Hepatitis C

Disease Plan

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Last updated: 6/28/2016, by Jeffrey T. Eason, MPH

Questions about this disease plan?

Contact the Utah Department of Health Bureau of Epidemiology: 801-538-6191.
WHY IS HEPATITIS C IMPORTANT TO PUBLIC HEALTH?

Hepatitis C virus (HCV) infection is a serious disease that can result in long-term health problems, including liver damage, liver failure, liver cancer, or even death. It is the leading cause of cirrhosis and liver cancer and the most common reason for liver transplantation in the U.S. Approximately 15,000 people die every year from HCV-related liver disease. It affects a diverse proportion of the population because prior to its identification, it had the opportunity to spread with little control through blood and organ tissue during transfusion and tissue transplant. Most individuals are unaware of their HCV infection status, which increases the probability of developing long-term health problems. Public health works to control HCV by increasing HCV awareness in the community, providing testing recommendations and education. With the recent advent of highly effective treatments that can cure many persons with chronic HCV infection, public health has a role in assessing the distribution and characteristics of persons who may be in need of treatment.

DISEASE AND EPIDEMIOLOGY

Clinical Description

Symptoms – Acute
Initial infection with HCV is often asymptomatic (~80% of cases) or mild; therefore, it is uncommon for people to be diagnosed with HCV infection in the acute stage. If clinical illness does occur, symptoms begin about seven weeks after infection and can include: jaundice, fatigue, dark urine, abdominal pain, loss of appetite, and nausea. About 15-25% of HCV-infected individuals are able to clear the infection without treatment; the rest develop chronic infection. Hepatitis C is a disease with varying rates of progression. In general, however, its course is slowly progressive.

Symptoms – Chronic
Most people are asymptomatic during the first decade or two of chronic HCV infection. Some patients may intermittently experience a range of symptoms, including fatigue, headache, joint aches, muscle aches, nausea, jaundice, loss of appetite, and/or abdominal pain.

For many people with chronic hepatitis C, signs and symptoms appear only when liver disease is advanced. Almost 70% of those with chronic HCV infection develop chronic liver disease, a situation in which the virus damages the liver. The damage may progress to severe disease, including cirrhosis, liver cancer, and liver failure.

Severe disease or cirrhosis symptoms include fatigue, muscle weakness, poor appetite, nausea, weight loss, itching, dark urine, fluid retention, and abdominal swelling.
**Causative Agent**

HCV is a spherical, enveloped, single-stranded RNA virus belonging to the Flaviviridae family and Hepacivirus genus. HCV is related to hepatitis G, dengue, and yellow fever viruses. HCV can produce at least 10 trillion new viral particles each day. Six major HCV genotypes and numerous subtypes have been identified.

**Genotypes**

The major HCV genotype worldwide is genotype 1, which accounts for 40-80% of all isolates.

![Figure 1: HCV Genotypes and Subtypes](image)

<table>
<thead>
<tr>
<th>Subtypes</th>
<th>Genotype 1</th>
<th>Genotype 2</th>
<th>Genotype 3</th>
<th>Genotype 4</th>
<th>Genotype 5</th>
<th>Genotype 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>U.S. Prevalence</td>
<td>a, b, c</td>
<td>a, b, c, k</td>
<td>a, b, k</td>
<td>a</td>
<td>a</td>
<td>a, b, d, g, h, k</td>
</tr>
<tr>
<td>70%</td>
<td>16%</td>
<td>12%</td>
<td>1%</td>
<td>&lt;1%</td>
<td>1%</td>
<td></td>
</tr>
</tbody>
</table>


- Genotypes 1a and 1b are most prevalent in the U.S. and worldwide.
  - HCV genotype 1, particularly 1b, does not respond to therapy as well as genotypes 2 and 3. Recent HCV treatments have increased the response rate to Genotype 1 therapy.
  - Genotype 1 also may be associated with more severe liver disease.
- Genotypes 2 and 3 are also found worldwide. However, in the U.S., they account for a minority of infections.
- Genotype 4, 5, and 6 are found worldwide, but are uncommon in the U.S. The largest proportions of genotypes 4 and 5 occur in lower-income countries, primarily in Africa. Genotype 6 is most prevalent in Vietnam, Cambodia, and the Philippines.

**Differential Diagnosis**

The major conditions that can be confused clinically with acute hepatitis C include:

- Acute hepatitis A and B
- Drug-induced hepatitis
- Alcoholic hepatitis
- Autoimmune disorders

The major conditions that can be confused clinically with chronic hepatitis C include:

- Autoimmune hepatitis
- Chronic hepatitis B and D
- Alcoholic hepatitis
- Non-alcoholic steatohepatitis (fatty liver)
- Sclerosing cholangitis
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- Wilson’s disease
- Alpha-1-antitrypsin-deficiency-related liver disease
- Drug-induced hepatitis

Laboratory Identification

Anti-HCV antibody (total antibody) testing is recommended for routine screening of asymptomatic persons based on their risk for infection, or based on a recognized exposure. For such persons, testing for HCV infection should include the use of an FDA-cleared test for antibody to HCV.

Persons tested for HCV infection and determined to be anti-HCV positive should be evaluated (by referral or consultation, if appropriate) for the presence of active infection, presence or development of chronic liver disease (CLD), and possible treatment. Nucleic acid testing, including reverse transcriptase polymerase chain reaction (RT-PCR) to detect HCV RNA (viral load), is necessary to confirm the diagnosis of current HCV infection, and an elevated ALT level is biochemical evidence of CLD (See Appendix A).

Several blood tests are performed to test for HCV infection (See Appendix B). Appendix B is data entry guidance – it will help investigators interpret the tests they receive. These tests can be characterized into two categories, anti-HCV antibody tests and HCV detection test.

