Hepatitis E

Signs and Symptoms	• Acute onset of gastrointestinal symptoms and jaundice • Hepatitis E virus (HEV) infection may be severe, particularly in pregnant women, (up to 20% fatal or immunocompromised (neurologic complications)
Incubation	2-9 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
	• Meets clinical criteria **and** IgM anti-HAV negative **and** anti-HCV negative **and** • 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, C, or D** (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	• Rare chronic infection with HIV infection coinfection or a certain Japanese HEV strain
Exposure	• Person-to-person fecal-oral spread or contaminated drinking water; rare secondary household cases; domestic pigs or wild animal species implicated rarely
Laboratory testing	• Confirmatory testing available at CDC • **Best specimens**: Acute and chronic sera including if possible specimens previously testing positive Also obtain stool specimen in sterile screw-top container *Specimen shipping (Section 4):* • Provider to keep all specimens **cold, ship cold** with serology/virology form: https://www.medialab.com/dv/dl.aspx?d=1615463&dh=e4b87&u=69790&uh=0e2a1
Public health actions	LHJ can contact Office of Communicable Disease Epidemiology at 877-539-4344 or 206-418-5500 for 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 • Exclude from food handling, child care or health care, or attending school or child care until diarrhea resolves • Recommend hepatitis A vaccine and hepatitis B vaccine *Infection Control:* standard precautions; enteric precautions if incontinent

Hepatitis E, Acute

(Previously Hepatitis, Unspecified)

1. DISEASE REPORTING

A. Purpose of Reporting and Surveillance

1. To better characterize the epidemiology of infections due to hepatitis E.
2. To recommend appropriate preventive measures, including immunization against other types of hepatitis which are vaccine-preventable.

B. Legal Reporting Requirements

1. **Health care providers** and **Health care facilities**: notifiable to local health jurisdiction within 24 hours
2. **Laboratories:** 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 the Washington State Public Health Laboratories for confirmatory testing.
3. Initiate appropriate infection control measures.
4. Hepatitis E virus infections should be reported to DOH as the appropriate condition. Report all *confirmed* cases to CDE. Complete the Hepatitis E report form http://www.doh.wa.gov/Portals/1/Documents/5100/210-033-ReportForm-HepDE.pdf and enter the data in the Washington Disease Reporting System (WDRS).

2. 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 https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6229a2.htm?s_cid=mm6229a2_e 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. Five of eight genotypes affect humans, with variation in geographic distribution and in epidemiologic patterns. See table: https://www.cdc.gov/hepatitis/hev/hevfaq.htm#section1

B. Description of Illness

The clinical course is usually like that of hepatitis A with a similar low case-fatality rate except in pregnant women, where the rate may reach 30% for those infected during the third trimester of pregnancy, and persons with existing liver damage. Severe cases of hepatitis E in Japan were associated with a more virulent genotype. https://wwwnc.cdc.gov/eid/article/15/5/08-1100_article Chronic infections are rare but occur in organ-transplant recipients in Europe (NEJM 2008;358(8):814) and may occur with HIV infection. Complications can be neurologic (particularly as chronic infections in immunocompromised persons https://wwwnc.cdc.gov/eid/article/17/2/10-0856_article or affect the kidney or pancreas.

C. Hepatitis E in Washington State

Of 21 cases reported in Washington during 2010-2020, 13 had travel to Asia, Africa or the Middle East.

D. Reservoirs

Humans as well as wild and domestic animals, particularly swine; also rabbits, chickens, rats, deer and camels. Risks for exposure may include contact with pigs and consuming pork products Emerg Infect Dis 2020 Feb and Emerg Infect Dis 2021 June.

E. Modes of Transmission

Hepatitis E virus is transmitted primarily by the fecal-oral route. Fecally contaminated drinking water is the most commonly documented vehicle of transmission. Contaminated food, including shellfish and sausage from raw pork livers, has been implicated; genotype 3 in particular is associated with food. Undercooked meat, particularly wild pig/boar or deer, may be a risk. Direct fecal-oral transmission probably can occur, though secondary household cases are not common during outbreaks. Outbreaks have occurred in camps for refugees or displaced persons where there was reduced sanitation. Transfusion, organ transplant, and perinatal transmission have been reported.

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. Estimated 1 week before to 1 month after onset of jaundice. Chronically infected persons continue to shed the virus.

H. Treatment

Supportive. Consider oral ribavirin chronic infection in solid-organ transplant recipients.

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

- 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 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 E but will forward specimens to the Centers for Disease Control and Prevention (CDC) for testing or confirmation. Please contact Office of Communicable Disease Epidemiology (CDE) for approval prior to submitting specimens. Obtain acute serum (if possible, previously tested specimen), chronic serum, and stool specimen. Specimens should be spun down, serum separated, and kept cold. See: https://www.cdc.gov/hepatitis/hdv/pdfs/cdc_50.34_specimensubmission.pdf CDE will complete the special hepatitis manifest form for CDC.

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: 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 international travel for hepatitis E. Rule out other infectious and non-infectious causes Facilitate transport of positive specimens to Washington State Public Health Laboratories for confirmatory testing at CDC. If the patient is pregnant, see Section 6E.

B. Identify Potential Sources of Infection

Ask the case about potential exposures 2–9 weeks before onset of illness, particularly food and water exposures during international travel. Identify any persons (e.g., household member, sex partners, those 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

Identify potential secondary cases exposed to the stools during the communicable period. Include household members and sexual 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 E infections in contacts.

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.

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 E virus who are still susceptible to hepatitis A or B should be vaccinated.
2. Hospitalized patients should be cared for using standard precautions. Also use contact precautions for diapered or incontinent individuals while they are symptomatic.

6. MANAGING SPECIAL SITUATIONS

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

Exclude a hepatitis E case from food handling, child care, healthcare, or attending school or child care until diarrhea resolves

B. 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

C. Case Is a Recent Blood Donor or Recipient

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

D. Case Is Pregnant

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

No vaccine exists for hepatitis E. Multiple viral hepatitis infections can result in liver damage, so recommend universal immunization to prevent hepatitis A and hepatitis B.

B. Prevention Recommandations

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. Immune globulin is not protective. For travel information related to hepatitis E see: https://wwwnc.cdc.gov/travel/yellowbook/2018/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

March 2018: Hepatitis E guideline separated from previous D/E guideline for WDRS conversion

June 2021: Routine review, references and case counts updated Section 2

February 2022: Routine review

December 2022: For 2023 WAC revision combined provider and facility reporting requirement (Section 1B2), updated laboratory submission (Section 1B3)