

Hepatitis C, Chronic

PROTOCOL CHECKLIST

- Merlin automatically assigns diagnosis status and reports chronic hepatitis C cases
- Follow up any special situations as time allows
 - Special situations may include:
 - Cases under the age of 30
 - Cases over the age of 60
 - Any cases where the initial notification includes information suggestive of an acute hepatitis C infection (provider diagnosis of acute hepatitis C, provider notes suggesting acute disease, symptoms of acute viral hepatitis, or elevated liver function tests)
- Enter additional data obtained from physician/ lab into Merlin
- Manually change disease code from chronic to acute pending laboratory/physician diagnosis if necessary
- Investigate acute hepatitis C cases according to corresponding guidelines

Hepatitis C, Chronic

1. DISEASE REPORTING

A. Purpose of reporting and surveillance

To identify those persons who are chronic carriers and may still be infectious; to educate and prevent further transmission. To identify chronic carriers so that they may seek treatment to prevent long term complications due to hepatitis C infection. To assess disease burden and estimate cost.

B. Legal reporting requirements

Laboratories and physicians are required to report chronic hepatitis C to the county health department (CHD) within one working day of identification/diagnosis.

C. County health department investigation responsibilities

Chronic hepatitis C cases are automatically reported in Merlin and may not require further investigation. Special situations, such as children and young adults, may require follow up. See Section 5, Case Investigation for further details.

2. THE DISEASE AND ITS EPIDEMIOLOGY

A. Etiologic agent

The Hepatitis C virus (HCV) is an enveloped positive single-stranded RNA virus of the Flavivirus family. There are eleven major genotypes, many subtypes, and approximately 100 different strains of HCV. Genotypes 1 to 3 have a worldwide distribution. Types 1a and 1b are the most common, accounting for approximately 60% of global infections, and predominate in North America. The determination of the infecting genotype is important for the prediction of response to antiviral treatment: genotype 1 is generally associated with a poor response to interferon alone, whereas genotypes 2 and 3 are associated with more favorable responses.

B. Description of illness

The majority of chronic HCV infections are asymptomatic. In 60% to 70% of persons with chronic infection, HCV will cause chronic liver disease, which can include cirrhosis or hepatocellular carcinoma (a type of liver cancer). Infection with HCV is the leading indication for liver transplantation among adults in the U.S.

When present, signs and symptoms can include:

- Fever
- Fatigue
- Loss of appetite
- Nausea
- Vomiting
- Abdominal pain

- Dark urine
- Clay-colored bowel movements
- Joint pain
- Jaundice
- Cirrhosis
- Liver failure
- Hepatocellular cancer

People with chronic hepatitis C remain infectious throughout their lifetime, unless successfully treated. Infected people should be counseled to avoid hepatotoxic agents, and should be informed of the risks of excessive alcohol ingestion which will exacerbate liver disease. All persons infected with HCV should be vaccinated against hepatitis A and hepatitis B.

C. Reservoirs

Hepatitis C does not have any other known reservoirs besides humans. Although the virus had been transmitted to chimpanzees experimentally, an animal reservoir in nature has not been identified.

D. Modes of transmission

Hepatitis C virus is transmitted primarily by parenteral exposure to blood of HCV-infected people. Sexual transmission of HCV may occur, but studies of monogamous serodiscordant partners have shown that sexual transmission is rare. HIV infection increases the risk of HCV transmission. The virus can be spread by:

- Contact with contaminated needles, especially injection drug equipment
- Tattoo and body piercing instruments if not sterilized; transmission rarely occurs in licensed commercial tattoo or piercing facilities
- Household contact with an infected person, usually through shared items that may be exposed to blood, such as toothbrushes, razors, and nail clippers
- Occupational exposure through accidental needle sticks
- Lack of infection control in the health care setting
- Unprotected sexual contact with an infected person, especially among persons with multiple sex partners or men who have sex with men (MSM)
- An infected mother to her infant during delivery (This is an uncommon route of transmission, requiring a high viremia. On average, it occurs in four out of 100 cases, but is more common in mothers co-infected with HIV.)

