstrated by the detection of viral-specific RNA in their serum with the use of the polymerase chain reaction.[10]

To have any impact on the spread of HCV it is essential to understand the epidemiologic features and modes of HCV transmission. We analysed the records of patients in a gastroenterology/hepatology practice in Ottawa who were found to be anti-HCV positive to determine the risk factors for and the clinical features of hepatitis C.

## Methods

### *Patient population*

We reviewed the records of 63 consecutive patients who were confirmed to be anti-HCV positive. These patients were seen by a hepatologist (L.J.S.) because of an unexplained abnormal serum aspartate aminotransferase (AST) level (40 patients), chronic hepatitis (15) or the presence of known chronic liver disease (8). None had been referred to our practice because of their anti-HCV status, because they had been seen before the diagnostic test was generally available.

The long-term sexual partners of the study patients were asked if they wished to undergo HCV antibody testing to assess the rate of sexual transmission in this population; only 29 of the 42 partners agreed to do so.

### *HCV antibody testing*

All serum samples were tested with the HCV ELISA Kit (Ortho Diagnostics, Raritan, NJ); only samples with an optical density of more than 2 were considered positive. All samples with a positive ELISA result were then tested with the RIBA; only those confirmed as being positive were included (two originally thought to be positive with the ELISA were excluded).

From the records we extracted information obtained at the first visit: the serum AST level and the presence of hepatitis B markers (the hepatitis B surface antigen [HBsAg] and antibodies to the hepatitis B surface and core antigens [anti-HBs and anti-HBc]). The three markers had been identified with the AUSRIA II, AUSAB and CORAB kits respectively (Abbott Laboratories, Chicago). We also noted the highest level of AST ever recorded by the attending physician for each subject. Investigation for other causes of liver disease such as hemochromatosis, autoimmune chronic active hepatitis, Wilson's disease and alcohol-induced liver disease had been carried out when appropriate.

## Results

Of the 63 patients 44 were men and 19 women;

the mean age was 41.4 (standard deviation 12.5) years. Intravenous drug use was the most common presumed mode of transmission (in 27 [43%] of the cases); the use of such drugs had often occurred more than 20 years previously. Transfusion of blood or blood products was presumably responsible for the HCV transmission in 21 patients (33%); 2 had hemophilia and had received Factor VIII concentrate. Eleven patients had no obvious risk factor (sporadic infection), but eight of these had lived for an extended period in a country where the prevalence rate of hepatitis C may be higher: three in Egypt, two in Europe and one each in Romania, Haiti and Vietnam. Only 3 of the 11 patients were from the Ottawa area. Finally, two of the subjects were health care personnel, and two were homosexual men; these four were not originally from Canada.

Nineteen (30%) of the patients had a history of acute hepatitis. The mean serum AST level recorded at the first visit was 140 (normally less than 40) IU/L; the mean highest level was 362 IU/L. The latter value includes the levels of patients with acute hepatitis, two of whom had markedly elevated serum AST levels recorded by their family physician. These values, however, had decreased by the time they were seen in our practice.

In 21 (33%) of the patients at least one hepatitis B marker was identified: HBsAg in 2 (3%), anti-HBc in 7 (11%), and anti-HBs and anti-HBc in 12 (19%). Of these, 12 had used intravenous drugs, 4 were from high-risk countries, 2 had received multiple transfusions, 2 had hemophilia, and 1 was a homosexual man.

Of the 29 sexual partners who underwent testing none was found to be anti-HCV positive. In one case, a man and woman in a common-law relationship were found to be anti-HCV positive, but both had been referred to the practice because of hepatitis and had used intravenous drugs. Parenteral exposure was assumed to be the mode of spread of HCV in this couple.

## Discussion

The recently developed diagnostic test for HCV antibody has been valuable for screening potential blood donors and for confirming a clinical diagnosis of hepatitis C. The availability of this test allowed us to study the epidemiologic features of hepatitis C in our practice and to analyse the clinical features and risk factors associated with such infection in the study population.

Whether our patients represent all those with hepatitis C in Ottawa requires further investigation. Giulivi and collaborators[11] recently reported the findings for 20 186 volunteer blood donors at the Ottawa Red Cross Blood Transfusion Centre. They found that in 59 (0.3%) repeat ELISA yielded positive results and in 31 (0.2%) the results were confirmed by means of a second-generation RIBA. In addition, Chaudhary and Mo[12] found confirmed anti-HCV positivity in only 3 (1.2%) of 256 federal public servants in Ottawa.

