Alberta Public Health Disease Management Guidelines

Hepatitis E

Alberta

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Health.CD@gov.ab.ca

Health and Wellness Promotion Branch

Public Health and Compliance Branch

Alberta Health

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Case Definition

Confirmed 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 six 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

Physicians, Health Practitioners and others

Physicians, health practitioners and others shall notify 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).

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).

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- 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 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 hepatitis E infection ranges from 0.1–4%.[8,9] Re-infection with HEV is possible.[4]

Women who acquire hepatitis E 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 genotype 1) may reach up to 25% in pregnant women in the third 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 hepatitis E infections (lasting more than six months) have been reported in immunosuppressed persons, especially those with solid organ transplants or who have HIV, lymphoma or leukemia.[8,9] Genotype 3, and to a lesser extent genotype4, 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 amyotrophy and acute transverse myelitis). particularly in immunocompromised persons with chronic infections.[1,8,13–15]

Diagnosis

HEV IgM antibody can be detected one to four weeks after the onset of clinical symptoms and persist for about three months.[16] 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 four to six 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 four to six weeks after the first sample will also confirm infection.[16] HEV IgG appears about 30 days after the initial infection by the virus and peaks two to four weeks after onset of clinical hepatitis. HEV 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.

Treatment

- 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]

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

Reservoir

HEV genotypes 1 and 2 are found exclusively in humans,[4,5] whereas genotypes 3 and 4 are more commonly found in pigs, wild boar, shellfish, and deer. Genotypes 5 and 6 have only been reported in boar meat, while genotypes 7 and 8 have been identified in camel meat and milk.[17]

Transmission

HEV is transmitted in endemic countries via fecal-oral route, mainly by contaminated drinking water;[18] genotypes 1 and 2 are the causative agents.

Person-to-person transmission is considered rare and much less frequent than for hepatitis A, with household secondary attack rates of HEV estimated to be 0.7–2.2%, as compared with 50–70% for HAV.[3,19–22]

Other reported routes of transmission include blood transfusion, solid organ transplantation and vertical transmission.[16,23–27] 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 hepatitis E 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 71°C for 20 minutes or heating water to 60°C for a few minutes has been shown to inactivate 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.[18,36–38]

Incubation Period

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

Period of Communicability

The period of communicability of HEV is not known; however, infected persons have been shown to excrete the virus approximately one week prior to onset to up to four weeks after the onset of jaundice.[18,24,39,40] Individuals who are immunocompromised or have a chronic infection can shed the virus as long as they are infected, sometimes six 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

Hepatitis E 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 third 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

Hepatitis E 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.[26,48–57] 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 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 hepatitis E infection and outbreaks are rare. Genotypes 1 and 2 are commonly the source of outbreaks affecting youths and adults in endemic countries.[8] In non-endemic areas, genotype 3 infections are more commonly reported in middle-aged and elderly males.

Public Health Management

Key Investigation

- Confirm that the individual 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 seventh day prior to the onset of jaundice, if prodrome is not known (See Clinical Presentation for more information).
  - Determine the dates of communicability (period of infectiousness).
  - Identify any underlying medical conditions that may increase host susceptibility.
- Determine the occupation of the case (e.g., food handler, childcare facility worker, health care worker) and identify specific duties at work that may pose a risk of transmission to others. Refer to Table 1 for more information on sensitive situations and 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,
  - 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., men who have sex with men, injection drug use),
  - whether the case attends a childcare facility or other type of institutional setting (e.g., living in a correctional facility or residential/institutional setting),
  - whether there was any contact with a confirmed case of HEV or contact with an ill person who had symptoms that were clinically compatible with hepatitis E infection,
  - a history of blood or blood product transfusion, or organ transplantation during the incubation period, and
  - similar symptoms in other members of the household (historical and present).
- Identify contacts, including those in SSO that may pose a risk of transmission to others, who may have had exposure to the feces of the case during the period that the case was infectious (period of communicability). Refer to Table 1 for more information on SSO. 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)

SSO	Definition
Food handler	• Touches unwrapped food to be consumed, and/or • Handles equipment or utensils that touch unwrapped food to be consumed.*
Health care, child care or other staff	• Has contact through serving food to highly susceptible persons. • Provides direct patient care and is involved in the care of young children, elderly or dependent persons.
Child attending a childcare facility or similar facilities	• 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.

∗ NOTE: Generally, food handlers who do not touch food, equipment or utensils in this way are not considered to pose a transmission risk; however, circumstances for each case should be assessed on an individual basis.

Management of a Case

- Consultation with an Infectious Disease Specialist is recommended.
- All cases should be advised:
  - about appropriate personal hygiene, disease transmission, routine infection prevention and control practices, and contact precautions,
  - to avoid food preparation for others until symptoms have resolved, and
  - to avoid sexual practices that facilitate fecal-oral transmission.
- In health care settings, if children or adults have poor hygiene or incontinence that cannot be contained, contact precautions should be used for at least one week after the onset of jaundice.[20]
- 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 they are asymptomatic, breastfeeding is considered safe, and
  - if they are 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 (more than six months).
- Notify and involve the Environmental Health Officer 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 seven 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. • 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.

**Specimens may still be submitted as determined by the MOH on a case-by-case basis.*

Management of Contacts

- Assess all contacts (see Key Investigation section), including visitors to the household, for potential of exposure during period of communicability.
- Provide information about HEV infection 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. • 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.

Preventive Measures

- Currently, there is no vaccine licensed in Canada for hepatitis E infection.
- Educate the public about.
  - taking precautions (avoiding 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, and 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 workers and veterinarians) who may be exposed to HEV need to ensure they take hygienic measures after contact with animals.[21]

Appendix 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” • To Confirmed Case added IgM with IgG seroconversion • Added Probable Chronic HEV Cases
	Reporting Requirements	• No change
	Rest of guideline	• New
October 2021	General	• Updated Template • Diagnosis and Treatment section moved to Epidemiology

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