Anti-HCV antibody tests

- Screening tests for total antibody to HCV (anti-HCV)
  - Enzyme immunoassay (EIA)
  - Enhanced chemiluminescence immunoassay (CIA)

HCV detection test

- Qualitative tests to detect presence or absence of virus (HCV RNA polymerase chain reaction [PCR])
- Quantitative tests to detect amount (titer) of virus (HCV RNA PCR)
- Genotype testing

Anti-HCV antibody can be detected as early as 4-10 weeks after infection and can be detected in >97% of persons by six months.

False positive anti-HCV antibody tests appear more often when persons at low risk for HCV infection (e.g., blood donors) are tested. Therefore, it is important to follow-up all positive anti-HCV antibody tests with an HCV detection test to establish current infection.
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**Figure 2: Laboratory test interpretation**

<table>
<thead>
<tr>
<th>Anti-HCV Antibody</th>
<th>Qualitative PCR</th>
<th>Quantitative PCR</th>
<th>Genotyping</th>
<th>Testing Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>-</td>
<td>&lt;n* and/or not detected</td>
<td>Negative or Indeterminate</td>
<td>Previously exposed, not currently infected or false positive antibody</td>
</tr>
<tr>
<td>+</td>
<td>+</td>
<td>Quantified viral load</td>
<td>Genotype Identified</td>
<td>Current Infection</td>
</tr>
</tbody>
</table>

*n will be dependent upon the detectable range of laboratory methodology used

Persons with early HCV infection might not yet have developed anti-HCV antibody levels high enough that the test can measure it (termed the “window” period). In addition, some persons might lack the immune response necessary for the test to work well. In these persons, further testing such as PCR for HCV RNA may be considered. HCV RNA appears in blood and can be detected as early as 2–3 weeks after infection.

**Figure 3: Laboratory description of Acute HCV (A) and Chronic HCV (B)**

In acute HCV, liver enzymes may be elevated up to, and in excess of, 10 times greater than normal values. This elevation is typically observed after two weeks of infection and will return to normal levels within 12 weeks. Fifteen to 25% of acute infections will self-resolve; the majority of acute cases (75-85%) will progress to chronic HCV infection.

It is common for patients with chronic HCV to have liver enzyme levels that go up and down, with periodic returns to normal or near normal levels. Liver enzyme levels can remain normal for over a year despite CLD.

Most patients with chronic hepatitis C have a viral load between 100,000 (1X10^5) and 10,000,000 (1X10^7) copies per mL. Expressed as IU, these averages are 50,000 to 5 million IU.

Viral levels as measured by viral load do not correlate with hepatitis severity or with a poor prognosis (as in HIV infection). However, viral load inversely correlates with the likelihood of a response to antiviral therapy (e.g., cases with low initial viral load levels have a better therapeutic outcome than cases with high initial viral load levels.)

**Utah Public Health Laboratory (UPHL):** UPHL has the ability to perform anti-HCV antibody testing on patients.
High Risk Group Screening Recommendations

“High-risk” is defined as persons with a current or past history of injection drug use, and persons who had a blood transfusion prior to 1992. Repeat screening for high-risk persons is recommended annually only for persons who have had continued injection drug use since a prior negative screening test.

The determination of “high-risk for HCV” is identified by the primary care physician or practitioner who assesses the patient's history, which is part of any complete medical history, typically part of an annual wellness visit, and considered in the development of a comprehensive prevention plan.

Birth Cohort – People Born 1945-1965

In 2012, the CDC issued a recommendation to test everyone born from 1945-1965 (“baby boomers”) for HCV. While anyone can get HCV, up to 75% of adults infected with hepatitis C were born from 1945-1965. Baby boomers are five times more likely to have HCV than other adults. This population was thought to have been infected in the 1970’s and 1980’s when HCV rates were highest. This was before education initiatives were implemented and the transmission risks of the virus were widely known. This recommendation is intended to encourage this population to get screened to know their HCV status and refer them to care. The longer people live with undiagnosed and untreated HCV, the more likely they are to develop serious, life-threatening liver disease.

Pregnancy

Routine testing for HCV infection is not recommended for all pregnant women. Pregnant women with a known risk factor for HCV infection should be offered counseling and testing. Approximately six of every 100 infants born to HCV-infected women become infected. This infection occurs predominantly during or near delivery, and no treatment or delivery method—such as cesarean section—has been demonstrated to decrease this risk. The risk of transmission is increased by the presence of maternal HCV viremia at delivery, and is 2-3 times greater if the woman is co-infected with HIV. HCV has not been shown to be transmitted through breast milk, although HCV-positive mothers should consider abstaining from breastfeeding if their nipples are cracked or bleeding. Children born to HCV-positive mothers should be tested for HCV infection and, if positive, evaluated for the presence of CLD.

HIV Infection

All persons with HIV infection should undergo serologic testing for HCV. People with HIV who have ongoing risk factors for HCV infection should be routinely screened. The progression of liver disease is more rapid in HIV/HCV co-infected persons, and the risk for cirrhosis is nearly twice that of persons with HCV infection alone. Co-infected persons receiving HIV antiviral regimens are now being treated for HCV after their CD4+ cell counts increase, optimizing their immune response.
Health Care Personnel

After a needle stick or sharps exposure to HCV-positive blood, the risk of HCV infection is approximately 1.8% (range: 0%–10%). Although a few cases of HCV transmission via blood splash to the eye have been reported, the risk for such transmission is expected to be very low.

Avoiding occupational exposure to blood is the primary way to prevent transmission of bloodborne illnesses among healthcare personnel. All healthcare personnel should adhere to Standard Precautions. Depending on the medical procedure involved, Standard Precautions may include the appropriate use of personal protective equipment (e.g., gloves, masks, and protective eyewear). In the event of an occupational exposure, the healthcare personnel should contact their employee health representative, follow OSHA bloodborne exposure recommendations, and be tested according to the CDC bloodborne infectious disease guidance.

