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Hepatitis E Virus Update December 2014

What is hepatitis E Virus?

Hepatitis E Virus (HEV) was first identified in 1983. It is a single stranded RNA virus belonging to the *hepeviridae* family that causes acute inflammation of the liver. HEV is the major cause of enterically transmitted non-A, non-B hepatitis worldwide and has been responsible for large waterborne outbreaks.

Mode of Transmission

- Fecal-oral: In endemic areas HEV is most commonly spread by fecal-contamination of drinking water (1).
- Food borne: through the ingestion of raw or undercooked meat - especially pig meat and pig liver (2-4).
- Vertical: Mother-to-child perinatal transmission has been documented to be around 50-100% (5-7).
- Blood borne: transmission via blood transfusion is possible but rare (8).
- Zoonotic: possible but unconfirmed.
- Person-to-person transmission is uncommon (1).

Epidemiology

HEV epidemiology is similar to that of hepatitis A virus (HAV), although less readily transmitted than HAV, with a narrower distribution worldwide. Although most cases of HEV occur in developing countries (Figure 1), it has recently become recognized that the incidence of HEV in developed countries is higher than previously thought.

Genotypes

There are at least 4 distinct HEV genotypes based on geographical origin.

- Genotypes 1 and 2: are more pathogenic, restricted to humans and responsible for the majority of cases /outbreaks in endemic regions.
- Genotypes 3 and 4: are less pathogenic; infect humans, pigs, and other animal species; generally are responsible for sporadic HEV infection cases within endemic and non-endemic regions

Figure 1. Distribution of hepatitis E infection 2012 (9).

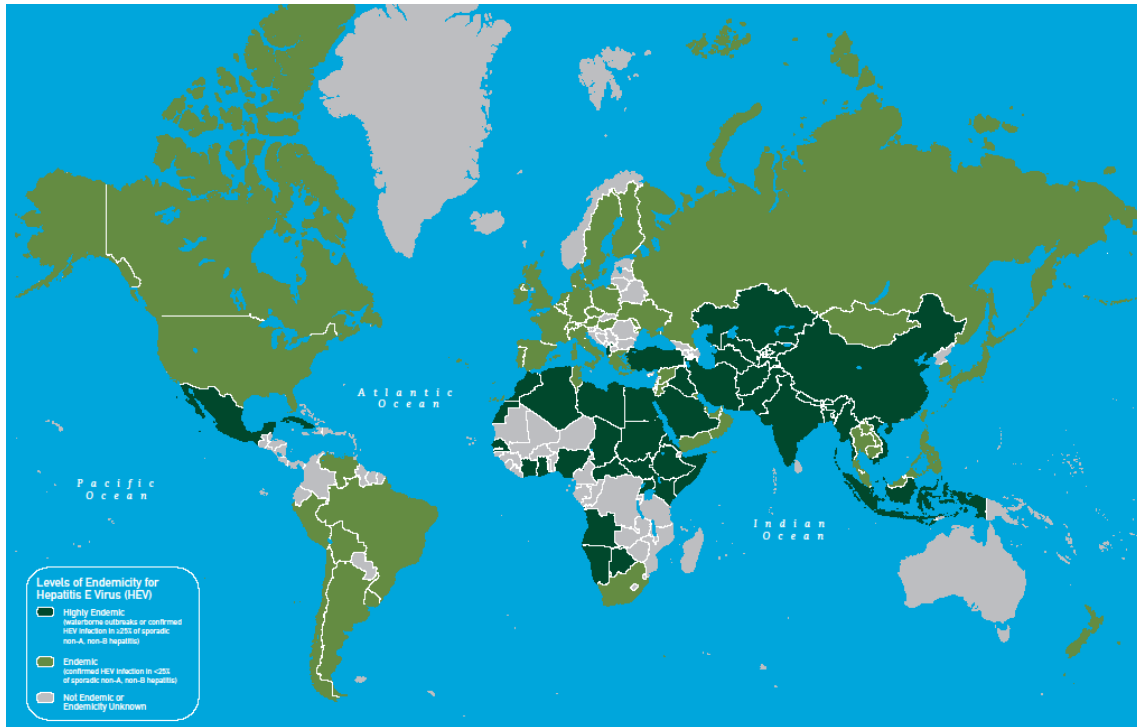


Figure 1: Distribution of Hepatitis E Infection. Traveller's Health Yellow Book: The Centre for Disease Control and Prevention. Retrieved on Sept 16, 2014 from <http://wwwnc.cdc.gov/travel/yellowbook/2012/chapter-3-infectious-diseases-related-to-travel/hepatitis-e.htm>

