Current Status of Hepatitis C in Canada

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Hepatitis C is a major public health concern around the world. It is estimated that approximately 3% of the world's population, or as many as 170 million persons worldwide, are infected with hepatitis C virus (HCV).[1] HCV was discovered by characterization of the viral genome in 1989,[2] without the actual isolation of the virus itself. The virus is a member of the flaviviridae family with a genome of single stranded RNA. Various genotypes exist in different regions of the world. So far, six major genotypes have been isolated with genotypes 1-3 described worldwide, genotypes 4 and 5 principally in Africa and genotype 6 primarily in Asia.[1] In Canada, the major genotypes are 1, 2, and 3.[3-5]

Hepatitis C is usually a subclinical infection with only 25% of patients with post-transfusion hepatitis developing jaundice.[6] In other prospective studies, only 20-30% of the patients had symptoms and approximately half of the symptomatic group developed jaundice.[7] Clinically and histopathologically, hepatitis C is similar to viral hepatitis caused by other pathogens.[8] The most important feature of hepatitis C is the high frequency (75-85%) with which acute disease progresses to chronic infection. Available studies of hepatitis C infection have shown that the disease has a protracted course and serious sequelae may not appear until decades after initial infection.[9] The pathogenesis of and the immune response to hepatitis C are poorly understood. Infection by HCV does not seem to induce a protective humoral response but it is becoming clear that some infected individuals do recover from their infection.

Hepatitis C is transmitted through blood or body fluids contaminated with the virus.[10,11] Important risk factors associated with transmission of HCV are the sharing of drug injection equipment and the receipt of unscreened blood or blood products. Vertical and sexual transmission can also occur. Inapparent parenteral exposure such as tattooing, body piercing and sharing of personal hygiene items, only if the instruments or items for such activities are contaminated with blood or body fluids, are also presumed to be risk factors. In different countries the relative importance of risk factors can vary both regionally and temporally. For example, until recently blood transfusion was an important route of transmission; however, with the development and implementation of sensitive (and specific) screening methods, the risk associated with blood transfusion and the use of blood products has been markedly reduced. In most developed countries such risk is minimal at the present time whereas in some developing countries the risk may still be at a relatively high level.[12]

As there are still many unanswered questions about HCV itself and the immune responses it induces, there is currently no vaccine developed for the disease. As a result, prevention and control rely primarily on the successful interruption of viral transmission and the management of cases. Treatment with interferon alone or combined with ribavirin has been shown to be effective in some cases, especially with the combination therapy for infections caused by certain genotypes of HCV.[13]

In Canada, surveillance and studies for HCV infection have been actively carried out to assess the risk of hepatitis C, to identify the major factors affecting the transmission of HCV, and to determine effective intervention measures for control of the disease.

Public health surveillance of hepatitis C in Canada

Public health surveillance for hepatitis C in Canada consists of the reporting of identified cases, enhanced surveillance and targeted research.

By January 1999, hepatitis C became reportable in all provinces and territories across the country. To determine the current status of surveillance activities for hepatitis C in different jurisdictions, a survey of the 12 provincial and territorial epidemiologists was conducted by Laboratory Centre for Disease Control (LCDC) in 1998. According to the survey, positive laboratory testing results were the criteria to stimulate reporting, with confirmed anti-HCV in all and HCV-RNA or seroconversion in some jurisdictions. Confirmatory testing was done either in central provincial laboratories, designated hospital laboratories or the federal laboratory. Health care sectors that must report HCV infections were laboratories (10 jurisdictions), physicians (11 jurisdictions), hospitals (8 jurisdictions) and the blood services (9 jurisdictions). A database had been set up for hepatitis C in 11 jurisdictions and duplicates had been checked in all 10 jurisdictions that answered this question.

While the nationwide reporting of hepatitis is important for the surveillance of hepatitis C, the data collected from such reporting are limited due to the nature of the infection, e.g., asymptomatic in most infections, the slow progression of the dis-

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ease, and the lack of a laboratory test to differentiate acute infection from remotely acquired infection. Likely, most of the reported hepatitis C cases have been remotely acquired infections.

