

Hepatitis, D and E, Acute

(Previously Hepatitis, Unspecified)

1. DISEASE REPORTING

A. Purpose of Reporting and Surveillance

1. To better characterize the epidemiology of infectious hepatitis not due to hepatitis A, B, or C viruses.
2. To recommend appropriate preventive measures, including immunization against other types of hepatitis which are vaccine-preventable.

B. Legal Reporting Requirements

1. Hepatitis D (acute and chronic)

- a. Health care providers: notifiable to local health jurisdiction within 3 business days
- b. Health care facilities: notifiable to local health jurisdiction within 3 business days
- c. Laboratories: Hepatitis D virus (detection of viral antigen, antibody or nucleic acid) notifiable within 2 business days
- d. Local health jurisdictions: notifiable to the Washington State Department of Health (DOH) Communicable Disease Epidemiology Section (CDES) within 7 days of case investigation completion or summary information required within 21 days.

2. Hepatitis E (acute)

- a. Health care providers: notifiable to local health jurisdiction within 24 hours
- b. Health care facilities: notifiable to local health jurisdiction within 24 hours
- c. Laboratories: Hepatitis E virus (detection of viral antigen, antibody or nucleic acid) notifiable within 24 hours
- d. Local health jurisdictions: notifiable to the Washington State Department of Health (DOH) Communicable Disease Epidemiology Section (CDES) within 7 days of case investigation completion or summary information required within 21 days.

C. Local Health Jurisdiction Investigation Responsibilities

1. Begin investigation within one working day.
2. Facilitate transport of specimens to Public Health Laboratories for confirmatory testing.
3. Initiate appropriate infection control measures.
4. Hepatitis D virus and hepatitis E virus infections should be reported to DOH as unspecified infectious hepatitis. Report all *confirmed* cases to CDES. Complete the hepatitis D or E report form (<http://www.doh.wa.gov/notify/forms/hepde.pdf>) and enter the data in the Public Health Issues Management System (PHIMS).

2A. HEPATITIS D AND ITS EPIDEMIOLOGY

Background

Hepatitis D infections occur globally, but the prevalence varies widely among countries. An estimated 10 million people worldwide have dual infections with hepatitis D and hepatitis B viruses. Hepatitis D infection occurs epidemically or endemically in populations at risk of hepatitis B virus infection, such as populations in countries where hepatitis B is endemic (e.g., Russia, Romania, southern Italy, Africa and South America); in hemophiliacs, intravenous drug addicts and others who come in frequent contact with blood; in institutions for the developmentally disabled; and, to a lesser extent, in male homosexuals. In the United States, seroprevalence may be over 50% in high risk groups such as urban injection drug users (JID 2010;200;822).

A. Etiologic Agent

Hepatitis D virus is an “incomplete virus” because it can only replicate in the presence of Hepatitis B virus. Hepatitis D virus has a small single-stranded RNA genome that only encodes one virus-specific protein (“delta antigen”). This genome is encapsulated within a protein coat of HBsAg that allows the hepatitis D virus to gain cell entry. During the period when hepatitis D virus is replicating in cells, hepatitis B replication is temporarily suspended.

B. Description of Illness

Onset is usually abrupt, with signs and symptoms resembling those of infections with hepatitis B virus; illness may be severe. Hepatitis D virus transmission can occur simultaneously with a new hepatitis B infection (“co-infection”) or can occur as a superinfection of a person with chronic hepatitis B. Hepatitis D may be self-limiting or it may progress to chronic hepatitis. Children may have a particularly severe clinical course with common progression to chronic active hepatitis. With superinfection, symptoms due to hepatitis D infection can be misdiagnosed as an exacerbation of chronic hepatitis B infection.

C. Hepatitis D in Washington State

An outbreak of acute hepatitis B infection among injecting drug users in Pierce County in April 2000 included 60 cases and also involved cases of hepatitis D infection. The three deaths in the outbreak were all infected with hepatitis B and D viruses.

D. Reservoirs

Humans.

E. Modes of Transmission

Transmission is similar to that of hepatitis B virus – by exposure to infected blood and serous body fluids, contaminated needles, syringes and plasma derivatives such as antihemophilic factor, and through sexual transmission. All people still susceptible to hepatitis B virus infection or who have chronic hepatitis B infection can be infected with hepatitis D virus.

F. Incubation Period

Approximately 2–8 weeks.