Large outbreaks, often waterborne, occur mostly in areas with inadequate environmental sanitation. The largest reported outbreak had over 100,000 individuals infected in the Xinjiang region of China between 1986 and 1988.

In developed countries acute HEV infections generally occur in travelers returning from HEV endemic or epidemic areas (9). However, HEV is prevalent in Canadian swine populations suggesting that swine HEV may be an important zoonotic agent for humans. In a study in 2001 which sampled almost 1,000 pigs, overall seroprevalence was 59% but varied by province highest in Quebec (90%) then Ontario (80%) and lower at 38% in Alberta and Saskatchewan (10)

Clinical attack rates are highest in ages 15–40 years, with males being more likely to develop clinical hepatitis when infected with HEV as compared to females.

Clinical Characteristics

HEV generally causes a self-limited acute hepatitis; typical symptoms include jaundice, malaise, anorexia, fever, abdominal pain, nausea, arthralgia, diarrhea, discoloured stool and/or urine, and hepatomegaly.

Disease severity increases with age but is also greater in pregnant women. Around 90% of children aged <10 years infected with HEV living in HEV endemic areas are asymptomatic. Fulminant hepatic failure can occur in pregnant women, in addition to their risk for spontaneous abortion and premature delivery. Chronic hepatitis does not develop after acute HEV infection except in the settings of organ transplantation and immunosuppression (1).

Incubation period: 15-64 days; mean ~40 days.

Infectious Period: is unknown, although maximal HEV shedding occurs during the incubation period and the early acute stage of the disease.

Recovery: 95% of people infected with HEV recover over 2-6 weeks. More persistent HEV cases can take up to 6 months to resolve without evidence of chronic HEV (6).

It has not been determined if HEV infection confers lifelong immunity. HEV infection can sometimes be fatal and has an overall case fatality rate of approximately 5% (11). The case fatality is higher in developing countries, which may be partly due to factors such as malnutrition. Risk factors that increase the mortality rate of HEV infection include pre-existing chronic liver disease and pregnancy. The case fatality rate in pregnant women can be as high as 10 to 30% (6, 7).

Diagnosis

Diagnosis depends on clinical and epidemiological features as stated above and exclusion of other causes of hepatitis by serology, especially hepatitis A.

Diagnostic methods include serological testing for HEV antibodies (IgM, IgA, IgG) via ELISA, and nucleic acid tests for detecting HEV RNA in serum/bile/stool samples via RT-PCR. Antibody tests against HEV alone are less than ideal since they have been associated with frequent false positive and negative results.

The availability of these tests varies between regions (12); they are not routinely performed in BC laboratories. Serum or plasma samples are sent from the BCCDC to the National Microbiology Laboratory where HEV serology, molecular detection and genotyping can be performed (13).

A HEV case is confirmed when anti-HEV IgM is detected or a 4-fold rise in anti-HEV IgG is determined.