To overcome the difficulties, at least in part, enhanced surveillance activities have been and are currently being carried out by LCDC in collaboration with certain regional health authorities to further define the risk of hepatitis C in Canada. Between 1993 and 1995, a sentinel health unit surveillance project was implemented involving eight health units across the country. In October 1998, an enhanced surveillance project was initiated in four health regions (Calgary Regional Health Authority, Capital Health of Edmonton, Winnipeg and the Ottawa-Carleton Health Department). In this enhanced surveillance, special effort was made to identify acute hepatitis C cases among all cases reported by laboratories, physicians, public health professionals and hospitals. Standardized case definitions (see footnote to Figure 4) and an investigational protocol including questionnaires were used to ensure consistency and comparability of data across regions or health units. In addition to clinical and laboratory information essential for the differentiation of acute versus chronic or remotely acquired cases, epidemiological data including risk factors potentially associated with the transmission for each case were also collected through case interview.

Furthermore, special research projects were carried out by public health agencies, physicians and university researchers in Canada to address specific research questions related to hepatitis C, including major transmission routes or risk behaviours, special population groups at higher risk, and long-term outcomes of HCV infection through follow-up of certain cohorts of the population.

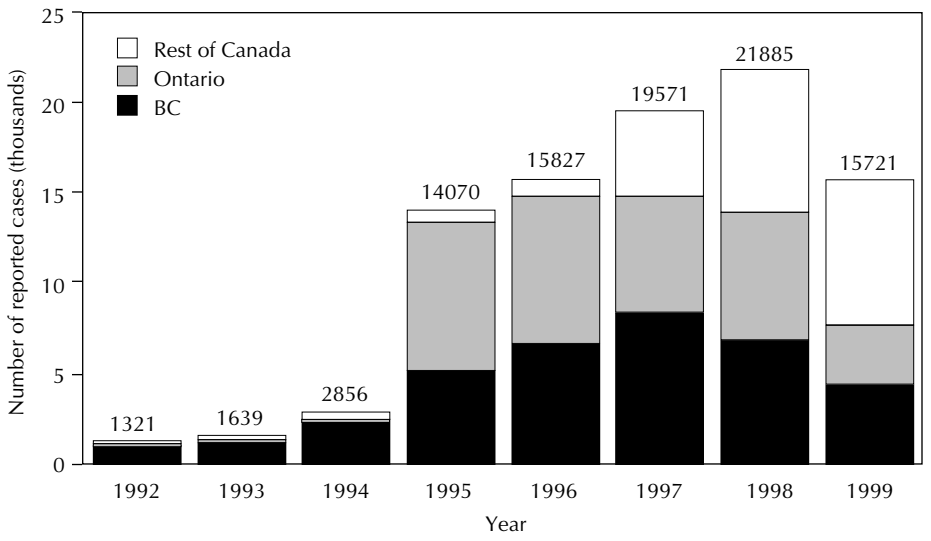

Figure 1. Annual nationally reported cases of hepatitis C infection in Canada by selected provinces, 1992-1999 (1999 incomplete).