There are no CDC recommendations to restrict a healthcare worker who is infected with HCV. The risk of transmission from an infected healthcare worker to a patient appears to be very low. All healthcare personnel, including those who are infected with HCV, should follow strict aseptic technique and Standard Precautions, including appropriate hand hygiene, use of protective barriers, and safe injection practices.

Treatment

The landscape of treatment for HCV infection has evolved substantially since the introduction of highly effective HCV protease inhibitor therapies in 2011. The pace of change is expected to increase rapidly, as numerous new drugs with different mechanisms of action will likely become available over the next few years. To provide healthcare professionals with timely guidance as new therapies are available and integrated into HCV regimens, the Infectious Diseases Society of America (IDSA) and American Association for the Study of Liver Diseases (AASLD), in collaboration with the International Antiviral Society–USA (IAS–USA), developed a web-based process for the rapid formulation and dissemination of evidence-based, expert-developed recommendations for HCV management. The IAS–USA provided the structure and assistance to sustain the process that represents the work of leading authorities in hepatitis C prevention, diagnosis, and treatment in adults, from 2013 to 2015.

The AASLD/IDSA Guidance on Hepatitis C (www.hcvguidelines.org) addresses management issues ranging from testing and linkage to care, the crucial first steps toward improving health outcomes for HCV-infected persons, to the optimal treatment regimen in particular patient situations. Recommendations are based on evidence and are rapidly updated as new data from peer-reviewed evidence become available. For each treatment option, recommendations reflect the best possible management for a given patient and a given point of disease progression. Recommendations are rated with regard to the level of the evidence and strength of the recommendation. The guidance should be considered a "living document" in that the guidance will be updated frequently as new information and treatments become available. This continually evolving report provides guidance on FDA-approved regimens. At times, it may also recommend off-label use of certain drugs or tests or provide guidance for regimens not yet approved by FDA.
Readers should consult prescribing information and other resources for further information. Of note, the choice of treatment may, in the future, be further guided by data from cost-effectiveness studies.

FDA maintains a complete list of viral hepatitis therapies that are approved for treatment of Hepatitis C.

**Treatment duration**
Treatment duration depends on genotype, liver health, previous treatment and other factors. Most treatments range from 8-24 weeks. The goal of treatment is to eliminate HCV RNA and achieve a sustained virologic response (SVR). An SVR has been demonstrated to result in a 97 to 100 percent chance of remaining HCV RNA negative after long-term follow-up. Individuals who achieve SVR are considered cured of the HCV infection. The definition of SVR is an absence of HCV RNA 24 weeks after treatment.

**Treatment response and success**
Each treatment has a different response rate and depends on several factors, including: genotype, race, age, weight, extent of liver damage, viral load, HIV Infection, previously treated or not, alcohol use, length of infection, and adherence.

When a person reaches SVR after completing treatment, this suggests that HCV infection has been cured. SVR can result in decreased cirrhosis and complications of liver disease, decreased rates of liver cancer (hepatocellular carcinoma), and decreased mortality. Most new medications are showing a SVR of 93-100%.

**Treatment Side Effects**
Each treatment has potential for a variety of adverse effects. However, most of the new medications that are interferon and ribavirin-free seem to be easily tolerated with very few minor side effects including headache, fatigue, and insomnia.

**Pegylated or standard interferon:** fatigue, flu-like symptoms, mood changes, drop in platelet count, drop in white blood cell count, drop in neutrophil count, loss of appetite, nausea or change in bowel habits, weight gain or weight loss, hair loss, changes in thyroid function, increase in blood sugar level, and insomnia may be associated with these medications.

**Ribavirin:** drop in red blood cell count, sore throat, cough, shortness of breath, rash, and birth defects may be associated with use of ribavirin.

**Clinical Trials**
Research facilities conduct clinical trials on hepatitis medications and are often looking for individuals to participate. For further information on current trials and qualifications, visit www.clinicaltrials.gov. Local agencies that have a history of HCV Medication Clinical trials include: The University of Utah Medical Center (http://healthcare.utah.edu/clinicaltrails), Jean Brown Research (www.jeanbrownresearch.com), and PRA Health Services.
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(www.crilifetree.com/clinicaltrialshepatitis), or contact the UDOH Bureau of Epidemiology, Prevention Treatment and Care Program (PTCP) at 801-538-6191 for additional resources.

Case Fatality

In the U.S., HCV is a contributing cause of death in approximately 15,000 people per year. According to the CDC, death certificates listing HCV as a cause of death have increased from 16,627 in 2010 to 19,368 in 2013.

Reservoir

Humans are the only known reservoir of HCV.

Transmission

HCV is a bloodborne pathogen that is predominantly spread via exposure to contaminated blood or blood products. Currently, the highest risk of transmission is sharing needles or syringes to inject drugs. Continued injection drug use increases the risk of HCV infection. Studies have shown up to a 33% seroprevalence among 18-30 year-old injection drug users (IDUs) and increases substantially (70-90%) among older and former IDUs.

Blood transfusions pose an extremely limited risk now. But, for patients who received a blood transfusion prior to June 1992, the risk of infection was approximately 1.5% per transfusion recipient.

Sexual transmission of HCV is very low, but can occur. The risk of sexual transmission increases with multiple partners, co-infection with HIV, MSM, anal sex, and any other sexual activity where blood may be exchanged.

Other potential risks for transmission include:

- Long-term hemodialysis
- Sharing straws for intranasal drug use
- Vertical (mother to infant) transmission (the risk of perinatal transmission is estimated to be about 5%, although if the mother is co-infected with HIV, the risk may be approximately 15–25%)
- Occupational blood exposure (the risk of occupational exposure for healthcare workers has been estimated to be 1.8% per incident of hollow-bore needle stick exposure to HCV-infected blood)
- Various medical procedures with non-sterile equipment (including dental)
- Tattooing or body piercing with non-sterile equipment

HCV is not spread through casual contact, kissing, sneezing, hugging, sharing glasses or utensils, or breast milk.
Susceptibility

HCV infection occurs among persons of all ages. The highest incidence of acute HCV infection (new cases) occurs among persons aged 20-40 years. Cases may be infected by more than one genotype, but this is rare. Patients can be treated for one genotype, and be re-infected via the same or another genotype.

