Primary Care Management of Chronic Hepatitis C
Professional Desk Reference 2009

WHO SHOULD BE SCREENED FOR THE HEPATITIS C VIRUS (HCV)?

(1) Anyone with RISK BEHAVIOURS/POTENTIAL EXPOSURES to HCV

**HIGH RISK**

- Injection drug use (IDU)
  - anytime in the past or present, even if only once
  - due to shared/contaminated drug preparation/injection materials (e.g., syringe/needle, spoon/cooker, water, drug solution, filter)

- Incarceration
  - exposures due to:
    - shared/contaminated drug preparation/injection materials (e.g., as above)
    - shared/contaminated tattooing materials (e.g., needles, inks)
    - physical trauma (e.g., fighting where blood is present)
    - unprotected sex where blood may be present (e.g., anal intercourse, fisting)

- Born, traveled, or resided in a region in which HCV infection is more common
  - due to lack of universal precautions and medical/dental practices using contaminated equipment (e.g., childhood immunizations, injections, multi-dose vials, surgery, transfusion, etc.)

**INTERMEDIATE RISK**

- Hemodialysis
- Infant born to mother with HCV infection
- Needle stick injuries

**OTHER RISKS SOMETIMES ASSOCIATED WITH HCV EXPOSURE**

- Sharing sharp instruments/personal hygiene materials with HCV+ person (e.g., razors, scissors, nail clippers, toothbrush)
- Tattooing, body piercing, scarification, female genital mutilation or other ceremonial rituals
  - due to shared/contaminated materials

- Intranasal (snorting) & inhalation drug use
  - due to shared/contaminated drug use materials (e.g., pipes, straws)

- Homelessness, residency in group homes or shelters

- Higher-risk sexual behaviour
  - Unprotected sex with HCV+ partner (non-monogamous relationship)
  - Unprotected sex with partner with STI (e.g., HIV, HBV, LGV)
  - Unprotected sex with multiple sexual partners
  - Unprotected sex where blood may be present (e.g., vaginal sex during menstruation; traumatic sex that can cause mucosal tearing e.g., fisting, sex toys; anal intercourse)

(2) Anyone with CLINICAL CLUES suspicious for hepatitis C infection (and above risk factors)

- Abnormal liver biochemistry (e.g., ↑ALT)
- Drug and/or alcohol dependency (past or present)
- Blood diseases requiring multiple transfusions of blood products (e.g., hemophilia, thalassemia, sickle cell anemia, vWD)
- HBV infection
- HIV infection
- Signs of chronic liver disease (e.g., hepatomegaly +/- splenomegaly, spider nevi, palmar erythema, jaundice)
- Vasculitis (due to associated cryoglobulinemia)
- History of unexplained renal impairment
- Non-Hodgkin’s lymphoma

MOST PEOPLE WILL HAVE NO SPECIFIC SYMPTOMS
SCREENING FOR HCV EXPOSURE & DETERMINING CHRONIC HEPATITIS C INFECTION

Has there been recent exposure to potentially HCV infected blood?

If YES — see Module 7 regarding acute hepatitis C infection

If NO — follow algorithm below

**START HERE**

**ANTI-HCV**

ALT, AST
Consider HIV antibody
Consider step 4 below

**ANTI-HCV POSITIVE**

Check HCV-RNA

HCV-RNA Negative

No chronic HCV infection

Resolved HCV infection or consider other liver diseases if ALT ↑

Repeat ALT, AST and HCV-RNA in 6 months
Do steps 1-5 below

HCV-RNA Positive

Chronic HCV infection

Refer to experienced colleague*
Do steps 1-7 below

**ANTI-HCV NEGATIVE**

If not at high risk, no HCV infection
No further action

If high risk (see Module 1) or immunocompromised
Check HCV-RNA

HCV-RNA Positive

Chronic HCV infection

Refer to experienced colleague*
Do steps 1-7 below

HCV-RNA Negative

No HCV infection
Do step 3 below

1. Complete physical exam

2. Evaluate for other liver diseases
   - Drugs (review history)
   - Alcohol (AST/ALT>1 Note: the same ratio may also be seen in cirrhosis)
   - Fatty liver (consider if central obesity or diabetic)
   - Hemochromatosis (check Fe, TIBC). Ferritin not useful because often elevated with
≤ALT or any inflammatory disease
   - Wilson’s disease (check ceruloplasmin)

3. Evaluate other viruses affecting liver health or potential treatment:
   a. Offer HIV testing (similar risk factors)
   b. Hepatitis A & hepatitis B testing — see step 4

4. Assure immunity to HAV & HBV
   - Check anti-HAV IgG, HBsAg, anti-HBs, anti-HBc
   - Offer hepatitis A & hepatitis B vaccine if negative
   - Consider verifying titres at 4 weeks post-hepatitis A & B immunization series in the HIV positive population or cirrhotic

