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1.0 INTRODUCTION

In British Columbia (BC), all cases of Hepatitis C Virus (HCV) that have not yet been entered into the electronic public health information system require documentation, geographical attribution and consideration for follow-up care. This guideline aims to meet the needs of BC health care professionals who are following-up individuals with newly identified HCV infection.

To meet the needs of the Regional Health Authorities (RHA's) and the communities they serve, this document presents information in a flexible way, to encourage client engagement with the health care system. Follow-up may occur directly by public health personnel with a client or indirectly through a primary care provider who is already engaged with the client.

1.1 Authority

Hepatitis C virus is a reportable condition under the Public Health Act (2008) and Schedule A of the Health Act Communicable Disease Regulation.

BC Public Health Act (2008) is available at:
http://www.bclaws.ca/EPLibraries/bclaws_new/document/ID/freeside/00_08028_01

Schedule A is available at: http://www.bclaws.ca/EPLibraries/bclaws_new/document/ID/freeside/12_4_83

1.2 Rationale for HCV Follow Up

Follow up of newly identified HCV infections can contribute to positive outcomes for both the individual and the community. Clients who test positive for HCV can be engaged into care to provide information around treatment options, transmission prevention, education around lifestyle and diet, and other clinical considerations including immunization updates and screening for sexually transmitted infections. This is a key moment in which appropriate counselling can be offered for alcohol and substance use, including harm reduction services, overdose prevention and naloxone training, and opioid substitution therapies.

1.3 Goals

To provide public health personnel and primary care providers with information to:

- Prevent transmission of hepatitis C infection
- Prevent newly identified HCV cases from acquiring coinfections, including Human Immunodefiniciency Virus (HIV), Hepatitis B (HBV) and Hepatitis A (HAV)
- Provide education and counselling to individuals infected with HCV and their contacts
- Reduce harms associated with illicit drug use by connecting individuals with HCV, including people who inject drugs (PWID) or who engage in non-injection drug use (IDU), with harm reduction, prevention and support resources. This can include distribution sites for harm reduction supplies, supervised injection facilities, detoxification, opioid substitution therapies (e.g.Buprenorphine/ naloxone therapy, methadone maintenance therapy (MMT)), mental health and substance use services, and outreach programs.
- Educate newly infected HCV cases about the risk associated with HBV infection if engaging in high risk activities, such as IDU, having unprotected sex with multiple sexual partners and engaging in high-risk sexual behaviours (1, 2).
- Immunize for HBV to reduce morbidity rates of cirrhosis and hepatocellular carcinoma (HCC) associated with coinfection (3).

- Increase engagement of clients who have HCV infection and who are at risk of HCV infection, into the cascade of care (see Figure 6-1)
- Increase access to treatment for clients with HCV infection
- Prevent adverse sequale in infants born to mothers who have HCV infection, by timely identification of cases of HCV vertical transmission.

2.0 DEFINITIONS

Alanine aminotransferase (ALT)/Aspartate Aminotransferase (AST) - Enzymes produced by the liver. Increased levels indicate inflammation of the liver, but do not always correlate with the severity of the disease process.

Attribution – Refers to the geographic area (e.g. RHA, outside of BC) for surveillance reporting purposes.

Case – Defined here for the purpose of surveillance reporting of acute HCV infections. Clinical criteria is not required. Laboratory criteria:

- For adults, adolescents & children > 18 months:
  - Anti-HCV positive **or** HCV RNA positive
    AND
  - There is an anti-HCV negative test result on record in the prior 12 months
- For Children ≤ 18 months:
  - HCV RNA positive ≥ 4 to 6 weeks of age
    OR
    Anti-HCV positive at 18 months of age

Cases may be further staged depending on the type of electronic public health information system being used in the RHA.

Contact - A contact includes any individual who has had a percutaneous or mucosal exposure to the blood or blood products of a HCV-infected person.

Direct Acting Anti-Virals (DAAs) - Class of drugs used for hepatitis C treatment that target the HCV at various stages in the HCV lifecycle (4). Includes:

- NS3/4A Serine Protease Inhibitors (PI's) (e.g. Simeprevir, Paritaprevir)
- Nucleotide analog inhibitor of NS5B polymerase (e.g. Sofosbuvir)
- NS5A Protein Inhibitors (e.g. Ledipasvir and Ombitasvir)
- Non-Nucleoside NS5B Polymerase Inhibitors (e.g. Dasabuvir) (5)

Documentation – Recording of results and follow-up care provided to those testing for HCV. Guidelines may vary by RHA and agency.

Genotype - There are now 7 genotypes of HCV currently identified, of which genotypes 1, 2 and 3 are the most common in North America and BC. Knowing the genotype with which an individual is infected can help inform the nature and duration of treatment.

HCV Antibody Test (anti-HCV) - A HCV antibody test determines if anti-HCV is present in the serum. HCV antibodies are produced when an individual is exposed to HCV and usually remain present for life. Anti-HCV becomes detectable 5-10 weeks after infection, and confirms that the individual has been infected at some time. Nucleic Acid Testing (NAT) is required to confirm if active infection is present.

Iatrogenic – Unintentional and unfavourable response to a medical treatment or procedure caused by a healthcare provider.

Immunocompromised - Where the immune response is attenuated by the administration of immunosuppressive therapy, malnutrition or disease processes. In immune compromised individuals the immune system functions at less than normal capacity. Those who have HIV infection and CD4+ cell count ≤ 200 cells/mm^3, chronic kidney infection, or who have been on long-term immune suppressants may not be able to mount a normal antibody response to HCV. Those with agammaglobulinemia are unable to make their own antibodies.

Liver fibrosis - An accumulation of extracellular matrix proteins that are produced in excess, inefficiently broken down, or both. Normal liver cells are replaced with fibrous tissue and this leads to disruption of the normal liver function. Main causes include chronic hepatitis B or C infection, excessive alcohol intake (>2-3 drinks/day) and non-alcoholic steatohepatitis (NASH), which is associated with obesity, diabetes or metabolic syndrome. Autoimmune hepatitis can also lead to chronic liver inflammation. Symptoms may not be present unless there is severe damage to liver function (5).

May be classified according to a histologic scoring system, such as METAVIR (6):

- F0 = no fibrosis
- F1 = portal fibrosis without septa
- F2 = portal fibrosis with few septa
- F3 = numerous septa without cirrhosis
- F4 = cirrhosis

    - **Cirrhosis** - Progression of fibrosis to scarring and disruption of normally functioning structures in the liver. The presence of extensive 'bridging fibrosis' (fibrosis forming bridges between portal-vascular structures) on liver histology can confirm this diagnosis. It can be predicted by non-invasive investigations, such as by Fibroscan®. Advanced cirrhosis is supported by marked coagulopathy, portal hypertension, ascites and liver failure (6).

    The gold standard for determining the severity of liver damage is liver biopsy.

    Non-invasive alternative tools to measure liver fibrosis:

    - **Fibroscan® (Transient Elastography)** - Ultrasound method used to detect advanced fibrosis and cirrhosis. A transducer probe mounted on a vibrator transmits vibrations toward the liver. The velocities of the pulse echos that follow the vibrations directly correlate with liver stiffness. These results can be correlated with the METAVIR scoring system. Results can be influenced by hepatic inflammation, obesity (less reliable results in BMI ≥ 25-28 kg/m^2), ascites, narrow intercostal spaces, and increased central venous pressure (5,6).
    - **Aspartate Aminotransferase-to-Platelet ratio index (APRI)** - An indirect method used to predict significant and severe fibrosis or cirrhosis. Uses an AST level, platelet count, and the upper limit of a normal AST level (most labs use 40 IU/L). APRI score > 1.5 indicates significant fibrosis or cirrhosis, and APRI < 0.7 indicates no significant fibrosis (6).

$$\text{APRI} = \frac{\frac{\text{AST level}}{\text{AST (Upper Limit of Normal)}}}{\text{Platelet Count } (10^9/\text{L})} \times 100$$

For an online calculator, see http://www.hepatitisc.uw.edu/page/clinical-calculators/apri

(cont'd liver fibrosis)

- **FIB-4** - An indirect method used to help with liver fibrosis staging. Uses age, AST, ALT and platelet count. FIB-4 < 1.45 indicates no significant fibrosis, and FIB-4 > 3.25 is predictive of advanced fibrosis or cirrhosis (6).

$$\text{FIB-4} = \frac{\text{Age (years)} \times \text{AST (U/L)}}{\text{Platelet Count } (10^9/\text{L}) \times \sqrt{\text{ALT (U/L)}}}$$

For an online calculator, see http://www.hepatitisc.uw.edu/page/clinical-calculators/fib-4

Nucleic Acid Test (NAT, NAAT, PCR, HCV RNA) - The NAT (or nucleic acid amplification testing (NAAT)) can determine if active infection is present by detecting hepatitis C RNA (i.e. the virus' genetic material). Quantitative NAT or a viral load measures the amount of HCV RNA in the blood. HCV RNA becomes detectable at 1-3 weeks post exposure. It does not determine the severity of liver damage.

Percutaneous Exposure - Contact through the skin with blood of a HCV-infected person, for example, through needlestick or other sharps injury, tattooing, body piercing, electrolysis, or acupuncture. Non-intact skin exposure when blood or body fluid comes in contact with a wound <3 days old, or with skin having compromised integrity (e.g. dermatitis, abrasions, fresh cutaneous scratches, burns, or other lesions).

Perinatal Exposure - Infection of an infant at birth from a HCV-infected mother. The likelihood of transmission of infection to the infant is dependent on the viral load of the mother. The risk increases if the viral load is > 10^6 genome copies/mL as determined by a quantitative HCV RNA test. Coinfection with HIV in the mother may increase the odds of transmission to the infant by approximately 3-fold (7).

Period of Communicability - All persons who are anti-HCV reactive are considered infectious unless there is documentation of a resolved infection or virological cure by treatment.

Permucosal Exposure - Contact of the mucous membrane lining body cavities of eyes, nose, mouth, vagina, rectum or urethra with blood or body fluids of a HCV-infected person.

Resolved Infection - HCV infections may resolve either spontaneously, usually within 6 months of infection, or following a course of antiviral therapy, resulting in a sustained virological response (SVR) indicating that the patient has cleared the virus. Individuals with resolved infection typically have serum that is anti-HCV reactive, but have no detectable HCV RNA. Resolved infection is confirmed after one negative HCV RNA test. If exposure is suspected to have occurred within the past 6 months, repeat HCV RNA testing ~ 6 months after the estimated time of infection.

Seroconversion - An immune response characterized by a change from the absence of HCV antibodies (anti-HCV non-reactive) to the presence of HCV antibodies (anti-HCV reactive) in the serum of an individual at any time.

Sustained virologic response (SVR) - No detectable HCV RNA in plasma 12 weeks (SVR12) after treatment completion. In the past, SVR was measured at 24 weeks after treatment completion.

3.0 HEPATITIS C VIRUS

Hepatitis C is a virus that can cause chronic liver disease. HCV is a single-stranded, enveloped, linear RNA virus from the *Flavivridae* family. HCV is a blood-borne virus that is highly transmissible via percutaneous exposures to infectious blood. Permucosal transmission may occur if blood is present, but is not as efficient.

3.1 Clinical Description

Most people (75%) who have just become infected with HCV have no symptoms. The remaining 25% may experience fatigue, loss of appetite, muscle aches, fever, nausea, or vague abdominal pain beginning approximately 6-7 weeks after infection and resolving after a few weeks. Jaundice, pale stools, and dark-coloured urine occur in less than 10% of cases. Individuals with newly acquired HCV infection may have elevated serum ALT levels. In very rare instances, severe and rapidly progressing hepatocellular death and hepatic failure may develop (fulminant hepatitis).

Approximately 75% of cases become chronically infected, while 25% will naturally clear the virus (spontaneous clearance or resolved infection). Among those with chronic infection, most remain asymptomatic for years, while some individuals will experience fatigue, depression, lethargy, digestive problems and/or other extrahepatic manifestations. Over decades, 10%-20% will develop cirrhosis. HCV is a leading cause of cirrhosis and end-stage liver disease. It is also an important cause of HCC, and is the major cause of liver transplantation. Cirrhosis is a condition that results from damage or scarring of the liver. This may be reversible in early stages, if the underlying cause is treated. It is the end-stage of many different forms of liver disease and is known to cause a number of other health problems, including variceal bleeding, ascites and hepatic encephalopathy. Approximately 1%-5% of all chronically infected individuals will develop hepatocellular carcinoma within two decades.

