

Hepatitis C



Communicable Disease Control Branch

1. Case Definition

Confirmed case that does not distinguish acute from chronic infection (1):

- Detection of anti-hepatitis C antibodies in blood (anti-HCV Ab) by enzyme immunoassay (EIA), confirmed by nucleic acid test (NAT) for hepatitis C virus RNA (HCV RNA), immunoblot or by a second manufacturer's EIA^a
- OR
- Detection of HCV RNA in blood

2. Reporting Requirements

2.1 Reporting to Manitoba Health and Healthy Living

- All positive laboratory results described above under "Case Definition" are reportable to the Communicable Disease Control Branch, Public Health Division, Manitoba Health and Healthy Living.
- All cases (acute and chronic) are reportable to the Communicable Disease Control Branch, Public Health Division, Manitoba Health and Healthy Living by the attending health care professional when it is believed that the cases will not be reported by laboratory.
- Cases are referred by Manitoba Health and Healthy Living to the regional health authority (RHA) of residence for follow-up.
- The *Manitoba Health and Healthy Living Investigation Form for Hepatitis B and C Positive Cases* should be completed for all clients testing positive (this applies to all cases new to Manitoba) and forwarded to the Communicable Disease Control Branch, Public Health Division, Manitoba Health and Healthy Living.

- Operators of Manitoba clinical laboratories are required to submit the residual serum or plasma specimens from individuals who tested positive for hepatitis C virus to Cadham Provincial Laboratory within seven days of report.
- Positive test results identified through the local Canadian Blood Services are reportable to the Communicable Disease Control Branch, Public Health Division, Manitoba Health and Healthy Living.

2.2 Reporting to Canadian Blood Services

- If there is reasonable possibility that the source of infection in a client testing positive for hepatitis C is the receipt of blood or blood products or there is a history of blood donation, Manitoba Health and Healthy Living will inform Canadian Blood Services.

3. Clinical Presentation/Natural History

Initial (acute) infection with hepatitis C virus (HCV) is mild or asymptomatic in more than 90 per cent of cases (2). When symptoms occur, they may include fatigue, anorexia, nausea and vomiting, jaundice and vague abdominal discomfort (2, 3). Symptoms usually subside after several weeks (4). While the signs and symptoms of HCV infection are indistinguishable from those of hepatitis A or hepatitis B virus (HBV) infections (5), jaundice, abnormalities in liver function tests and extrahepatic manifestations are less frequent in HCV infection (2, 5, 6). Abnormalities in liver function tests generally are less pronounced in patients with HCV infection than in patients with HBV infection (5). Extrahepatic manifestations are not prominent in acute HCV infection (6).

^a In the event of a discrepancy between the two EIA tests (when EIA is used as a confirmatory test), NAT for HCV RNA or immunoblot should be performed and the specimen considered positive or negative based on the NAT or immunoblot result.

Chronic Infection: The lack of an effective T-lymphocyte response and the high propensity of the virus to mutate appear to promote a high rate of chronic infection (4). Chronic HCV infection develops in 75 to 85 per cent of HCV-infected individuals (7). Spontaneous clearance of HCV infection appears most frequently with younger age, female gender and specific major histocompatibility complex genes (4).

Sixty to 70 per cent of chronically infected persons have evidence of active liver disease; however, the majority of infected persons might not be aware of their infection because they are not clinically ill (8). The most commonly reported symptom of chronic HCV infection is fatigue (9). Children with chronic infection are usually asymptomatic (5).

The most important sequelae of chronic HCV infection are progressive liver fibrosis leading to cirrhosis, end-stage liver disease and hepatocellular carcinoma (HCC) (4). Alcohol is an important cofactor in the progression to cirrhosis and HCC in persons with HCV liver disease (4). These long-term complications generally occur more than 20 years after the onset of infection, although more rapid progression has been reported (6). It is not known why only some immunocompetent persons with chronic hepatitis C develop cirrhosis (6). Virologic factors including viral load, viral genotype and quasi-species diversity may significantly affect the risk of progression of liver disease (4). Relatively little is known about how chronic HCV infection leads to cancer (6).

