# Protocol for Surveillance of Hepatitis C

#### Public Health Action

- 1. Educate the general public about hepatitis C risk factors and prevention of hepatitis C transmission.
- 2. Educate providers and the general public about appropriate testing indications.
- 3. Educate laboratories and providers to report any positive test for hepatitis C to Infectious Disease Epidemiology Program (IDEP), West Virginia Bureau for Public Health(WVBPH) within one week.
- 4. Educate laboratories to include the full name, date of birth, address of the patient and the name, address and telephone number of the ordering physician or health provider on each report (as required by 64CSR7-8.2.b.2.A and 64CSR7-8.2.b.2.G)
- 5. Educate laboratories to do reflex supplemental testing if screening test for anti-HCV is positive (MMWR February 7,2003, vol. 52, No. RR-3).
- 6. Educate providers about proper diagnosis, management and treatment of hepatitis C.
- Educate correctional facilities health care providers: (MMWR January 24, 2003/ Vol. 52/ No. RR-1)

a) to evaluate inmate risk factors for HCV infection during the entry medical evaluation, and test inmates reporting risk factors for HCV.

b) to do appropriate diagnostic testing to differentiate acute hepatitis A, hepatitis B, or hepatitis C for inmates with signs and symptoms of acute hepatitis and to determine if the patient has chronic HBV or HCV infection.

c) to report cases of acute and chronic (past or present) hepatitis C to Infectious Disease Epidemiology Program at West Virginia Bureau for Public Health.

d) to do prompt epidemiologic investigation in collaboration with the public health authorities to identify the source of the infection for all inmates with acute hepatitis C, including those incarcerated >6 months.

- 8. When a Hepatitis C Case Report is received, evaluate to determine if the case meets the acute case definition by checking the following information:
  - a) Does the patient have signs and symptoms of hepatitis?
  - b) Is the patient's alanine aminotransaminase (ALT) or serum glutamicpyruvic transaminase (SGPT) level more than 7 times the upper limit of normal?

c) Is the patient positive for EIA or CIA with a positive confirmatory test (RIBA or PCR) or a high positive signal to cutoff ratio?

- 9. If the patient meets the acute Hepatitis C case definition, investigate by using the yellow card and the CDC viral hepatitis case report form and return to IDEP with the completed hepatitis Case Report. Attach copies of the laboratory data.
- 10. If the patient does not meet the acute case definition complete Hepatitis C Case Report form and return to IDEP.
- 11. Assure that cases are educated about hepatitis C transmission, prevention and control measures to prevent complications of hepatitis C such as: hepatitis A and B vaccines; reduction of alcohol intake; and referral for medical evaluation.

#### **Disease Prevention Objectives**

- 1. Prevent transmission of hepatitis C through education of persons who have tested positive for hepatitis C.
- 2. Reduce the incidence of acute hepatitis C through community education and programs to prevent drug use and sharing of needles.
- 3. Prevent nosocomial transmission of hepatitis C through effective infection control measures.
- 4. Prevent transmission of hepatitis C through screening of blood and organ donors.
- 5. Prevent complications of hepatitis C by assuring that persons with hepatitis C receive education about hepatitis A and B vaccines, and use of alcohol.

# **Disease Control Objectives**

1. Reduce transmission through timely identification and investigation of community-based and nosocomial outbreaks of hepatitis C so that appropriate control measures can be applied.

# Surveillance Objectives

- 1. Determine the incidence of acute hepatitis C in West Virginia.
- 2. Estimate the annual number of newly diagnosed chronic cases of hepatitis C.
- 3. Prospectively identify the risk factors associated with acute hepatitis C.

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- 4. Periodically identify the risk factors associated with chronic hepatitis C through special studies.
- 5. Identify demographic characteristics of persons with acute and chronic hepatitis C.
- 6. Periodically assess access to care and quality of care for patients with hepatitis C.