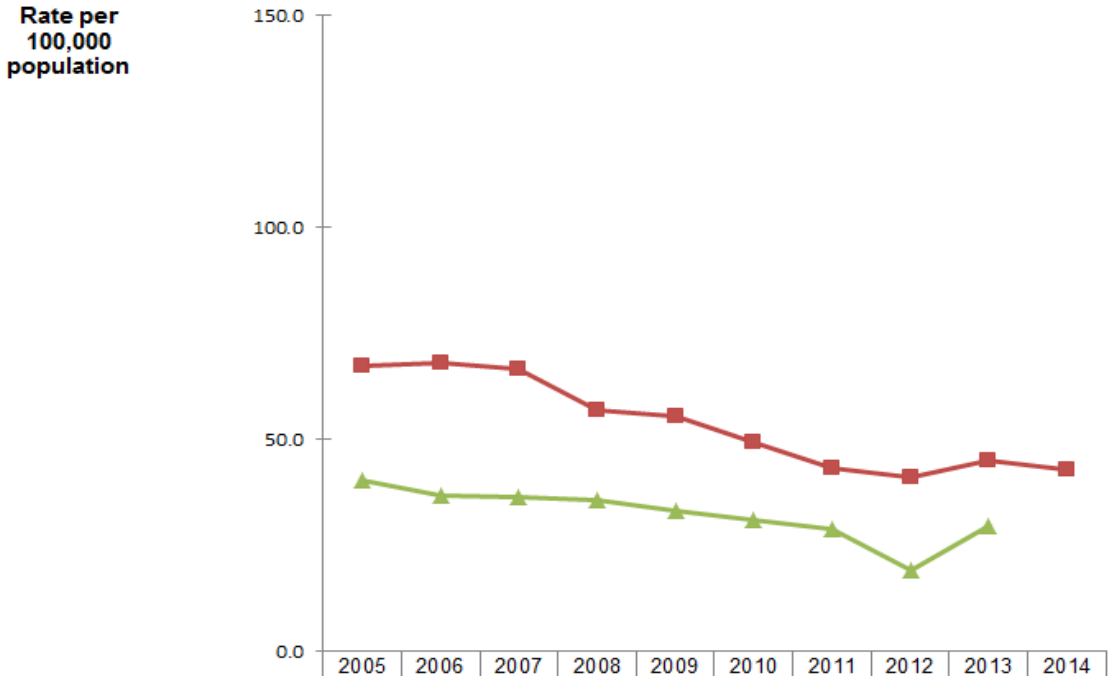
Factors that accelerate liver disease include alcohol consumption (>2-3 drinks per day), older age at the time of infection (> 40 years old), male gender, obesity, and coinfection with HIV or HBV (8, 9). Individuals who are chronically infected with HCV have an increased risk of developing fulminant hepatitis if they are acutely infected with HAV.

3.2 Epidemiology

After the discovery of hepatitis A (1973) (10) and hepatitis B (1963) (11), it became clear that many cases of hepatitis that occurred following blood transfusions were due to neither hepatitis A nor hepatitis B. By the mid-1970's, the term "non-A, non-B hepatitis" was used to refer to the virus presumed responsible for these infections. In 1989 the virus was identified and renamed hepatitis C (12, 13). As a result of this discovery and subsequent work to detect infection, Canadian Blood Services has implemented anti-HCV screening of all blood donors since 1990 and HCV NAT testing since October 1999 (14).

It is estimated that between 230,000-450,000 (0.66%-1.3%) Canadians were HCV-infected in 2011. In BC, there were an estimated 73,000 anti-HCV positive persons in 2012, of which 20,000 were undiagnosed and 50,000 chronically infected.

Figure 3-1: Annual rates of newly diagnosed HCV cases by Health Authority, BC (2005-2014)



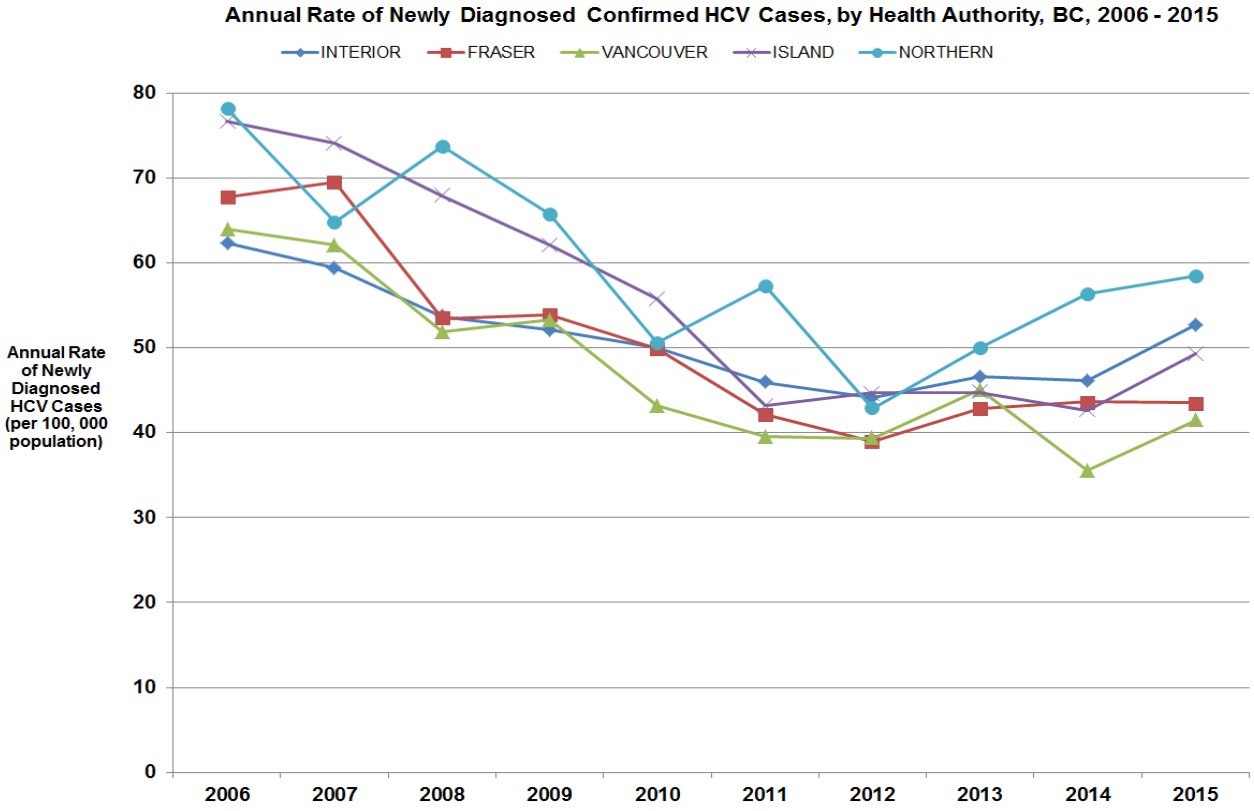
	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
BC Hepatitis C Reports	2822	2891	2863	2473	2452	2201	1950	1866	2058	1985
BC Hepatitis C Rate	67.3	68.2	66.7	56.9	55.6	49.3	43.3	41.1	44.9	42.9
Canadian Hepatitis C Rate	40.3	36.9	36.6	35.8	33.3	31.1	28.9	19.3	29.6	

The annual rate of newly diagnosed HCV cases (acute and chronic) reported in BC has declined over the last decade but remains considerably above the Canadian rate. In 2013, the rate of newly diagnosed HCV cases was 44.9 per 100,000 population in BC, and 29.6 per 100,000 in Canada (see Figure 3-1) (15). In 2014, the overall rate of HCV infection in BC was 42.4 cases per 100,000 people. Fraser East had the highest rate at 71.8 per 100,000 followed by Northern Interior at 70.5. Richmond had the lowest rate at 17.1 per 100,000 (see Figure 3-2).

HCV is endemic among people who inject drugs (PWID), the core group involved in the forward transmission of the present epidemic. As PWID also have higher prevalence of HIV, HBV, mental illness and social and material deprivation, prevention strategies need to be multi-factorial to address co-occurring conditions. Prevalent infections are common in people born in 1945-64, immigrants from endemic countries, and people who have used illicit drugs in the past. In developed nations, iatrogenic transmission is uncommon.

There is no vaccine to prevent HCV infection. Treatment based on interferon/pegylated-interferon and ribavirin has been available in BC since 2000. While HCV cure is associated with reduced morbidity and mortality, less than 15% of those infected had been treated by 2012 (16) in part due to poor tolerability and variable cure rates by genotype. In 2014, better-tolerated, short-course (8-12 weeks), interferon-free, direct-acting antiviral (DAA) drugs with cure rates approaching 95% became available, drastically improving the opportunity to prevent progressive liver disease in the population (5).

Figure 3-2: Newly Diagnosed cases of Hepatitis C by Health Authority (2006-2015)



Higher net healthcare costs have been reported in individuals with HCV-related sequelae compared to individuals in the initial stages of disease ($6,000/person/yr vs. $1,850/person/yr respectively). Although illicit drug use, mental illness, and HIV coinfection were significant predictors of cost in the initial stages of disease, costs were largely attributable to hospitalizations. In 2005, BC is estimated to have had a net incremental expenditure of $136M/yr for HCV-related disease (17). Although updated cost information is not currently available, this figure is presently estimated to be significantly higher.

3.2.1 HCV/HIV Coinfection

HIV has a significant impact on HCV infection. HCV/HIV coinfected individuals tend to have higher HCV viral loads, impacting HCV treatment response, and lower CD4+ counts. Coinfected individuals with a high degree of immunosuppression have a greater risk of fibrosis and death compared to those with a lower degree of immunosuppression. Coinfected individuals with cirrhosis also progress more quickly to HCC than HCV mono-infected individuals (18).

HCV coinfection is estimated to occur in 20% of Canadians infected with HIV and 50-90% of HIV-positive PWID (19). Compared to HIV mono-infected individuals, HCV/HIV coinfected groups are characterized by a higher prevalence of injection drug use, poverty, and psychiatric disorders. In BC, Buxton et al. (2010) found that of 3,219 HIV positive subjects, 53% were HCV/HIV coinfected. More importantly, for those diagnosed with HCV first, the median time to HIV infection was 3.5 years.

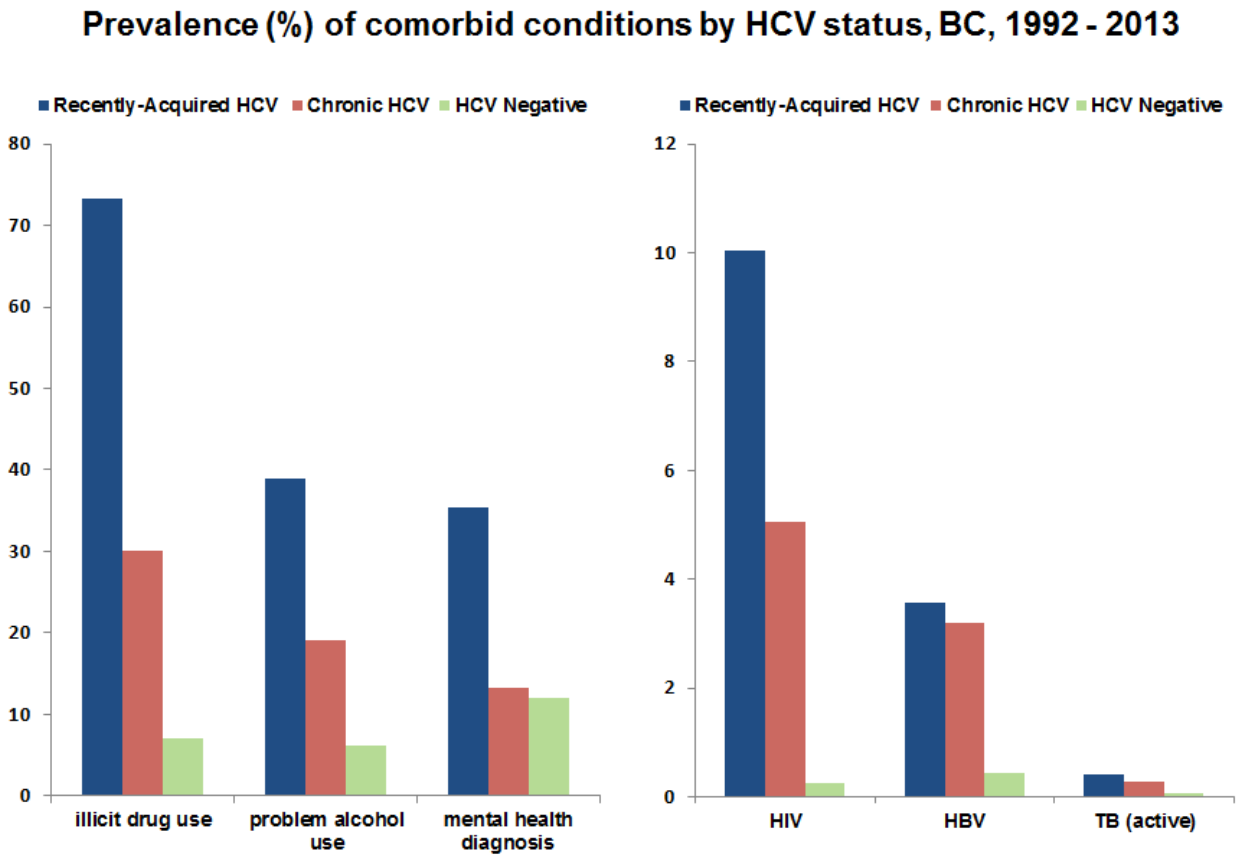
3.2.2 Harm Reduction

Mortality in those with newly acquired infections (incident cases) is associated with HCV acquisition risk activities and behaviours (see Figure 3-3). In BC, incident cases have a risk of drug-related mortality that is approximately 38 fold higher than the general population (20). Prevalent cases, on the other hand, are more likely to have a composite of risks and behaviours related to HCV acquisition as well as a greater risk of liver-related mortality that is about 20 fold higher than the general population.

