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Hepatitis E

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OVERVIEW

Background

Hepatitis E is an enterically transmitted infection that is typically self-limited. [1, 2] It is caused by the hepatitis E virus (HEV) and is spread by fecally contaminated water within endemic areas or through the consumption of uncooked or undercooked meat. [3, 4, 5] Outbreaks can be epidemic and individual. Hepatitis E has many similarities with hepatitis A. Hepatitis E has been associated with chronic hepatitis in solid-organ transplant recipients, patients infected by human immunodeficiency virus (HIV), and in an individual on rituximab treatment for non-Hodgkin lymphoma. [6, 7, 8, 9] A study has shown that among patients receiving hemodialysis, the seroprevalence of anti-HEV immunoglobulin G (IgG) was found to be high. However, no evidence of chronic infection was found. [10]

The course of infection has 2 phases, the prodromal phase and the icteric phase. The infection is self-limited. Whether protective immunoglobulins develop against future reinfection remains unknown. The overall case fatality rate is 4%, although pregnant women and liver transplant recipients may be at substantially higher risk.

Therapy should be predominantly preventive, relying on clean drinking water, good sanitation, and proper personal hygiene. A successful recombinant hepatitis E vaccine has been developed. [11, 12]

Etiopathophysiology

The hepatitis E virus (HEV) genome contains 3 open reading frames (ORFs). The largest, ORF-1, codes for the nonstructural proteins responsible for viral replication. ORF-2 contains genes encoding the capsid. The function of ORF-3 is unknown, but the antibodies directed against ORF-3 epitopes have been identified.

Hepatitis E results from HEV infection and is spread by fecally contaminated water within endemic areas. However, in nonendemic areas, the major mode of the spread of HEV is foodborne, especially consumption of undercooked pork, raw liver, and sausages. [13, 14]

HEV is an RNA virus of the genus *Hepevirus*. It was discovered during electron microscopy of feces contaminated with enteric non-A, non-B hepatitis. The virus is icosahedral and nonenveloped. It has a diameter of approximately 34 nanometers, and it contains a single strand of RNA approximately 7.5 kilobases in length. Five HEV genotypes have been identified. Genotypes 1 and 2 are considered human viruses; genotypes 3 and 4 are zoonotic and have been isolated from humans and animals (eg, pigs, boars, deer), and genotype 7 primarily infects dromedaries. [14, 15]

Epidemiology

United States statistics

Population-based surveys from 1988-1994 indicate that 21% of US adults had anti–hepatitis E virus (HEV) antibody, a rate lower than that of anti–hepatitis A virus antibody (38.3%) but higher than that of antibodies against hepatitis B (5.7%) or hepatitis C (2%). [16]

Anti-HEV antibody rates increased markedly with age, from less than 10% among persons aged 6-19 years to more than 40% among those older than 60 years. Age-adjusted rates of anti-HEV antibody were lower among blacks (14.5%) than among non-Hispanic whites (22.1%); among men who had sex with men (23.1%) than among those who did not (23.9%); among cocaine users (16.8%) than among nonusers (23.6%); and among people living in the southern United States (14.7%) than among people living in the Northeast (20.8%), Midwest (26.6%), or West (25%). Rates of anti-HEV antibody were minimally higher among men than among women (21.6% vs 20.4%). Among men who had sex with men, the rates of anti-HEV antibody were lower among men with HIV infection (12.8%) than among men without HIV infection (19.2%). [17]

The route of exposure is unknown but is generally attributed to travel in endemic areas such as China, Nepal, India, Southwest France, North African countries, and Borneo. Exposure to pigs and consumption of undercooked pork are other methods of spread in autochthonous (nonendemic) areas, as testing of samples of pig liver and sausage from commercial groceries in the United States identified HEV RNA in a high percentage of samples. [18]

International statistics

The global disease burden of hepatitis E has been reported to be at least 20 million cases/year with 70,000 fatalities and 3,000 stillbirths. [19] Hepatitis E has worldwide distribution, but predominating factors include tropical climates, inadequate sanitation, and poor personal hygiene. It is found most often in developing countries near the equator, in both the Eastern and Western hemispheres. Regions with a prevalence rate of more

than 25% include Central America, the Middle East, and large parts of Africa and Asia. [20] Outbreaks are associated with rainy seasons, floods, and overcrowding.

Water supply contamination with human feces is a frequent source of epidemics. The largest outbreak was reported in Northeast China, with 100,000 people affected between 1986 and 1988. [21] The reservoir of HEV is unknown, but it is believed that the virus may be transmitted by animals. Waterborne epidemics of hepatitis E mainly affect young adults, the clinical attack rate being highest among those aged 15–35 years. [22] Men are clinically infected 2-5 times more commonly than women in most outbreaks. [21, 23] However, no sex difference exists in exposure to HEV. [24, 25]

Prognosis

No chronic cases of acute hepatitis E have been reported. The infection is self-limited. Whether protective immunoglobulins develop against future reinfection remains unknown. The overall case fatality rate is 4%.

Among pregnant women, the case fatality rate is 20%, and this rate increases during the second and third trimesters. Reported causes of death include encephalopathy and disseminated intravascular coagulation. The rate of fulminant hepatic failure in infected pregnant women is high.

In a 3-year (2010-2013) prospective observational study of 55 symptomatic anti-HEV IgM-positive Indian women, the overall maternal mortality was 5%, including one antenatal death. The most common fetal complications were prematurity (80%) and premature rupture of membranes (11%), with a 28% rate of vertical transmission. [26]

Liver transplant recipients may be at a greater risk for hepatitis E virus (HEV) infection, which can lead to chronic hepatitis and rapid progression of liver fibrosis. [27, 28] The presence of anti-HEV-IgG titer in pretransplantation measurements do not lead to protection of hepatitis E in posttransplantation patients. [29]

Clinical Presentation

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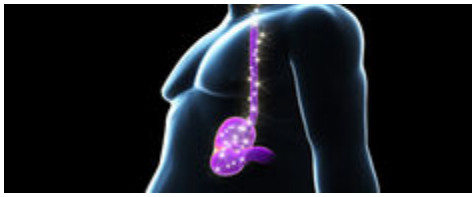

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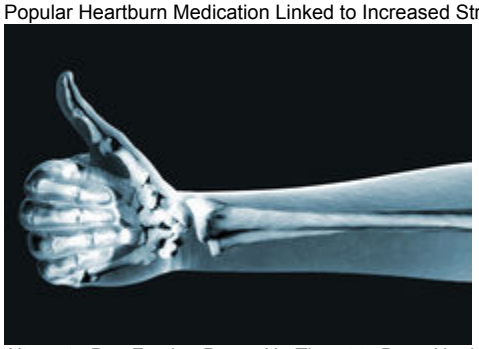

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