# Public Health Significance

Hepatitis C is the most common blood borne infection in the United States and the leading cause of chronic liver disease in US. It is a common cause of cirrhosis and hepatocellular carcinoma as well as the most common reason for liver transplant. According to NHANES (National Health and Nutrition Examination Survey, 1988-1994), 1.8% of persons in the United States are infected with Hepatitis C. Sixty to 85 percent of HCV-infected persons develop chronic infection. The most important sequelae of chronic HCV infection are progressive liver fibrosis leading to cirrhosis, end-stage liver disease, and hepatocellular carcinoma(HCC). Estimates of the proportion of persons who develop chronic infection 20 years after exposure vary from 2 to 4 percent in children and young women, to 20 to 30 percent in middle-aged transfused subjects. HCV accounts for an estimated one-third of HCC cases in the United States. Workplace and health care expenditures for hepatitis C are currently estimated at 600 million dollars per year in the US. There are 10,000 to 20,000 deaths attributed to HCV infection in 1999.

Public health must estimate the number of persons infected in our state and in each county. This information will help to raise awareness and result in improved allocation of resources to treat and prevent hepatitis C and its complications. Public health must also raise community awareness about prevention. Treatment is expensive, carries substantial side effects, and is not always successful.

# **Clinical Description**

Persons with acute hepatitis C are usually asymptomatic. About 25-35% of persons with acute hepatitis C will experience the classic symptoms of hepatitis, including malaise, anorexia, abdominal pain, jaundice, nausea, vomiting, diarrhea, etc. Acute hepatitis C is completely indistinguishable from acute hepatitis due to another virus. A full set of tests for viral hepatitis, including hepatitis A IgM, HBsAg, HBcIgM, and Hepatitis C EIA (with confirmation according to current guidelines) should be ordered, because of the frequency of coinfections. Acute hepatitis A superimposed on chronic hepatitis C infection can cause fulminant hepatitis.

An estimated 60-85% of HCV infected persons develop chronic infection. Again, most of these patients are asymptomatic, yet 2-4 % of children and young women and 20-30% in middle-aged transfused subjects may develop cirrhosis over a period of about 20 years. Persons with cirrhosis may develop edema, ascites, jaundice, bleeding or easy bruisability, loss of body mass, thinning of the skin, sleep disturbance, confusion,

exhaustion, and loss of sexual drive or performance. Hepatocellular carcinoma is estimated to occur in about 1-4% of persons with cirrhosis every year.

#### Etiologic Agent

Hepatitis C virus (HCV) is a 50 nm positive-stranded RNA virus, classified in its own genus: Hepacivirus. It is related to the genus Flavivirus (dengue and yellow fever).

#### <u>Reservoir</u>

This virus is found only in humans. Chimpanzees and mice have been infected experimentally, but they play no known role in transmission to humans.

#### Mode of Transmission

Hepatitis C is efficiently transmitted by the parenteral route. Injection drug users, even those who have used drugs only once, are considered to be at risk. Risk factors for transmission of HCV include: first-time use with an older user, frequent use, cocaine injection, and sharing of paraphernalia. Other important risk factors include: transfusion or organ transplantation, especially prior to July, 1992; hemodialysis; high-risk sexual activity; unsafe injections (in developing countries); occupational exposure to blood; and perinatal exposure.

Sexual transmission does occur, but is very inefficient; in the United States, the estimated seroprevalence of HCV is 2 to 3 percent among partners of HCV-infected persons who are in long-term monogamous relationships and is 4 to 6 percent among persons with multiple sex partners, sex workers, and men who have sex with men (those at risk for sexually transmitted diseases). One study found the risk of HCV infection to be threefold higher for female than male sexual partners. Therefore, sexual partners of male and female patients with hepatitis C should be tested for this infection. For heterosexual, discordant monogamous couples, the risk of transmission is estimated to be only 0 to 0.6 percent annually. However, HCV-infected individuals with multiple sexual partners or in short-term relationships should be advised to use condoms to prevent transmission of HCV and other sexually transmitted diseases.

The risk of perinatal transmission is approximately 2 percent for infants of anti-HCV seropositive women. When a pregnant woman is HCV RNA positive at delivery, this risk increases to 4 to 7 percent. Higher HCV RNA levels appear to be associated with a greater risk. HCV transmission increases up to 20 percent in women co-infected with HCV and HIV. There are no prospective studies evaluating the use of elective cesarean section for the prevention of mother-to-infant transmission of HCV. However, avoiding fetal scalp monitoring and prolonged labor after rupture of membranes may reduce perinatal transmission. Breast-feeding does not appear to transmit HCV. Infants born to HCV-positive mothers should be tested for HCV infection by HCV RNA tests on two

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occasions between the ages of 2 and 6 months and/or have tests for anti-HCV after 15 months of age. Positive anti-HCV in infants prior to 15 months of age may be due to transplacental transfer of maternal anti-HCV antibody.