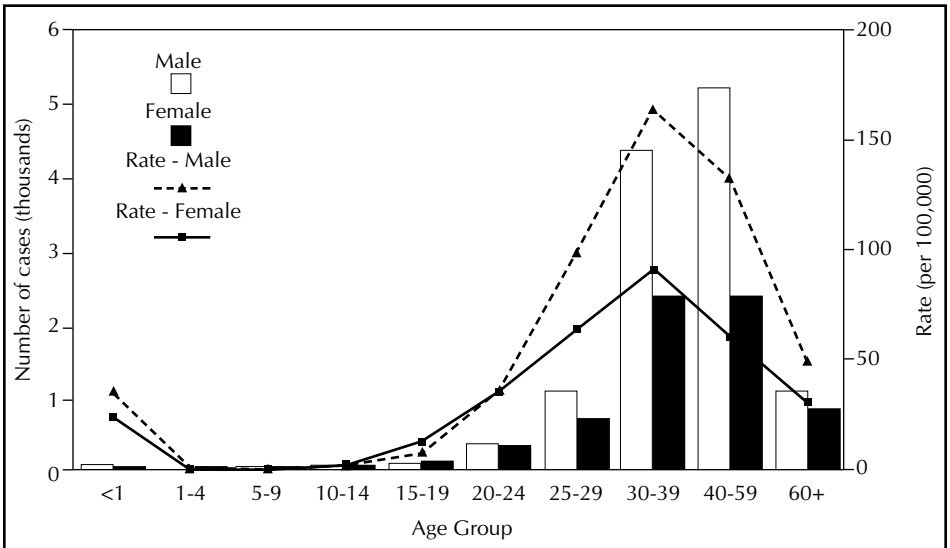

Figure 2. Number of nationally reported hepatitis C cases and rates in Canada by gender and age, 1997.

Prevalence and incidence of hepatitis C

Nationally Notified Cases of Hepatitis C

Reporting of hepatitis C started in British Columbia in 1992 and gradually more provinces began to report the disease. Figure 1 shows the number of reported cases each year in British Columbia, Ontario and the rest of the country (data source: Division of Surveillance, LCDC). The case definition employed was confirmed anti-HCV seropositivity. Data for 1999 are incomplete. While there has been an exponential increase in the number of reported cases over time, this is primarily a result of increasing recognition and reporting of remotely acquired cases as opposed to an epidemic of new infections.

Regional differences in reported hepatitis C cases exist across jurisdictions. Of the 19,571 cases reported in 1997, 42.3% (8,286) were from the province of British Columbia (BC) and 33.1% (6,472) were from Ontario. Due to variations in reporting practices, comparison of rates of reported cases among jurisdictions may not be reasonable.

The age distribution of the reported cases of hepatitis C showed that the age-specific rates were very low in infants and children, gradually climbing to a peak rate among those 30-39 years of age and declining thereafter (Figure 2, data source: Division of Surveillance, LCDC). As indicated above, these reported cases are largely prevalent cases and the bulge among those

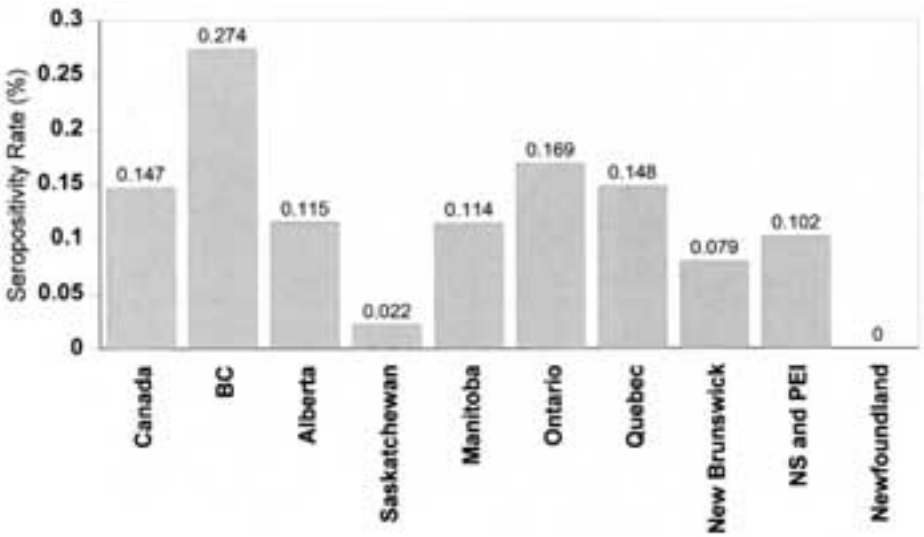

Figure 3. Hepatitis C seropositivity rate (%) among first-time blood donors in Canada and the provinces, 1997.