Incubation Period

The incubation period for HCV ranges from two weeks to six months, with an average incubation period of 6-7 weeks.

Period of Communicability

Communicability of HCV is variable; anyone with a positive test for anti-HCV antibody should be considered infectious until ruled out by negative HCV detection tests. The virus can usually be detected by the presence of viral RNA in an infected person's blood within 1-3 weeks after the initial exposure. The degree of correlation between quantity of circulating virus and communicability is not clearly established.

Epidemiology

HCV has a worldwide distribution. In the U.S., an estimated 3.5 million (range 2.5-4.7 million) people are infected with HCV. The CDC estimates approximately 29,718 acute HCV cases (newly infected individuals) occurred in 2013. Prevalence is highest among groups with specific risk factors, especially IDUs, patients with hemophilia, on long-term hemodialysis, prison inmates, and people who received blood or organ products prior to June 1992.

Most of these newly reported cases are not people with new (acute) disease, but those with chronic infection who have been newly diagnosed. There remains a large population of undiagnosed people who were infected in the past. It is estimated that only 25% of individuals with HCV know they are infected.

A segment of the population of particular interest is the baby boomers, or those U.S. citizens born between 1945 and 1965. Statistics show that baby boomers account for more than 75% of all American adults living with HCV, and they are considered five times more likely to be infected than other adults. CDC estimates that more than 2 million (nearly 1 in 30) Baby boomers have been infected with hepatitis C, with most unaware of their infection. CDC recommends that all baby boomers get a one-time test for hepatitis C. This approach will address the largely preventable consequences of this disease, especially in light of newly available therapies that can cure up to 75% of infections. For more information, see the CDC press release from May 18, 2012: http://www.cdc.gov/nchhstp/newsroom/HepTestingRecsPressRelease2012.html.
PUBLIC HEALTH CONTROL MEASURES

Public Health Responsibility

- To provide information to HCV-infected patients on the importance of medical evaluation, why continued care is needed, how to reduce disease progression, and to provide referrals to medical or supportive facilities for these services.
- To provide current treatment information and resources.
- To provide information to HCV-infected persons on how to prevent exposing others.
- To provide education to HCV-infected pregnant women on the importance of prenatal care and strategies to reduce the transmission risk to their child.
- To determine the incidence and prevalence of HCV in specific populations and geographic locations to help guide HCV prevention and education activities, and other public health interventions.
- To identify clusters of HCV cases or outbreaks.
- To investigate all suspect acute cases of disease, as explained in the investigation protocol below.
- To investigate individuals co-infected with HIV/AIDS or hepatitis B without evidence of previously documented investigation.
- To provide education to the general public, clinicians, and first responders regarding disease transmission and prevention.
- To identify sources of exposure and prevent further transmission.

Prevention

The goals of HCV prevention and control efforts are:

1) To reduce the incidence of new infections by reducing HCV transmission.
2) To reduce the risk of chronic liver disease in HCV-infected individuals through appropriate medical management and counseling by ensuring linkage to care.
3) To educate infected persons on how to care for themselves and how to avoid spreading infection to others.

Chemoprophylaxis

There is currently no post-exposure prophylaxis for HCV, although treatment is available for infected individuals.

Vaccine

There is currently no vaccine for HCV. It is recommended that HCV infected individuals receive hepatitis A and hepatitis B immunizations to prevent further liver disease. There are currently HCV vaccines under development; the progress of these vaccines can be monitored on the U.S. Food and Drug Administration website.
Isolation and Quarantine Requirements

Isolation: None.

Hospital: Standard Precautions.

Quarantine: None.

No restrictions except for exclusion from organ and blood donation.

HCV positive healthcare workers: As long as Standard Precautions and other infection control practices are used consistently, medical and dental procedures performed in the U.S. generally do not pose a risk for the spread of HCV. There are no restrictions on healthcare workers that are HCV positive. There are no specific regulations regarding HCV infection in daycare, school, or community residential programs. HCV is not spread via casual contact or through food or water. As long as standard precautions are maintained, HCV will not be spread to others in these settings. No one who is HCV-infected should be excluded from attending or working in any of these settings on the basis of his/her HCV infection.

CASE INVESTIGATION

Reporting

All cases of HCV infection are reportable to public health.

Criterion for reporting HCV

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Reporting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthcare record contains a diagnosis of hepatitis C</td>
<td>S</td>
</tr>
<tr>
<td>Death certificate lists hepatitis C as a cause of death or a significant condition contributing to death</td>
<td>S</td>
</tr>
<tr>
<td>Antibodies to hepatitis C virus (anti-HCV)</td>
<td>S</td>
</tr>
<tr>
<td>Nucleic Acid Test (NAT) for HCV RNA positive</td>
<td>S</td>
</tr>
<tr>
<td>Positive test for hepatitis C antigen(s)*</td>
<td>S</td>
</tr>
</tbody>
</table>

Notes:
S = This criterion alone is sufficient to report a case.
*When and if a test for HCV antigen(s) is approved by FDA and available.
Clinical Descriptions

Acute Clinical Description
An illness with discrete onset of any sign or symptom consistent with acute viral hepatitis (e.g., fever, headache, malaise, anorexia, nausea, vomiting, diarrhea, and abdominal pain), including jaundice and/or peak elevated serum alanine aminotransferase (ALT) level >200 IU/L during the period of acute illness.

Chronic Clinical Description
Most HCV infected persons are asymptomatic; however, many have CLD, which can range from mild to severe. Testing for HCV RNA (by PCR) confirms chronic HCV and documents that viremia is present; almost all patients with chronic infection will have the viral genome detectable in serum by PCR.