Co-infection with HIV or the parasite *Schistosoma* (Schistosomiasis) has been associated with viral persistence (6). Concurrent chronic hepatitis B infection appears to increase the risk of progressive liver disease (4).

4. Etiology

Hepatitis C virus, identified in 1989 (10), is a small, enveloped, single-stranded RNA virus that is a member of the Flaviviridae family (5). Multiple HCV genotypes and subtypes occur (5). Genotype 1 is the most common genotype reported in Canada (3).

5. Epidemiology

5.1 Reservoir and Source

Humans; the virus has been transmitted experimentally to chimpanzees (2). Injection drug users are the most common reservoir for new infections (11). The duration of HCV viability in the environment is at least 16 to 23 hours (7).

5.2 Transmission

Hepatitis C virus is usually transmitted by percutaneous exposure to HCV-infected blood (6). In economically developed countries, most new HCV infections are related to illicit injection drug use (6). Current or past injection drug use (IDU) accounts for more than 56 per cent of all reported HCV infections in Canada. (11). Sharing of equipment for inhalation drug use (e.g., crack pipes, straws, etc.) has also been associated with HCV transmission (12). HCV may be transmitted by other percutaneous exposures not associated with drug use (e.g., tattooing or syringe reuse) (6).

In the past, HCV transmission via contaminated blood transfusions was common (6, 12). Currently the risk of acquiring HCV infection from the receipt of donated blood or blood products in Canada is very low (approximately one in 3,100,000 per unit component) with current donor screening and viral inactivation/reduction processes (13-15).

Sexual transmission among monogamous couples is uncommon (5). Sexual activity during menstruation may increase the risk of transmission (10). It is unknown whether sexual transmission of HCV might be increased with concurrent HIV infection or other sexually transmitted infections (8).

Transmission among family contacts is uncommon, but could occur from direct or inapparent percutaneous or mucosal exposure to blood (5). There is no evidence of HCV transmission with kissing, hugging, sneezing, coughing, food, water, sharing eating utensils or drinking glasses, casual contact or other contact without exposure to blood (4).

The risk of perinatal transmission is approximately two per cent for infants of anti-HCV Ab seropositive women (4). When a pregnant woman is HCV RNA positive at delivery, this risk increases to four to seven per cent (4). Both intrauterine and intrapartum transmission of HCV have been described (16). Maternal co-infection with human immunodeficiency virus (HIV) has been associated with increased risk of perinatal transmission of HCV (5). Although HCV RNA and antibody to HCV (anti-HCV Ab) have been detected in colostrum, breastfeeding has not been shown to be a risk for HCV transmission from an infected mother to an infant (5).

Nosocomial exposure through contaminated needles and syringes is a leading cause of infection in developing countries, but rare where resources are adequate and appropriate health care practices are followed (6). There are isolated reports in developed countries linking health care procedures to transmission of HCV from infected to susceptible individuals when appropriate practices have not been followed (17, 18). The risk for HCV transmission from an infected health care worker to patients appears to be low (19). HCV is not transmitted efficiently through occupational exposures to blood; the average incidence of anti-HCV seroconversion after accidental percutaneous exposure from an HCV-positive source is 1.8 per cent, with one study indicating that transmission occurred only following injury with hollow-bore needles (7).

5.3 Occurrence

General: Worldwide, it is estimated that approximately 130 to 170 million individuals (approximately two to three per cent of the world population) are chronically infected with HCV (2). Most populations in Africa, the Americas, Europe and Southeast Asia have anti-HCV prevalence rates under 2.5 per cent (2). Prevalence rates for the Western Pacific regions average 2.5 to 4.9 per cent (2). In the Middle East, the prevalence of anti-HCV ranges from one per cent to more than 12 per cent (2). The highest seroprevalences of HCV infection (60 to 90 per cent) occur in individuals with large or repeated direct percutaneous exposure to blood or blood products such as injection drug users (5).