The BC Provincial Health Officer's Report on HIV and HCV incidence among injection drug users in BC notes that the largest recent decrease in new HIV diagnoses is among injection drug users of younger ages (21). Although this supports the notion that fewer young adults are taking up injection drug use, prospective cohort studies of at-risk youth in the Downtown Eastside (DTES) of Vancouver have found that 30% - 43% ended up engaging in drug injection over time (22, 23).

Among PWID in major urban centres in BC, needle sharing ranges from 8% to 23%, depending on factors such as accessibility of harm reduction supplies and safe injection sites (24).The HIV prevalence among street-involved youth in Canada ranges from 0.2% to 1.9% (25), and HCV prevalence ranges from 10.6% to 21.5% (26). Targeting prevention and harm reduction strategies at youth thus remains an important focus of hepatitis C care to prevent HIV infection.

Figure 3-3: Hepatitis C and comorbid conditions in BC (1992-2013)



Other factors that have contributed to the declining incidence of HIV among PWID include an increased uptake of highly active antiretroviral treatment (HAART), decreased sexual transmission of HIV, aging population, and changing patterns of drug use from IDU to smoking crack cocaine in the DTES of Vancouver and elsewhere in the province (21).The risk of HCV acquisition due to sharing smoking paraphernalia is much lower than the risk of acquiring HIV through sharing used needles.

Opioid overdose (OD) is a public health concern in BC. In 2009, it was reported that 70 deaths were attributed to prescription opioid medication. In 2011, BC Coroner's Service reported 275 deaths were attributed to drug overdose, a cluster of which were associated with high purity heroin. In 2015, Fentanyl emerged as a highly potent drug driving up the number of overdose deaths. Overdoses that do not lead to death can still cause lifelong harms from the lack of oxygen to the brain (http://towardtheheart.com/).

Harm Reduction Programs

Harm reduction programs that involve the distribution of harm reduction supplies are effective at reducing the transmission of blood-borne infections. Needle exchange programs began in BC in 1988. In 2002, the provincial policy shifted to focus on the supply distribution and safe disposal of needles. The BC Centre for Disease Control (BCCDC) has tracked the distribution of products to reduce drug-related harms since 2004. There is evidence to suggest that distribution programs are more effective in preventing HIV infection related to injection drug use than one-to-one needle exchange programs (27). The effect of needle/syringe distribution programs on decreasing the rate of HIV transmission is supported in the literature (28-30). Supervised injection facilities also play a role in harm reduction by connecting medical and nursing staff with PWID, distributing harm reduction supplies, and connecting a marginalized population with the health care system. The use of supervised injection facilities has been associated with reduced syringe sharing in comparison with those who do not use these facilities (31).

The BC Provincial Health Officer's Report also suggests that the incidence of HCV and HIV infections among injection drug users in BC is decreasing. Greater access to harm reduction supplies, MMT, condom distribution, mental health and substance use services, outreach programs and other support services, are cited as factors contributing to the decrease in HCV and HIV incidence (21). Albeit ecological, this is further evidence that policies aimed at reducing harms from substance use have had a positive impact on population HCV and HIV rates.

Long term MMT has been shown to mitigate risk behaviours associated with IDU (39) and to reduce the risk of HIV infection (32, 33). However, it has not been shown to decrease HIV sex-related risk behaviours (34). Other reported benefits of MMT include cessation of drug use in some individuals (35) , and reductions in criminal activity (36) , unemployment (37), and mortality rates (38). In 2010, Buxton et al., showed that of the those engaged in MMT, 45% were already anti-HCV positive at the time of MMT initiation (19).

Naloxone (aka Narcan®) is an opioid-blocking drug that has been used to quickly reverse heroin, morphine, OxyContin®, and other opioid overdoses. It is a safe drug with minimal side effects and has been approved for use in emergency settings in Canada for over 40 years. In 2011, the BC ambulance service administered the life-saving medication 2,367 times. In 2012, the BC Take Home Naloxone Program was launched. Since then over 5500 persons have been trained and Take Home Naloxone kits have been dispensed across 150 locations in BC, including correctional facilities. As of February 2016, there have been 434 documented overdose reversals in which 60% called 911 (39).

3.3 Risk Factors

The risk for acquiring an HCV infection depends upon the nature of the activity and exposure, with the parenteral and percutaneous route being considered higher risk. Permucosal exposure is lower risk, with greater concern when the integrity of the mucosa in question has been compromised.

Table 3-1: Risk factors for HCV infection

Category	Activity	Comments
High Risk	Injection drug use	Greatest risk in those who have: • shared drug preparation or injecting equipment • not used new, sterile syringe each time • not used sterile water each time • not used a new or disinfected cooker each time • poor injection technique (leading to bleeding)
	Incarceration	High level of needle sharing in PWID and unsterile tattooing practices
	Potential iatrogenic exposures	For foreign-born BC residents or travelers to BC from HCV endemic countries (high prevalence areas include regions of Central and East Asia, and North Africa/Middle East (40)*), are at increased risk if medical care was received where basic infection control practices are not followed and where the blood supply is not tested.
		In Canada, increased risk if: • Blood-derived coagulation products before July 1988 • Organ or tissue transplant before 1990 • Blood transfusion or blood product before May 1992
Mod-Low Risk	Non-injection drug use	Transmission can occur when sharing drug use equipment, as the integrity of the mucosa can be compromised or ulcerated (e.g. snorting can irritate nasal mucosa, smoking crack pipes can damage oral mucosa)
	Unprotected sexual activity with multiple partners	• Where blood is exchanged, as in sex causing mucosal tearing • Coinfection with HIV, HBV or other STI's that can cause sores or lesions can increase the risk • Theoretical risk when engaging in unprotected vaginal sex during menstruation
	Tattooing, body piercing or acupuncture	In unregulated premises where unsterile equipment or improper technique is used
Low Risk	Unprotected sexual activity in long-term, monogamous relationships	Where blood is exchanged, as in sex causing mucosal tearing
	Vertical transmission	• ~6% risk of transmission to infants born to anti-HCV positive mothers • Increased risk with increased RNA titres and when clinical symptoms of acute hepatitis • 3-fold increased risk if mother has HIV/HCV coinfection
	Sharing personal hygiene items	Such as nail clippers or toothbrushes that may have traces of blood
	Accidental needle stick injury	The average incidence of anti-HCV seroconversion after percutaneous exposure from a HCV positive source is 1.8%

* For estimated rates by region, see Figure 3 in http://www.natap.org/2013/HCV/26141_ftp.pdf (40)

3.4 Transmission

Hepatitis C virus is mainly spread by parenteral exposure to HCV-infected blood (41). Estimates suggest that 54% to 70% of HCV infections in Canada are related to injection drug use (42).Sharing equipment for snorting and smoking drug use (e.g. crack pipes, straws, etc.) has also been associated with HCV transmission (43). Transmission of HCV may also occur in relation to other activities involving percutaneous exposure such as tattooing, piercing, electrolysis and acupuncture in unsterile and/or unregulated premises (44, 45).

Sexual transmission is uncommon in long-term monogamous relationships (46). The risks increase with high-risk sexual activities causing mucosal tearing (e.g. receptive anal sex) and coinfection with HIV and other STIs (44).

The risk of vertical transmission is about 6% for infants born to anti-HCV positive mothers, and higher if the mother is coinfected with HIV (47, 48). There is limited understanding of the mechanisms of HCV vertical transmission and it may occur intrauterine, peri-partum and/or post-partum.

There is a theoretical but unproven risk of HCV transmission to an infant via breastfeeding. Unless mothers are coinfected with HIV, a HCV infected mother should be advised to breastfeed (49-51). If the nipples become cracked or bleed, mothers can abstain from breastfeeding until they are healed.

Transmission through household exposure has been reported through sharing personal hygiene equipment such as toothbrushes, nail scissors and clippers, and razors (44).

HCV is not transmitted efficiently through occupational exposures to blood. The average incidence of anti-HCV seroconversion after percutaneous exposure from an HCV positive source is 1.8% (range is 0 to 7%) (52).

There is no evidence that HCV is spread by coughing, sneezing, hugging, kissing, using the same dishes or cutlery, swimming in a chlorinated pool when a case has cuts or scrapes or when menstruating, being bitten or stung by an insect which then bites or stings someone else or skin contact by others with the body fluids of a case that are not exposed to blood (such as saliva, urine, feces or vomit) (53).

Refer to Table 3-1 and Appendix A for a summary of activities, associated level of transmission risk, and resources for health care providers.

4.0 LABORATORY INFORMATION

4.1 HCV Testing

The BCCDC Public Health Laboratory performs the majority (95%) of HCV antibody and all HCV RNA and genotype testing for BC. A sensitive enzyme immunoassay (EIA) screen is used to detect antibodies to HCV. All samples reactive by this initial screen are retested using an EIA test from an alternative manufacturer.

All persons infected with anti-HCV are considered infectious unless there is documented evidence of a resolved infection. While approximately 25% of HCV infected individuals resolve their infection (usually within 6 months of infection) without treatment, most HCV infections become chronic. To distinguish active from resolved infection, individuals who test anti-HCV reactive require nucleic acid testing (NAT) of plasma for HCV RNA. The BCCDC Public Health Lab uses a quantitative HCV RNA test which has a lower limit of detection of 15 IU/mL for both diagnosis and monitoring.

HCV genotyping is routinely performed after confirmation of a newly acquired infection or chronic infection, as it will inform the type and length of treatment.