Most patients with chronic HCV have levels of HCV RNA (viral load) between 100,000 (10^5) and 10,000,000 (10^7) copies per mL. Expressed as IU, these averages are 50,000 to 5 million IU.

Laboratory Criteria
A positive test for antibodies to HCV (anti-HCV).

HCV detection test:
- Nucleic acid test (NAT) for HCV RNA positive (including qualitative, quantitative or genotype testing)
- A positive test indicating presence of HCV viral antigen(s) (HCV antigen)*
  * When and if a test for HCV antigen(s) is approved by FDA and available.

In 30-40% of patients, anti-HCV is not detected until 2-8 weeks after onset of symptoms. In this situation, testing for HCV RNA is helpful, as this marker is present even before the onset of symptoms and lasts through the acute illness.

Case Classification

Acute, confirmed
- A case that meets clinical criteria and has a positive HCV detection test (HCV NAT or HCV antigen*), OR
- A documented negative HCV antibody, HCV antigen* or NAT laboratory test result followed within 12 months by a positive result of any of these tests (test conversion)

Acute, probable
- A case that meets clinical criteria and has a positive anti-HCV antibody test, but has no reports of a positive HCV NAT or a positive HCV antigen* tests, AND
- Does not have test conversion within 12 months or has no report of test conversion
  * When and if a test for HCV antigen(s) is approved by FDA and available.
Chronic, confirmed

- A case that does not meet clinical criteria or has no report of clinical criteria, AND
- Does not have test conversion within 12 months or has no report of test conversion, AND
- Has a positive HCV NAT or HCV antigen* test.
  *When and if a test for HCV antigen(s) is approved by FDA and available.

Chronic, probable

- A case that does not meet clinical criteria or has no report of clinical criteria, AND
- Does not have test conversion within 12 months or has no report of test conversion, AND
- Has a positive anti-HCV antibody test, but no report of a positive HCV NAT or positive HCV antigen* test.
  *When and if a test for HCV antigen(s) is approved by FDA and available.

Criteria to distinguish a new case of HCV

A new case is an incident case (new acute, or newly diagnosed chronic) that has not previously been reported, which meets case criteria for hepatitis C. A new probable acute case may be re-classified as confirmed acute case if a positive NAT for HCV RNA, or a positive HCV antigen(s) test is reported within the same year. A confirmed acute case may be classified as a confirmed chronic case if a positive NAT for HCV RNA, or a positive HCV antigen is reported one year or longer after acute case onset. A confirmed acute case may not be reported as a probable chronic case (e.g., HCV antibody positive, but with an unknown HCV RNA NAT or antigen status).

Criterion for classification of HCV

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Acute</th>
<th>Chronic</th>
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<tbody>
<tr>
<td></td>
<td>Confirmed</td>
<td>Probable</td>
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<tr>
<td><strong>Clinical Evidence</strong></td>
<td></td>
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</tr>
<tr>
<td>Discrete onset</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>Fever</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>Headache</td>
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</tr>
<tr>
<td>Malaise</td>
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<td>Abdominal Pain</td>
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</tr>
<tr>
<td>Jaundice</td>
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<tr>
<td>ALT &gt;200 IU/L</td>
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<td>N</td>
</tr>
<tr>
<td>No available evidence of clinical and relevant laboratory information indicative of acute infection</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td><strong>Laboratory Evidence</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive anti-HCV antibody</td>
<td>N</td>
<td>N</td>
</tr>
</tbody>
</table>
Report of a positive HCV detection test (NAT for HCV RNA or HCV antigen(s)*)

| Criteria to distinguish a new case | N | N | N
---|---|---|---
Absence of a negative NAT for HCV RNA or negative HCV antigen(s)* | N | N | N
Report of HCV antibody or virus detection test conversion from negative to positive within 12 months | S |
Not previously reported as a case | N | N | N | N
Not previously reported as an acute case within one year | N | N

Notes:
* = When and if a test for HCV antigen(s) is approved by FDA and available.
N = This criterion in conjunction with all other “N” and any “O” criteria in the same column is required to classify a case.
O = At least one of these “O” criteria in each category in the same column (clinical evidence and laboratory evidence) in conjunction with all other “N” criteria in the same column is required to classify a case.
S = This criterion alone is Sufficient to classify a case.

Nosocomial Outbreaks
Nosocomial outbreaks are uncommon with hepatitis C, but could occur with lack of infection control. Contact UDOH for assistance with any suspect or confirmed nosocomial HCV outbreaks or occurrences.

Resolved infection: ‘Treated and Cured’ or ‘Self Resolved’

Treated HCV infected patient
When a patient has completed HCV treatment and receives a (1) negative HCV detection test ≥24 weeks after treatment (SVR), that individual is considered ‘Treated and Cured’. ‘Treated and Cured’ individuals can become re-infected with HCV. When a ‘Treated and Cured’ individual is determined to be re-infected, as evident through a positive HCV detection test, their case will be treated as a new event and managed according to the investigation algorithm in Figure 4.

Note: An automated process using Utah’s All Payer Claims Database is being developed, but is currently unavailable.

Untreated HCV infected patients
Individuals that are not known to have been treated, who through laboratory evidence, demonstrate negative results on an HCV detection test will be considered ‘Self-resolved’ after two negative HCV detection tests on different collection dates or collected on the same date but tested using differing HCV detection laboratory methodologies. ‘Self-resolved’ individuals can become re-infected with HCV. When a ‘Self-resolved’ individual is determined to be re-infected, as evident through a positive HCV detection test, their case will be treated as a new event and managed according to the investigation algorithm in Figure 4.
Case Investigation Process

All acute cases will be investigated (asymptomatic cases with documented seroconversion in the past 12 months, and symptomatic cases with elevated ALT (>200 IU/L) or jaundice with other symptoms of acute hepatitis (e.g., nausea, vomiting, RUQ pain, etc.) Chronic cases and cases that are determined not to be acute will be considered surveillance events.

