### 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: [http://www.doh.wa.gov/Portals/1/Documents/5230/302-017-SerVirHIV.pdf](http://www.doh.wa.gov/Portals/1/Documents/5230/302-017-SerVirHIV.pdf)

**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. 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 (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. 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, and persons with existing liver damage. 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) as well as impaired renal function and pancreatitis.

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

- 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 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: http://www.doh.wa.gov/Portals/1/Documents/5230/302-017-SerVirHIV.pdf

5. ROUTINE CASE INVESTIGATION

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. 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 2–9 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 HEV 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:

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 for hepatitis E. Multiple viral hepatitis infections can result in liver damage, so universal immunization is recommended to prevent hepatitis A and hepatitis B.

B. Prevention Recommendations

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: https://wwwnc.cdc.gov/travel/yellowbook/2018/infectious-diseases-related-to-travel/hepatitis-e

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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.