G. Period of Communicability

Blood is potentially infectious during all phases of active hepatitis D infection. Peak infectivity probably occurs just prior to onset of acute illness, when particles containing the hepatitis D antigen are readily detected in the blood. Following onset of symptoms, viremia probably falls rapidly to low or undetectable levels but experimental evidence suggests infectivity may persist even if antigen is not detectable.

H. Treatment

Treatment for acute hepatitis D infection is supportive. For chronic hepatitis B and D virus infection, antiviral treatment for hepatitis B or, in severe cases, liver transplantation may be considered.

2B. HEPATITIS E AND ITS EPIDEMIOLOGY**Background**

After hepatitis A, hepatitis E virus is the second most common etiologic agent of enterically transmitted viral hepatitis throughout the world. Outbreaks and sporadic cases of hepatitis E infection occur over a wide geographic area especially in areas with inadequate environmental sanitation including Egypt, India, and China. Outbreaks are often waterborne, but sporadic cases and epidemics not clearly related to water have been reported; foodborne and waterborne outbreaks have been reported. The highest rates of hepatitis E infection are in young to middle-aged adults although lower rates in younger age groups may reflect undiagnosed milder hepatitis E infections without jaundice. In the United States and most other industrialized countries, almost all cases result from travel to hepatitis E virus endemic areas although rare sporadic endemic cases occur. Seroprevalence is reported elevated in homeless persons including in California and France (<http://www.cdc.gov/eid/content/16/11/1761.htm>).

A. Etiologic Agent

The hepatitis E virus (HEV) is a single-stranded RNA virus with four genotypes. The major geographic distributions are genotype 1 in Asia and Africa, genotype 2 in Mexico and Africa, genotype 3 in developed countries, and genotype 4 in Asia. Genotypes 1 and 2 circulate in humans while genotypes 3 and 4 are generally zoonotic diseases.

B. Description of Illness

The clinical course is usually like that of hepatitis A. The case-fatality rate is similar to that of hepatitis A except in pregnant women, where the rate may reach 20% for those infected during the third trimester of pregnancy. Fulminant hepatitis is more common during outbreaks particularly in children under two years and pregnant women. Severe cases of hepatitis E in Japan have been associated with a more virulent genotype of the virus (Emerg Infect Dis 2009 May). Rare chronic hepatitis E has been described in a small number of organ-transplant recipients in Europe (NEJM 2008;358(8):814) and other persons with immunocompromise including HIV infection.

C. Hepatitis E in Washington State

Two cases have been reported in the past five years, both associated with travel to India.

D. Reservoirs

Humans for genotypes 1-4. Wild and domestic animals, particularly domestic pigs and wild swine, for genotypes 3 and 4. Other wild game (e.g., deer) and rats may be infected.

E. Modes of Transmission

Hepatitis E virus is transmitted primarily by the fecal-oral route and fecally contaminated drinking water is the most commonly documented vehicle of transmission. Fecal-oral transmission probably can occur from person-to-person; secondary household cases occur but are not common during outbreaks. Transfusion-associated cases have occurred. Recent studies have suggested that hepatitis E is likely a zoonotic infection transmitted from domestic pigs and other wild animal species; pig contact does not explain all endemic cases in the United States. Shellfish may be a source of exposure.

F. Incubation Period

The range is 2 to 9 weeks; mean incubation period is around 6 weeks but has varied from 26 to 42 days in different epidemics.

G. Period of Communicability

Not known. However, hepatitis E virus has been detected in stools 14 days after the onset of jaundice and approximately 4 weeks after ingestion of contaminated food or water and persists for about 2 weeks.

H. Treatment

Treatment is supportive.

3. CASE DEFINITIONS

A. Clinical Description

Acute Infection, Hepatitis D or E

An illness with a) discrete onset of symptoms **and** b) jaundice or elevated serum aminotransferase levels.

Chronic Infection, Hepatitis D

May be no symptoms or chronic liver disease, which can range from mild to severe.

B. Laboratory Criteria for Diagnosis

Hepatitis D

- Serum aminotransferase levels > 2.5 times the upper limit of normal, AND
- Immunoglobulin M (IgM) anti-HAV negative, AND
- Anti-HCV negative, AND
- HBsAg or IgM anti-HBc positive, AND

- Positive result from a research laboratory for hepatitis D RNA or detection of antibody to hepatitis D virus.

Hepatitis E

- Serum aminotransferase levels > 2.5 times the upper limit of normal, AND
- Immunoglobulin M (IgM) anti-HAV negative, AND
- IgM anti-HBc negative (if done) or HbsAg negative, AND
- Anti-HCV negative, AND
- Positive result from a research laboratory for hepatitis E RNA or detection of antibody to hepatitis E antigen.