The hepatitis C virus is not an airborne virus, and never transmits through casual contact such as coughing, sneezing, being in the same area as an infected person, or by consuming contaminated food or water. The most common route of transmission is through injection drug use. Transmission due to transfused blood and blood products, including those used to treat hemophilia, used to be common and has been essentially eradicated by testing of products for hepatitis C.

E. Incubation period

The incubation period for chronic hepatitis C is difficult to determine due to the absence of clinical symptoms, and the lack of a serologic marker of infection. The incubation period is

estimated to average six to seven weeks but has been shown to have a range of two weeks to six months. Chronic hepatitis C may persist for up to 20 years before onset of cirrhosis or liver cancer.

F. Period of communicability

All persons with detectable HCV RNA in their blood are potentially infectious to others. Infectivity of chronically infected persons varies from high to moderate depending on the severity of disease and viremia.

G. Treatment

Guidance on treatment can be found at the following sites:

http://www.aasld.org/practiceguidelines/Documents/Bookmarked%20Practice%20Guidelines/Diagnosis_of_HEP_C_Update.Aug%2009pdf.pdf

and

http://www.hcvadvocate.org/hepatitis/factsheets_pdf/AASLD%20HCV%20Practice%20Guidelines%20Genotype%201%202011%20update.pdf

Therapy for hepatitis C is a rapidly changing area of clinical practice and many advances have been made in recent years. Combination therapy with pegylated interferon and ribavirin is approved by the Food and Drug Administration (FDA) and is the treatment of choice for most patients with chronic hepatitis C. Therapies can be expensive and may not be covered by all health insurance plans. Treatment can also have significant adverse reactions. Side effects will vary from person-to-person and can include flu-like symptoms and depression. Response to treatment varies depending on the genotype with which the person is infected. A sustained viral response occurs in 40% to 45% of treated adult patients infected with genotype 1 and approximately 80% in patients with genotype 2 or 3. Recently approved combination therapies for genotype 1 now include direct acting antiviral agents in combination with pegylated interferon and ribavirin. These combination therapies have improved sustained viral response rates from 50% to 80% for patients with HCV genotype 1.

H. Prophylaxis

On the basis of lack of clinical efficacy in humans and data from animal studies, use of immune globulin for post-exposure prophylaxis against HCV infection is not recommended.

I. Vaccination

There is currently no vaccine for hepatitis C. All persons with chronic HCV infection should be immunized against hepatitis A and hepatitis B because of the very high rate of severe hepatitis in patients with chronic liver disease from HCV who become co-infected with hepatitis A or B virus.

J. Chronic Hepatitis C in Florida

Chronic hepatitis C became reportable in Florida in 2001. There has been a steady increase in the number of reports received up to at least 21,000 cases a year from 2009 to 2011. The majority of reports occur in the baby boomer generation (those born between 1946 and 1964). In recent years however, the rate of newly reported chronic hepatitis C cases in those

over the age of 50 has leveled off while the rate in young adults has been rising steadily since 2008.

3. CASE DEFINITION

A. Clinical case definition

Persons with chronic hepatitis C may have no evidence of liver disease or may have a spectrum of disease ranging from chronic hepatitis to cirrhosis or liver cancer. Persons with chronic infection may be asymptomatic.

B. Laboratory criteria for diagnosis

- Antibody to HCV (anti-HCV) positive (repeat reactive) by enzyme immunoassay (EIA), verified by an additional more specific assay (e.g., RIBA or PCR for HCV RNA),
OR
- HCV RIBA positive,
OR
- Nucleic acid test for HCV RNA positive,
OR
- Report of HCV genotype,
OR
- HCV antibody positive (repeat reactive) with a signal to cut-off ratio predictive of a true positive as determined for the particular assay as defined by CDC. (Web link for the signal to cut-off ratios: http://www.cdc.gov/ncidod/diseases/hepatitis/c/sc_ratios.htm)

C. Case classification

Confirmed: A case that is laboratory confirmed AND that does not meet the case definition of acute hepatitis C.