For requisitions and information about testing performed at the BCCDC Public Health Laboratory, refer to the serology and virology sections:
http://www.bccdc.ca/health-professionals/professional-resources/laboratory-services

For information on sample collection and processing instructions, refer to the BCCDC Public Health Laboratory Guide to Programs and Services:
http://www.bccdc.ca/health-professionals/professional-resources/laboratory-services

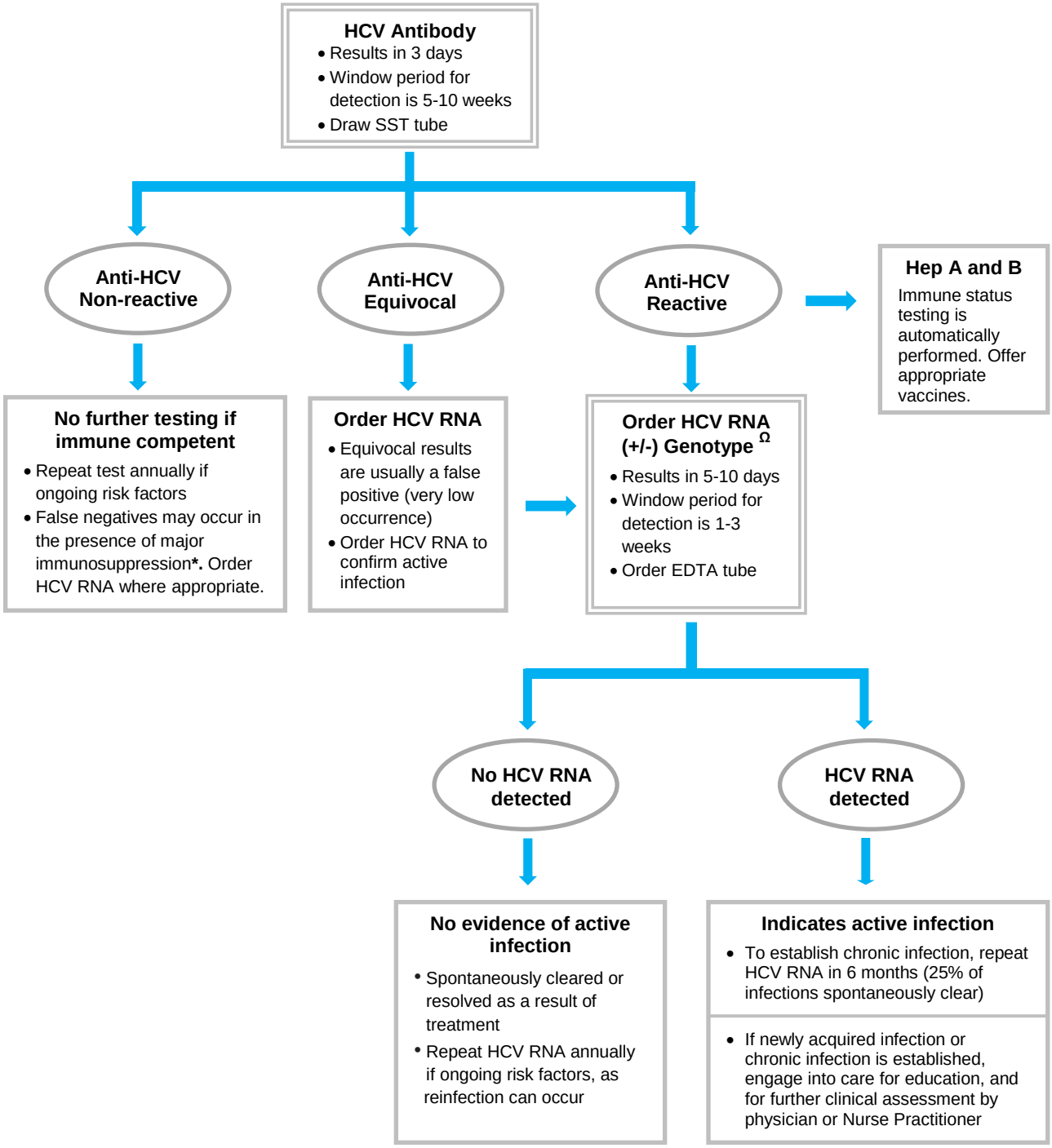
4.2 Reflex Testing

The BCCDC Public Health Laboratory automatically performs hepatitis A and B immune status testing on the first reactive anti-HCV result but it is not unusual to have these tests performed on subsequent samples. Sera are tested for total antibody to hepatitis A (anti-HAV total) and hepatitis B surface antibody (anti-HBs). Further testing for hepatitis B surface antigen (HBsAg) and total hepatitis B core antibody (anti-HBc total) is performed for sera non-reactive for anti-HBs. Based on the results, recommendations can be made on the appropriate vaccines to administer.

If HAV and HBV results are not available on a reactive anti-HCV laboratory report, check local electronic lab results systems or call the BCCDC Public Health Laboratory.

If HAV and HBV tests have not been reflexively performed, call the BCCDC Public Health Laboratory to request them. Testing for HAV and HBV immune status can be completed within 7 days of the laboratory receiving the HCV sample.

Figure 4-1: HCV Testing Flowchart



* HIV+ (CD4+ < 200 cells/mm^3), chronic kidney disease, long-term use of immunnosuppressants and agammaglobulinemia

Ω BCCDC Public Health Laboratory can do genotype testing on 'HCV RNA detected' specimens only. If requested at the same time as the HCV RNA, the genotype will be done and a new EDTA tube is **NOT** required

4.3 Interpretation of Test Results

The following sections outline information about how to interpret HCV testing results (Section 4.3.1 and Section 4.3.2).

4.3.1 HCV Antibody Test Results

Two sensitive enzyme immunoassay (EIA) screens are used to detect antibodies to HCV. The incidence of false positive EIA results is extremely low (0.2 - 0.4%).

Practitioner Alert!

Anti-HCV antibodies usually persist for life. Anti-HCV does **NOT** need to be repeated once result is reactive. A reactive result does **NOT** differentiate between a resolved case and an active infection.

Anti-HCV antibodies are **NOT** protective. Inidividuals who clear the HCV either spontaneously or from treatment (i.e. HCV RNA not detected), can get reinfected again with any type of HCV.

Table 4-1. Interpretation of HCV antibody test results

HCV Antibody test result	Screening HCV antibody assay	Supplemental HCV antibody assay	Interpretation
Anti-HCV reactive	EIA test is reactive	EIA test is reactive	• Person has antibodies to HCV and therefore has been infected with the hepatitis C virus at some point in their life • Reactive result does not indicate active infection or immunity • Antibodies usually persist for life
Anti-HCV non-reactive	EIA test is non-reactive	N/A	• HCV infection is ruled out in most immunocompetent persons. No further testing is required. • It is possible that the test was performed before this marker became detectable. If the person has high risk behaviours, consider a repeat anti-HCV test after 1-2 months. • In an immunocompromised* person, the anti-HCV response may be blunted and further confirmatory HCV RNA testing may still be required
Anti-HCV equivocal	EIA test is reactive	EIA test is non-reactive	• If clinically indicated, a HCV RNA test is required to determine if active infection exists • Equivocal results usually indicate a false positive

* HIV+ (CD4+ < 200 cells/mm^3), chronic kidney disease, long-term use of immunnosuppressants and agammaglobulinemia

4.3.2 HCV RNA Test Results

Table 4-2. Interpretation of HCV RNA test results

HCV RNA Test Result	Interpretation
HCV RNA detected	• Indicates active infection with HCV (i.e. the virus is actively replicating) • HCV RNA viral load and log values are used to predict and monitor treatment response but do not correlate with disease progression
No HCV RNA detected	• No evidence of active infection • The infection has resolved either spontaneously or as a result of therapy • Re-infection can occur if the client has on-going risk factors

The HCV RNA test is quantitatively accurate between 15 and 100,000,000 IU/mL. Note that the viral load may be reported outside of this range at < 15 IUmL, but an active infection can still be detected and reported as “HCV RNA detected”.

There are 3 options when the HCV RNA results are reported out by the BCCDC Public Health Laboratory. Examples are provided below:

1. HCV RNA detected (active infection)
   Specimen Description Plasma
   Test Name Results
   HCV RNA 316732
   HCV RNA (log 10IU/mL) 5.50 | HCV RNA detected

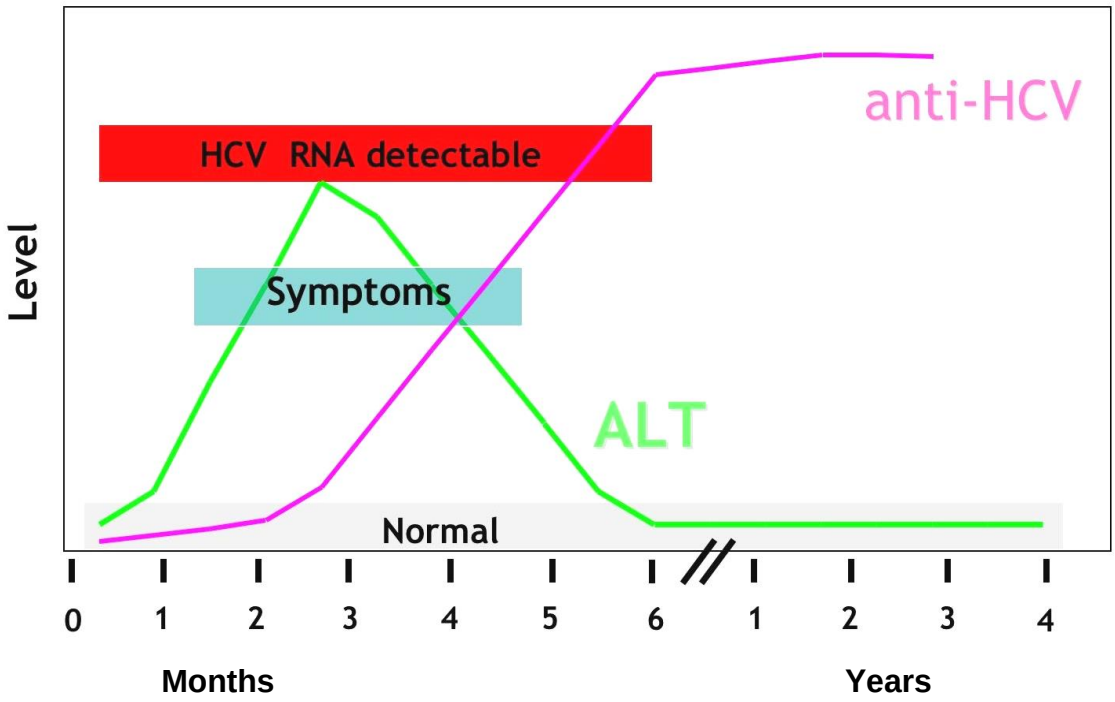
2. HCV RNA detected (active infection)
   Specimen Description Plasma
   Test Name Results
   HCV RNA < 15
   HCV RNA (log 10IU/mL) Not calculated | HCV RNA detected at < 15 IU/mL

3. No HCV RNA detected (no active infection)
   Specimen Description Plasma
   Test Name Results
   HCV RNA 0.021548657
   HCV RNA (log 10IU/mL) Not calculated | No HCV RNA detected

Contact the BCCDC Public Health Laboratory if unsure of how to interpret HCV testing results.

4.4 HCV Testing Window Periods

Figure 4-2: Acute HCV Infection with Recovery



During the acute phase of HCV infection, ALT/AST levels are markedly elevated, while they can fluctuate widely in chronic cases. Antibodies to HCV are usually detectable 5 to 10 weeks after infection and persist. HCV RNA becomes detectable by NAT within 1-3 weeks of infection.

The development of antibodies can be delayed or absent in immunocompromised individuals (e.g. HIV with CD4+<200 cells/mm^3, chronic kidney disease, long-term immunosuppressant use, agammaglobulinemia). A HCV RNA test may be ordered if clinically indicated (i.e. symptoms, risk factors) after an anti-HCV nonreactive result.

5.0 PUBLIC HEALTH MANAGEMENT

The following case definitions described in this section are specific to Public Health documentation and attribution of HCV cases in BC. Definitions employed in daily clinical practice may employ the same terminology, but can differ significantly in their use and meaning.

> ***Practitioner Alert!***
>
> Case definitions used for the purposes of surveillance in BC can differ from their use in a clinical setting.

The information presented in this section may be used to guide the documentation and geographical attribution of confirmed (not suspect, or Person Under investigation, or PUI) HCV cases using an electronic public health information system. One key distinction in how HCV case definitions are used by public health reporting is the focus on seroconversion. In BC, individuals who have a documented seroconversion ('anti-HCV not detected' to 'anti-HCV detected' within a 12-month time period) are considered an 'acute' case, regardless of whether HCV RNA results are available or not, and regardless of clinical presentation. HCV cases attributed to BC that have not been reported elsewhere in Canada, are reported to the Public Health Agency of Canada (PHAC).

'Acute' cases of HCV are an important population whose risks represent current transmission and acquisition risk factors. The documentation and attribution of 'acute' HCV cases can support case management by gathering acquisition risk factors. From this information, the linkage to care can be facilitated by the provision of timely education and service referrals (see Section 6.0).

> ***Practitioner Alert!***
>
> The identification of acute HCV cases provides key opportunities to engage individuals with HCV infection into care.

Laboratory results available to public health may not be adequate to meet clinical requirements for staging the infection, but will generally be sufficient for surveillance purposes of documenting and attributing cases appropriately. From a surveillance perspective, the acute stage of infection is important to capture. The documentation of other stages is useful to have, but is not crucial (see Table 5-1 for Panorama staging).