C. Case Definition (DOH)

Confirmed: A case that meets the clinical case definition (for acute) and is laboratory confirmed.

4. DIAGNOSIS AND LABORATORY SERVICES

A. Diagnosis

Diagnosis of hepatitis D depends on clinical and epidemiologic features and exclusion of other etiologies of hepatitis, especially hepatitis A, by serologic means. EIA is available to detect total antibody to hepatitis D virus (anti-HDV). A positive IgM titer indicates ongoing replication; reverse transcription PCR is the most sensitive assay for detecting hepatitis D viremia.

Diagnosis of hepatitis E depends on clinical and epidemiologic features and exclusion of other etiologies of hepatitis, especially hepatitis A, by serologic means. Anti-HEV IgM is detectable before onset and persists 4-6 months. Anti-HEV IgG appears soon after IgM.

Several diagnostic tests are available including enzyme immunoassays and Western blot assays to detect IgM and IgG anti-HEV in serum; polymerase chain reaction tests to detect hepatitis E virus RNA in serum and stool; and immunofluorescent antibody blocking assays to detect antibody to hepatitis E antigen in serum and liver. Nucleic acid amplification tests detect HEV two weeks before onset to one week after in blood, later in stool.

B. Tests Available at the Washington State Department of Health Public Health Laboratories (PHL)

PHL does not perform testing for hepatitis D or E but will forward specimens to the Centers for Disease Control and Prevention for testing or confirmation. Please contact Communicable Disease Epidemiology Section for approval prior to submitting specimens.

C. Specimen Collection

Serum should be refrigerated and transported cold. Specimens should be submitted with a completed DOH PHL Virus Examinations form available at:
<http://www.doh.wa.gov/EHSPHL/PHL/Forms/SerVirHIV.pdf>

5. ROUTINE CASE INVESTIGATION

Interview the case or others who may be able to provide pertinent information.

A. Evaluate the Diagnosis

Confirm that the case's illness is consistent with acute viral hepatitis. Diagnosis is supported by presence of risk factors such as intravenous drug use for hepatitis D or international travel for hepatitis E. Facilitate transport of positive specimens to Washington State Public Health Laboratories which will arrange confirmatory testing.

B. Identify Potential Sources of Infection**1. Hepatitis D**

For acute infections and those suspected to have been infected through medical, dental or commercial procedures, collect information about possible exposures, including high risk behaviors, during the period 2–8 weeks before onset of illness. Include close contacts with recent or chronic hepatitis, receipt of blood products, blood exposure through needles or other route, or occupational exposure to blood. Also identify any persons sharing risks (e.g., household member, sex partners, those sharing injection equipment) who had a compatible illness. Obtain each person's name and contact information. Newly identified suspected cases should be reported and investigated in the same manner as the index case.

2. Hepatitis E

Collect information about possible exposures, including high risk behaviors, during the period 2–9 weeks before onset of illness. Include close contacts (particularly foreign arrivals) with recent hepatitis as well as travel-associated food and water exposures. Also identify any persons sharing risks (e.g., household member, sex partners, shared a meal, others in a travel group) who had a compatible illness. Obtain each person's name and contact information. Newly identified suspected cases should be reported and investigated in the same manner as the index case.

C. Identify Close Contacts or Others Potentially Exposed to the Patient

1. For hepatitis D investigations, identify secondary cases, that is, persons potentially exposed to the case during the communicable period. These include household members, sexual contacts, and needle sharing contacts and others potentially exposed to blood or sexual fluids. Evaluate for symptoms and educate about preventing transmission. Recommend hepatitis B vaccination to contacts susceptible to hepatitis B virus.
2. Secondary cases of hepatitis E infection are not common. Household and sexual contacts should be evaluated for symptoms and educated about preventing transmission.
3. If the case has donated blood or plasma in the 8 weeks before onset, see Section 7D.
4. If the patient is pregnant, see Section 7E.

D. Environmental Evaluation

None, unless a commercial food service facility, child care center, or public water supply appears to be implicated as the source of infection.

6. CONTROLLING FURTHER SPREAD

A. Infection Control Recommendations / Case Management

1. Hepatitis D: Hospitalized patients should be cared for using standard precautions.
2. Hepatitis E: Hospitalized patients should be cared for using standard precautions. In addition, contact precautions should be used for diapered or incontinent individuals for the duration of symptoms.
3. Patients infected with hepatitis D or hepatitis E viruses who are still susceptible to hepatitis A should be vaccinated against hepatitis A.