The similarity of the observations of Giulivi and collaborators to ours suggests that the patients we studied do represent the Ottawa population. In our study HCV was presumably transmitted through the use of intravenous drugs in 27 patients (43%) and parenteral administration of blood or blood products in 21 (33%). Similarly, in the Ottawa blood donor study 67% of donors who were anti-HCV positive (as determined by an optical density of more than 2, as in our study) had a history of parenteral exposure to the virus (16 received blood transfusions, 5 used intravenous drugs, and 1 was a member of a blood-brother sect). The screening questionnaire used in the donor study excluded those who had used intravenous drugs since 1977. Therefore, the five donors who had used such drugs had been exposed through that route more than 15 years before the study. All people who use intravenous drugs are now excluded from donating. In our study several of the patients who had used intravenous drugs had experimented with them more than 20 years earlier and had presumably been in the HCV carrier state since then. Parenteral HCV transmission has been well documented: 80% of well-characterized post-transfusion hepatitis is associated with the development of HCV antibody.[2] Some people have hepatitis C but for unexplained reasons do not have detectable antibody levels.[2] Studies in other countries have shown that 64% to 85% of people with hemophilia and 30% to 70% of those who use intravenous drugs are anti-HCV positive.[12] Similar results have been observed in Canada (54% and 43% respectively).[12]

According to our data sporadic hepatitis C in Ottawa natives is rare. Only 3 of the 11 patients with an unknown risk factor had always lived locally, whereas the other 8 had been born or had lived for an extended period in a country where the prevalence rate of hepatitis C may be higher. Similar results were found in a study in a Detroit suburb: five of eight patients with sporadic infection had been born outside North America.[13] Also, in our study the two health care personnel and the two homosexual men were from European or Middle Eastern countries and most likely did not acquire their infection in Canada. The prevalence rate of hepatitis C may be extrapolated from the proportion of blood donors who are anti-HCV positive. For example, the incidence rate of HCV antibody in the Canadian blood donor population is only 0.52%, as compared with 0.68% in France,[14] 0.87% in Italy,[15] 1.2% in Japan[16] and 5% in Saudi Arabia.[17] Assuming

that HCV is spread at low levels by some inapparent route, the chance of acquiring hepatitis C in Ottawa through a route other than the obvious parenteral ones is extremely low and could be as much as 10 times lower than in Saudi Arabia.

HCV is obviously transmitted through blood-blood contact, but other modes of transmission are not well documented. Alter and colleagues[3] and Tajima, Shimotohno and Oki[18] suggested that sexual contact is an important mode of infection, but this conclusion is controversial.[3,19,20] Our data and those from other studies involving spouses of anti-HCV-positive patients do not support sexual contact as a frequent route of transmission. However, some of the sexual partners in our study refused to be tested, and whether this introduced any significant bias is difficult to determine. In another study none of 13 spouses of anti-HCV-positive people were anti-HCV positive.[19] Everhart and coworkers[20] were unable to detect HCV antibody in any of 62 sexual or family contacts of people in the HCV carrier state. In addition, a study involving homosexual patients in Spain indicated that only 2 (8%) of 26 were anti-HCV positive, whereas the prevalence rate of markers of the hepatitis B virus, which is easily transmitted sexually, was usually closer to 75% in the same population.[6] Of the three local patients with sporadic hepatitis in our study, two worked in a restaurant and had had more than 10 heterosexual partners. The third patient had had only one sexual partner, who was anti-HCV negative. With the present HCV serologic techniques we cannot determine whether the sexual partners of the anti-HCV-positive patients had been remotely infected, cleared the virus and not produced antibody. However, since the development of the chronic carrier state is reported to be identical in sporadic and parenterally acquired cases of infection, one would expect more sexual partners to be anti-HCV positive if sexual transmission were occurring at any significant rate. The recent finding that HCV RNA is not detectable in saliva or semen of those in a chronic carrier state[21] may explain the rarity of transmission through this route. Larger studies are required to assess this important issue.

The method of transmission in sporadic cases is unclear. Maternal-fetal spread is uncommon.[22] Transmission by insect vectors or inapparent percutaneous spread, during dental procedures for example, is possible, but further work is required to clarify the role of these routes in HCV transmission.

