Hepatitis C, Acute

PROTOCOL CHECKLIST

- ☐ Enter available information into Merlin upon receipt of initial report
- ☐ Review background on disease, case definition, and laboratory testing
- ☐ Contact provider
- ☐ Interview patient
  - ☐ Review disease facts
    - ☐ Modes of transmission (see page 3)
    - ☐ Incubation period
    - ☐ Symptoms
    - ☐ Risk of co-infection with hepatitis A and B
      - ☐ Provide information on obtaining hepatitis A and B vaccines
  - ☐ Ask about exposure to relevant risk factors
    - ☐ Blood to blood contact with someone with hepatitis C
    - ☐ Occupational exposure
    - ☐ Drug use
    - ☐ Tattoos/body piercings
    - ☐ Sexual contact
  - ☐ Identify contacts
    - ☐ Refer symptomatic contacts to a health care provider
  - ☐ Determine if patient can be epi-linked to an existing case and if patient is part of an outbreak
  - ☐ Provide information on how to prevent further transmission (see page 3)
  - ☐ Address patient's questions or concerns
- ☐ Follow-up on special situations, including outbreaks or cases in sensitive situations
- ☐ Enter additional data obtained from interview into Merlin

Hepatitis C, Acute

1. DISEASE REPORTINGTHE DISEASE AND ITS EPIDEMIOLOGY

A. Purpose of reporting and surveillance

1. To identify those persons who are carriers and may still be infectious to educate and prevent further transmission
2. To identify carriers so that they may seek treatment to prevent long-term complications due to hepatitis C infection
3. To identify outbreaks and other undiagnosed patients
4. To determine if there is a source of infection of public health concern and to stop transmission from such a source

B. Legal reporting requirements

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

C. County health department investigation responsibilities

1. Begin investigation within one business day of receiving report from a provider or laboratory.
2. Contact patient and/or provider to complete case interview.
3. Report all confirmed and probable cases in Merlin.
4. Report liver enzyme results for all patients where these are available.

2. THE DISEASE AND ITS EPIDEMIOLOGY

A. Etiologic agent

The hepatitis C virus (HCV) is an enveloped positive single-stranded RNA virus of family Flaviviridae. There are eleven major genotypes, many subtypes, and about 100 different strains of HCV. Genotypes 1 to 3 have a worldwide distribution. Types 1a and 1b are the most common, accounting for about 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

Signs and symptoms of hepatitis C infection are indistinguishable from those of hepatitis A or hepatitis B infection. Acute disease tends to be mild and insidious in onset. Most infections are asymptomatic. Jaundice occurs in fewer than 20% of patients.

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

Persistent infection with HCV (hepatitis C, chronic) occurs in up to 80% of those infected. 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 has 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,
- 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) (uncommon),

- 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,
- Household contact with an infected person, usually through shared items that may be exposed to blood, such as toothbrushes, razors, and nail clippers (uncommon).

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 transfusion of 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 hepatitis C is difficult to determine due to 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.

F. Period of communicability

All persons with detectable HCV RNA in their blood are potentially infectious to others.

G. Treatment

Guidance on treatment can be found at the following site:
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 FDA and is the treatment of choice for most patients with 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 genotypes 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 the hepatitis A or B virus.

J. Hepatitis C, Acute in Florida

Hepatitis C, acute infection became reportable in Florida in 2001. The incidence rate for acute hepatitis C has been variable over the last ten years. It was low from 2005 to 2008 but has been increasing since 2008. In 2011, there was a 50% increase in comparison to the average incidence from the previous five-year average (2006 – 2010). A total of 100 cases were reported in 2011, for an incidence rate of 0.53 cases per 100,000 persons. The most common reported risk factor was injection drug use (41%), followed by non-injection drug use (33%), recent tattoo (14%) and recent body piercing (4%). Sixty-four percent of the cases were classified as confirmed. The hepatitis C acute surveillance case definition changed in 2008, leading to more cases being classified as confirmed compared to previous reporting years (2006: 36.0%, 2007: 34.7%, 2008: 60.4%, 2009: 68.8%, 2010: 53.3%). There is no seasonal trend for acute hepatitis C infection. Overall, the highest incidence rates for 2011 occurred among those 25 to 34 years-old, which is consistent with historical trends. Because many HCV infections are asymptomatic, some acute infections may have been erroneously reported or classified as chronic infections.

