HEPATITIS E

(Enterically Transmitted non-A non-B Hepatitis [ET-NANB],
Epidemic non-A non-B Hepatitis, Fecal-Oral non-A non-B Hepatitis)

REPORTING INFORMATION

- **Class B:** Report by the end of the next business day after the case or suspected case presents and/or a positive laboratory result to the local public health department where the patient resides. If patient residence is unknown, report to the local public health department in which the reporting health care provider or laboratory is located.
- Reporting Form(s) and/or Mechanism: The Ohio Disease Reporting System (ODRS) should be used to report lab findings to the Ohio Department of Health (ODH). For healthcare providers without access to ODRS, you may use the Ohio Confidential Reportable Disease form (HEA 3334).
- The Centers for Disease Control and Prevention (CDC) Viral Hepatitis Case Report is available for use to assist in local disease investigation and contact tracing activities. Information collected from the form should be entered into ODRS and not sent to the Ohio Department of Health (ODH), unless otherwise requested.
- Key fields for ODRS reporting include: sensitive occupation (e.g. direct patient care, child care provider, food handler), sensitive setting (e.g. day care or preschool attendee, long term care facility resident), is patient symptomatic, is patient jaundiced, and the fields in the Epidemiology Information module.

AGENT

Hepatitis E virus (HEV) is a spherical, non-enveloped, single-stranded RNA virus, 32-34 nm in diameter. HEV is classified in the Hepeviridae family.

Note: Hepatitis A, hepatitis B and hepatitis C are each reportable as individual entities (see entries elsewhere in this manual). Hepatitis D occurs only in association with hepatitis B. Other viruses (e.g. cytomegalovirus and Epstein-Barr virus) can cause hepatitis or abnormally elevated liver enzymes. Hepatitis E is the cause of non-A, non-B, non-C hepatitis that will be discussed here.

CASE DEFINITION

The Centers for Disease Control and Prevention (CDC) has not established a clinical case definition, laboratory criteria for diagnosis or case classification for hepatitis E. Diagnosis of hepatitis E based on clinical signs and laboratory criteria are included in the Ohio case definition below.

Clinical Case Definition

An illness with:

- Discrete onset of symptoms and
- Jaundice, dark urine or elevated serum aminotransferase levels (ALT) >200 IU/L.

Laboratory Criteria for Diagnosis

- IgM anti-HAV negative *and*
- IgM anti-HBc negative (if done) or HBsAg negative *and*
- Antibody to hepatitis C virus (anti-HCV) negative (if done) *and*
- IgM anti-HEV positive.

Case Classification

Confirmed: A case that meets the clinical case definition and the laboratory criteria for diagnosis.

SIGNS AND SYMPTOMS

Hepatitis E commonly presents with abdominal pain, anorexia, dark urine, pale stools, fever, fatigue, hepatomegaly, jaundice, malaise, nausea and emesis. Less frequent symptoms include arthralgia, diarrhea, pruritus and urticaria. The ratio of symptomatic to asymptomatic infection in outbreak settings is reported to range from 1:2 to 1:13. Fulminant disease is rare, except in pregnant women. Chronic hepatitis E infection is rare and has only been reported in organ transplant patients and people with severe immunodeficiency. The case fatality rate overall is 1%-3%, except in pregnant women where it may reach 10%-25% among those infected during the third trimester.

DIAGNOSIS

Hepatitis E is a diagnosis of exclusion. Diagnosis depends on clinical and epidemiologic features, as well as exclusion of other etiologies of hepatitis, especially Hepatitis A, by serologic laboratory tests. Hepatitis E is characterized by symptoms indicative of liver inflammation, with a negative history of exposure to toxic substances, and the laboratory profile noted in the **CASE DEFINITON** above. No serologic tests to diagnose HEV infection are commercially available in the United States. Diagnostic tests available in research laboratories include: enzyme immunoassays (EIAs) and Western blot assays to detect IgM and IgG anti-HEV in serum, polymerase chain reaction (PCR) tests to detect HEV RNA in serum and stool, immunofluorescent antibody blocking assays to detect antibody to HEV antigen in serum and liver and immune electron microscopy to visualize viral particles in feces.

EPIDEMIOLOGY

Source

Humans are the natural host for HEV. The occurrence of sporadic cases may maintain transmission during interepidemic periods, but a nonhuman reservoir for HEV is also possible. Non-human primates (e.g. chimpanzees, cynomolgus monkeys, rhesus monkeys, pig-tail monkeys, owl monkeys, tamarins, African green monkeys) are susceptible to natural infection with humans HEV strains. Pigs, chicken and cattle have been found to have natural HEV infections, especially in highly endemic areas.

Occurrence

Hepatitis E outbreaks have occurred over a wide geographic area, primarily in developing countries with inadequate sanitation. It has occurred in epidemics or sporadically in parts of Asia, Africa and Mexico. Outbreaks often manifest as waterborne epidemics, but sporadic cases and outbreaks not related to water have occurred. The attack rate is highest in young adults, with cases uncommon in children and the elderly. In the United States and other industrialized countries, hepatitis E has been diagnosed only among travelers returning from HEV-endemic countries. In the United States and other nonendemic areas where outbreaks of hepatitis E have not been documented, a low prevalence of anti-HEV (<2%) has been found in healthy populations. The source of infection for these persons is unknown.