Canada: It is estimated that the prevalence of HCV infection in Canada is 0.8 per cent to one per cent, is increasing over time (11) and that 250,000 Canadians are chronically infected with HCV (3). Perhaps only 65 per cent of the estimated cases in Canada have been identified (11). Approximately 20 per cent of reported hepatitis C infections in Canada occur in the immigrant community, 13 per cent are from transfusion of blood products (prior to donor screening)^b and 56 per cent in current or past injection drug users (11). Reported HCV infection rates vary among the provinces. In 2007, highest rates were found in the Yukon (132.3 per 100,000) and British Columbia (65.3 per 100,000) (20). The lowest rate in 2007 was found in Newfoundland (18.8 per 100,000) (20). Manitoba's rate in 2007 (29.4 per 100,000) was below the national average (35.8 per 100,000) (20).

Manitoba: The number of reported cases newly diagnosed in Manitoba was 329 for 2006 and 349 for 2007 (21). For most cases, it was not known whether they were acute or chronic at the time of reporting. Since 1999, 65 per cent of reported cases occurred in the 30-to-49-year age group (21). The lowest incidence of reported infection with HCV during this time period was in children under one year of age and 62 per cent of all cases reported were in males (21). As many asymptomatic cases would not be detected and reported, the true number of cases in Manitoba is likely higher than those reported.

5.4 Incubation Period

The incubation period for HCV disease averages six to seven weeks, with a range of two weeks to six months (5). The time from exposure to development of viremia is generally one to two weeks (5). Long-term complications (e.g., cirrhosis and HCC) generally occur more than 20 years after the onset of infection, although more rapid progression has been reported (6).

^b Donor screening for anti-HCV, which detects antibodies to hepatitis C (implemented in 1990) and donor screening by a nucleic acid test (NAT) which detects the actual hepatitis C virus (implemented in October 1999) (24).

5.5 Host Susceptibility and Resistance

All humans are susceptible (2). It is not known whether protective immunity develops following infection (2). Repeated infections with HCV have been demonstrated in an experimental chimpanzee model (2).

5.6 Period of Communicability

Communicability begins from one or more weeks before onset of symptoms (2). All individuals with HCV infection should be considered infectious (5).

6. Diagnosis

NOTE: Where the testing for HCV is being done pursuant to an order issued under *The Testing of Bodily Fluids and Disclosure Act*, see Manitoba Health and Healthy Living's *Integrated Post-Exposure Protocol for HIV, HBV and HCV: Guidelines for Managing Exposures to Blood and Body Fluids* for testing procedure.

Cadham Provincial Laboratory (CPL) performs serological and nucleic acid testing for HCV in clinical specimens. Currently available laboratory tests cannot distinguish acute from chronic HCV infection (17).

The initial screening test for detection of HCV infection is an enzyme immunoassay (EIA) test which detects antibody to HCV (anti-HCV Ab). A positive anti-HCV Ab test may be an acute, chronic or resolved infection. It may take 12 to 14 weeks or longer after infection with HCV for the antibodies to be detected. A positive result from the EIA test is confirmed with either a recombinant immunoblot (antibody) assay (RIBA) or nucleic acid testing (NAT) for HCV nucleic acid (HCV RNA). Only confirmed positive results are reported.

HCV RNA testing (NAT) can detect the presence of HCV infection as early as one to three weeks after exposure and may be indicated in the following circumstances:

- For individuals undergoing testing who are suspected to be in the “window period” (i.e., infected but not yet producing detectable antibody)

- For immunocompromised individuals who may not develop detectable anti-HCV Ab (e.g., HIV infection with CD4 counts < 50)
- For infants younger than 18 months of age (refer to section below)
- To predict the likelihood of response to antiviral therapy and to monitor the response to antiviral therapy (22)

Determination of the viral genotype may be useful in predicting the duration of and response to therapy (6). HCV genotyping in clinical specimens is performed by CPL.