Probable: A case that is HCV antibody positive (repeat reactive) by EIA and has alanine aminotransferase (ALT or SGPT) values above the upper limit of normal, but the HCV antibody EIA result has not been verified by an additional more specific assay and the signal to cut-off ratio that does not meet the above criteria or is not reported.

Suspect: A case that is HCV antibody positive, but absent other diagnostic criteria and does not meet the clinical or laboratory criteria for hepatitis C, acute.

D. Note

Multiple laboratory tests indicative of chronic HCV infection may be performed simultaneously on the same patient specimen as part of a “hepatitis panel.” Testing performed in this manner may lead to seemingly discordant results (e.g., for the purposes of this case definition, any positive result among the three laboratory tests mentioned above is acceptable, regardless of other testing results). HCV RNA levels below positive the cut-off level do not confirm the absence of HCV infection.

A chart for assisting in interpreting hepatitis C serology can be found on the CDC site below:
http://www.cdc.gov/hepatitis/HCV/PDFs/hcv_flow.pdf

4. LABORATORY TESTING

A. Criteria for diagnosis

Hepatitis C serology is the only way to determine the state of infection. Chronic hepatitis C is classified as the presence of HCV antibodies and/or HCV RNA in blood.

B. Services available at the BPHL

The Bureau of Public Health Laboratories (BPHL) runs a chronic hepatitis screen when testing patients for chronic hepatitis. The chronic hepatitis screen includes hepatitis B surface antigen, hepatitis B surface antibody, hepatitis B core total antibody, hepatitis A total antibody and hepatitis C antibody.

C. Testing requests

1. Submitting specimens/isolates to BPHL
 - a. All submissions should be accompanied by Clinical Lab Submission Form 1847



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- b. Electronic Laboratory Ordering (ELO) may also be used by entering request into the HMS State Laboratory System, placing bar coded label on the O&P vial, and writing the date collected on the vial.

2. Specimen collection

Three ml of serum or 6 to 8 ml of whole blood that is properly labeled (name, date of birth, date collected) should be submitted for testing.

3. Packaging and shipping

- a. Testing for chronic hepatitis C is done at all BPHL facilities.
 - b. Place labeled specimen in the proper biohazard transport bag with the Clinical Lab Submission Form 1847. Package according to International Air Transport Association (IATA) regulations, labeling the outer shipping container: *UN3373, Biological Substance Category B.*
 - c. Specimens and isolates should be sent at ambient temperature or cooler, but cool packs should not be in direct contact with vials.
 - d.



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4. Contact the regional laboratory with questions:
- | | |
|--------------|--------------|
| Jacksonville | 904-791-1500 |
| Miami | 305-324-2432 |
| Tampa | 813-974-8000 |
| Pensacola | 850-595-8895 |

D. Interpretation of results:

The fact that many people with chronic HCV infection are asymptomatic and have no evidence of liver disease makes interpretation of laboratory results difficult. The following is a chart used to help determine the status of the patient based on serological testing. Other testing and liver biopsy may be necessary to determine the progression of disease. The following information is available on the CDC website:

http://www.cdc.gov/hepatitis/HCV/PDFs/hcv_graph.pdf

HCV antibody screening test (anti-HCV): The presence of HCV antibodies indicates exposure to the hepatitis C virus. This test cannot distinguish between an acute or chronic infection.

HCV antibody with reported signal to cut-off (S/CO) ratio: Samples with high S/CO ratios confirm positive by supplemental testing more than 95% of the time and thus do not require further testing. Less than five of every 100 might represent false positives and more specific testing can be requested. Specific S/CO ratios have been determined for each HCV antibody assay. A list of confirmatory S/CO ratios for approved HCV antibody assays can be found here: <http://www.cdc.gov/hepatitis/hcv/labtesting.htm>.