Follow RHA guidelines, and refer to recommendations in the Surveillance of Reportable Conditions, Chapter 6 of the BCCDC CDC Manual (http://www.bccdc.ca/health-professionals/clinical-resources/communicable-disease-control-manual), for individuals with HCV infection who are newly identified in BC, but who reside (permanent residence) out of province.

5.1 Case Classification

There is no single serological test available for identification of newly-acquired infections. Seroconversion and time parameters are used as a proxy. As local surveillance systems may be limited by the current reporting of laboratory testing results, refer to RHA guidelines for further specific classification requirements related to a particular electronic public health information system (see Table 5-1 for Panorama HCV staging guidelines).

Table 5-1: Confirmed case classification of Hepatitis C for the purposes of Public Health reporting in Panorama

Staging	Age	Baseline anti-HCV test result	Present HCV test result
Unstaged*	Adults, adolescents & children > 18 months	Anti-HCV negative result on record > 12 months ago **OR** No documentation available	Anti-HCV positive **AND** No HCV RNA result available
Unstaged**	Children ≤ 18 months	N/A	HCV RNA positive ≥ 4 to 6 weeks of age **OR** Anti-HCV positive at 18 months of age
Acute	Adults, adolescents & children > 18 months	Anti-HCV negative result on record ***within*** the prior 12 months	Anti-HCV positive **OR** HCV RNA positive
Chronic^	Adults, adolescents & children > 18 months	Anti-HCV negative result on record > 12 months ago **OR** No documentation available	HCV RNA positive
Resolved^,Ω	Adults, adolescents & children > 18 months	Anti-HCV positive	HCV RNA negative

* Update case within the same investigation when HCV RNA result arrives

** In the case of children ≤ 18 months, leave unstaged until further testing has been completed. This can be revised to chronic or resolved if further HCV RNA results are available after 18 months.

^ If an anti-HCV reactive and a HCV RNA positive result are received at the same time, report as an 'acute' case and then change to 'chronic' or 'resolved' using the same date.

Ω For the purposes of surveillance, for all cases > 18 months only a ***single*** negative HCV RNA is required to confirm resolution (no time parameter)

Individual client testing report flow can vary, but in general anti-HCV test results are received first, followed by HCV RNA, and then genotyping. A confirmed HCV case may consist of a single 'anti-HCV detected' test result, with or without other results. An antibody positive client who then receives HCV RNA results ('HCV RNA detected' or 'No HCV RNA detected') remains a confirmed case.

If the only information available on a client is a 'HCV RNA detected' test result or a stand-alone genotype result, this is also a confirmed case.

5.2 New case follow-up

This section describes a suggested practice for follow-up of new HCV cases, carried out by public health personnel with the assistance of a primary health care provider when possible. Refer to local agency guidelines for further guidance.

Case Identification

- Lab notification received confirming HCV infection (usually anti-HCV results)
- Document result in the electronic public health information system
- Review prior testing history to determine if new HCV case
- Classify according to age and prior baseline anti-HCV test result (see Table 5-1 for staging information specific to Panorama)

Reporting

- Use the electronic public health information system available in your RHA to report confirmed cases of HCV
- If reporting a new acute HCV, complete the 'Hepatits C Acute Case Report Form' (http://www.bccdc.ca/health-professionals/professional-resources/surveillance-forms)

Case Management

- Engage into care. If appropriate offer:
  - Immunization update (review reflex HAV/HBV testing)
  - Alcohol and drug harm reduction strategies
  - Mental health and addictions counselling
  - STI screening
  - General health and education resources (e.g. diet, housing resources)
  - Community support groups and services
  - Explore treatment options (may prefer to wait until confirmed chronic)
- Recommend confirmation of infection by HCV RNA (copy primary care provider on results)
- Review transmission information and prevention
- Connect client with primary care provider for further clinical evaluation
- Discuss potential for stigma and that disclosure is voluntary
- Where possible, offer to assist client with notifying contacts and provide local testing resources
- Also see Section 6.0 for Case Management information

6.0 ACUTE CASE MANAGEMENT

The following section outlines suggested follow-up for cases of acute HCV. Many of the recommendations below are not exclusive to acute cases, and may also be applicable to the case management of chronic HCV.

Individuals may avoid seeking follow-up care due to stigma and discrimination. Stigma may be greater in rural and remote areas. The creation of an environment by the health care practitioner that respects the privacy and culture of each individual will help to foster the trust needed to develop a partnership of care. The challenges that face individuals in the context of the broader determinants of health (e.g. housing, social support networks, coping skills, gender, education, etc.) must be acknowledged in addressing the concerns that can arise when reviewing new HCV lab test results or diagnosis.

For healthcare provider HCV pre- and post-discussion checklists and patient support information, including partner disclosure, see Hepatitis Education Canada: www.hepatitiseducation.ca. Refer to Figure 6-1 for Hepatitis Education Canada's cascade of care flow diagram and Appendix B for links to information that health care professionals and clients may find useful.

6.1 Management of Adults

6.1.1 First Contact

If direct contact with a client is part of a RHA's routine practice, attempt to confirm that the client is aware of their diagnosis with the primary care provider before initiating contact. In situations where confirmation with the primary care provider cannot be established, direct contact with a client may be appropriate.

Recommend confirmation of infection by HCV RNA. Ensure that the primary care provider (PCP) is copied on the results, and advise client to follow-up with their PCP for results. It is within the scope of practice of a STI certified nurse to order a HCV RNA test (see STI assessment DST, https://www.crnbc.ca/Standards/CertifiedPractice/Pages/DSTs_all.aspx).

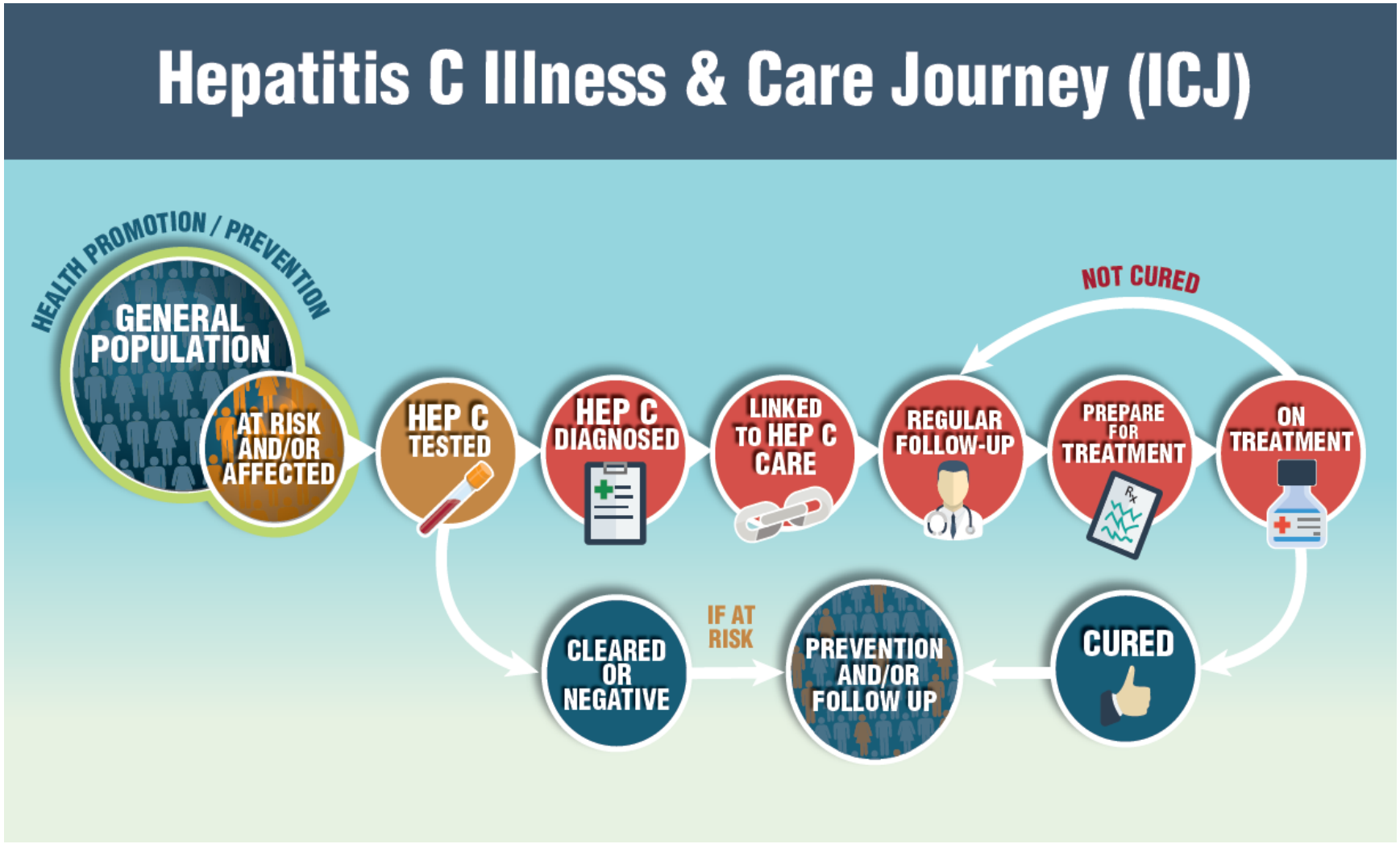
6.1.2 Contact Tracing and Disclosure

Give a rationale as to why the case report information is being collected to provide reassurance regarding privacy and confidentiality. Where possible, provide assistance to clients with notifying contacts who may need testing and counselling. Provide local HCV testing resources and educational materials.
It is recommended that interviewing for contact information be done by the first health care professional (e.g. public health personnel, primary care provider) who interviews the client, as there may not be another opportunity to do so.

There is no effective post-exposure prophylaxis currently available for hepatitis C.

Provide counselling regarding transmission. Refer to Section 3.3, Section 3.4 and Appendix A for further information on risk factors and transmission risk.

Figure 6-1: Hepatitis Education Canada: Hepatitis C Stages of Care



http://hepatitiseducation.med.ubc.ca/

6.1.3 Health Teaching to Prevent HCV Transmission

Advise how to prevent transmission and recommend the following since there is no preventative HCV vaccine:

- Do not share drug injection, snorting or smoking equipment such as needles, syringes, straws and pipes
- Do not share needles and ink used for tattooing
- Do not share needles used for body piercing
- Do not share toothbrushes, dental floss, razors, earrings or manicure equipment (articles that might have traces of blood)
- Do not donate blood, semen, breast milk, body organs or tissues
- Keep all open cuts and sores covered until healed
- Put articles with blood on them (e.g. tampons, pads, tissue, dental floss and bandages) in a separate plastic bag before disposing of them into household garbage
- Dispose of bloody sharp items (e.g. razor blades, needles, etc.) into a hard-sided container, taped shut
- Clean blood spills by using absorbent materials first, such as paper towels, and wearing clean, disposable gloves. The area should then be cleaned more thoroughly with soap and water, and finally disinfected with household bleach. A fresh solution of bleach should be used for disinfecting and can be prepared by mixing 1 part bleach to 9 parts water and left sitting for 10 minutes before wiping off.
- If considering pregnancy discuss the risk of transmission to the infant. Breastfeeding is generally considered safe (see Section 6.1.6).
- For additional information on reducing the risk of transmission from blood and body fluids, refer to
    - HealthLink BC File #97, Contact with Blood or Body Fluids: Protecting Against Infection: http://www.healthlinkbc.ca/servicesresources/healthlinkbcfiles/index.html
    - BCCDC Communicable Disease manual, Chapter 1, Blood and Body Fluid Exposure Management: http://www.bccdc.ca/health-professionals/clinical-resources/communicable-disease-control-manual

6.1.4 General Health and referrals

Assist in obtaining a referral to a primary care provider (physician or nurse practitioner) if needed. The primary care provider will conduct further assessments and tests prior to referring the client to a specialist (e.g. gastroenterologist, hepatologist or infectious disease specialist) for more specialized care and treatment consideration. See Figure 4-1 for the HCV testing flow chart.

If appropriate, assess for other STI's and offer harm reduction education and counseling. If needed, refer to other STI clinics and support services such as harm reduction, safer sex counseling, and drug use supply, distribution and recovery sites, supervised injection facilities, opioid substitution therapies, and other harm reduction strategies aimed at reducing the risk of acquiring HIV infection and reducing harms associated with illicit drug use.