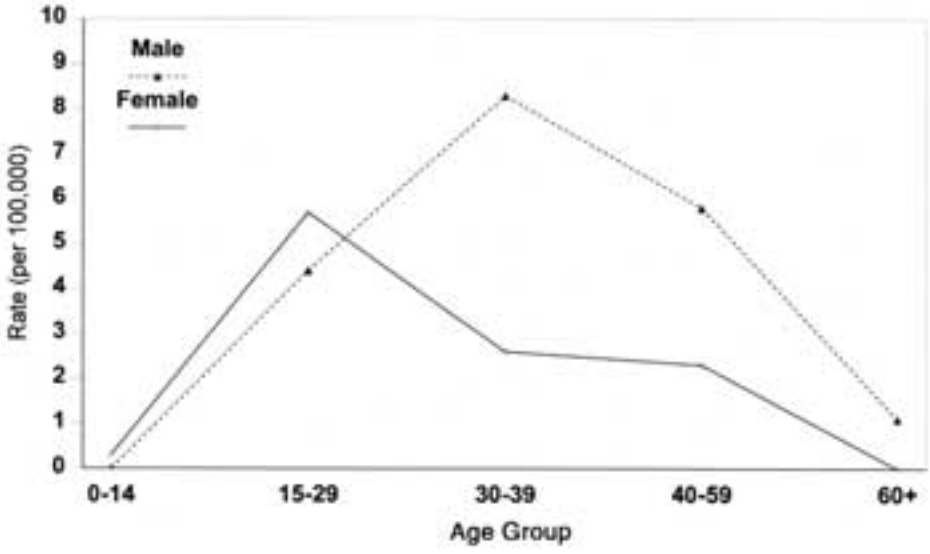

Figure 4. Incidence rates of acute hepatitis C in Canada by gender and age, 1998-1999, from enhanced surveillance in four health regions: Calgary, Edmonton, Winnipeg and Ottawa-Carleton

30-39 and 40-59 years old may represent infection acquired in the 1960s and 1970s. Males have close to twice the reported rate of females (83.3 vs 45.6 per 100,000); males have higher rates in all age groups beyond 20-24 years. Nevertheless, rates by age follow a similar pattern for males and females.

Prevalence of Hepatitis C

Remis et al.[14] estimated from available data that the prevalence of anti-HCV positivity was approximately 0.8% (0.68-0.94%) in Canada, with 0.96% in males and 0.53% in females. Those in age groups <5 years, 6-14 years, 15-19 years, 20-39 years, 40-64 years, and 65+ were estimated to have a prevalence rate of 0.2%, 0.05%, 0.10%, 1.51%, 0.75% and 0.6%, respectively. Based on the positive rates of anti-HCV among first-time blood donors from different jurisdictions, it was further projected that the anti-HCV prevalence rate (%) in each province was 1.36, 0.91, 0.43, 0.54, 0.94, 0.49, 0.37, 0.51, 0.25, and 0.08 for British Columbia, Alberta, Saskatchewan, Manitoba, Ontario, Quebec, New Brunswick, Nova Scotia, Prince Edward Island, and Newfoundland, respectively. Figure 3 shows the seropositivity rates for first-time blood donors in 1997 (Canadian Red Cross, unpublished data). While the rates are low, there are evident differences among the provinces with BC having the highest seropositive rate (0.27%) and Newfoundland having the lowest (0.0%).

