Alberta

# Public Health Disease Management Guidelines

## Hepatitis E

Ministry of Health, Government of Alberta
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Hepatitis E Public Health Disease Management Guideline
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For further information on the use of this protocol contact:
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# Case Definition

## Confirmed Acute Case

Laboratory confirmation with clinical illness[A] in the absence of other infectious causes of hepatitis[B]:

- Positive Anti-HEV IgM with an IgG seroconversion in an appropriate clinical sample (e.g., serum) tested at least four to six weeks apart,

  **OR**

- Detection of HEV nucleic acid (e.g., PCR) in an appropriate clinical sample (e.g. stool, serum).

## Probable Acute Case

One of the following with clinical illness[A]:

- A single positive anti-HEV IgM ***and*** absence of other infectious causes of hepatitis ***and*** exposure history[C],

  **OR**

- Epidemiologically linked to a confirmed case.

## Probable Chronic Case

Laboratory confirmation with clinical illness[A]:

- Detection of HEV nucleic acid (e.g., PCR) in an appropriate clinical sample (e.g. stool, serum) persisting for at least 6 months.[1]



[A] Clinical illness is characterized by elevated alanine aminotransferase (ALT), discrete onset of symptoms and jaundice or elevated serum aminotransferase levels.
[B] Testing should be done to rule out other infectious causes of hepatitis: IgM anti-HAV negative, IgM anti-HBc negative (if done) or HbsAg negative and anti-HCV negative.
[C] Exposure history: refer to ***Transmission*** and ***Incidence*** sections.

# Reporting Requirements

## 1. Physicians/Health Practitioners and others

A physician, health practitioner or others shall notify the Medical Officer of Health (MOH) (or designate) of the zone, of all confirmed and probable cases in the prescribed form by mail, fax or electronic transfer within 48 hours (two business days).

## 2. Laboratories

All laboratories shall report all positive laboratory results by mail, fax or electronic transfer within 48 hours (two business days) to the:

- MOH (or designate) of the zone, and
- the Chief Medical Officer of Health (CMOH) (or designate).

## 3. Alberta Health Services and First Nations and Inuit Health Branch

- The MOH (or designate) of the zone where the case currently resides shall forward the initial Notifiable Disease Report (NDR) of all confirmed and probable cases to the CMOH (or designate) within two weeks of notification and the final NDR (amendment) within four weeks of notification.
- For out-of-province and out-of-country reports, the following information should be forwarded to the CMOH (or designate) by phone, fax or electronic transfer within 48 hours (two business days) including:
  - name,
  - date of birth,
  - out-of-province health care number,
  - out-of-province address and phone number,
  - positive laboratory report, and
  - other relevant clinical/epidemiological information.

# Epidemiology

## Etiology

Hepatitis E, a non-enveloped RNA virus (HEV), is classified within the genus Hepevirus of the family *Hepeviridae*.[2,3] While HEV comprises a single serotype, there are eight known genotypes (G1–8) found in human and other species.[4,5]

## Clinical Presentation

Hepatitis E (HE) infection is similar in presentation to hepatitis A infection and, depending upon the infectious dose, ranges from asymptomatic to non-specific symptoms (e.g., fatigue, itching, nausea) in the **prodromal phase**.[2,6,7] Dark urine and/or jaundice and elevated liver enzymes occur a few days later in the **icteric phase**. Most individuals recover completely, however a small number can develop prolonged viremia and acute liver failure (fulminant hepatitis).
The mortality rate of HE infection ranges from 0.1–4%.[8,9] Re-infection with HEV is possible.[4]

Women who acquire HE during pregnancy are at higher risk of fulminant hepatitis than men or non-pregnant women.[9–12] The mortality rate for fulminant hepatitis (mainly due to HEV G1) may reach up to 25% in pregnant women in the 3rd trimester. Other obstetrical complications include intrauterine fetal death, preterm delivery, stillbirth, prematurity and low birth weight, making HEV the most severe hepatitis virus in pregnancy.