Children and personnel should not be excluded from day care centers, schools, or sports on the basis of HCV infection. Standard(universal precautions should be used in any situation where exposure to blood occurs.

Nosocomial transmission has rarely been reported. Dialysis patients are at increased risk for hepatitis C; probably because of unrecognized transmission during dialysis.

Transmission does <u>not</u> occur through casual contact (kissing, hugging, touching, coughing, sneezing, food, water, sharing eating utensils or drinking glasses, or other contact without exposure to blood etc.)

Healthcare workers have a similar or slightly lower prevalence of HCV infection than the general population, although they may have acquired their infection from occupational sources. Transmission from healthcare workers to patients has also been documented, but is rare and confounded by other risk factors. HCV-infected healthcare workers should use standard (universal) precautions to prevent transmission and should not be restricted from work.

The risk of HCV infection from a needlestick injury is estimated to be 2 percent. The source and exposed individual should be tested for antibody to HCV. If the source individual is HCV EIA positive, RIBA or HCV RNA assay should be done in the exposed individual. Since HCV RNA is first detected in the blood 2 weeks after transmission, the exposed individual should be tested for HCV antibody, HCV RNA, and ALT at exposure and again between 2 and 8 weeks after injury. If seroconversion occurs, that person should be referred for consideration of treatment.

Body piercing and tattooing are other potential sources of transmission if contaminated equipment or supplies are used. However, transmission due to these activities is rare and confounded by other risk factors.

#### **Incubation Period**

Incubation period is two weeks to six months; usually 6-9 weeks.

#### **Infectious Period**

Persons with hepatitis C are infectious (viremic) from about two weeks after exposure for an indefinite period of time. Persons with chronic hepatitis C are intermittently viremic. Persons who test positive for hepatitis C should be assumed to be infectious unless repeated testing for hepatitis C RNA is documented to be negative.

# **Outbreak Recognition**

Outbreaks have been described in association with cardiac surgery, colonoscopy and outpatient surgery. If, two or more *acute cases* of hepatitis C occur in association with surgery, dialysis, another invasive procedure or another common source within the 2 week to 6 month incubation period, WVDHHR should be notified that a possible outbreak has been identified. Outbreak identification should be facilitated by use of the CDC hepatitis investigation form to investigate acute cases of hepatitis C.

# Case Definition for Acute Hepatitis C

# Clinical case definition:

An acute illness with a) discrete onset of symptoms (such as nausea, vomiting, abdominal pain and diarrhea) and b) jaundice or abnormal serum aminotransferase levels.

# Laboratory criteria for diagnosis:

Serum alanine aminotransferase levels greater than 7 times the upper limit of normal, and

IgM anti-HAV negative, and

IgM anti-HBc negative, or if not done, HBsAg negative, and one of the following: Antibody to hepatitis C virus (anti-HCV) screening-test-positive verified by an additional more specific assay (e.g. RIBA for anti-HCV or nucleic acid testing for HCV RNA) OR

Anti-HCV screening-test-positive with a signal to cut-off ratio predictive of a true positive as determined for the particular assay (e.g.,  $\geq$  3.8 for the enzyme immunoassays).

Note for above: New testing platform chemiluminescence immunoassay (VITROS anti-HCV assay) data not available yet to calculate signal to cut-off ratio.

# Case classification

**Confirmed**: A case that meets the clinical case definition and is laboratory confirmed.

# Comment

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

# Case Definition for Viral Hepatitis C Infection (past or present) 2003 Case Definition (proposed)

#### **Clinical description**

Most hepatitis C virus (HCV) infected persons are asymptomatic. However, many have chronic liver disease, which can range from mild to severe including cirrhosis and liver cancer.

#### Laboratory criteria for diagnosis

- 1. Anti-HCV positive (repeatedly reactive) by EIA, verified by an additional more specific assay (e.g. RIBA for anti-HCV or nucleic acid testing for HCV RNA), OR
- 2. HCV-RIBA positive, OR
- 3. Nucleic acid test for HCV RNA positive, OR
- 4. Anti-HCV positive (repeat reactive) by EIA with a signal to cut-off ratio >=3.8 (as this becomes available).