Mode of Transmission

HEV is transmitted primarily by the fecal-oral route, with contaminated water the most commonly documented vehicle of transmission. Person-to-person transmission of HEV appears to be uncommon; however, nosocomial transmission, presumably by person-to-person contact, has been reported to occur. Recent studies suggest that hepatitis E may be a zoonotic disease in areas with concurrent human infection. In developed countries sporadic outbreaks have occurred following consumption of uncooked/undercooked pork or deer meat.

Period of Communicability

The period of infectivity of hepatitis E following acute infection has not been determined, but virus excretion in stool has been demonstrated up to 14 days after onset of illness.

Incubation Period

From 15-64 days, with a mean incubation period of 26-42 days.

PUBLIC HEALTH MANAGEMENT

Case

Treatment

No therapeutic measures have been proven effective following the onset of disease. Diet and rest should be dictated by the individual's sense of well-being.

Isolation

None.

Contacts

Immune Globulin (IG) prepared from plasma collected in non-HEV endemic areas is not effective in preventing clinical disease during hepatitis E outbreaks. The efficacy of IG prepared from plasma collected in HEV endemic areas is unclear.

Prevention and Control

Prevention of hepatitis E relies primarily upon the provision of clean water supplies. Educational programs should be designed to stress sanitary disposal of feces and careful handwashing after defecation and before handling food. There is no evidence that IG manufactured in the United States or Europe will prevent infection. Travelers to endemic areas should take precautions to avoid contaminated food and water, including avoidance of drinking water, beverages with ice of unknown purity and eating uncooked shellfish and uncooked fruits or vegetables not peeled or prepared by the traveler. A recombinant hepatitis E vaccine using recombinant capsid protein was evaluated in a phase III clinical trial and was demonstrated to be effective in preventing disease but is not available outside the research setting. No FDA-approved vaccine for Hepatitis E is currently available in the United States.

What is hepatitis E?

Hepatitis E is a serious liver disease caused by the hepatitis E virus that usually results in a self-limited, acute infection. It does not lead to a chronic infection. While rare in the United States, hepatitis E is common in many parts of the developing world.

Where is hepatitis E most common?

Hepatitis E is most common in developing countries with inadequate environmental sanitation. Hepatitis E epidemics have been reported in Asia, the Middle East, Africa and Central America. Some epidemics of hepatitis E have involved tens of thousands of persons affected over a short period of time. People living in refugee camps or overcrowded temporary housing after natural disasters can be at particular risk. Hepatitis E is believed to be uncommon in the United States. When hepatitis E infection does occur, it is usually the result of travel to a developing country where hepatitis E is endemic. However, rare cases have been reported among persons with no history of travel to hepatitis E-hyperendemic countries. Furthermore, some recent studies have found a high prevalence of antibodies to HEV in the general population.

What are the signs and symptoms of hepatitis E?

Persons with hepatitis E virus infection commonly have abdominal pain, loss of appetite, dark urine, pale-colored stools, fever, enlarged liver, jaundice (yellowing of the skin and eyes), nausea and vomiting. Less frequently, persons with hepatitis E virus infection have joint pain, diarrhea, itchy skin, and hives. Hepatitis E does not lead to a chronic infection. Most people with hepatitis E recover completely. The overall fatality rate is ≤4%. However, for pregnant women, hepatitis E is more serious, and the disease is fatal in 15-25% of pregnant women, particularly those in their third trimester.

How is hepatitis E diagnosed?

Talk to your doctor or someone from your local health department if you suspect that you have been exposed to hepatitis E or any type of viral hepatitis. A physician would diagnose hepatitis E virus infection in a patient through a physical exam, assessment of the patient's symptoms and history (especially travel history) and exclusion of other possible causes of hepatitis (like hepatitis A, hepatitis B and hepatitis C viruses). There is no commercial test available in the United States to diagnose hepatitis E infection.

How is hepatitis E virus transmitted?

Hepatitis E virus is spread from person-to-person by putting something in the mouth that has been contaminated with the stool of a person with hepatitis E. This type of transmission is called "fecal-oral." For this reason, the virus is more easily spread in areas where there are poor sanitary conditions. Thus, outbreaks are usually associated with contaminated water supply in countries with poor sanitation.

How soon after exposure will symptoms appear?

When symptoms occur, they usually develop 15 to 64 days (average: 26-42 days) after exposure.

How is hepatitis E treated?
Hepatitis E usually resolves on its own without treatment. There is no specific antiviral therapy for hepatitis E. Physicians may offer supportive therapy. Patients are typically advised to rest, get adequate nutrition and fluids, and avoid alcohol. Hospitalization is sometimes required in severe cases and should be considered for pregnant women.

Is there a vaccine to prevent hepatitis E virus infection?
There is currently no FDA-approved vaccine for hepatitis E. However, several studies are in progress for the development of an effective vaccine to prevent hepatitis E. A Hepatitis E vaccine (Hecolin) has been tested and is currently in use in China for the prevention of Hepatitis E, although it is not available globally.