PRIMEVIEW

HEPATITIS E VIRUS INFECTION

nature REVIEWS DISEASE PRIMERS

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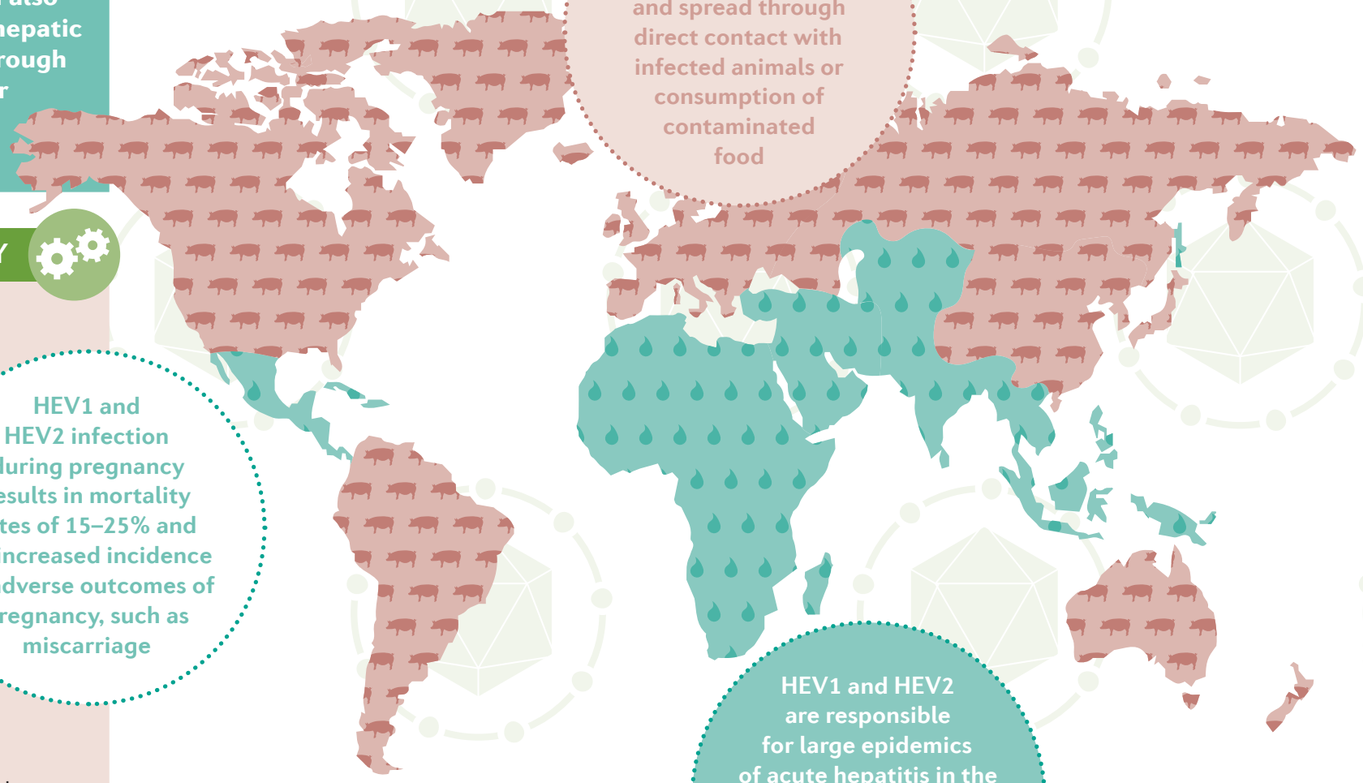
Infection with the hepatitis E virus (HEV) is the most common cause of acute viral hepatitis globally but can also result in chronic hepatitis and extrahepatic manifestations. The virus spreads through the food chain via the drinking water or infected animals but iatrogenic transmission is also possible.

EPIDEMIOLOGY



HEV3 and HEV4 are endemic in the developed world and spread through direct contact with infected animals or consumption of contaminated food

HEV1 and HEV2 infection during pregnancy results in mortality rates of 15–25% and an increased incidence of adverse outcomes of pregnancy, such as miscarriage

HEV1 and HEV2 are responsible for large epidemics of acute hepatitis in the developing world and spread via contamination of drinking water supplies with human faeces

The seroprevalence rates as a marker for current or past HEV infection vary substantially between regions. Rates of 10–40% are reported in developing areas, whereas they are 10–30% in Europe and ~6% in the United States; France is hyperendemic, with rates of >50%.

PATHOPHYSIOLOGY

HEV is an RNA virus that belongs to the Hepeviridae family. Seven genotypes exist but only four are responsible for most infections in humans. HEV genotype 1 (HEV1) and HEV2 are obligate human pathogens, whereas HEV3 and HEV4 are zoonotic — meaning that infection is propagated via animal reservoirs (mainly swine). HEV is an noncytopathic virus and clinical consequences of infection are determined by the host's immune response. The pathogenesis consists of an incubation period, acute hepatitis E with various clinical phenotypes (including asymptomatic disease in the majority of patients, acute icteric hepatitis in 5–30% of patients and acute liver failure in <4% of patients) and gradual recovery.

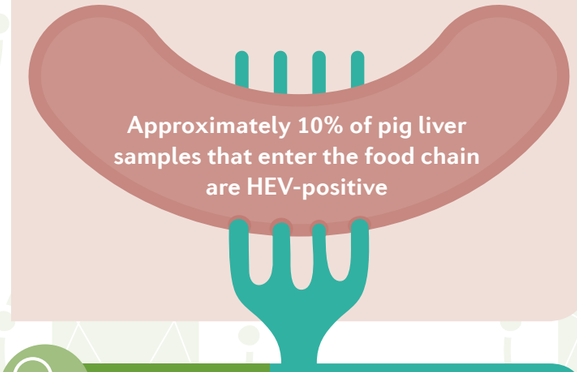
In addition to the hepatic manifestations, HEV infection can be associated with the development of neurological and renal manifestations, such as Guillain–Barré syndrome and kidney injury

SCREENING

HEV can be transmitted iatrogenically through tainted blood or blood products. The proportion of viraemic donors is surprisingly high, ranging from 1 per 600 individuals in the Netherlands to 1 per ~14,000 individuals in Australia. Most individuals receiving tainted blood remain asymptomatic, although immunocompromised individuals might fail to mount an immune reaction and clear the virus. Several countries have introduced universal, targeted or partial screening for HEV in donor blood.

PREVENTION

To prevent HEV infection, the risk of exposure should be minimized. For HEV1 and HEV2, this entails better sanitation of drinking water. For HEV3 and HEV4, consuming undercooked meat should be avoided and/or taking protective measures when handling infected animals should be encouraged. An effective vaccine is available but is so far only licensed in China.



Approximately 10% of pig liver samples that enter the food chain are HEV-positive

DIAGNOSIS

When HEV infection is suspected based on clinical symptoms or abnormal liver enzyme levels, anti-HEV IgM is measured first, given the wide availability and good performance of this test. HEV RNA detection is the gold standard to confirm acute infection, but the presence of viral capsid antigens could be an alternative test in resource-poor settings.

MANAGEMENT

Most HEV infections are self-limiting and do not require treatment. In immunocompromised individuals who are at risk of chronic infection, the dose of the immunosuppressive drug should be lowered, if possible, and treatment with the antiviral drug ribavirin might be needed.

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