Liver fibrosis can progress in the presence of coinfection with HBV or HIV, alcohol consumption (> 2-3 drinks/day), non-alcoholic fatty liver disease, obesity and insulin resistance. Discuss limiting or avoiding alcohol, avoiding hepatotoxic drugs (e.g. acetaminophen) and eating a well-balanced diet, as part of a healthy lifestyle and to minimize liver damage. Clients should consult with their primary care provider before using over-the-counter medications and herbal remedies[1].

- For general healthy living guidelines for those with liver disease:
  http://www.liver.ca/liver-disease/having-liver-disease/healthy-living-guidelines/default.aspx
- For the Harm Reduction Training Manual for frontline staff and information on BC Harm Reduction Strategies and Services, refer to:
  http://www.bccdc.ca/health-professionals/clinical-resources/harm-reduction
- For more information on Insite – Supervised Injection Site refer to:
  http://supervisedinjection.vch.ca/
  For information on the College of Physicians and Surgeons of BC Methadone Maintenance Program (includes Burprenorphine/Suboxone):
  https://www.cpsbc.ca/programs/drug-programs/mmp
- For the Primary care management of chronic Hepatitis C: Professional desk reference 2009:
  http://www.cfpc.ca/uploadedFiles/Resources/Resource_Items/HEP_C_Guide_eng_2.pdf
- For a sample letter that public health can send to a physician informing them of follow-up for newly identified anti-HCV cases, refer to Appendix C.
- For requisitions and information about testing performed at the BCCDC Public Health Laboratory refer to:
  http://www.bccdc.ca/health-professionals/professional-resources/laboratory-services

6.1.5 Immunizations

All persons with an anti-HCV reactive result are considered to be at higher risk for certain infections. Regardless of HCV RNA results, offer the following immunizations free of charge to anyone with an anti-HCV reactive result:

- hepatitis A vaccine series if susceptible[2]
- hepatitis B vaccine series if susceptible[2]
- pneumococcal vaccine
- annual influenza vaccine

Timely HBV immunization is important, as a better immune response to HBV vaccine is observed in persons chronically infected with HCV if immunization occurs ***before*** the onset of cirrhosis (54)

Engaging individuals into care also provides an opportunity to assess for any other outstanding routine adult immunizations, such as Tetanus Diphtheria (Td).

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[1] Herbal remedies include herbs, herbal materials, herbal preparations, and finished herbal products that contain parts of plants or other plant materials as active ingredients (55). Clients may refer to them as, but are not limited to, the following examples: “natural”, “alternative”, “traditional” or “Chinese” medicine.

[2] Refer to reflexive testing results for hepatitis A and hepatitis B, that is automatically done by the BCCDC Public Health Laboratory on all new anti-HCV reactive test results. Refer to Section 4.2.

Practitioner Alert!

Individuals who spontaneous clear a HCV infection (i.e. resolved infection) should be offered these immunizations for free as well, as they are still considered to be at higher risk for certain infections.

For more information on routine immunizations for the general adult population and those recommended for persons with chronic liver disease, refer to Communicable Disease Manual, Chapter 2, Section IIa Immunization Schedules and Section III Immunization of Special Populations:
http://www.bccdc.ca/health-professionals/clinical-resources/communicable-disease-control-manual

6.1.6 Pregnancy and Breastfeeding

Recommend pregnant women who are anti-HCV positive have confirmatory HCV RNA testing. If active infection is confirmed, recommend liver function testing to identify those with compromised liver functioning who may require specialist referral.

Recommend breastfeeding to mothers who are infected with HCV. If the nipples become cracked or bleed, mothers can abstain from breastfeeding until they are healed. To prevent cessation of milk supply, mothers may consider expressing and discarding breast milk until their nipples are healed. Breastfeeding is not recommended for mothers co-infected with HIV.

6.1.7 Private Insurance Testing

Clients identified through insurance applications may go through a different process when reporting to Public Health. The elements of follow up are the same as for other all other newly identified cases. These clients may be contacted directly by public health personnel to begin follow-up and/or identify a primary care provider who may complete the follow-up process. Information regarding the appropriate vaccinations, testing and counselling for a case can be provided to the primary care provider.

6.1.8 Transfusion Transmission

If risk factors indicate the possibility of a transfusion transmissible infection, where the client has been a donor or recipient, follow the reporting process in the Transfusion Transmissible Infections section of Chapter I in the Communicable Disease Manual:

http://www.bccdc.ca/health-professionals/clinical-resources/communicable-disease-control-manual

6.2 Management of Neonates to Determine Vertical Transmission

Infants with HCV infection born to HCV positive mothers (i.e. anti-HCV reactive) should be followed up by a paediatric infectious disease specialist or hepatologist.

HCV antibody testing is not appropriate as a screening test for infants less than 18 months since maternal antibodies can cross the placenta and yield a false positive result (see Figure 6-2). In 95% of cases maternal antibody will no longer be detectable in the infant by 12 months of age. In the remaining 5%, maternal antibody will no longer be detectable by 15 to 18 months of age. The BCCDC Public Health Laboratory will not normally process requests for antibody testing on infants less than 18 months

HCV RNA testing may be done when infants are between 4-6 weeks. If this is negative, anti-HCV testing can be done at 18 months to ensure that the passive maternal antibody has cleared.

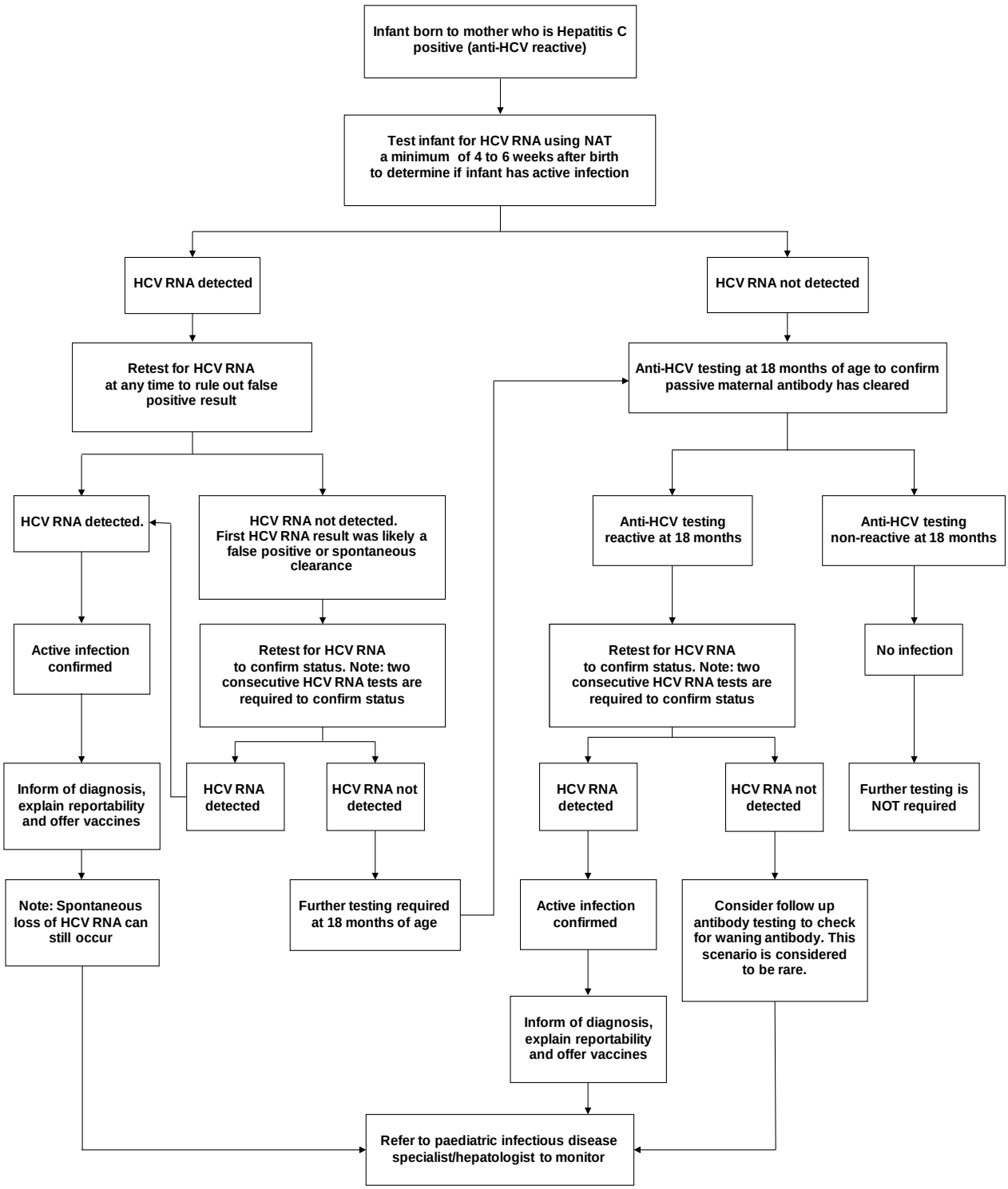
For children older than 18 months of age, the adult recommendations for hepatitis C testing are appropriate to confirm infection.

For requisitions and information about testing performed at the BCCDC Public Health Laboratory refer to: http://www.bccdc.ca/health-professionals/professional-resources/laboratory-services

For information on vaccines recommended for infants infected with hepatitis C, see the Communicable Disease Manual, Chapter 2, Section III Immunization of Special Populations, and for specific vaccine schedule information, refer to Chapter 2, Section VII Biological Products:http://www.bccdc.ca/health-professionals/clinical-resources/communicable-disease-control-manual

For a sample letter that public health can send to a physician informing them of testing that should be performed for an infant born to a HCV positive mother, refer to Appendix D.

Figure 6-2: Neonate flowchart: management of vertical transmission



6.3 Treatment

The goal of antiviral therapy for chronic hepatitis C infection is to reduce liver-related morbidity (e.g. hepatocellular carcinoma) and mortality. The introduction of direct-acting antiviral agents (DAA's) has dramatically changed treatment options for chronic HCV infections. Depending on the genotype, prior treatment with ribavirin and injectable pegylated interferon typically lasted 24 to 48 weeks, and cure rates ranged from 40 to 80%. Newer regimens can be all oral and interferon free for those with genotype 1, and can be completed within 8-12 weeks. Cure rates for newer therapies are consistently around 95%, and side effect profiles have significantly improved. It is hoped that therapy options for those with genotype 2 and 3 will be just as good in the near future.

The type and duration of hepatitis C treatment is determined on an individual basis. Treatment type and duration varies depending on multiple factors such as the HCV genotype, prior treatment history, co-morbidities, and stage of infection (i.e. liver fibrosis, cirrhosis). Stage of infection is important since curability rates vary depending on the amount of liver damage. Consultation with a specialist is generally required.

After a chronic HCV infection has been confirmed (i.e. potential for a HCV infection to resolve spontaneously has been ruled out) the primary care provider can undertake further clinical evaluation prior to a referral to a specialist to help expedite evaluation for treatment readiness. This may include:

- bloodwork to determine genotype
- bloodwork for liver enzymes and clinical exam to assess for acute infection
- imaging to assess for cirrhosis or focal hepatic masses
- fibrosis staging (e.g. Fibroscan®, liver biopsy, APRI, FIB-4)

Treatment can result in a sustained virologic response, defined as having no detectable HCV RNA in plasma or serum 12 weeks after treatment completion. This is synonymous with a virological cure, but patients can still be re-infected if they have on-going risk exposures (56, 57).

For CASL recommended treatment options, see Hepatitis Education Canada's interactive tool designed for front-line health care providers and clients:
http://hepatitiseducation.med.ubc.ca/

For treatment information, see the 2015 Canadian Consensus Guidelines on Management of Chronic Hepatitis C from the Canadian Association for the Study of the Liver (CASL): http://www.hepatology.ca/

For guidelines on the treatment of HCV/HIV co-infected adults, refer to the Canadian Association for the Study of the Liver Hepatitis Guidelines (2015): http://www.hepatology.ca/

Information on available treatments and requirements for coverage in BC can be found:
http://www2.gov.bc.ca/gov/content/health/health-drug-coverage/pharmacare-for-bc-residents

Up to date treatment information contextualized to BC for health care providers and clients, can be found on the Pacific Hepatitis C Network webpage: http://www.pacifichepc.org/

For Hepatitis C information for health care providers and clients, see: www.hepcinfo.ca

7.0 MANAGEMENT OF ACCIDENTAL EXPOSURES

Needle stick accidents should be reported and documented as per agency guidelines.