The prevalence of HCV infection is much higher in certain at-risk population groups. For example, Strathdee et al.[15] showed that 88% of 1,006 injection drug users in Vancouver who had injected illicit drugs in the previous month were positive for anti-HCV. Inmates in prisons were found to have anti-HCV positive rates in the range of 28-40%.[16,17] A study of 437 street youth in Montreal indicated a prevalence of 12.6% (Roy et al., Hepatitis B and C among street youth in Montreal - final report, 1997) whereas another study of street youth in Ottawa showed a lower prevalence of 4%.[18] Finally, in a northern Alberta dialysis population, the prevalence of hepatitis C infection was 6.5%.[19]

Incidence of Hepatitis C

As indicated earlier, the rates of reported hepatitis C cases from the national reporting data over time were affected by increasing recognition and reporting of remotely acquired cases. To assess the occurrence of acute hepatitis C in Canada, an enhanced surveillance system was initiated in four health regions: Edmonton and Ottawa-Carleton in October 1998, and Calgary and Winnipeg in January 1999. The four regions cover a population of approximately 3 million, or 10% of the total population in this country. According to preliminary data collected up to October 1999, the incidence rate of recognized acute hepatitis C was 3.2 per 100,000 person years in these four regions. Males had higher incidence rates than females except in the 0-14 and 15-29 age groups (Figure 4). Incidence of acute hepatitis C peaked at 30-39 years of age for males and 15-29 years for females (Figure 4). There were substantial regional variations among the four regions with the highest incidence rate being in Edmonton at 6.7 per 100,000

person-years, followed by Winnipeg, Calgary and Ottawa-Carleton at 3.7, 2.2 and 0.5, respectively. Note that these were identified clinically recognized acute cases with symptoms, elevated liver enzyme and positive anti-HCV test results.

Based on the incidence data from this enhanced surveillance in the four health regions from October 1998 to October 1999, namely, 3.2 per 100,000 person-years for acute hepatitis C, an extrapolation to the entire population of Canada would suggest that an estimated 1,000 cases of clinically recognized acute hepatitis C could be identified annually in Canada. However, this is a conservative estimate as not all acute cases would have been recognized and not all clinically recognized acute cases would have been identified by this enhanced surveillance. Nevertheless, these data provide a consistent and comparable measure across these four jurisdictions.

Transmission patterns and risk factors

A few studies have looked at transmission patterns and risk factors for hepatitis C. In a report of a series of 63 consecutive patients by Scully et al.,[20] 43% of infections could be attributed to injection drug use and 33% to blood use. Among 54 cases reported in Prince Edward Island (PEI) from 1991 to 1995 and followed up by the Chief Medical Officer of Health, 46% were attributed to injection drug use, 39% to blood use, 6% to both and for 9% a risk factor was not identified.[21] In the Capital Regional District, British Columbia (BC), among 698 anti-HCV positive general population cases reported to the public health department in 1995 and 1996, 69.6% admitted to intravenous drug use and 16% to receipt of blood (LCDC, unpublished data).

Among the 720 community cases from eight health departments (Edmonton, Guelph, Kelowna, Kingston, Prince Edward Island, Saskatoon, Sherbrooke and Winnepeg) cooperating in the Sentinel Health Unit Surveillance Study from October 1993 to March 1995, 68% admitted to injection drug use and 30% to therapeutic blood receipt. For the 585 persons for whom full information was known, 67% had injection drug use (IDU) but not blood exposure, 17% had IDU and blood exposure, 6% had blood exposure but not IDU and 9% had neither (LCDC, unpublished data).

TABLE I
Distribution of Mutually Exclusive Risk Factors for Acute Hepatitis C*

Risk Factor	No. of Cases	% of All Cases	% of Cases with Known Risk Factors
Injection drug use	32	46.4	60.4
Drug snorting	3	4.3	5.7
Blood contact	1	1.4	1.9
Blood transfusion	1	1.4	1.9
Haemodialysis	1	1.4	1.9
Tattooing	2	2.9	3.8
Body piercing	2	2.9	3.8
Incarceration	2	2.9	3.8
Sex with hepatitis C	2	2.9	3.8
Hepatitis C in family	3	4.3	5.7
Hospitalization	2	2.9	3.8
History of dental visit	2	2.9	3.8
Unknown	16	23.2	
Total (w/o unknown)	53		100
Total (with unknown)	69	100	

* from enhanced surveillance, Oct. 1998 - Oct. 1999, in Calgary, Edmonton, Winnipeg and Ottawa-Carleton.