HCV RNA, qualitative: Detects the presence or absence of HCV RNA.

HCV RNA, qualitative (viral load): Detects and measures the number of viral RNA particles in the blood; often used before and during treatment to determine response to treatment. Successful treatment can lead to undetectable levels of HCV RNA.

HCV RIBA: A more specific anti-HCV assay, used as a confirmatory supplemental test.

Hepatitis C Genotype: Viral genotyping by RT-PCR determines the HCV genotype; usually done prior to treatment to give an idea of the likelihood of treatment success and the necessary length of treatment

If HCV Test Result is:			Interpretation		Action
HCV Antibody Screening Test*	HCV Antibody Supplemental Test RIBA [†]	HCV RNA	HCV Antibody	HCV Infection	Additional Testing or Evaluation
Negative	Not Needed	Not Needed	Negative	None	No
Positive	Not Done	Not Done	Not Known	Not Known	Supplemental anti-HCV (RIBA) or HCV RNA
Positive	Not Done	Negative	Not Known	Not Known [♦]	Supplemental anti-HCV (RIBA)
Positive (high S/CO ratio [‡])	Not Done	Not Done	Positive	Past/Current	Evaluate for chronic infection and liver disease
Positive	Negative	Not Needed	Negative	None	No
Positive	Positive	Not Done	Positive	Past/Current	Evaluate for chronic infection and liver disease
Positive	Positive	Negative	Positive	Past/Current [♦]	Repeat HCV RNA; Evaluate for chronic infection and liver disease
Positive	Positive/Not Done	Positive	Positive	Current	Evaluate for chronic infection and liver disease
Positive	Indeterminate	Not Done	Indeterminate	Not Known	Test for HCV RNA or repeat anti-HCV testing
Positive	Indeterminate	Positive	Positive	Current	Evaluate for chronic infection and liver disease
Positive	Indeterminate	Negative	Indeterminate	Not Known [♦]	Test for HCV RNA or repeat anti-HCV testing

* EIA (enzyme immunoassay) or CIA (enhanced chemiluminescence immunoassay)

[†] RIBA (recombinant immunoblot assay), a more specific HCV antibody assay

[♦] Single negative HCV RNA result cannot determine infection status, as persons might have intermittent viremia

[‡] Samples with high S/CO ratios usually (>95%) confirm positive, but supplemental serological testing was not performed. Less than 5 of every 100 might represent false positives; more specific testing should be requested, if indicated.

5. CASE INVESTIGATION

A. Chronic Hepatitis case management

In most populations, investigation of chronic cases of hepatitis C is not required. Children and young adults with chronic hepatitis C are unusual and should be investigated as time allows, as this could also be an indication of an acute hepatitis C infection. A viral Hepatitis Case Report Form is available to guide the investigation and assist in follow-up:

[http://www.floridahealth.gov/diseases-and-conditions/disease-reporting-and-management/disease-reporting-and-surveillance/ documents/crf-hepatitis-viral.pdf](http://www.floridahealth.gov/diseases-and-conditions/disease-reporting-and-management/disease-reporting-and-surveillance/documents/crf-hepatitis-viral.pdf).

Hepatitis cases are automatically reported in Merlin. If laboratory results or physician notes indicate a diagnosis of acute hepatitis C, the disease code should be manually changed and a case investigation will be conducted following the corresponding guidelines.