5. Patient education (see Modules 4 & 5)

6. Further evaluation of chronic infection:
   a. Risk factor review (see Module 1)
   b. Determine duration of infection (use proxy measures: “in what year did you first inject drugs?”)
   c. Targeted physical exam for signs of advanced liver disease
   d. ALT, AST, T-Bili, GGT, INR, Albumin
   e. HCV viral load
   f. HCV genotype

7. If cirrhotic:
   a. Hepatocellular carcinoma surveillance – ultrasound every 6 months
   b. Annual influenza vaccination
   c. One-time pneumococcal vaccination

* Experienced colleague may be a hepatologist, gastroenterologist, infectious diseases specialist, or family physician with experience in HCV management.
EVALUATION OF THE HCV INFECTED ADULT

All patients with chronic hepatitis C infection (HCV-RNA +) should be referred to an experienced colleague* for further assessment & possible treatment

**Special clinical considerations**

- Evaluate liver function – measure T-Bili, Albumin, INR (Note: low platelets suggest cirrhosis in this population)
- Probable cirrhosis – screening liver ultrasound for HCC. If suspicious mass found, refer urgently to specialist
- HIV positive
  - refer to experienced colleague* with expertise in HCV-HIV co-infection
- Extra-hepatic HCV (e.g., PCT, skin vasculitis, renal failure, NHL) – needs to see experienced colleague* urgently
- Pregnant women with chronic hepatitis C infection – no change to routine obstetrical care unless cirrhotic
- Pregnant women with cirrhosis require referral to an expert in high risk obstetrical care
- HCV positive moms can breastfeed as long as nipples are not cracked/bleeding. Can resume breastfeeding when nipples healed
- Children & Adolescents – no urgent care required. Test newborns of HCV-rNA positive mothers at 1 year using HCV-rNA test. (Note: anti-HCV may be positive if infant is tested before 1 year old.) Children rarely develop end-stage liver disease.

EDUCATION FOR CHRONIC HCV INFECTED ADULTS

Natural history of chronic HCV infection

PROJECTION OF LIFETIME OUTCOMES IN HCV INFECTION

100 ACUTE HCV INFECTIONS

- 20% recovery
- 80% persistent infections

20 PATIENTS

- 30% severe progressive hepatitis†
- 40% variable progression†
- 30% chronic, nonprogressive††

24 patients

- End-stage disease, HCC, liver transplantation, death

80 PATIENTS

- Treatment failure (10-60%)
- Antiviral therapy 56 patients (see Module 6)
- Genotype/host dependent

- Sustained response/cure (40-90%)**

22 patients

34 patients

†† For reasons unknown, disease is more rapidly progressive with age and requires ongoing monitoring.


† Risk factors which may contribute to liver damage (fibrosis progression)

- Older age (> 40yrs) when infected
- Alcohol intake > 50g/day (3 drinks)
- Male sex
- Coinfection with HBV or HIV
- Longer duration of infection
- Advanced fibrosis at time of diagnosis
- Central obesity (WC>80cm♀, >102cm♂)
- Smoking (daily tobacco/marijuana increases risk of HCC)

**Note: undetectable HCV-RNA at 6 months after full course of hepatitis C treatment
Adhere to and be actively involved in the follow-up and monitoring of your hepatitis C infection

Be informed. Obtain current/accurate information about hepatitis C

Be physically active

Reduce stress and maintain an active support network

Limit alcohol intake (less than 2 drinks/week)

Promote smoking cessation (e.g., tobacco, marijuana)

Maintain a healthy weight (ideal BMI 20-25, ideal WC <80cm ♀, <102cm ♂)

Ensure hepatitis A & hepatitis B immunity

Consider therapy for hepatitis C

Never donate blood, organs, semen, tissues

Never share materials used to prepare, inject, or inhale drugs (e.g., syringe/needle, pipe, straw, spoon/cooker, water, drug solution, filter)

Never share sharp instruments/personal hygiene materials with others (e.g., razors, scissors, nail clippers, toothbrush)

Consider the potential health risks of tattooing and body piercing

Discuss your HCV status with drug using partners

Sexual activity is safe unless it involves trauma or higher risk sexual behaviours (see Module 1)

In non-monogamous relationships and for new sexual partners – use condoms/dental dams for sex to limit potential HCV transmission as well as the transmission of STI

There is currently no proven method to reduce the risk of vertical transmission (approx. 5%)

HCV+ mother can breastfeed unless nipples are cracked or bleeding. Can resume breastfeeding when nipples are healed

Avoid benzodiazepines, aminoglycosides, and narcotics including codeine

No ASA or NSAIDs if possible

Acetaminophen (e.g., Tylenol), oral contraceptive pills, and statins are safe to use

Keep your health care provider informed of any complementary/alternative therapies or supplements taken

Adhere to and be actively involved in the follow-up and monitoring of your hepatitis C infection

Be informed. Obtain current/accurate information about hepatitis C

Be physically active

Reduce stress and maintain an active support network

Therapy for hepatitis C can cure HCV infection in up to 90% of cases (40-90%)

