

Hepatitis D and E

Signs and Symptoms	<ul style="list-style-type: none"> • Acute onset of gastrointestinal symptoms and jaundice • Hepatitis D virus (HDV) infection may be severe, particularly in children • Hepatitis E virus (HEV) infection may be severe, particularly in pregnant women, (up to 20% fatal or immunocompromised (neurologic complications))
Incubation	HDV 2-8 weeks, HEV 2-9 weeks
Case classification	<p>Clinical criteria: acute illness, discrete onset of any consistent symptoms (fever, headache, anorexia, nausea, vomiting, diarrhea, abdominal pain) and either jaundice or serum aminotransferase levels > 2.5 times the upper limit of normal</p> <p>Meets clinical criteria and IgM anti-HAV negative and anti-HCV negative and</p> <ul style="list-style-type: none"> • Confirmed HDV: HBsAg or IgM anti-HBc positive and positive research laboratory result for HDV RNA or detection of antibody to HDV • Confirmed HEV: IgM anti-HBc negative (if done) or HbsAg negative and positive research laboratory result for HEV RNA or detection of antibody to HEV
Differential diagnosis	Hepatitis A, B or C (do laboratory testing), chemical hepatitis (e.g., alcoholism, use of risk medication, natural remedy, specialty tea), autoimmune hepatitis , biliary disease (cholangitis, gallstones), malignancy (liver, pancreas), metabolic disease (e.g., Wilson's)
Treatment	Supportive
Duration	<ul style="list-style-type: none"> • HDV may be self-limiting or progress to chronic infection • HEV has rare chronic infection with HIV infection or a Japanese strain
Exposure	<ul style="list-style-type: none"> • HDV: infected blood, serous body fluids, or plasma derivatives such as anti-hemophilic factor; contaminated needles or drug works; sexual transmission • HEV: person-to-person fecal-oral spread or contaminated drinking water; rare secondary household cases; domestic pigs or wild animal species implicated rarely
Laboratory testing	<ul style="list-style-type: none"> • Confirmatory testing available at CDC • Best specimens: Acute and chronic sera including if possible previously tested specimens For HEV also obtain stool specimen in sterile screw-top container <p><i>Specimen shipping (Section 4):</i></p> <ul style="list-style-type: none"> • Provider to keep all specimens cold, ship cold with serology/virology form: http://www.doh.wa.gov/Portals/1/Documents/5230/302-017-SerVirHIV.pdf
Public health actions	<p>LHJ can contact Office of Communicable Disease Epidemiology at 877-539-4344 or 206-418-5500 for diagnosis and treatment</p> <ul style="list-style-type: none"> • Identify potential sources of exposure • Identify symptomatic close contacts or those sharing an exposure with the case • Determine if case donated blood and if so notify blood bank • Exclude HEV case from food handling, child care or healthcare, or attending school or child care until diarrhea resolves • Recommend hepatitis A vaccine; for HEV also recommend hepatitis B vaccine • Recommend hepatitis B vaccination for any susceptible contacts of HDV case <p><i>Infection Control:</i> standard precautions; for HEV enteric precautions if incontinent</p>

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. Healthcare providers: notifiable to local health jurisdiction within 3 work days
2. Healthcare facilities: notifiable to local health jurisdiction within 3 work days
3. Laboratories: no requirements for reporting
4. Local health jurisdictions: notifiable to Washington State Department of Health (DOH) Office of Communicable Disease Epidemiology (OCDE) 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 the appropriate condition. Report all *confirmed* cases to OCDE. Complete the Hepatitis D or E report form (<http://www.doh.wa.gov/Portals/1/Documents/5100/210-033-ReportForm-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 much lesser extent, in men having sex with men.

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 including gastrointestinal symptoms and jaundice; 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

Three of five cases during 2010-2015 used injection drugs, one had close contact with a drug user, and one had no information about risk. An April 2000 Pierce County outbreak of acute hepatitis B infection among injecting drug users included 60 cases, some with hepatitis D infections; three fatal cases were infected with both hepatitis B and D viruses.

D. Reservoirs

Humans.

E. Modes of Transmission

Transmission is similar to hepatitis B virus – 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 worldwide, particularly in Asia and Africa. Outbreaks and sporadic cases occur especially with inadequate environmental sanitation. Hepatitis E virus outbreaks are often waterborne, but foodborne outbreaks (pork, venison), sporadic cases, and epidemics not clearly related to water have been reported. Parenteral transmission may occur. Refugee camps in conflict areas can have outbreaks. Highest rates are in young to middle-aged but younger age groups may have undiagnosed milder illness without jaundice. In the United States and most other industrialized countries, almost all cases result from travel to endemic areas.

A. Etiologic Agent

The hepatitis E virus (HEV) is a single-stranded RNA virus. There are four genotypes.

B. Description of Illness

The clinical course is usually like that of hepatitis A with a similar case-fatality rate except in pregnant women, where the rate may reach 20% for those infected during the third trimester of pregnancy. Severe cases of hepatitis E in Japan were associated with a more virulent genotype (Emerg Infect Dis 2009 May). Chronic infections are rare but occurred in organ-transplant recipients in Europe (NEJM 2008;358(8):814) and may occur with HIV infection. Neurologic complications have been reported, particularly in immunocompromised persons with chronic infections (Emerg Infect Dis 2011 Feb).