In addition to an assessment of the magnitude of acute hepatitis C cases, potential routes of transmission for each identified case were also investigated in the enhanced surveillance described previously by interviewing identified cases. For analysis of potential transmission routes, a ranking of risk factors was compiled according to available epidemiological information. From October 1998 to October 1999, 95 acute hepatitis C cases were identified, of whom 69 were interviewed (72.6%) for history of risk factors during the six months prior to the onset of the disease. Table I shows the distribution of risk factors reported by acute hepatitis C cases. Among the 53 acute hepatitis C cases who reported one or more risk factors, 60.4% (32) reported a history of IDU, among whom 78% (25) reported sharing needles. Higher frequency of IDU history was reported among those who were 15-39 years of age (67.7%), female (68.4%) and born in Canada (62.0%). One of the 69 cases reported a history of blood transfusion (see below in discussion). Finally, sex with HCV-infected individuals was identified as a risk factor for only 2.9% (2/69) of the acute hepatitis C cases.

Nine hundred and five (905) of the 2,505 identified chronic or likely chronic hepatitis C cases were also interviewed for risk factor information. Of 885 cases who reported one or more risk factors, 55.5% reported having ever injected drugs and 7.0% having ever snorted drugs without IDU. History of blood transfusion before 1990 was identified as a potential risk factor for 20.9% of these 885 cases. However, bias could have existed due to the fact that only 36.1% of chronic or likely chronic cases were interviewed and a disproportionately higher number of injection drug users might not have been interviewed. Nevertheless, a higher proportion of chronic cases reported a history of blood transfusion in comparison with acute hepatitis C cases.

Taken together, the data presented above indicate that injection drug use and blood exposure were the two most important routes of transmission for hepatitis C. However, injection drug use is the single most important route of HCV transmission currently in Canada, accounting for at least 60% of all HCV transmissions.

Prediction of hepatitis C burden in Canada

To assess the current risk of hepatitis C in Canada and to predict the burden this disease may pose to Canadian society in the near future, expected numbers of persons at different stages of the disease currently and in the next decade were estimated by simulation using a published hepatitis C natural history model with no treatment effect being applied (LCDC, unpublished analysis). Based on the estimate that 240,000 persons are currently infected

with hepatitis C virus in Canada,[14] the simulation analysis showed that the number of prevalent hepatitis C cirrhosis cases would likely double (increasing by 92%) from 1998 to the year 2008. It was also projected that the number of prevalent cases of liver failure and hepatocellular carcinoma related to hepatitis C would be expected to increase by 126% and 102%, respectively, for the same period. The number of liver deaths associated with hepatitis C would be expected to increase by 126% in 10 years. The medical and social care systems in Canada may not be ready to support these large increases.

It should be noted that these predictions are based on currently available data and the progression probabilities in the natural history model that were used in the simulation. Most recently, Seeff et al.[22] published their results of a 45-year follow-up of hepatitis C virus infection in healthy young adults. Their findings suggest that healthy HCV-positive persons may be at less risk for progressive liver disease than is currently thought. If the results are confirmed by other studies with representative HCV-infected populations and adequate sample sizes, the above predictions may need to be revisited.

In addition to patients with sequelae from existing hepatitis C cases, an estimated 1,000 clinically recognized acute hepatitis C cases will be identified annually in Canada, according to data from the enhanced surveillance system (see above). Based on the proportion of asymptomatic HCV infections (approximately 75% of all HCV infections), 4,000 new HCV infections may be expected each year in Canada; this does not take into account underreporting.

These results highlight the importance of both the control of disease progression of HCV-infected persons and the primary prevention of hepatitis C infections in this country.