The HCV surveillance system is designed to focus investigator efforts on likely acute cases based on the first reported laboratory test. This is accomplished by first identifying likely acute cases based on the test type (e.g., acute hepatitis panel) or diagnostic facility (e.g., blood component donor facilities). Individuals that do not meet investigation criteria are not investigated. Individuals that are reported as HCV positive (either anti-HCV antibody or HCV detection test) from the likely acute categories have met investigation criteria and are investigated by one of two methods:

1. Individuals reported as HCV positive from a blood component donation center will have their last negative test date ascertained from the donor center. If the donor’s last negative HCV test was less than 12 months from their HCV positive test they will continue to meet investigation criteria and will be contacted by public health to assess exposure risks and provide education. If the donor was a first time donor, or the last negative donation was greater than 12 months prior, the case will be considered a surveillance event with no further investigation.

2. Individuals reported from an acute hepatitis panel will have their ALT and total bilirubin (Tbili) requested from the reporting lab. If ALT is greater than 200 IU/L or Tbili is greater than 3.0 mg/dL they will continue to meet investigation criteria. Investigators will then request clinical notes from the ordering provider to identify if the individual presented with clinically compatible symptoms of acute hepatitis. If the individual meets the clinical definition of acute HCV, he/she will be contacted by public health to assess exposure risks and provide education. If the clinical definition of acute HCV is not met, the case will be considered a surveillance event with no further investigation.

UDOH enhanced reports: UDOH receives an automated report providing ALT and Tbili from individuals identified as HCV positive from acute hepatitis panels at some medical facilities. This information is entered into UT-NEDSS to assist investigators. UDOH will continue to work with medical providers to expand the use of automated data collection to support investigational efforts.
### (1) Investigation Criteria

- Anti-HCV antibody + from Acute Hepatitis Panel
- HCV detection test + from a Donor Center
- HCV + Suspect acute based on circumstantial evidence and/or health department discretion
- Co-infected (HIV/AIDS, HBV) and not previously investigated

### (2) Donor Screening

Complete a “Limited Call” to Donation Center
Collect donor history (Last Negative Donation)
If negative HCV result in <12 months proceed. If criteria not met or not done, Surveillance event.

### (2) Acute Panel

Complete a “Limited Call” to Laboratory
Collect: ALT, Total Bilirubin
If ALT is >200 IU/L, or T Bili is >3.0 mg/dL proceed to step 3. If criteria not met or not done, Surveillance event.

### (3) Request clinical Notes from facility or Clinician listed on Laboratory Report.

If acute onset/symptomatic according to disease plan or if Co-infected (HIV/AIDS, HBV) and not previously investigated, proceed to step 4. If criteria not met or not done, Surveillance event.

### (4) Full Investigation (Case Contact)

Identify individual risk and behavior
Assess place exposure and contacts.

### Surveillance Events. ELR check for previous results

Update: Current Infection, Resolved, Treated and Cured

### Previous Negative (Seroconversion)

Separate Database
Outbreaks

An outbreak is defined as:

- Two (2) or more cases of HCV clustered in time AND
- At least one (1) confirmed case AND
- At least one of the following:
  - A common exposure
  - Laboratory evidence of highly related viral sequences

Occasionally, a healthcare-associated outbreak may be identified by a single sentinel case, e.g., a frequent blood donor with no identified risk who has had contact with the healthcare system where parenteral exposure to blood or blood-contaminated products may have occurred. Investigation of such outbreaks can be quite complex and requires strong collaboration among involved parties and expert advice.

Identifying Case Contacts

Identification of case contacts for an acute case should focus on individuals that may have been exposed to the case’s blood (e.g., sharing needles, sharing drug preparation equipment [i.e. spoons, cotton, syringes, water bottles], or tattoo equipment and supplies). Otherwise, encourage the case to speak to people who may have been exposed to his/her blood since the time he/she is estimated to have been exposed, infected, or seroconverted.

Case Contact Management

Percutaneous and Mucosal Exposure to HCV Infection

Recommend baseline anti-HCV antibody testing and HCV detection test if indicated. If baseline testing is negative, recommend testing for anti-HCV antibody and ALT 4-6 months after exposure. Recommend HCV detection testing at 4-6 weeks if earlier diagnosis of HCV is desired. Reactive anti-HCV antibody tests should be confirmed with an HCV detection test to identify current infection. Contacts with a positive anti-HCV antibody and/or HCV detection test should be reported and investigated according to the HCV disease plan.

Pregnant women

Routine testing for HCV infection is not recommended for all pregnant women. Pregnant women with a known risk factor for HCV infection should be offered counseling and testing. Patients should be advised that approximately six out of every 100 infants born to HCV-infected woman become infected. Infection occurs predominantly during or near delivery, and no treatment or delivery method—such as caesarian section—has been demonstrated to decrease this risk. The risk is increased, however, by the presence of maternal HCV viremia at delivery, and is 2-3 times greater if the woman is co-infected with HIV.

Infants born to HCV positive mothers

The American Academy of Pediatrics (AAP) recommends screening infants born to mothers who are HCV infected. The diagnosis of HCV is based on detection of HCV RNA. In infants, passively
acquired maternal antibodies can last up to 12 months. The AAP recommends that testing for anti-HCV antibodies be performed after 18 months of age. However, an HCV detection test should be performed if detection of current infection is required earlier.

A negative HCV detection test strongly suggests that the infant is not infected, although a confirmatory re-test at least three months after the initial test is advised. A positive HCV detection test increases the post-test probability that the infant is infected with HCV.