Refer to the Communicable Disease Manual, Chapter 1, Blood and Body Fluid Exposure Management section for:

- Blood and Body Fluid Exposure Procedures
- Blood and Body Fluid Exposure Management Tool
- Blood and Body Fluid Laboratory Requisition Form
- Management of Percutaneous or Permucosal Exposure to Blood and Body Fluid Physician Letter

http://www.bccdc.ca/health-professionals/clinical-resources/communicable-disease-control-manual

Appendix A: Summary of Transmission Risk, Advice, and Resources

Risk Level	Activities	Advice	Resource examples
High risk: injection drug use	People who inject drugs (PWID), or who have ever used injection drugs or shared drug equipment (i.e. needles, syringes, swabs, filters, spoons, tourniquets, and water) have the greatest risk of acquiring HCV infection	Offer access to appropriate harm reduction support services. Counselling and referral to detox and addiction treatment facilities should be based on the client's readiness to engage in behaviour change. Harm reduction activities should be discussed and supported including: • Do not reuse or share needles, syringes, water or drug preparation equipment or any drug paraphernalia (pipes, spoons, snorting equipment, etc.) • Use syringes obtained from a reliable source and safely dispose after one use. Ensure a new, sterile syringe and needle is used for each injection, not just each session • Use sterile water to prepare drugs; otherwise use clean water from a reliable source • Prior to injection, clean the site with a new alcohol swab • Save one vein for medical use	BC Harm Reduction Strategies and Services (HRSS) at the BCCDC, refer to and the Harm Reduction Training Manual for Frontline staff refer to ('Resources' tab): http://www.bccdc.ca/health-professionals/clinical-resources/harm-reduction For specific information on HRSS Policy and Guidelines, refer to the Communicable Disease Manual, Chapter 3, BC HRSS Policy and Guidelines section: http://www.bccdc.ca/health-professionals/clinical-resources/communicable-disease-control-manual
	Inmates report a high level of needle sharing. In 2007, approximately 44% of male inmates who inject drugs reported sharing needles while incarcerated. The risk of transmission from unsterile tattooing practices in prisons has been reported and carries a high risk of HCV transmission.	Same harm reduction advice as above for IDU. Advise clients that single-use needles and ink containers should be used to prevent infection.	For information on infectious disease surveillance in Canadian federal Penitentiaries, refer to: http://www.csc-scc.gc.ca/publications/index-eng.shtml For information on tattooing and the risk of transmission of HCV, refer to: http://journal.cpha.ca/index.php/cjph/article/viewFile/3039/2624

(cont'd) Appendix A: Summary of Transmission Risk, Advice, and Resources

High Risk: potential iatrogenic exposures	For foreign-born BC residents or travelers to BC from HCV endemic countries (high prevalence areas include regions of Central and East Asia, and North Africa/Middle East (40)*), are at increased risk if medical care was received where routine infection control practices are not followed and where the blood supply is not tested. In Canada, increased risk if: • Blood-derived coagulation products before July 1988 • Organ or tissue transplant before 1990 • Blood transfusion or blood product before May 1992	If risk factors indicate the possibility of a transfusion transmissible infection, where the client has been a donor or recipient, follow the reporting process in the Transfusion Transmissible Infections section of Chapter 1 in the Communicable Disease Manual	Refer to the Transfusion Transmissible Infections section of Chapter I in the Communicable Disease Manual: http://www.bccdc.ca/health-professionals/clinical-resources/communicable-disease-control-manual For estimated rates by region, see Figure 3 in Hanafiah et al. Hepatology 2013;57:1333–1342 http://www.natap.org/2013/HCV/26141_ftp.pdf
Moderate to low risk: non-injection drug use	Transmission can occur through sharing crack pipes when users have superficial burns on the lip. Cocaine snorting can cause irritation and ulceration of the nasal mucosa with bleeding. This can contaminate straws used for snoring cocaine.	Offer access to appropriate harm reduction support services. Counselling and referral to detox and addiction treatment facilities should be based on the client's readiness to engage in behaviour change Advise clients to not share crack pipes and snorting straws.	BC Harm Reduction Strategies and Services (HRSS) at the BCCDC, refer to and the Harm Reduction Training Manual for Frontline staff refer to ('Resources' tab): http://www.bccdc.ca/health-professionals/clinical-resources/harm-reduction For specific information on HRSS Policy, refer to the Communicable Disease Manual, Chapter 3, BC HRSS Policy and Guidelines section: http://www.bccdc.ca/health-professionals/clinical-resources/communicable-disease-control-manual

(cont'd) Appendix A: Summary of Transmission Risk, Advice, and Resources

Moderate to low risk: sexual contact	Having multiple sexual partners and engaging in sex that may cause mucosal tearing (e.g. anal intercourse, sex toys and fisting), increases the risk of acquiring HCV Coinfection with HIV, HBV and other STIs that cause sores or lesions (e.g. herpes, LGV, etc.) also increases the risk of transmission Unprotected vaginal sex during menstruation carries a theoretical transmission risk	Advise clients to engage in safe sex practices including condom use for all sexual encounters	For more information on sexual transmission refer to: Canadian AIDS Society. HIV Transmission: Guidelines for Assessing Risk (2004): http://www.cdnaids.ca/hivtransmissionguidelinesforassessi Hepatitis C in Canada: 2005-2010 Surveillance Report: http://www.phac-aspc.gc.ca/sti-its-surv-epi/nat_surv-eng.php
Moderate to low risk: Tattoos and Piercings	Tattoos and piercings acquired in unregulated premises with unsterile needles and re-usable ink containers carry a risk of transmitting HCV.	Single-use needles and ink containers should be used to prevent infection	For more information on tattooing and the risk of transmission of HCV, refer to: http://journal.cpha.ca/index.php/cjph/article/viewFile/3039/2624
Low risk: sexual contact	In long-term, monogamous relationships the risk of acquiring HCV by sexual contact is low. Where blood is exchanged, as in sex causing mucosal tearing	Once disclosed and discussed, the use of condoms is a personal choice of the couple.	
Low risk: vertical transmission	The risk of vertical transmission is about 6% for infants born to anti-HCV positive mothers. Transmission risks increase when the mother has high RNA titres, has clinical symptoms of acute hepatitis or is co-infected with HIV (3 fold ↑ risk with coinfection)	Breastfeeding is not contraindicated for anti-HCV sero-positive, HIV sero-negative mothers The follow-up of infants and children with proven hepatitis C infection is complex. Consultation with a paediatric infectious disease specialist or hepatologist is recommended.	For more information on the reproductive care of women infected with HCV, refer to: http://sogc.org/wp-content/uploads/2013/01/gui96ECPG0010wDisclaimer.pdf and http://www.perinatalservicesbc.ca/Documents/Guidelines-Standards/Maternal/PostpartumNursingCarePathway.pdf

(cont'd) Appendix A: Summary of Transmission Risk, Advice, and Resources

Low risk: household contacts	Sharing personal hygiene items such as toothbrushes, dental floss, razors, nail files, or other items which could have tiny amounts of blood on them carries a low but real risk of transmission	Advise clients to not share toothbrushes, dental floss, razors, nail files etc. Open cuts and sores should be kept bandaged until healed Place articles stained with blood in a separate plastic bag before disposing into household garbage (e.g. tampons, razors, tissues, bandages, etc.)	Refer to Healthlink BC file Number #40b Living Well with Hepatitis C Virus Infection: http://www.healthlinkbc.ca/servicesresources/healthlinkbcfiles/index.html#section-l
Low risk: accidental needle stick injury	The average incidence of anti-HCV sero-conversion after percutaneous exposure from a HCV positive source is 1.8%	Needle stick accidents should be reported and documented according to RHA guidelines	Refer to the Communicable Disease Manual, Chapter 1, Blood and Body Fluid Exposure Management section for procedures, post-exposure treatment to hepatitis C and an occupational exposure fact sheet: http://www.bccdc.ca/health-professionals/clinical-resources/communicable-disease-control-manual

Appendix B: Resources for Public Health Personnel and Clients

1) BCCDC Contact Information
   a) BCCDC Public Health Laboratory: 1-877-747-2522
2) HCV Testing
   a) BCCDC Provincial Health Laboratory serology and virology requisitions: http://www.bccdc.ca/health-professionals/professional-resources/laboratory-services
   b) Online STI testing, including HCV (not available in all areas, see website for frequent updates)
      - GetCheckedOnline: https://getcheckedonline.com/Pages/default.aspx
3) Information on Immunizations
   a) BCCDC Immunization Manual: http://www.bccdc.ca/health-professionals/clinical-resources/communicable-disease-control-manual/immunization
   b) Immunize BC: http://www.immunizebc.ca/healthcare-professionals/patient-education-print-resources-print-resources
   c) Health Link BC: www.healthlinkbc.ca/healthfiles
      - Number 12b,c,d,e Influenza (Flu) Vaccine
      - Number 25a Hepatitis B Vaccine
      - Number 33 Hepatitis A Vaccine
      - Number 62b Pneumococcal Polysaccharide Vaccine
4) General Information about HCV
   a) BCCDC: http://www.bccdc.ca/health-info/diseases-conditions/hepatitis-c
   b) Hepatitis Education Canada: www.hepatitiseducation.ca
      - Hepatitis C: The Basics self-learning course
      - Pre/Post Test Discussion checklist
      - Frequently Asked Questions About Hepatitis C (booklet & video)
      - Getting Ready for Hepatitis C Treatment (booklet & video)
      - Tests Used for Diagnosing Hepatitis C
      - Qustions People Frequently Ask Their Provider (card)
   c) Health Link BC: www.healthlinkbc.ca/healthfiles
      - Number 40a Hepatitis C Virus Infection
   d) Canadian Liver Foundation: http://www.liver.ca/
      - Hepatitis C - General information
      - Hepatitis C Self-Learning Online Course
      - Video Gallery
      - Support Research and education programs
   e) Canadian AIDS Treatment Information Exchange (CATIE): www.hepcinfo.ca
      - Key Messages
      - Basic and in-depth information

- Multilingual resources
- Local area services
- What's new in hepatitis C
- Hepatitis C resources

f) Organization To Achieve Solutions In Substance-Abuse (O.A.S.I.S): http://www.oasiscliniconline.org/#materials
- Hepatitis C: Get the Facts Workbook
- Hepatitis C: Quik FAQs Reference Guide
- Videos: medication, coinfection, prevention and education

g) Canadian Hemophilia Society:
http://www.hemophilia.ca/files/HepCBooklet.pdf
- Hepatitis C: An Information Booklet for People Infected with Hepatitis C Virus, and Their Families and Friends

5) Healthy Living with HCV Infection and Nutrition

a) Health Link BC: www.healthlinkbc.ca/healthfiles
- Number 40a Hepatitis C Virus Infection
- Number 40c Healthy Eating for Chronic Hepatitis

b) Canadian Liver Foundation: www.liver.ca
- LIVERight: Healthy Living with Viral Hepatitis
- LIVERight: Healthy Living with Hepatitis C
- Hepatitis C Information for Pregnant Women
- Hepatitis C – a liver disease (multi-languages)
- Fatigue and Hepatitis C
- Alcohol and the Liver
- Liver Healthy Home Checklist
- Nutrition and Liver disease

c) Dieticians of Canada: www.dietitians.ca

d) Liver Foundation
http://www.liverfoundation.org/downloads/alf_download_871.pdf
- 50 Ways to Love Your Liver

6) Information and Services for Aboriginal Clients

a) BCCDC: www.bccdc.ca
- Chee Mamuk Aboriginal Program http://www.bccdc.ca/our-services/programs/chee-mamuk-aboriginal-health
- Hepatitis Education Canada http://hepatitiseducation.med.ubc.ca/resources/aboriginal-resources/

b) Two-Spirit Resources
   - Dancing to Eagle Spirit Society
     http://www.dancingtoeaglespiritsociety.org/
   - Two-Spirit Journal
     http://twospiritjournal.com/

c) Vancouver Native Health Society
   http://www.vnhs.net/

7) Advocacy Tools

a) BCCDC Hepatitis Education Resources:
   http://www.bccdc.ca/health-info/diseases-conditions/hepatitis-c
   - Advocacy Skills Workshop Slides
   - Hep C Youth Education Project
   - Negotiating for Hepatitis Care and Support
   - Disclosing your Hepatitis C Infection
   - Stigma and HCV – A Question and Answer Resource for People Living with Hepatitis C
   - Using Your Voice: A Guide for Getting Hepatitis C Care and Support