Efficacy depends on the HCV genotype. People respond best in the following order: genotype 2 > 3 > 4 > 1. Genotypes 5 & 6 not yet known

Treatment duration also depends on HCV genotype or HIV status: 24 to 72 weeks

For those who opt not to have treatment, regular follow-up should be encouraged to monitor disease progression and desire for treatment

Side effects from hepatitis C medications are common. Before starting hepatitis C therapy consider and discuss the balance between side effects and potential benefits. Experienced colleagues are prepared to deal with most side effects that may occur

Remember: Not everybody needs or wants treatment. Many people live well with hepatitis C. As symptoms do not correlate with disease severity, sophisticated tests are required to assess the degree of hepatic fibrosis (e.g., liver biopsy, fibroscans/fibrotest if available)
Has there been recent exposure to potentially HCV infected blood (e.g., recent needle stick injury, recent injection drug use)? Investigate for acute hepatitis C if the patient meets the following criteria:

**Clinical Case definition:** an acute illness with a discrete onset of any sign or symptom consistent with acute viral hepatitis (e.g., anorexia, RUQ abdominal discomfort, nausea, vomiting, malaise) and elevated serum ALT, +/- jaundice.

**Laboratory Criteria for diagnosis:**

One or more of the following criteria:
1) Anti-HCV becomes positive at 4-12 weeks post exposure

OR
2) HCV-RNA becomes positive at 2-4 weeks post exposure

AND, meets the following two criteria:
1) Anti-HAV IgM negative

AND
2) Anti-HBc IgM negative

**Case Classification**

**Confirmed:** a case that meets the clinical case definition, is laboratory confirmed, and is not known to have chronic hepatitis C.

**Unconfirmed:** consider other causes of acute hepatitis (e.g., alcohol, hepatitis A or hepatitis B, medications, other toxins, autoimmune hepatitis).

Adapted from www.cdc.gov/ncphi/diss/nndss/print/hepatitisacutecurrent.htm

Diagnosis of acute HCV infection is reason for an urgent referral to an experienced colleague*. If viral clearance does not occur within 12 weeks of exposure, antiviral therapy should be started as there is a very high rate (>90%) of viral clearance following treatment of acute HCV.

*Experienced colleague may be a hepatologist, gastroenterologist, infectious diseases specialist, or family physician with experience in HCV management.

**Acute hepatitis C infection suspected – recent exposure to potentially HCV infected blood**

**ORDER THESE TESTS AT FIRST VISIT**

- **Anti-HCV** (to ensure not previously infected. This will become positive at 4–12 weeks post exposure)
- **HCV-RNA (qualitative PCR)** (this will become positive at 2–4 weeks post exposure)
- **ALT AST**
- **HIV**
- **Anti-HAV IgM** (to rule out acute hepatitis A)
- **HBsAg Anti-HBcTotal, Anti-HBc IgM** (to help rule out acute hepatitis B)

**HCV-RNA POSITIVE**

- **Anti-HCV Positive**
  - Test result at less than 4 weeks post exposure
  - Pre-existing chronic HCV infection likely
  - See Module 2 – Chronic HCV infection
  - Immediate referral to experienced colleague* for evaluation of need for antiviral therapy (call your colleague)
  - Immediate treatment recommended
  - Repeat HCV-RNA at 12 weeks required to confirm persistent infection

- **Anti-HCV Negative** with seroconversion (Anti-HCV positive) 4–12 weeks post exposure
  - Acute HCV infection
  - Repeat HCV-RNA at 2-4 wks and if RNA positive, repeat in 12 more weeks

**HCV-RNA NEGATIVE**

- **Anti-HCV Negative**
  - Still possible acute HCV infection
  - Resolved HCV infection or false positive serology
  - Repeat HCV-RNA in 1 year (to confirm viral clearance)
  - HCV-RNA Positive
  - HCV viral clearance (Anti-HCV persists)

- **Anti-HCV Positive** at time of 1st test
  - Resolved HCV infection or false positive serology
  - Repeat HCV-RNA in 1 year (to confirm viral clearance)

- **HCV-RNA Negative**
  - Still possible acute HCV infection
  - Resolved HCV infection or false positive serology
  - Repeat HCV-RNA in 1 year (to confirm viral clearance)
WEB RESOURCES

Patients:
Canadian Liver Foundation: www.liver.ca
Health Canada: www.hc-sc.gc.ca/iyh-vsv/diseases-maladies/hepc_e.html
Public Health Agency of Canada: www.phac-aspc.gc.ca/hepc

Health Care Providers:
Canadian Association for the Study of the Liver: www.hepatology.ca
Management of chronic hepatitis C: consensus guidelines: www.hepatology.ca/cm/FileLib/hepC.pdf
Canadian Medical Association: www.cma.ca
Hepatitis C: a review for primary care physicians (Wong, Lee, 2006): www.cmaj.ca/cgi/content/full/174/5/649
A study to characterize the epidemiology of hepatitis C infection in Canada, 2002 (Remis RS, 2004): www.phac-aspc.gc.ca/hepc

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