Signs and symptoms of chronic hepatitis C are usually absent but may include fatigue and a minimally elevated serum AST level. In our group only 30% of the patients had any history of acute hepatitis. Most (63%) of the patients had been found to be anti-HCV positive when investigated for an asymptomatic persistently elevated serum AST level initially discovered on routine testing. Giulivi and collaborators[11] reported that 90% of their anti-HCV-positive patients had an elevated serum AST level, but the levels were not given. The mean level at the first visit in our study was only moderately elevated; however, the values ranged from 44 to 345 IU/L, and unexplained AST fluctuations in individual patients were frequent.

Other studies have shown that a significant number of anti-HCV-positive patients also have markers for hepatitis B.[1,16,23] At least one marker was detected in 21 of our patients, 12 of whom had used intravenous drugs. Presumably there had been a common route of transmission for the two viruses.

Whether hepatitis C will have the same epidemiologic features in all cities across Canada requires further investigation. The recent introduction of screening for HCV by the Canadian Red Cross will significantly reduce the incidence of post-transfusion hepatitis but will have little impact on other forms of transmission. Improved HCV antibody testing with more sensitive second-generation assays, less frequent transfusion of blood and blood products, the provision of free needles to people who use intravenous drugs and, ultimately, the development of a protective vaccine will also help to reduce the incidence of hepatitis C.

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23. Richards C, Holland P, Kuramoto K et al: Prevalence of antibody to hepatitis C virus in a blood donor population. *Transfusion* 1991; 31: 109-113

## *Conferences*
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**June 9, 1993:** Ambulatory Care Conference
Vancouver
Professional services, Canadian College of Health Service Executives, 201-17 York St., Ottawa, ON K1N 5S7; tel (613) 235-7218, fax (613) 235-5451

**June 9-11, 1993:** Approaches to Design and Development of Cost Effective Laboratory Animal Facilities
Ottawa
Lori Creelman, Canadian Council on Animal Care, 1000-151 Slater St., Ottawa, ON K1P 5H3; tel (613) 238-4031, fax (613) 238-2837

**June 10-12, 1993:** Addictions '93 — Emerging Issues and the Health Care Professional (cosponsored by the American Society of Addiction Medicine, the Canadian Medical Society on Alcohol and Other Drugs and the College of Family Physicians of Canada)
Guelph, Ont.
Karen Maki, program manager, Office of Continuing Education, Rm. 160, Johnston Hall, University of Guelph, Guelph, ON N1G 2W1; tel (519) 767-5000, fax (519) 767-0758

**June 20-25, 1993:** International Adolescent Health Week in Israel — 2nd International Conference on Youth and Disability, 2nd European Forum on Adolescent Health and Symposium on "Quality of Life, Youth and Disability"
Jerusalem, Israel
Ortra Ltd., 2 Kaufman St., PO Box 50432, Tel Aviv 61500, Israel; tel 011-972-3-664825, fax 011-972-3-660952

**June 23-24, 1993:** IMAC '93 — 3rd International Conference on Image Management and Communication (followed by CAR '93 — Computer Assisted Radiology)
Berlin, Germany
*Official language: English*
IMAC '93, Professor Heinz U. Lemke, Institut für Technische Informatik, Technische Universität, Sekr. CG FR 3-3, Franklinstrasse 28/29, W-1000, Berlin 10, Germany

**June 24-26, 1993:** CAR '93 — Computer Assisted Radiology (preceded by IMAC '93 — International Conference on Image Management and Communication)
Berlin, Germany
*Official language: English*
CAR '93, Professor Heinz U. Lemke, Institut für Technische Informatik, Technische Universität, Sekr. CG FR 3-3, Franklinstrasse 28/29, W-1000, Berlin 10, Germany

**June 27-30, 1993:** Canadian Ophthalmological Society 56th Annual Meeting and Exhibition
Montreal
Hubert Drouin, executive director, or Kimberley Ross, office administrator, Canadian Ophthalmological Society, 610-1525 Carling Ave., Ottawa, ON K1Z 8R9; tel (613) 729-6779, fax (613) 729-7209

**Sept. 20-22, 1993:** Alzheimer's Disease International 9th Annual Conference — Global Challenge, Local Action
Toronto
Alzheimer Society of Canada, 201-1320 Yonge St., Toronto, ON M4T 1X2; tel (416) 925-3552, fax (416) 925-1649

**Oct. 20, 1993:** A Day in Geriatrics
Toronto
Cindy Stolarchuk, conference coordinator, Sunnybrook Health Science Centre, 2075 Bayview Ave., North York, ON M4N 3M5; tel (416) 480-5904