3. CASE DEFINITION

A. Clinical case definition

An acute illness with:

1. Discrete onset of symptoms that commonly include fever, headache, malaise, anorexia, diarrhea, vague abdominal discomfort, nausea and vomiting;
   AND EITHER
2. Jaundice **or** serum alanine aminotransferase (ALT) levels over 400 IU/L.

A documented negative HCV antibody laboratory test result followed within six months by a positive test result (as described in the laboratory criteria for diagnosis, below) does not require an acute presentation to meet the surveillance case definition.

B. Laboratory criteria for diagnosis

1. One or more of the following three criteria:

- Hepatitis C Virus Recombinant Immunoblot Assay (HCV RIBA) positive,
  OR
- Nucleic Acid Test (NAT) for HCV RNA Positive (including quantitative, qualitative and genotype testing),
  OR
- Antibodies to hepatitis C virus (anti-HCV) screening test positive with a signal to cut-off ratio predictive of a true positive as determined for the particular assay as defined by CDC. The website for signal to cut-off ratios is available at: http://www.cdc.gov/hepatitis/HCV/LabTesting.htm

AND, meets the following two criteria (if done):

- IgM anti-HAV negative (if done),
  OR
- IgM anti-HBc negative (if done).

2. A documented negative HCV antibody laboratory test followed within six months by a positive test result.

C. Case classification

Confirmed:
- A case that meets the clinical case definition and is laboratory confirmed, and is not known to have chronic hepatitis C,
  OR
- A case that does not have acute clinical illness but has a documented negative HCV antibody laboratory test followed within six months by a positive test result **AND** is not known to have chronic hepatitis C.

Probable: A hepatitis C case with a clinically compatible illness and with positive HCV antibody laboratory results with a signal to cut-off ratio that does not meet the above criteria or is not reported.

Comment

Up to 20% of acute hepatitis C cases will be HCV antibody negative when reported and will be classified as non-A, non-B hepatitis because some (5% to 10%) have not yet seroconverted and others (5% to 10%) remain negative even with prolonged follow-up. Available serologic tests for HCV antibodies do not distinguish between acute and chronic or past infection. Thus, other causes of acute hepatitis should be excluded for HCV antibody positive patients who have an acute illness compatible with viral hepatitis.

Report liver enzymes results for all cases where these are available.
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. Hepatitis C, acute 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 hepatitis screen when testing patients for hepatitis. The hepatitis screen includes hepatitis B surface antigen, hepatitis B surface antibody, hepatitis B core total antibody, and 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: http://www.floridahealth.gov/diseases-and-conditions/disease-reporting-and-management/disease-reporting-and-surveillance/surveillance-and-investigation-guidance/_documents/dh1847clinicallabsubmissionform.pdf.
   b. Electronic Laboratory Ordering (ELO) is also available by entering a request into the HMS State Laboratory System, placing a 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 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.
   Packaging and Shipping of Diagnostic Specimens Flowchart:
   http://www.floridahealth.gov/diseases-and-conditions/disease-reporting-and-management/disease-reporting-and-surveillance/surveillance-and-investigation-guidance/_documents/packagingflowchar0422051.pdf

   Packaging and Shipping of Diagnostic Specimens Notes:
   http://www.floridahealth.gov/diseases-and-conditions/disease-reporting-and-management/disease-reporting-and-surveillance/surveillance-and-investigation-guidance/_documents/packagingflowchartnotes0422051.pdf

4. Contact the regional laboratory with questions: http://www.floridahealth.gov/diseases-and-conditions/disease-reporting-and-management/disease-reporting-and-surveillance/_documents/investigationunitmap_11-22-13color.pdf

D. Interpretation of results:

The fact that some people with acute HCV infection are asymptomatic and have no evidence of liver disease makes interpretation of laboratory results difficult. Below 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. The 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 (generally >11.0) 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 at: 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 HCV antibody 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 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 HCV antibody (RIBA) or HCV RNA
Positive	Not Done	Negative	Not Known	Not Known♦	Supplemental HCV antibody (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. Contact the physician or hospital

1. Confirm acute hepatitis C infection has been diagnosed in the reported patient and symptoms are consistent with an acute hepatitis C infection.