Chronic infections (HE infection > 6 months) have been reported in immunosuppressed persons, especially solid organ transplants (SOTs), or who have HIV, lymphoma or leukemia.[8,9]
Genotype 3, and to a lesser extent genotype 4, are associated with chronic infections in this group of patients.[4]

Extrahepatic manifestations have been reported, such as acute glomerulonephritis, pancreatitis and neurological disorders (e.g., Guillain-Barré syndrome, Bell's palsy, neurologic amylotrophy and acute transverse myelitis). particularly in immunocompromised persons with chronic infections.[1,8,13–15]

## Reservoir

Genotypes G1 and G2 are found exclusively in humans,[4,5] whereas genotypes, G3 and G4 are more commonly found in pigs, wild boar, shellfish, and deer. Genotypes 5 and 6 have only been reported in boar meat, while genotype 7 and G8 have been identified in camel meat and milk.[16]

# Transmission

HEV is transmitted in endemic countries via fecal-oral route, mainly by contaminated drinking water.[17], and genotypes 1 and 2 are the causative agents.

Person-to-person transmission is considered rare and much less frequent than hepatitis A with household secondary attack rates of HEV estimated to be 0.7–2.2%, as compared with 50–70% for HAV.[3,18–21]

Other reported routes of transmission include: blood transfusion, solid organ transplantation and vertical transmission.[22–27] In Canada, infections from blood donations are rare.[28]

HEV has a 50% vertical transmission rate.[11,29] There is no reliable data on whether asymptomatic HE infection may influence pregnancy outcomes.[8] The risk of transmission of HEV via breastmilk is increased if the mother has acute hepatic disease or an increased viral load.[29–33]

Cooking meat at 71ºC for 20 minutes or heating water to 60ºC for a few minutes has been shown to inactivate a HEV.[7,34,35] Although there is no direct evidence that chlorine inactivates HEV, several large outbreaks of HEV in other countries have been related to failure of chlorination.[17,36–38]

# Incubation Period

The incubation period is 26–42 days but can range from 15–64 days.[3]

# Period of Communicability

The period of communicability is not known, however infected persons have been shown to excrete the virus approximately 1 week prior to onset to up to 4 weeks after the onset of jaundice.[17,23,39,40] Individuals who are immunocompromised or have a chronic infection can shed the virus as long as they are infected, sometimes 6 months or longer.[39,41]

Viremia does not necessarily equate with infectivity, although this continues to be under investigation. Maximal viral shedding occurs during the incubation period and the early stages of acute illness. The infectious dose is unknown.

## Host Susceptibility

HE infection occurs most frequently among displaced persons and refugees due to the nature of their living conditions (e.g., overcrowding, poor hygiene) as well as travellers from developed countries to areas where HEV is endemic.[9]

Disease is more severe in the following:[9,42]

- Pregnant women in the 3rd trimester,
- Persons with pre-existing liver disease, and
- Immunosuppressed persons (e.g., organ or stem cell transplant recipients, HIV-infected patients with low CD4 cell counts).

In developed countries, though much more rare, numerous studies have identified an increased risk of autochthonous infection among older males (average age of 60) that may have a history of excessive alcohol consumption with or without liver damage.[43–47]

## Incidence

HE infection is not notifiable nationally. It is uncommon in Alberta and generally occurs in people who have travelled to or recently emigrated from an endemic country.

A number of developed countries, including Canada, have reported the presence of HEV antibodies in commercial swine populations and HEV RNA in food products containing raw pork and pig liver.[25,48–57] However, the risk of acquiring HEV from exposure to pigs or pork in Canada is considered to be small.[52]

Hepatitis E is endemic to subtropical and tropical countries in in Asia, Africa and Central America.[58] In developing countries, HEV is the most common cause of viral hepatitis reported and water-borne outbreaks are common.[59]

In developed countries, local HE infection and outbreaks are rare. HEV G1 and HEV G2 are commonly the source of outbreaks in endemic countries affecting youths and adults.[8] HEV G3 infections are more commonly reported in non-endemic areas in middle-aged and elderly males.

# Public Health Management

## Diagnosis

HEV IgM antibody can be detected 1 – 4 weeks after the onset of clinical symptoms and persist for about 3 months.[26] The demonstration of HEV IgM antibody (anti-HEV IgM) in the serum of acutely or recently ill persons is also useful for diagnosis, but due to the probability of false positives more than one test is required for definitive diagnosis. It is recommended that a follow-up specimen is collected 4 – 6 weeks later.