B. Merlin data entry

Create a case in Merlin under disease code **HEPATITIS C-07054**. Enter available data. The hepatitis C disease code is automatically assigned as chronic and reported in Merlin. Based on the completeness of the laboratory results, the diagnosis status will be set as confirmed, suspect or probable. In the instance of an incomplete case status, the case will automatically be assigned a blank diagnosis status until completed information is entered. Once the completed data are entered, the case will automatically be reported. When laboratory results and/or physician diagnosis are received that specifically indicate acute hepatitis C, the CHD user can access the case, enter relevant results and manually change the disease code from chronic to acute. If the case has already been reported it will remain so, if not, it will move to the hepatitis C, acute task list for further investigation and completion by the CHD. Merlin will not automatically match hand entered cases of acute hepatitis C with cases that have been automatically reported as chronic. Checking the CHD "Chronic Hepatitis B and C" list for preexisting cases before entering a new one will save time and reduce duplication of cases.

6. CONTROLLING FURTHER SPREAD

A. Patient/Household education on prevention recommendations

1. Disinfect all items that may come in contact with blood and body fluid.
2. Do not share personal items that may have blood on them: razorblades, toothbrushes.
3. Cuts and sores on the skin should be covered to prevent the spread of infected blood or body fluid.
4. Patients should be informed of the risk of sexual transmission. While sexual transmission of HCV is not well-documented, hepatitis C virus-positive persons engaged in high-risk sexual activities* should be counseled to use latex barriers correctly every time they have sex. Special populations such as MSM and HIV positive individuals may be susceptible to sexual transmission of HCV.
5. Do not share needles or syringes. Disposable needles should be used only once then discarded. As a last resort, undiluted household bleach can be used to clean syringes and needles.
6. Active injection drug users should be directed to needle exchange programs and drug rehabilitation services.

7. Blood spills, including dried blood, still carry a risk of infection. All blood spills should be cleaned using 1:10 dilution of one part bleach to 10 parts water.

B. Isolation of cases

Standard precautions should be observed to prevent exposures to blood and body fluids in health care settings.

C. Management of contacts

To identify who may be a contact, see [Modes of Transmission](#).

Symptomatic contacts: May still be in the acute stage of HCV infection; if the suspect or probable case definition is met, the contact should be reported, investigated, and managed in the same manner as a confirmed case.

Asymptomatic contacts: If the suspect or probable case definition is met, the contact should be reported, investigated, and managed in the same manner as a confirmed case.

* High-risk sexual activities are any type of penetrative sexual contact without using barrier protection, especially if the person has multiple sexual partners (even if one is steady) regardless of vaccination status.

7. MANAGING SENSITIVE SITUATIONS

A. Work or child care restrictions

No occupational, school, or child care restrictions are necessary for hepatitis C infected individuals.

B. Needle stick and similar exposure

Accidental needle sticks carry a risk for transmission of hepatitis C

C. Case is a recent blood donor or recipient

Notify the blood bank immediately so that any unused product can be recalled.

8. IMPORTANT LINKS

A. Viral Hepatitis Case Report Form

<http://www.floridahealth.gov/diseases-and-conditions/disease-reporting-and-management/disease-reporting-and-surveillance/documents/crf-hepatitis-viral.pdf>

B. CDC Hepatitis C Page

<http://www.cdc.gov/hepatitis/C/index.htm>

C. Florida Department of Health Bureau of HIV/AIDS and Hepatitis

<http://www.floridahealth.gov/diseases-and-conditions/aids/index.html>

D. Health care Investigation Guide

<http://www.cdc.gov/hepatitis/Outbreaks/PDFs/HealthcareInvestigationGuide.pdf>

9. REFERENCES

- A. American Academy of Pediatrics. (2012). *Red Book: 2012 Report of the Committee on Infectious Diseases* (29th ed.). Grove Village, IL: American Academy of Pediatrics.
- B. Heymann, D.L. (2008). *Control of Communicable Disease Manual* (19th ed.). Washington DC: American Public Health Association.
- C. CDC. (2001). *MMWR: Updated U.S. Public Health Service Guidelines for the Management of Occupational Exposures to HBV, HCV, and HIV and Recommendations for Postexposure Prophylaxis*. June 29, 2001/ 50(RR11);1-42.