2. Obtain as much information as possible about the case, such as:
   a. Contact information
   b. Demographic information (e.g., DOB, gender, race, ethnicity)
   c. Date of onset
   d. Symptoms
   e. Laboratory tests performed
   f. Hepatitis A and B vaccine history
   g. Underlying conditions

3. Ask what information has been given to the patient, including whether the patient knows about the diagnosis.

4. Notify the physician that you will be contacting the patient as DOH follows up on all cases of hepatitis C, acute to assess risk factors, to better characterize the occurrence of hepatitis C, acute in Florida and to take necessary steps to prevent additional cases. Also, review infection control recommendations and address any concerns in regards to the CHD contacting the case.

B. Interview the case

1. Complete an interview as soon as possible after the case is reported to optimize recall.

a. Make at least three phone call attempts to reach the case; calls should be made at different times of the day with at least one call being made in the evening.
b. If phone calls are unsuccessful, mail a letter to the patient requesting that he/she contact the CHD and/or conduct a home visit or leave a letter for the patient.
c. If the patient is unable to provide information, interview a proxy (e.g., a spouse, parent) to gather further information.

2. Once contact is made, education about hepatitis C infection should be provided and an interview should be conducted to obtain any further information not already gathered from the provider or hospital. A viral Hepatitis Case Report Form is available to guide the investigation and assist in follow-up at: http://www.floridahealth.gov/diseases-and-conditions/disease-reporting-and-management/disease-reporting-and-surveillance/_documents/crf-hepatitis-viral.pdf.

3. Pertinent items to cover during the interview include:
   a. Education
   b. Demographic information
   c. Identification of possible exposures and risks during exposure period (six weeks to six months prior to onset of symptoms)
      i. Close contact (e.g., household member, sexual partner) with any person who had an illness compatible with hepatitis C or any person with a known acute or chronic hepatitis C infection
      ii. Injection and non-injection drug use
      iii. Tattoos and/or body piercings
      iv. Surgery, dental work, other invasive procedures
   d. Information on where to obtain the hepatitis A and hepatitis B vaccines

C. Merlin data entry

Create a case in Merlin under disease code **HEPATITIS C, ACUTE-07051**. Enter available data, being sure to include all required fields on the Basic Data screen, complete the Case Symptoms screen, and attach all relevant laboratory results. Please note that liver function test results should be entered as a laboratory result. The extended data screens (Hepatitis Common, and Hepatitis C, Acute) should also be completed in Merlin.

Chronic hepatitis cases are automatically reported in Merlin. However, Merlin does 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. Case contacts should be Epi-linked in Merlin.

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

Asymptomatic contacts: May be in the chronic stage of infection; if the probable case definition is met, the contact should be reported, investigated, and managed in the same manner as a confirmed case.

Use universal precautions for individuals in contact with body fluids in health care settings. High-risk groups for infection include:
- drug abusers who share needles,
- health care workers who have contact with infected blood,
- men who have sex with men,
- people who have multiple sexual partners,
- household contacts of infected persons,
- infants born to mothers who are hepatitis C carriers.

* 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 a steady) regardless of vaccination status.

7. MANAGING SENSITIVE SITUATIONS

A. Identifying a sensitive situation

As defined by *Florida Administrative Code* 64D-3.028, a sensitive situation is a setting in which the presence of a case would increase significantly the probability of spread of the diagnosed or suspected disease or condition and would, therefore, constitute a public health

hazard. Examples of such settings are schools, childcare facilities, hospitals and other patient care facilities.

B. Work or childcare restrictions

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

C. Needle stick and similar exposure

Accidental needle sticks carry a risk for transmission of hepatitis C.

D. 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.