Infants younger than 18 months of age: There is passive transfer of maternal HCV antibodies to infants, so the diagnosis of infant HCV infection must be based on detection of viral RNA or on the persistence of antibody after 18 months of age (6). Cord blood should not be used to test for HCV because of potential cross-contamination with maternal antibody (1). The recommended laboratory test for otherwise well infants born to HCV-infected mothers is anti-HCV Ab, performed at 12 to 18 months of age. A positive test obtained prior to 18 months must be repeated at 18 months to confirm that it is still positive (16).

HCV RNA testing might be considered after two months of age, in consultation with an appropriate specialist and in select circumstances (e.g., significant parental anxiety, concern that the infant will be lost to follow-up care) (16). However, as false negatives may be observed with HCV RNA testing, a negative HCV RNA test should be confirmed by performing anti-HCV Ab testing at or after 18 months of age.

Testing of co-infected infants (HIV, hepatitis B) may be more complex and should be conducted under the guidance of an appropriate specialist.

7. Key Investigations

- Efforts to identify the potential source of acquisition of infection by the case and any subsequent transmission from the case to contacts.

- Interviewing cases for contact identification if applicable.

8. Control

For the purposes of this protocol, “Public Health” refers to provincial regional public health authorities as well as First Nations Inuit Health.

8.1 Management of Cases

NOTE: It is recommended that interviewing for contact information be done by the first health professional (e.g., physician, public health nurse) who interviews the case as there may not be a subsequent opportunity to do so.

- Immunization against hepatitis A virus (HAV) and hepatitis B virus (HBV) is recommended for all HCV cases who have not been previously immunized or infected with HAV and/or HBV (23). Individuals testing positive for hepatitis C for the first time are routinely screened by CPL for hepatitis A and hepatitis B.
 - Where testing indicates susceptibility to both HAV and HBV, the combined or bivalent hepatitis vaccine (offering protection against both hepatitis A and hepatitis B) is recommended (24).
 - Where the case is susceptible to HAV but not HBV, the monovalent hepatitis A vaccine is recommended.
 - Where testing indicates that the case is susceptible to HBV, but not HAV, the monovalent hepatitis B vaccine is recommended.
- When indicated, Manitoba Health and Healthy Living provides the vaccines at no charge to HCV-infected individuals. Refer to the most recent edition of the *Canadian Immunization Guide* for vaccine schedules and clinical use information.
- Hepatitis A, B and combined A/B vaccines are available in adult and pediatric formulations and may be ordered using the Biologics/Vaccine Order Form. A current Biologics/Vaccine Order Form is available at www.gov.mb.ca/health/publichealth/cdc/protocol/index.html#forms or by calling the Provincial Vaccine Warehouse (weekdays 8:30 a.m.-5 p.m.) at 204-633-2621 or 800-665-7315; fax: 204-694-2380. After 5 p.m., call 204-781-5342.
- Post-immunization testing for antibody to hepatitis B virus (anti-HBs), one to two months following receipt of the third dose of hepatitis B vaccine is recommended only when there is likely to be repeated exposure to hepatitis B (e.g., injection drug user) to confirm development of a protective response (≥ 10 IU/L). If results are < 10 IU/L, a second three-dose series of HBV vaccine should be completed, again followed by anti-HBs post-immunization testing (24, 25). The high response rate to hepatitis A virus (HAV) immunization makes routine post-immunization serologic testing unnecessary (24). HAV vaccine may have reduced efficacy in individuals who are immunosuppressed (24).
- HIV antibody testing with appropriate pretest and post-test counseling is recommended for HCV-infected clients (4).
- Cases should be advised to limit or avoid alcohol and not to initiate therapy with any new medicines (including OTC and herbals) without checking with their health care provider (8).
- HCV-positive women do not need to avoid pregnancy or breastfeeding (8). However, mothers who experience a flare of chronic HCV infection with postpartum jaundice or who develop cracked, bleeding nipples should abstain from breastfeeding (16).