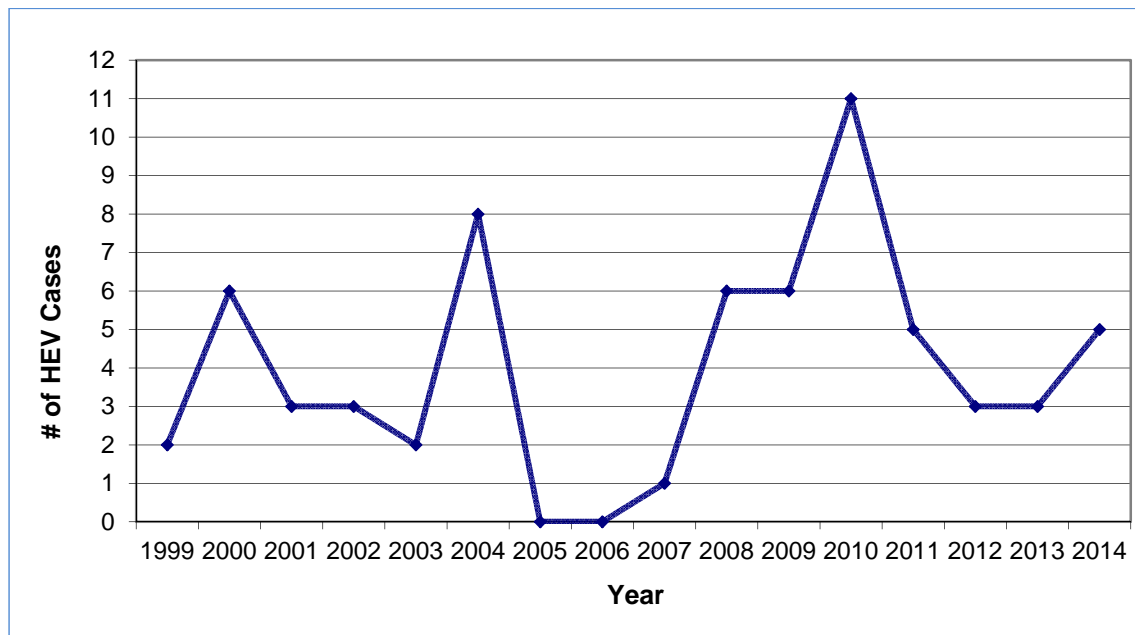
Occurrence of HEV in BC

HEV is reportable to public health in BC. However not all regional health authorities follow up HEV cases to identify risk factors. Between January 1, 1999 and December 31st, 2014 there have been 64 reported cases of HEV in BC, with numbers ranging from 0 to 11 new cases per year (median = 3). The majority of the cases were from Fraser Health Authority (33 of 64 cases - 51%) and Vancouver Coastal Health (23 of 64 cases – 36%). Island and Interior Health each had four cases, and Northern Health Region had one.

The possible source of exposure was identified in 45% of the reported cases; of these the majority (90%) reported a significant travel history prior to HEV diagnosis. Most of the cases (95%) with relevant travel history were to endemic or highly endemic regions as shown in Figure 1, including South and Southeast Asia (India, Bangladesh, Laos, Philippines, China/Hong Kong), Mexico region, South America and Russia. India was the most commonly reported place of travel in the documented cases (15 of 26 cases with identified travel history).

The majority of the patients (64%) were male. The age of patients at disease onset ranged from 14 to 79 years (Median = 41). Figure 2 demonstrates reported HEV cases in BC between January 1, 1999 and December 31st, 2014.

Figure 2: HEV cases reported in BC Jan 1, 1999 to Dec 31st, 2014



Treatment

Management for those infected with HEV is supportive only. Typical recommendations include rest, consuming adequate nutrition and fluids, and avoiding alcohol. Post exposure prophylaxis with immunoglobulin is not recommended in managing those exposed to, or infected with, HEV.

Prevention

There is currently no commercially available HEV vaccine. However, phase II and III clinical trials have been performed with a recombinant HEV vaccine, which have demonstrated an efficacy of ~95% (14, 15). HEV prevention is currently based on practicing good sanitary techniques and avoiding consuming unboiled or unchlorinated, water or ice.

Food products containing raw pork and pork liver such as French sausage Figatellu are suspected to transmit HEV (4). HEV can be heat inactivated by thorough cooking at 71°C for 20 minutes.

'Consumers at high risk of developing severe forms of HEV e.g. solid-organ transplant recipients, persons having underlying liver conditions or pregnant women, should be informed about the HEV risk and avoid eating such pork liver products without thoroughly cooking them' (4).

For more information on HEV visit:

- 1) The Public Health Agency of Canada website at: <http://www.phac-aspc.gc.ca/lab-bio/res/psds-ftss/hepe-eng.php>
- 2) The Centre for Disease Control and Prevention website at: <http://wwwnc.cdc.gov/travel/yellowbook/2010/chapter-5/hepatitis-e.aspx#1574>

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