Definitive diagnosis of hepatitis E is made by demonstrating viral RNA in serum or stool by means of reverse transcriptase-polymerase chain reaction assay (RT-PCR).[D] A rise of IgG antibody titres (in the absence of another viral hepatitis) in a second sample collected approximately 4–6 weeks after the first sample will also confirm infection.[26] IgG appears about 30 days after the initial infection by the virus and peaks 2 to 4 weeks after onset of clinical hepatitis. IgG response is long-lasting but it is currently unclear how long it lasts and whether sero-reversion may occur after many years. There is strong cross-reactivity between HEV genotypes 1–4.

## Key Investigation

- Confirm that the case meets the case definition.
- Obtain a history of illness including the date of onset, signs and symptoms. For the purpose of public health follow-up, date of onset is the first day of prodromal phase **OR** the 7th day prior to the onset of jaundice, if prodrome is not known (See Clinical Presentation for more information).
- Identify any underlying medical conditions that may increase host susceptibility.
- Determine the estimated dates of communicability (period of infectiousness).
- Determine the occupation of the case (e.g., food handler, childcare facility worker, healthcare worker) and identify specific duties at work. Refer to Table 1 for more information on sensitive situations or occupations (SSO).
- Determine the possible source of infection taking into consideration the incubation period, reservoir, and mode of transmission. Assessment may include:
  - a history of recent travel or immigration, especially in areas with poor sanitation including improper water treatment and sewage disposal;
  - For cases with no history of travel:
    - a detailed food history especially consumption of contaminated ice/water; uncooked or undercooked food (especially pork products) or food washed in contaminated water; a history of risk behaviours including lifestyle risks for infection (e.g., MSM, IDU);
    - any contact with a confirmed case of HEV or contact with an ill person who had symptoms that were clinically compatible with HE infection;

[D] PCR testing is restricted to certain cases (e.g., transplant patients) and should be discussed with the Virologist-on-call at the Alberta Public Health Laboratories (formerly ProvLab) prior to ordering.

    - a history of blood or blood product transfusion, or organ transplantation during the incubation period;
  - if the case attends a childcare facility or other type of institutional setting (e.g. living is a correctional facility or residential/institutional setting); and
  - similar symptoms in other members of the household (historical and present).
- Identify contacts, including those in a sensitive situation or occupation (SSO), that may pose a risk of transmission to others – Refer to Table 1 that may have had exposure to the feces of the case during the period that the case was infectious (period of communicability).
- Contacts include:
  - persons living in the household,
  - children and child care workers in a day care/day home, and
  - individuals exposed to the same source (if identified).

## Table 1: Sensitive Situations or Occupations (SSO)

| Sensitive Situation or Occupation | Definition |
|---|---|
| Food handler | • Touches unwrapped food to be consumed, and/or<br>• Handles equipment or utensils that touch unwrapped food to be consumed.<br><br>*NOTE: Generally, food handlers who touch wrapped food, or food, equipment or utensils only prior to cooking, are not considered to pose a transmission risk however, circumstances for each case should be assessed on an individual basis.* |
| Healthcare, childcare or other staff | • Has contact through serving food to highly susceptible persons.<br>• Provides direct patient care and are involved in the care of young children, elderly or dependent persons. |
| Child attending a child care facility or school | • Is diapered or unable to implement good standards of personal hygiene. |
| Any individual (older child or adult) attending a public place | • Is unable to implement good standards of personal hygiene (e.g., those with disabilities/challenges that may impact ability to perform good hand hygiene) and is involved in an activity that may promote disease transmission. |

# Management of a Case

- Consultation with an Infectious Disease Specialist is recommended.
- All cases should be advised of the following:
  - Disease transmission, appropriate personal hygiene, routine infection prevention and control practices, and contact precautions,
  - To avoid food preparation until symptoms have resolved, and
  - To avoid sexual practices that facilitate fecal-oral transmission.
- Contact precautions should be used in healthcare settings where children or adults have poor hygiene or incontinence that cannot be contained for at least one week after the onset of jaundice.[19]
- Pregnant cases should be referred to their OB/GYN to discuss potential risks to mother and fetus.
- Breastfeeding women should be advised that:[29]
  - If asymptomatic, breastfeeding is considered safe; and
  - If symptomatic (with acute hepatic disease), breastfeeding is not recommended.
- Advise the case to refrain from preparing food for others during the period of communicability.
- Case should refrain from donating blood for 14 days after the onset of symptoms, unless diagnosed with chronic infection (>6 months).
- Notify and involve the Environmental Health Officer (EHO) when a food source is suspected.
- Refer to Table 2 for case exclusion criteria.