- There is insufficient evidence to recommend caesarian section in HCV-positive women as a means of preventing transmission to the newborn (16).
- Individuals need not be excluded from work, school, play, child care or other settings on the basis of their HCV infection status (19).
- Although there is a theoretical risk of HCV transmission during contact sports, there are no firm recommendations for exclusion. The exception in Manitoba is boxing and other sports covered under boxing regulation 14 (1)(b) of *The Boxing Commission Act* (C.C.S.M. c. B80) where to be eligible to participate in a boxing contest, a boxer must within six months before the boxing contest, have negative tests for HIV, hepatitis B and C.

8.1.1 Treatment

- Factors considered in recommending treatment include favourable genotype, presence of hepatic fibrosis, patient motivation, symptoms, severity or comorbid illness and the patient's age (4).
- Treatment is often associated with significant side effects and is expensive, so it is recommended that HCV-infected patients be referred to the Viral Hepatitis Investigative Unit (VHIU) (204-787-3630) or appropriate specialist for treatment.
- Timing of treatment in the disease course is an important consideration; therefore, early referral is recommended.
- Loss or reduction in HCV RNA is the primary indicator of response to antiviral therapy; the resolution of elevated alanine aminotransferase (ALT) levels with antiviral therapy is also an indicator of disease response (4).
- Herbal remedies have not been shown to be effective (9).

8.1.2 Management of Infants Younger than 18 Months of Age

- Infected infants may be more likely than adults to have a transient infection that does not progress to chronic disease; therefore, no immediate intervention is recommended.
- HCV-infected infants should be referred to a specialist with expertise in HCV infection for further assessment and monitoring.

8.1.3 Public Health Investigation and Management

NOTE: Cases more likely to have poor outcomes (e.g., individuals with alcohol dependency or co-infected with HIV or HBV) or to transmit infection to others (e.g., injection drug users) should be given priority for public health follow-up.

Once a positive laboratory report of a newly detected case is received by the Communicable Disease Control Branch, Manitoba Health and Healthy Living, a referral is made to the appropriate regional health jurisdiction. It is recommended that the public health nurse responsible for the case liaise with the primary care provider before contacting the client. The purposes of this liaison are as follows:

- Confirm receipt of the referral.
- Verify the primary case manager.
- Determine the reason for the test. The primary care provider should be informed that HCV is reportable (completion of the *Manitoba Health and Healthy Living Investigation Form for Hepatitis B and C Positive Cases*) and of the requirements for public health investigation (i.e., patient education and interview, contact follow-up, provision of resources).
- Recommend referral of the case to the VHIU or appropriate specialist (if not already referred by primary care provider) for additional testing, investigation and possible treatment.

- Confirm who (primary care provider or Public Health) will advise on and provide case with immunization for HAV and/or HBV if indicated.
- Provide literature/information for the primary care provider and/or client.

Where possible, case follow-up should consist of an in-person meeting for the following purposes:

- education and recommendations regarding future management;
- contact identification and follow-up; and
- completion of the *Manitoba Health and Healthy Living Investigation Form for Hepatitis B and C Positive Cases*. If the primary care provider elects to manage the case on his/her own, he/she should complete the investigation form and return it to Manitoba Health and Healthy Living. The public health nurse may contact the client for further education and an interview. In many instances, the public health nurse responsible for the case will be expected to complete the investigation form.

8.1.4 Education of Cases

Cases should be educated about how hepatitis C virus is spread and advised on harm reduction measures to limit/prevent transmission to others. Specifically, it is recommended that cases:

- not share toothbrushes, razors or injection/inhalation drug use equipment (e.g., needles, pipes), or donate blood or organs.
- prevent their blood (e.g., cover open wounds) and other potentially infective body fluids from coming into contact with other individuals.
- know how to safely clean up blood spills.
- inform individuals providing health care or other personal services who may be exposed to their blood (e.g., piercing, tattooing) that they have been infected with HCV (9).
- limit or avoid alcohol consumption as alcohol consumption is a risk factor for more rapid progression to cirrhosis (6).
- advise their sex partners and practice safer sex (e.g., condoms) (3) due to the low, but possible risk of sexual transmission to partners.