8) Community Support Groups

a) Pacific Hepatitis C Network: http://www.pacifichepc.org/
b) Vancouver Area Network of Drug Users: http://www.vandu.org/
c) Society of Living Illicit Drug Users: http://solidvictoria.org/
d) Positive Living Society of BC: http://www.positivelivingbc.org/
e) Hep C BC: http://hepcbc.ca/

9) Men's Health

a) Health Initiative for Men: http://checkhimout.ca/?s=hepatitis
b) CDC - Gay and Bisexual Men's Health: http://www.cdc.gov/msmhealth/viral-hepatitis.htm

10) LGBT Community Resources

a) QMUNITY: http://qmunity.ca/
b) Here to Help: http://www.heretohelp.bc.ca/visions/lgbt-vol6/lgbt-resources

11) Harm Reduction

a) Insite Supervised Injection Site: http://supervisedinjection.vch.ca/
b) Harm Reduction Training Manual for Frontline staff:
   http://www.bccdc.ca/health-professionals/clinical-resources/harm-reduction
   BC Harm Reduction Strategies and Services (HRSS) at the BCCDC:
   http://www.bccdc.ca/health-professionals/clinical-resources/harm-reduction
c) Communicable Disease Manual, Chp 3, BC HRSS Policy and Guidelines section:
   http://www.bccdc.ca/health-professionals/clinical-resources/communicable-disease-control-manual
d) Canadian Harm Reduction Network:
   http://canadianharmreduction.com/

e) Guideline for the Clinical Management of Opioid Addiction:
http://www.vch.ca/media/Opioid-Addiction-Guideline.pdf

f) For information on the College of Physicians and Surgeons of BC Methadone Maintenance Program (includes Burprenorphine/Suboxone):
https://www.cpsbc.ca/programs/drug-programs/mmp

12) HCV Disclosure

a) HCV Advocate Guide to Disclosure:
http://hcvadvocate.org/publications/fact-sheets/guides/work-related/

b) Information on the impact and consequences of disclosing HCV infection, top 11 counselling messages and dispelling HCV myths
http://hcvadvocate.org/resources/

13) Drug Interactions

a) HCV Advocate: http://hcvadvocate.org/publications/fact-sheets/

b) Canadian Liver Foundation: http://www.liver.ca/files/LIVERight/pdf/livertips_takingdrugs.pdf

c) Health Canada: http://www.hc-sc.gc.ca/dhp-mps/prodnatur/about-apropos/cons-eng.php

d) Lexicomp: http://www.wolterskluwercdi.com/

e) Micromedex: http://micromedex.com/

14) Professional Associations

a) Canadian Association for the Study of the Liver: www.hepatology.ca

b) Canadian Association of Hepatology Nurses: http://livernurses.org/cahn-library

c) American Association for the Study of the Liver: www.aasld.org

d) European Association for the Study of the Liver: http://www.easl.eu/

15) HCV SURVEILLANCE REPORTS

a) BCCDC Annual Summaries of Reportable Diseases
http://www.bccdc.ca/health-professionals/data-reports/annual-summaries-of-reportable-diseases

b) 2005-2010 HCV SURVEILLANCE REPORT – PUBLIC HEALTH AGENCY OF CANADA:
http://www.phac-aspc.gc.ca/sti-its-surv-epi/nat_surv-eng.php

Appendix C: Sample Letter to Physician

{Print on letterhead}

Date

Confidential

Physician Address

Dear:

RE: patient name DOB: PHN:

We have recently received a reactive anti-HCV laboratory report for your patient listed above. It is recommended that active hepatitis C infection be confirmed by nucleic acid amplification testing (NAAT) to detect the presence of HCV RNA. Hepatitis C Virus is a reportable condition under the BC Public Health Act (2008) and Schedule A of the Health Act Communicable Disease Regulation.

All persons anti-HCV reactive are eligible to receive the following publicly funded vaccinations, in addition to those listed in the routine schedules:

- ❑ Hepatitis A vaccine (if susceptible)
- ❑ Hepatitis B vaccine (if susceptible)
- ❑ Pneumococcal vaccine
- ❑ Annual Influenza vaccine

The vaccines are available by *{enter method the jurisdiction prefers vaccines be administered}*.

Please contact me if you have any questions.

Sincerely,

{First Name Last Name}
{Position}

Appendix D: Sample Letter to Physician regarding testing of infants born to mothers who are anti-HCV positive

{Print on letterhead}

Date

Confidential

Physician Address

Dear:

RE: patient name DOB: PHN:

We have been advised that your patient listed above is hepatitis C positive and delivered *{name of the infant}* on *{DOB of the infant}.*

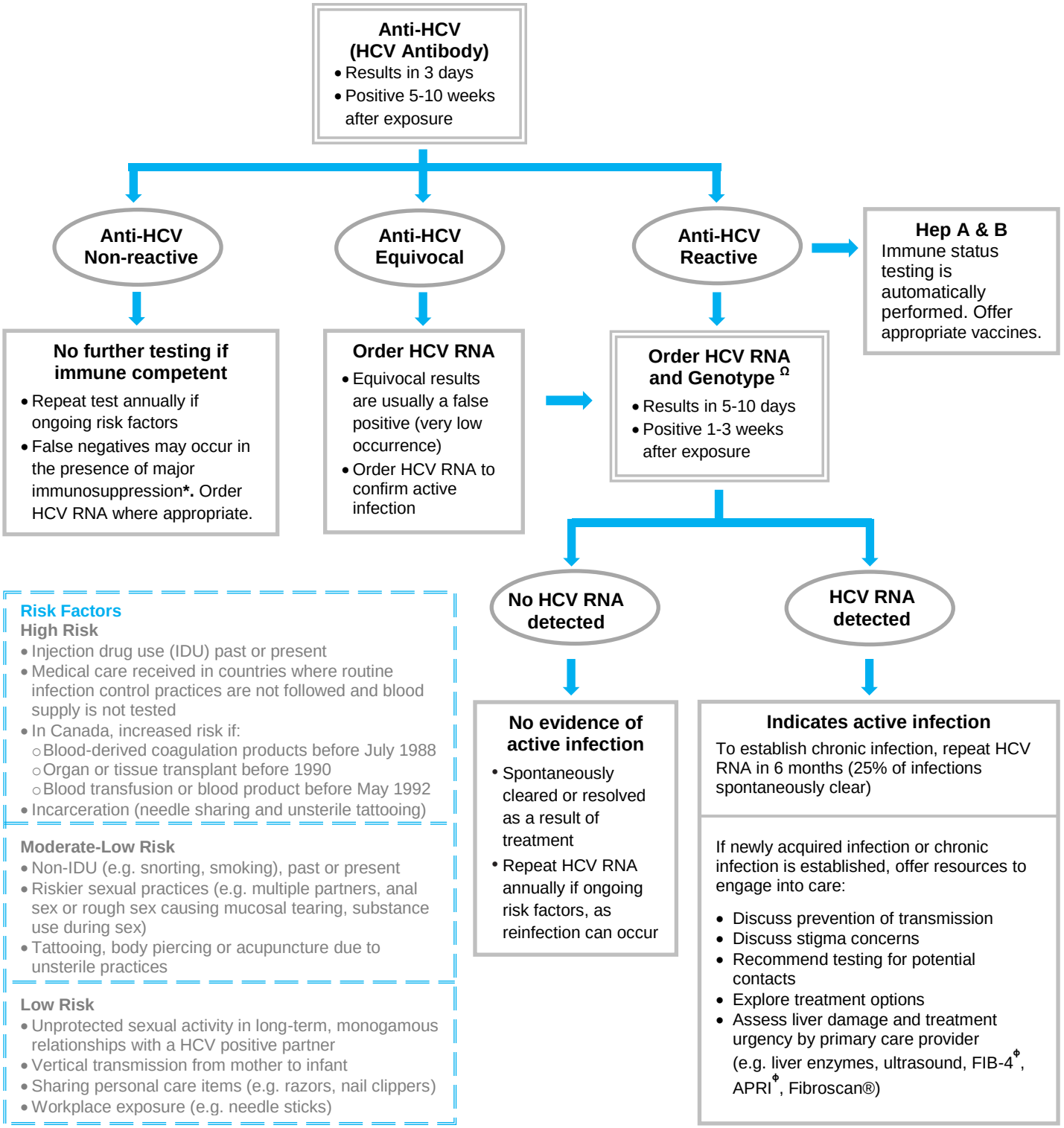
It is recommended that testing for HCV RNA be performed at six weeks of age and/or HCV antibody testing at 18 months of age to determine if this infant has become infected with HCV. Please refer to the attached infant testing algorithm.

Please contact me if you have any questions.

Sincerely,

{First Name Last Name}
{Position}

APPENDIX E: Quick Reference Guide for Health Care Providers



* HIV+ (CD4+ < 200 cells/mm^3), long-term use of immunosuppressants, chronic kidney disease and agammaglobulinemia

Ω BCCDC Public Health Laboratory can do genotype testing on 'HCV RNA detected' specimens only. If requested at the same time as the HCV RNA, the genotype will be done and a new EDTA tube is **NOT** required

ϕ For an online calculator, see http://www.hepatitisc.uw.edu/page/clinical-calculators/apri

Page 2 - Quick Reference Guide for Health Care Providers

Background

Injection drug use is the major source of new infections. As people who inject drugs also have a higher prevalence of HIV, HBV, mental illness and social and material deprivation, prevention strategies need to be multi-factorial.

Prevalent infections are commonly seen in people born in 1945-64, immigrants from endemic countries (high prevalence areas include regions of Central and East Asia, and North Africa/Middle East*) and people who have used illicit drugs in the past.

There are 7 genotypes of HCV, of which 1, 2 and 3 are the most common in North America and BC. Treatment previously consisted of 24 to 48 weeks of ribavirin and injectable pegylated interferon, and cure rates ranged from 40 to 80%. Newer direct acting antiviral agents are well tolerated can achieve cure rates of ~ 95% within 12 weeks of treatment.

Key education points to provide with HCV testing
Engage into care
• Ensure immunizations are up to date (see special populations and routine adults schedules) • Assess and counsel about safer alcohol use • Assess for substance use and need for counselling, harm reduction services and opioid substitution therapy. • Offer STI screening • Clinical supports and general healthy liver education (e.g. diet and acetaminophen use)
Key education points to provide with active infection
Transmission prevention
• Do not share personal care items • Do not donate blood, semen, breast milk or body organs/tissues • Dispose items and sharps with blood in separate bags or containers • Keep all open cuts and sores covered • Blood spills can be cleaned with a solution of 1 part bleach to 9 parts water. Apply and let sit for 10 minutes before rinsing. • There is no immunization and no post-exposure prophylaxis for HCV

* For estimated rates by region, see http://dx.doi.org/10.1002/hep.26141

Clinical Description

Newly acquired HCV infection: symptoms are usually absent, but can include a wide spectrum of illness, including jaundice.

Chronic HCV infection: symptoms are absent. Over decades, 20% will develop cirrhosis and 1-5% will develop hepatocellular carcinoma. Chronic HCV is a major cause of liver transplantation.

Laboratory

HCV Antibody: produced when exposed to HCV and usually remains present for life. A reactive anti-HCV test does not distinguish between resolved or current HCV infection. Does **NOT** need to be repeated once result is reported as reactive.

HCV RNA: confirms current active infection. Used to predict and monitor treatment response, but does not correlate with disease progression.

HCV Genotype: determines appropriate HCV treatment and counselling.

Resources

BCCDC virology requisition and program information
http://www.bccdc.ca/health-professionals/professional-resources/laboratory-services

Acute HCV case report form
http://www.bccdc.ca/health-professionals/professional-resources/surveillance-forms

For Health Care Providers:

Canadian Association for the Study of the Liver – 2015 Hepatitis C Guidelines
http://www.hepatology.ca/

University of Washington – Hepatitis C Online
http://www.hepatitisc.uw.edu/

For clients and Health Care Providers:

BCCDC Hepatitis Prevention & Care
http://www.bccdc.ca/our-services/programs/hepatitis-prevention-care

HealthLinkBC Files
http://www.healthlinkbc.ca/servicesresources/healthlinkbcfiles/

Hepatitis Education Canada
http://hepatitiseducation.med.ubc.ca/resources/

Hepatitis Education Canada
Programme canadien d'éducation sur l'hépatite

Questions?
BCCDC Public Health Laboratory
1-877-747-2522

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