In several studies, high maternal viremia and positive HCV-RNA are predictors for vertical transmission rate, as well as maternal co-infection with HIV. Co-infection with HIV both accelerates the clinical progression of HCV and increases the risk of perinatal HCV transmission from 5% (range, 3-8%) to 17% (range, 7-36%).

HCV has not been shown to be transmitted through breast milk, although HCV-positive mothers should consider abstaining from breastfeeding if their nipples are cracked or bleeding. Infants born to HCV-positive mothers should be tested for HCV infection and, if positive, evaluated for the presence of chronic liver disease.
REFERENCES


VERSION CONTROL

1. 05.15. This disease plan contains updated testing, treatment, and investigation processes and information. The major changes in the investigation process change the investigation criteria from age based investigation criteria to acute case investigation.

2. 06.15. Updated plan with new CSTE position statement classification tables and narrative descriptions.

3. 02.16. HCV disease plan workgroup updates. Complete guidance and investigation revamp. Chronic case definition included and shift to acute case investigation.

3.11.16. Added guidance for ‘Treated and Cured’ and ‘Self-resolved.’
### UT-NEDSS Minimum/Required Fields by Tab

#### Demographic
- Age
- Area Code
- Birth Gender
- City
- County
- Date of Birth
- Ethnicity
- First Name
- Last Name
- Phone Number
- Race
- State
- Street
- Zip Code

#### Clinical
- Clinician First Name
- Clinician Last name
- Date Diagnosed
- Date of Death
- Diagnostic Facility (DF)
- DF State
- DF City
- DF County
- Died
- Disease
- Pregnant
- Does patient have jaundice?
- ALT (SGPT) results:
- ALT interpretation:
- Hepatitis B?, Date of diagnosis
- HIV/AIDS?, Date of diagnosis
- Abdominal pain/tenderness/cramping?
- Acute onset?
- Anorexia?
- Diarrhea?
- Fever?
- Headache?
- Malaise?
- Nausea?
- Vomiting

#### Laboratory
- Collection Date
- Lab
- Organism
- Result Value
- Test Result
- Test Type
- Units
- Bilirubin results:
- ALT (SGPT) results:
- ALT interpretation:

#### Epidemiological
- None

#### Contacts
- None

#### Reporting
- Date first reported to public health

#### Administrative
- LHD investigation/ intervention started
- State case Status
- Outbreak name
- Outbreak Associate
APPENDICES

Appendix A: HCV Testing Algorithm

Recommended Testing Sequence for Identifying Current Hepatitis C Virus (HCV) Infection

- **HCV antibody**
  - Nonreactive: No HCV antibody detected → STOP*
  - Reactive: HCV RNA
    - Not Detected: No current HCV infection
      - Additional testing as appropriate†
    - Detected: Current HCV infection → Link to care

* For persons who might have been exposed to HCV within the past 6 months, testing for HCV RNA or follow-up testing for HCV antibody is recommended. For persons who are immunocompromised, testing for HCV RNA can be considered.
† To differentiate past, resolved HCV infection from biologic false positivity for HCV antibody, testing with another HCV antibody assay can be considered. Repeat HCV RNA testing if the person tested is suspected to have had HCV exposure within the past 6 months or has clinical evidence of HCV disease, or if there is concern regarding the handling or storage of the test specimen.

# Appendix B: HCV Laboratory Report Guidance

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Total Ab (EIA, IFA, TRF, ETC.)</th>
<th>Western (immune) blot (RIBA)</th>
<th>Viral Load</th>
<th>Genotype</th>
<th>ALT</th>
<th>AST</th>
<th>Bilirubin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Common Test Codes</td>
<td>HCV ab, HCVDA, Hepatitis C ab, Hepatitis C antibody, Ab s/CO, s/co</td>
<td>RIBA</td>
<td>PCR, NAT, NAAT, qualitative, quantitative</td>
<td>Genotype, Sequencing</td>
<td>• (ALT) alanine aminotransaminase</td>
<td>• (AST) aspartate aminotransaminase</td>
<td>• (Bilirubin), T bil, Bill,</td>
</tr>
<tr>
<td>Reporter</td>
<td>Local Hospitals, Cat-C, Donor Centers, Reference Laboratories</td>
<td>Reference Laboratories</td>
<td>Reference Laboratories, Donation Centers, some Local Hospitals</td>
<td>Reference Laboratories</td>
<td>Local Hospitals, some Reference Laboratories</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Results</td>
<td>Reactive, Positive, Equivocal, Indeterminate, &gt;11, 11, Reactive HI, Low Positive, reactive (number), Low s/com, HI s/co</td>
<td>Positive, Negative, reactive, non-reactive</td>
<td>Numbers, reactive, non-reactive, positive, negative, HI, detected, not detected, &lt;43**</td>
<td>Genotype 1a, 1b, 2a, 2b, 2c, 2d, 3a, 3b, 3c, 3d, 3e, 3f, 4a, 4b, 4c, 4d, 4e, 4f, 4g, 4h, 4i, 4j, 5a, 6a</td>
<td>Number</td>
<td>Number</td>
<td>Number</td>
</tr>
<tr>
<td>Units</td>
<td>None, IV, s/co</td>
<td>None</td>
<td>IU/mL, LOG IU/mL, Copies, copies/mL</td>
<td>None</td>
<td>U/L</td>
<td>U/L</td>
<td>mg/dL</td>
</tr>
<tr>
<td>Hints</td>
<td>Hint: All antibody tests are considered equivalent and must be confirmed by a more specific assay</td>
<td>Hint: This lab is not routinely used anymore so it will be very rare to see one</td>
<td>Hint: Tests have numbers over 10,000 is a clue that it is a Viral Load.</td>
<td>Hint: Some laboratories do not differentiate between similar genotypes and will report both (ex. 1a or 1b)</td>
<td>Hint: These 3 tests are components of clinical testing. They can be found in laboratory panels called: “Liver Function Panel”, Liver Function Test (LFT)”, and “Comprehensive Metabolic Panel (CMP)”</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