8.2 Management of Contacts

- There is no effective post-exposure prophylaxis available for hepatitis C (26).
- Individuals who are contacts of injection drug users should be given priority for follow-up by Public Health.
- Generally, contacts with exposure within one year of the first positive test obtained from the index case should be followed up. However, there may be situations where more distant contact identification and notification are indicated depending on the period of infectivity, the significance of the exposure, the feasibility of notification and prioritization of contacts at risk.
- Needle-sharing partners who test negative for HCV should be re-tested every six to 12 months if needle-sharing continues.
- As most long-term sex partners of HCV-positive persons test anti-HCV Ab negative, long-term sex partners need not be followed by Public Health. However, sex contacts may choose to be screened for HCV by their health care provider.
- **Perinatal Contacts:** It is important to establish whether HCV was transmitted to the child to ensure appropriate medical follow-up of infected children, and to reassure the large majority of women (over 95 per cent) where transmission of HCV to their infants does not occur (16). It is recommended that perinatal contacts who are well not be tested for HCV until after one year of age. Additional testing (e.g., at 18 months) may be necessary to

confirm results obtained from earlier testing. Refer to section 6 for testing procedure.

8.3 Preventive Measures

- There is no vaccine or immune globulin product available to prevent HCV infection (6, 26).
- Individuals who are HCV-positive should refrain from donating blood, organs, tissues or semen, and sharing sharp items potentially contaminated with blood (e.g., razors, nail clippers, scissors, toothbrushes) (3).
- Use of condoms can minimize the risk of sexual transmission from an infected to an uninfected partner. If condoms are not used, avoidance of unprotected sexual intercourse during menses may limit transmission.
- Screening of individuals at high risk of infection including individuals with a history of injection drug use, incarceration, body piercing, tattooing, blood transfusion in Canada prior to April 1992 or any other high risk exposures (9). Early detection of HCV infection is important, so that treatment may be initiated if indicated and infected persons may initiate lifestyle changes to reduce other exposures that might increase the risk of liver damage (25). Response to treatment may also be enhanced in individuals with a shorter duration of infection (25).
- Identification of needle-sharing contacts and re-testing of contacts (who initially test negative for HCV) every six to 12 months if needle-sharing continues.
- Follow-up of individuals who have sustained an exposure to blood and body fluids (e.g., needlestick injury in a health care worker) and are deemed at risk of acquiring infection. See Manitoba Health and Healthy Living's *Integrated Post-*

Exposure Protocol for HIV, HBV and HCV: Guidelines for Managing Exposures to Blood and Body Fluids.

- Health care precautions:
 - routine practices including safe disposal of sharps
 - adequate sterilization of instruments used in invasive procedures, including personal care services (e.g., piercing, tattooing)
 - avoidance of personal care services where there may be a possibility of transmission through blood exposure (e.g., piercing, tattooing)
 - appropriate disinfection measures following body fluid spills
- Harm reduction activities:
 - The risk of HCV transmission through injection drug use (IDU) can be significantly reduced by use of a new needle, syringe and all other IDU equipment (e.g., filters, water, spoon) for each injection.
 - Harm reduction activities such as safe injection practices may help to reduce HCV transmission within injection drug using populations.
- Education of individuals at high risk of infection.

9. Additional Resources

- 9.1 Canadian Liver Foundation (www.liver.ca/Home.aspx)
- 9.2 Canadian Association for the Study of the Liver (www.hepatology.ca)
- 9.3 Cadham Provincial Laboratory Guide to Services (www.gov.mb.ca/health/publichealth/cpl/docs/manual2009.pdf)

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