B. Contact Management

1. Symptomatic Contacts

Symptomatic close contacts of a confirmed case should be referred to a healthcare provider and tested.

2. Postexposure Prophylaxis

No products are available to prevent hepatitis D or E in contacts.

3. Education

All persons exposed to the case or the same source as the case should be educated about signs and symptoms of hepatitis in both children and adults, and methods to prevent transmission. They should be informed that persons may be infectious without being ill.

4. Vaccination

For contacts of hepatitis D cases who are still susceptible to hepatitis B virus, recommend hepatitis B vaccination.

7. MANAGING SPECIAL SITUATIONS

A. Case is a Health Care Worker with Hepatitis D

If the case is a dentist, physician, nurse, or other health care worker with potential for exposing patients by blood or other body fluids:

1. Discourage the person from working until the acute clinical illness has resolved;
2. Recommend that upon return to work, the worker practice special precautions be practiced until no longer infectious, including:
 - a. wearing gloves for all procedures during which the hands will be in contact with patients' mucosal surfaces or broken skin;
 - b. avoiding situations involving sharps that could lead to exposures of susceptible patients to blood or objects contaminated with blood of the case;
 - c. careful and frequent hand washing.
3. Chronically infected health care workers should be encouraged to voluntarily seek confidential counseling from employee health services regarding risk reduction strategies, which evaluation would include a review of their practice by an expert panel.

B. Outbreak of Hepatitis D

When two or more cases occur with a likely common exposure, such as associated with the same health care setting, conduct a search for additional cases. If a plasma derivative such as antihemophilic factor, fibrinogen, pooled plasma or thrombin is implicated, notify the bloodbank to withdraw the lot from use and cooperate with other agencies to trace all recipients of the same lot.

Outbreaks are typically associated with intravenous drug use. During an outbreak provide education and outreach to intravenous drug users in the affected area to reduce bloodborne transmission. In addition, make available hepatitis B vaccination for those still susceptible to that infection.

C. Outbreak of Hepatitis E

Follow investigation guidelines for foodborne or waterborne outbreaks.

See: Said B, Ijaz S, Kafatos G, Booth L, Thomas HL, et al. Hepatitis E outbreak on cruise ship. *Emerg Infect Dis* [serial on the Internet]. 2009 Nov [cited 10/26/2009]. <http://www.cdc.gov/EID/content/15/11/1738.htm>

D. Case Is a Recent Blood Donor or Recipient

The blood bank should be notified so that any unused product can be recalled.

E. Case Is Pregnant

Follow the perinatal hepatitis B recommendations if the pregnant woman is hepatitis B virus DNA or HBsAg-positive.

Hepatitis E virus infection can be severe in a pregnant woman, causing acute liver failure and premature delivery or stillbirth. Refer the patient to a gastroenterologist and consult with Communicable Disease Epidemiology Section.

8. ROUTINE PREVENTION

A. Immunization Recommendations

None. Multiple viral hepatitis infections can result in liver damage, so universal immunization is recommended to prevent hepatitis A and hepatitis B.

B. Prevention Recommendations

1. Hepatitis D

Preventing hepatitis B virus infection prevents infection with hepatitis D virus. For at-risk persons such as injection drug users, follow prevention recommendations for hepatitis B including vaccination for those susceptible to hepatitis B virus infection. Among persons with chronic hepatitis B virus, the only effective measure is avoiding exposure to any potential source of hepatitis D. Immune globulin, hepatitis B immune globulin, and hepatitis B vaccine do not protect persons with chronic hepatitis B virus from infection by hepatitis D virus. Studies suggest that measures which decrease sexual exposure and needle sharing have been associated with a decline in the incidence of hepatitis D virus infection.

2. Hepatitis E

Routine precautions should be taken during travel in risk areas to assure safe food and water, particularly for women who may be pregnant. Hepatitis E is highly endemic in many parts of Asia and Africa, but is also endemic in the Americas and Europe. For travel information related to hepatitis E see:

<http://wwwnc.cdc.gov/travel/yellowbook/2010/chapter-5/hepatitis-e.aspx>

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UPDATES

January 2011:

Condition renamed from Hepatitis, Unspecified.

The Legal Reporting Requirements section has been revised to reflect the 2011 Notifiable Conditions Rule revision.