Prevention and control of hepatitis C in the new era

Prevention and control of hepatitis C involves prevention of HCV infection, slowing disease progression, and reducing the likelihood of premature death. As indicated above, the transmission of hepatitis C has evolved from an illicit drug use and blood safety issue to an issue associated with illicit drug use and other likely routes of transmission. Accordingly, strategies for the prevention and control of hepatitis C have to change to effectively cope with the challenges in the new era. In October 1998, LCDC held a national consensus conference in Ottawa: *Hepatitis C - Prevention and Control: A Public Health Consensus* and a report was published.[23] The report provides a general guide for activities to be utilized across the country for the prevention and control of hepatitis C.

Prevention of Disease Transmission

This includes preventing transmission of HCV through high-risk behaviours such as the sharing of needles and other gear (injection drug use), preventing transmission through blood or blood components, organs, tissues, semen, unsafe medical or health care practices, as well as reducing the likelihood of blood and body fluid exposure in health care settings or through contaminated personal hygiene items.

For injection drug use, it is realized that effort should be made on different fronts to reduce the transmission of HCV and other bloodborne pathogens. These include prevention of initiation, harm reduction among illicit drug users, programs targeting special population groups at higher risk for injection drug use and for hepatitis C such as street youth, and research to explore new ways to contain the spread of HCV through illicit drug use. At the federal level, an interdepartmental committee has been working with different partners to collectively tackle the issue of drug abuse. This will not only benefit the prevention of HCV infection but will also help to reduce the transmission of other bloodborne pathogens such as human immunodeficiency virus (HIV) and hepatitis B virus (HBV).

Although the risk associated with blood, blood components and blood products is currently very low (less than 1/100,000), it is nevertheless essential to ensure the highest safety possible with these products because of their potentially disastrous impact should they be contaminated with HCV. In Canada, the Canadian Blood Services (CBS) and HemaQuebec (HQ) are responsible for blood donor screening, blood collection, and distribution. The Therapeutic Products Programme (TPP) of Health Canada is the regulatory body for the safety of blood and blood products, whereas LCDC is responsible for surveillance and risk assessment for blood and blood products. A Transfusion Transmitted Injuries Surveillance System is being piloted by LCDC in collaboration with certain provinces and the blood agencies (CBS and HQ). Once established, the system will be able to monitor transfusion-transmitted injuries including bloodborne infections among recipients to assess the risk of these injuries.

For nosocomial, occupational, and other inapparent parenteral transmission routes of HCV, LCDC has prepared several guidelines for the prevention and control of HCV transmission through these routes. These include *An Integrated Protocol to Manage Health Care Workers Exposed to Bloodborne Pathogens,*[24] *Proceedings of the Consensus Conference on Infected Health Care Workers: Risk for Transmission of Bloodborne Pathogens,*[25] and *Infection Prevention and Control Practices for Personal Services: Tattooing, Ear/Body Piercing, and Electrolysis.*[26]

Counselling of anti-HCV positive persons to prevent transmission is another component of primary prevention.[23] HCV-infected women of childbearing age should be informed that there is a risk of transmission to any infants born, that the risk increases if a woman is infected with both HIV and HCV, and that the infants should be tested for infection. Household contacts of HCV-infected people should not share their personal hygiene items. Household contacts should take "common sense measures" to protect themselves from exposure to the blood of an infected person. Although the risk may be low, HCV can be transmitted through sexual activities especially with risky sexual behaviours such as unprotected sex with multiple partners. The Canadian Liver Foundation is preparing a brochure for hepatitis C-infected individuals, with support from Health Canada and the Canadian Association for the Study of the Liver. The brochure should also serve as a source of general

information about the infection, the disease and the measures to prevent transmission of the virus.

Prevention of Disease Progression and Management of Hepatitis C Cases

This includes reduction of consumption of alcohol, consideration of vaccination against other hepatitis viruses such as hepatitis A virus, and treatment with interferon and ribavirin. The Canadian Association for the Study of the Liver (CASL) has prepared a guideline for the management of hepatitis C cases[13] which is available on the CASL website (http://www.lhsc.on.ca/casl/cont.htm).

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