C. Hepatitis E in Washington State

Of 11 cases 2010-2015, six had travel to Asia or the Middle East.

D. Reservoirs

Humans. Wild and domestic animals, particularly swine, also rabbits, chickens, rats, deer.

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, though secondary household cases are not common during outbreaks. Recent studies have suggested that hepatitis E is likely a zoonotic infection transmitted from domestic pigs and other wild animal species.

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. Hepatitis E virus was detected in stools 14 days after onset of jaundice and about 4 weeks after consuming contaminated food or water, persisting for about 2 weeks.

H. Treatment

Treatment is supportive.

3. CASE DEFINITIONS

A. Clinical Description

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

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 and is laboratory confirmed.

4. DIAGNOSIS AND LABORATORY SERVICES

A. Diagnosis

Diagnosis of hepatitis D infection 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 infection depends on clinical and epidemiologic features and exclusion of other etiologies of hepatitis, especially hepatitis A, by serologic means.

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.

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

PHL does not test for hepatitis D or E but will forward specimens to the Centers for Disease Control and Prevention for testing or confirmation. Please contact Office of Communicable Disease Epidemiology for approval prior to submitting specimens. Obtain acute (if possible, previously tested specimen) and chronic sera. For hepatitis E also obtain stool specimen. Specimens should be kept cold.

Note that PHL require all clinical specimens have two patient identifiers, a name **and** a second identifier (e.g., date of birth) both on the specimen label and on the submission form. Due to laboratory accreditation standards, specimens will be rejected for testing if not properly identified. Also include specimen source and collection date.

C. Specimen Collection

Serum and other specimens 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/Portals/1/Documents/5230/302-017-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 for confirmatory testing. If the patient is pregnant, see Section 6E.

B. Identify Potential Sources of Infection

Ask the case about potential exposures 2–8 weeks before onset of illness, including any persons (e.g., household member, sex partners, shared injection equipment, 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

For hepatitis D investigations, identify potential secondary cases exposed to the case's blood or sexual fluids during the communicable period. Include household members, sexual contacts, and needle sharing contacts. Evaluate for symptoms, educate about preventing transmission, and inform that persons with hepatitis may be infectious without being ill. Also educate persons exposed to the same source as the case. No products are available to prevent hepatitis D or E infections in contacts. Recommend hepatitis B vaccination to contacts susceptible to hepatitis B virus.

1. Symptomatic close contacts of a confirmed case should be referred to a healthcare provider and tested.
2. Secondary cases of hepatitis E infection are rare, but recommend hygiene measures.
3. If the case has donated blood or plasma in the 8 weeks before onset, see Section 6D.

4. Recommend hepatitis B vaccination for all susceptible household and other close contacts of a hepatitis D case.

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.

E. Infection Control

1. Patients infected with hepatitis D virus who are still susceptible to hepatitis A should be vaccinated against hepatitis A. Patients infected with hepatitis E virus who are still susceptible to hepatitis A or B should be vaccinated against hepatitis A or B.
2. Hepatitis D: Hospitalized patients should be cared for using standard precautions.
3. Hepatitis E: Hospitalized patients should be cared for using standard precautions. Also use contact precautions for diapered or incontinent individuals while symptomatic.

6. MANAGING SPECIAL SITUATIONS**A. Case is a Health Care Worker with Hepatitis D**

If the case is a dentist, physician, nurse, or other healthcare 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:
 - Wearing gloves for all procedures during which the hands will be in contact with patients' mucosal surfaces or broken skin;
 - Avoiding situations involving sharps that could lead to exposures of susceptible patients to blood or objects contaminated with blood of the case;
 - 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 associated with a common exposure, such as a 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 trace all recipients of the same lot.

Provide education and outreach to intravenous drug users in the community to reduce bloodborne transmission and make available hepatitis B vaccination for those still susceptible to that infection.

C. Hepatitis E Case Works or Volunteers in a Risk Setting

Exclude HEV case from food handling, child care, healthcare, or attending school or child care until diarrhea resolves

D. 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 5/12/2014].

http://wwwnc.cdc.gov/eid/article/15/11/09-1094_article

E. Case Is a Recent Blood Donor or Recipient

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

F. Case Is Pregnant

Follow perinatal hepatitis B recommendations if a pregnant woman had hepatitis D.

Hepatitis E virus infection can be severe in pregnancy, causing acute liver failure and premature delivery or stillbirth. Consult with Office of Communicable Disease Epidemiology.

7. 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 present in the Americas and in Europe. For travel information related to hepatitis E see:

<http://wwwnc.cdc.gov/travel/yellowbook/2014/chapter-3-infectious-diseases-related-to-travel/hepatitis-e>

ACKNOWLEDGEMENTS

This document is a revision of the Washington State Guidelines for Notifiable Condition Reporting and Surveillance published in 2002 which were originally based on the Control of Communicable Diseases Manual (CCDM), 17th Edition; James Chin, Ed. APHA 2000. We would like to acknowledge the Oregon Department of Human Services for developing the format and select content of this document.

UPDATES

May 2014: Combined Routine Case Investigation with Controlling Further Spread

May 2016: Added first page.