Hepatitis D

Signs and Symptoms	• Acute onset of gastrointestinal symptoms and jaundice (for acute hepatitis D) • Hepatitis D virus (HDV) infection may be severe, particularly in children • HDV can be an acute, short-term infection or a long-term chronic infection • HDV can be acquired either as a coinfection with HBV or as superinfection in people with chronic HBV infection
Incubation	2-8 weeks
Case classification	**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.
	Laboratory criteria: • **Confirmed HDV:** Presence of Hepatitis B (HBsAg, IgM anti-HBc, or HBV DNA positive) **and** HDV RNA or HDV antigen positive or detection of antibody to HDV. Only laboratory criteria is required to confirm a hepatitis D case.
Differential diagnosis	**Hepatitis A, B, C, or E** (history and laboratory testing)**, chemical hepatitis** (e.g., alcoholism, risk medication/natural remedy, specialty tea), **autoimmune hepatitis**, **biliary disease** (cholangitis, gallstones), **malignancy** (liver, pancreas), **metabolic disease** (e.g., Wilson's)
Treatment	Supportive
Duration	• HDV may be self-limiting or progress to chronic infection
Exposure	• HDV: infected blood, serous body fluids, or plasma derivatives such as anti-hemophilic factor; contaminated needles or drug works; sexual transmission
Laboratory testing	• Communicable Disease Epidemiology (CDE) will arrange confirmatory testing, genotyping, and sequencing available at CDC • **Best specimens**: Acute and chronic sera including previously tested specimens – spin down, separate, and ship cold or frozen at -70°C. Contact CDE to discuss specimen shipping and handling for each situation. CDE will complete the special hepatitis shipping manifest. *Specimen shipping (Section 4):* • Relay specimen handling instructions to provider and have them submit specimen to Washington State Public Health Laboratories (PHL) with this form: https://www.medialab.com/dv/dl.aspx?d=1615463&dh=e4b87&u=69790&uh=0e2a1
Public health actions	Local Health Jurisdiction (LHJ) can contact CDE at 877-539-4344 or 206-418-5500 for assistance with diagnosis and treatment • 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 • Recommend hepatitis A vaccine • Recommend hepatitis B vaccination for any susceptible contacts • Complete the CDC questionnaire for hepatitis D surveillance • Enter in WDRS as subtype: Hepatitis D co-infected; also assure entry as a hepatitis B case *Infection Control:* standard precautions

Hepatitis D

1. DISEASE REPORTING

A. Purpose of Reporting and Surveillance

1. To better characterize the epidemiology of infectious hepatitis not due to hepatitis A, B, C, or E 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 and Healthcare facilities: notifiable to local health jurisdiction within 24 hours.
2. Laboratories: hepatitis D positivity notifiable to local health jurisdiction within 24 hours; submission on request – specimen associated with positive result, within 2 business days
3. Local health jurisdictions: notifiable to Washington State Department of Health (DOH) Office of Communicable Disease Epidemiology (CDE) 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 Washington State Public Health Laboratories for confirmatory testing.
3. Initiate appropriate infection control measures.
4. Report all *confirmed* hepatitis D virus infections cases to CDE. Complete the CDC's Hepatitis D questionnaire and fax the completed form to CDE (206-364-1060).
5. Note that hepatitis D occurs only with a hepatitis B virus infection. If the patient has not been reported to DOH as a hepatitis B case, enter the relevant information into the Washington Disease Reporting System (WDRS).

2. HEPATITIS D AND ITS EPIDEMIOLOGY

Background

Hepatitis D virus infections occur globally as a dual infection with hepatitis B, but the prevalence varies widely among countries. An estimated 10 million people worldwide have dual infections. 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 persons who inject drugs, hemophiliacs, and others who come in frequent contact with blood or receive blood products; 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 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 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 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 person who inject drugs, and one had no information about risk. An April 2000 Pierce County outbreak of acute hepatitis B infection among persons who inject drugs 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.

3. CASE DEFINITION

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

- HBsAg or IgM anti-HBc or HBV DNA positive , **and**
- Hepatitis D RNA or HDV antigen positive or detection of antibody to hepatitis D virus.

C. Case Definition (DOH)

Confirmed: A case that 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.

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

PHL does not test for hepatitis D but will forward specimens to the Centers for Disease Control and Prevention for testing or confirmation. Please contact Office of Communicable Disease Epidemiology (CDE) for approval prior to submitting specimens. Obtain acute (if possible, previously tested specimen) and chronic sera. Specimens should be spun down, separated, and kept cold. CDE will complete the special CDC shipping manifest.

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: https://www.medialab.com/dv/dl.aspx?d=1615463&dh=e4b87&u=69790&uh=0e2a1

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. Case should have a prior or concurrent hepatitis B diagnosis (acute or chronic). 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 drug paraphernalia) with 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 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. If the case has donated blood or plasma in the 8 weeks before onset, see Section 6D.
3. 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.
2. Hepatitis D: Hospitalized patients should be cared for using standard precautions.

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 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 persons who inject drugs in the community to reduce bloodborne transmission and make available hepatitis B vaccination for those still susceptible to that infection.

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.

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 persons who inject drugs, 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.

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UPDATES

May 2014: Combined Routine Case Investigation with Controlling Further Spread

May 2016: Added first page.

April 2018: Separated from Hepatitis D and E guideline, updated for WDRS.

April 2019: Reviewed.

December 2022: For 2023 WAC revision combined provider and facility reporting requirement, updated laboratory submission (Section 1B)