## Table 2: Case Exclusion

| Cases | Category | Exclusion Criteria |
|---|---|---|
| Symptomatic | **SSO*** | • The MOH may by order exclude a symptomatic case until diarrhea has resolved and for at least 7 days after the onset of jaundice or at least 14 days after the initial onset of symptoms, whichever comes earlier.** |
| Asymptomatic | **SSO*** | • No exclusion - cases should monitor themselves for gastrointestinal symptoms, maintain good hand hygiene and food handling practices and seek medical attention if symptoms develop. |
| Symptomatic | **Non-SSO** | • No exclusion required, however cases should remain home from work, school or daycare while they are acutely ill.<br>• Refer to their physician for assessment. |
| Asymptomatic | **Non-SSO** | • No exclusion required however, if symptoms develop they should be told to seek their physician for assessment. |

**Persons who are involved in sensitive situations or occupations.*
***Specimens may still be submitted as determined by the MOH on a case-by-case basis.*

# Treatment of a Case

- In general, there is no specific therapy; treatment is supportive.
- Antiviral treatment may be required for people with pre-existing liver disease or immunosuppression.[2]
- Currently, liver transplantation is the only valid treatment available for patients with fulminant hepatic failure.[8]

# Management of Contacts

- Assess all contacts (see ***Key Investigation***), including visitors to the household for potential of exposure during period of communicability.
- Provide information about HEV disease and to seek medical attention if symptoms should develop.
- Refer symptomatic contacts for serology for anti-HEV IgG and anti-HEV IgM.
- Refer to Table 3 for contact exclusion criteria.

### Table 3: Contact Exclusion

| Contacts | Category | Exclusion Criteria |
|---|---|---|
| Symptomatic | SSO* | • The MOH may by order exclude until contact has been assessed by a physician to rule out disease. |
| Asymptomatic | SSO* | • No exclusion is required.<br>• Contacts should be told to monitor themselves for gastrointestinal symptoms, maintain good hand hygiene and food handling practices and seek medical attention if symptoms develop. |
| Symptomatic | Non-SSO | • No exclusion - refer to health care provider for assessment, as indicated. |
| Asymptomatic | Non-SSO | • No exclusion - contacts should monitor themselves for gastrointestinal symptoms, maintain good hand hygiene and food handling practices and seek medical attention if symptoms develop. |

**Persons who are involved in sensitive situations or occupations.*

## Preventive Measures

- Currently, there is no vaccine licensed in Canada for hepatitis E infection.
- Educate the public about the following:
  - Take precautions (avoid improperly cooked foods, unpasteurized milk/milk products, tap water, ice cubes, unpeeled fruits and uncooked vegetables) when travelling to endemic areas where HEV is known to occur,[3]
  - personal hygiene, especially the sanitary disposal of items containing feces,
  - careful hand washing before/after preparing or eating food, after defecation and sexual contact,
  - washing cutting boards, counter tops and utensils with soap and water after contact with raw meat (and other foods of animal origin), and
  - the risk of sexual practices that permit fecal-oral contact.
- Individuals that handle raw pork and swine products (e.g., pig handlers, butchers, abattoir works and veterinarians) who may be exposed to HEV need to ensure they take hygienic measures after contact with animals.[20]

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# ANNEX 1: Revision History

| Revision Date | Document Section | Description of Revision |
|---|---|---|
| December 2019 | Case Definition | • To Confirmed Case added “in the absence of other infectious causes of hepatitis”<br>• To Confirmed Case added IgM with IgG seroconversion<br>• Added Probable Chronic HEV Cases |
| | Reporting Requirements | • No change |
| | Rest of guideline | • New |