** Viral loads may result <43 but state HCV RNA Detected. This is a positive test. The quantity of IU was less than the tests sensitivity range.
Prevention and education includes providing information on how the disease is transmitted, how to prevent spread of infection, how patients can protect themselves from other potential sources of liver damage, and treatment options available. Offer the information and support below to newly identified cases:

- Provide basic instruction on transmission of HCV and emphasize the need for ongoing medical evaluation. Treatment is available and effective, and the case should be referred to his/her health care provider for a discussion of treatment options.
- Discuss sexual transmission of HCV. Indicate that HCV may be transmitted during sex. Monogamous sexual partners are at lower risk of transmission than those with multiple partners. All contact with blood during sex should be avoided. Emphasize latex barrier protection as a way to prevent the spread of HCV, as well as a way to prevent exposure to and transmission of other pathogens.
- Discuss household transmission of HCV. Household transmission is rare, but to ensure that it does not happen, the case should not share razors, toothbrushes, nail clippers, or any other item that could be contaminated with blood.
- If the patient is a current injection drug user, provide referrals to drug treatment and needle exchange programs if the case needs, or wants, support to stop using. This will help prevent the spread to other individuals.
- Educate the case on the need to abstain from alcohol to help protect the liver. If a case needs, or wants, support to stop drinking, provide referrals to appropriate treatment or support services.
- Discuss medications that should be avoided (e.g., acetaminophen) as high doses can damage the liver. All cases should discuss medications (including over-the-counter medications), dietary supplements, and herbs with a healthcare provider to be certain that they will not damage their livers.
- Determine hepatitis A or B immunization status. If not immunized, provide information on hepatitis A and hepatitis B immunization. (Refer to the Hepatitis A and Hepatitis B disease plans for more information.)
- Inform the case that he/she should not be restricted from working, preparing food, or taking part in his/her daily activities unless he/she has specific symptoms that make it difficult to do so. There are no recommendations suggesting that HCV-infected persons should change their exercise routines or have any dietary restrictions.
- Encourage them to consult with their healthcare provider, or suggest involvement in a research study. Research facilities conduct clinical trials on hepatitis medications and are often looking for individuals to participate. For further information on current trials and qualifications, visit www.clinicaltrials.gov. Local agencies that have a history of HCV Medication Clinical trials include: The University of Utah Medical Center (http://healthcare.utah.edu/clinicaltrials), Jean Brown Research (www.jeanbrownreasearch.com), and PRA Health Services (www.crilifetree.com/clinicaltrialshepatitis), or contact the UDOH Bureau of Epidemiology, Prevention Treatment and Care Program (PTCP) at 801-538-6191 for additional resources.
Appendix D: LHD Action Steps

This is for LHD use as a quick-reference guide to HCV case investigation activities. It is a suggested sequence of investigation and information that should be reviewed with each case. This guidance corresponds with the investigation algorithm above.

Upon receiving a report of acute HCV infection from UDOH, a laboratory, or a healthcare provider, please follow the process detailed below:

1. Decide if report meets investigation criteria:
   - Anti-HCV antibody positive from an acute hepatitis panel
   - HCV detection test from donor screening
   - HCV+ Suspect acute based on circumstantial evidence and/or health department discretion
   - Co-infected (HIV/AIDS, HBV) If previously not investigated

If the investigation criteria are not met, no further investigation is needed.

For individuals that meet the investigation criteria, proceed with investigation.

2. Make a call or fax request for ALT, Tbili, or last negative donation result from the lab or Donation Center respectively. The following are criteria for moving to step 3 (or 4):
   - ALT >200 IU/L
   - Tbili >3.0 mg/dL
   - Negative HCV <12 months (move directly to step 4)

If the investigation criteria are not met, no investigation is needed.

For individuals that meet the investigation criteria, proceed with investigation.

3. Request medical records to review clinical presentation. The following are criteria for moving to step 4:
   - Co-infected (HIV/AIDS, HBV) If previously not investigated OR
   - Clinically compatible symptoms (jaundice, fever, nausea, vomiting, abdominal pain, etc.) AND
   - Absence of other etiologies/underlying conditions to explain clinical elevated LFT, Tbili, jaundice

If the investigation criteria are not met, no investigation is needed.

For individuals that meet the investigation criteria, proceed with investigation.

4. Contact case for full investigation as described:
   - Complete form (risk factor) questionnaire
   - Attempt to identify place exposure and contacts
   - Assist with education to disrupt transmission
Hepatitis C: Utah Public Health Disease Investigation Plan

Start

Is case being reported an existing "Hepatitis C, acute" case?

Y  |  Is specimen collection date from new lab result <12 months from specimen collection date of 1st positive lab result?  
N  |  Add the laboratory results to the existing CMR (including negatives). Update Case Status as appropriate.

Y  |  Enter as a "Hepatitis C, acute" case
N  |  Deep copy the "Hepatitis C, acute" case and save as a "Hepatitis C virus infection, chronic" case. Add the laboratory results to the new CMR (including negatives). No further follow up is necessary.

Does the case have symptoms consistent with acute Hepatitis C?

Y  |  Call the diagnostic facility and request clinical notes.
N  |  Change to "Hepatitis C virus infection, chronic". No further investigation is necessary. Case can be closed.

Does the case have symptoms consistent with acute Hepatitis C?

Y  |  Call the performing laboratory and ask for ALT and Bilirubin values
N  |  Are ALT and Bilirubin values available?

Y  |  Were results from donors last negative donation included in original report?
N  |  Enter as (or change to) a "Hepatitis C, acute" case. Complete a full investigation.

Y  |  Were previous HCV test results negative?
N  |  Were results from previous donation (within the past 12 months) available?

Symptoms: Acute Onset, Jaundice, Fever, Headache, Malaise, Anorexia, Nausea, Vomiting, Diarrhea, Abdominal Pain