# **Case Classification**

Probable: a case that is anti-HCV positive (repeat reactive) by EIA and has alanine aminotransferase (ALT or SGPT) values above the upper limit of normal, but the anti-HCV EIA result has not been verified by an additional more specific assay or the signal to cutoff ratio is unknown.

Confirmed: a case that is laboratory confirmed and that does not meet the case definition for acute hepatitis C.

# Laboratory Diagnosis of Hepatitis C

During acute infection, HCV RNA is first detectable within 1-3 weeks after exposure. The patient is viremic and potentially infectious at this time. Elevated ALT generally occurs at about 6-7 weeks after exposure, and the EIA becomes positive at about 6-12 weeks. Only 50-70% of individuals have a positive EIA at the onset of symptoms; 90% will seroconvert within 3 months.

Here are the recommendations for reporting results of testing for antibody to hepatitis C virus (anti-HCV) by type of reflex supplemental testing performed (MMWR, February 7, 2003, vol. 52, No. RR-3). Not all laboratories are using these guidelines yet. Encourage laboratories in your jurisdiction to adopt these guidelines.

Anti-HCV screening test results	Supplemental test results	Interpretation	Comments
Screening test*- negative	Not applicable	Anti-HCV-negative	Not infected with HCV, unless recent infection is suspected or other evidence exists to indicate HCV infection
Screening-test*- positive with high signal-to-cut-off (s/co)ratio	Not done	Anti-HCV-positive	Probably indicates past or present HCV infection; supplemental serologic testing not performed. Samples with high s/co ratios usually (≥95%) confirm positive, but <5 of every 100 might represent false- positives; more specific testing can be requested, if indicated
Screening-test- positive	Recombinant immunoblot assay (RIBA®)-positive	Anti-HCV-positive	Indicates past or present HCV infection
Screening-test*- negative	RIBA-negative	Anti-HCV-negative	Not infected with HCV, unless recent infection is suspected or other evidence exists to indicate HCV infection

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Anti-HCV screening test results	Supplemental test results	Interpretation	Comments
Screening-test*- positive	RIBA-indeterminate	Anti-HCV- indeterminate	HCV antibody and infection status cannot be determined; another sample should be collected for repeat anti-HCV testing (>1 month) or for HCV RNA testing.
Screening-test*- positive	Nucleic acid test (HCV-RNA)-positive	Anti-HCV-positive, HCV RNA-positive	Indicates active HCV infection
Screening-test*- positive	Nucleic acid test (HCV-RNA)- negative RIBA-positive	Anti-HCV-positive, HCV RNA-negative	The presence of anti-HCV indicates past or present HCV infection; a single negative HCV RNA result does not rule out active infection
Screening-test*- positive	HCV-RNA-negative RIBA-negative	Anti-HCV-negative, HCV RNA-negative	Not infected with HCV
Screening-test*- positive	HCV-RNA-negative RIBA-indeterminate	Anti-HCV- indeterminate HCV RNA-negative	Screening test anti- HCV result probably a false- positive, which indicates no HCV infection

\*Screening immunoassay test results interpreted as negative or positive on the basis of criteria provided by the manufacturer.

To send specimens for hepatitis C antibody testing (EIA) to the Office of Laboratory Services, collect in a serum separator (tiger top), not yellow top tube. If testing for hepatitis C virus only, a minimum of 3 mls must be collected. Fill out the lab request form completely and describe what specific test you are requesting for (i.e. hepatitis B and C or hepatitis C only). If you have any questions regarding hepatitis C lab testing please contact Sherry (Sherian Nestor) at 304-558-3530.

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# Preventive Interventions

For persons who are HCV-positive, share the following information:

- 1. Don't donate:
  - a. Blood;
  - b. Body organs or other tissue; or
  - c. Semen.
- 2. Don't share personal items, including:
  - a. Toothbrushes or dental appliances;
  - b. Razors; or
  - c. Nail-grooming equipment.
- 3. Cover cuts or skin lesions.
- 4. Stop using or injecting illegal drugs. Enter and complete substance abuse treatment, including relapse prevention. If still injecting, follow risk reduction practices.
- 5. Consult a physician regarding treatment. Some people benefit from treatment. Additional testing may be required to determine if treatment will be beneficial, including blood tests and a liver biopsy. Be sure to select a physician who is knowledgeable about hepatitis C.
- 6. Stop drinking alcohol or drastically reduce consumption.
- 7. Get immunized against hepatitis A.
- 8. If using drugs or engaged in high-risk sexual activity, get immunized against hepatitis B.
- 9. Counseling regarding sexual behavior:
  - a. For persons who have <u>only one</u> sex partner:
    - i. While it is advisable to inform that partner, no change in sexual practices is necessary.
    - ii. Risk of transmission is about 1%.
  - b. For persons who have <u>multiple</u> partners:
    - i. Reduce the number of partners;
    - ii. Inform all partners of their status; and
    - iii. Use latex condoms.
    - iv. Risk of transmission is approximately 5 to 10%.

For persons regardless of serostatus who are still using drugs:

- 1. Never reuse or share syringes, water, or preparation equipment.
- 2. Use only syringes obtained from a reliable source. In West Virginia, syringes can be obtained without a prescription at veterinary supply stores.
- 3. Use a new sterile syringe to prepare and inject drugs.
- 4. Use sterile water to prepare drugs. If sterile water is not available, clean tap water is preferable to water from other sources.
- 5. Use a new or disinfected container ('cooker') and a new filter ('cotton') to prepare drugs.
- 6. Clean the injection site with a new alcohol swab prior to injection

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7. Safely dispose of syringes after one use.

#### Postexposure Prophylaxis and Follow-Up

The prevention of HCV infection with immunoglobulin (IG) is not effective for postexposure prophylaxis of hepatitis C. There is no vaccine available for hepatitis C.

#### **Treatment**

According to NIH 2002 Consensus Development Conference on the Management of Hepatitis C meeting, combination therapy has a better response than monotherapy and the highest response rates have been achieved with pegylated interferon in combination with ribavirin. Currently the best indicator of effective treatment is an sustained viral response (SVR), defined by the absence of detectable HCV RNA in the serum as shown by a qualitative HCV RNA assay with lower limit of detection of 50 IU/mL or less at 24 weeks after the end of treatment.

Factors associated with successful therapy included genotypes other than 1, lower baseline viral levels, less fibrosis or inflammation on liver biopsy, and lower body weight or body surface area. Two studies reported that SVRs of 42 to 46 percent were achieved for genotype 1 using pegylated interferon and ribavirin for 48 weeks. Patients with genotype 2 and 3 achieved SVRs of 76 to 82 percent after 24 weeks of treatment. These studies demonstrated that 24 weeks of treatment appears to be sufficient for persons with genotypes 2 and 3, while patients with genotype 1 need 48 weeks of treatment. One study suggested that higher dose of ribavirin -1,000 to 1,200 mg/day versus 800 mg/day had a slightly greater SVR at 48 weeks (51 percent versus 40 percent).

Early viral response (EVR), defined as a minimum 2 log decrease in viral load during the first 12 to 24 weeks of treatment, is predictive of SVR and should be a routine part of patient monitoring. Treatment need not be extended in patients who fail to achieve an EVR at week 12 or week 24 because there is only a small chance of achieving an SVR even if therapy is continued for a full year.

Selected patients who fail to achieve an SVR may benefit from retreatment with pegylated interferon-based regimens. Decisions regarding re-treatment should be based on (1) previous type of response, (2) the previous therapy and the difference in potency of the new therapy, (3) the severity of the underlying liver disease, (4) viral genotype and other predictive factors for response, and (5) tolerance of previous therapy and adherence.

#### Surveillance Indicators

- Proportion of acute cases of hepatitis C with complete demographic information
- Proportion of acute cases of hepatitis C with complete information on risk factors
- Proportion of chronic cases of hepatitis C with complete demographic information.
- Presence of current data on lifetime risk factors among chronic cases of hepatitis C.
- Proportion of cases with information on whether the case is chronic or acute.
- Proportion of cases that have been educated about hepatitis C.
- Presence of data on quality and access to care.

# Public Health Surveillance for ACUTE VIRAL HEPATITIS C

West Virginia Infectious Disease Epidemiology Program

June 24, 2003



Refer to the Hepatitis C Information Sheet to educate the patient about receiving medical attention, including hepatitis A and hepatitis B vaccination, hepatitis C transmission, and hepatitis C prevention. Consider contact tracing for hepatitis C.