Hepatitis Viruses

Many viruses cause hepatitis. Of these, five medically important viruses are commonly described as "hepatitis viruses" because their main site of infection is the liver. These five are hepatitis A virus (HAV), hepatitis B virus (HBV), hepatitis C virus (HCV), hepatitis D virus (HDV, delta virus), and hepatitis E virus (HEV) . Other viruses, such as Epstein-Barr virus (the cause of infectious mononucleosis), cytomegalovirus, and yellow fever virus, infect the liver but also infect other sites in the body and therefore are not exclusively hepatitis viruses (sporadic viruses).

Clinical Features of Hepatitis Viruses

Virus	Mode of Transmission	Chronic Carriers	Laboratory Test Usually Used for Diagnosis	Vaccine Available	Immune Globulins Useful
HAV	fecal–oral	No	IgM HAV	Yes	Yes
HBV	Blood, sexual, at birth	Yes	HBsAg, HBsAb, IgM HBcAb	Yes	Yes
HCV	Blood, sexual[1]	Yes	HCV Ab	No	No
HDV	Blood, sexual[1]	Yes	Ab to delta Ag	No	No
HEV	fecal–oral	No	None	No	No

[1]Sexual transmission seems likely but is poorly documented.

Hepatitis A Virus

Disease; HAV causes hepatitis A.

Important Properties; HAV is a typical **enterovirus** classified in the picornavirus family. It has a single-stranded RNA genome and a nonenveloped icosahedral nucleocapsid and replicates in the cytoplasm of the cell. It is also known as enterovirus 72. It has one serotype, and there is no antigenic relationship to HBV or other hepatitis viruses.

Summary of Replicative Cycle; HAV has a replicative cycle similar to that of other enteroviruses.

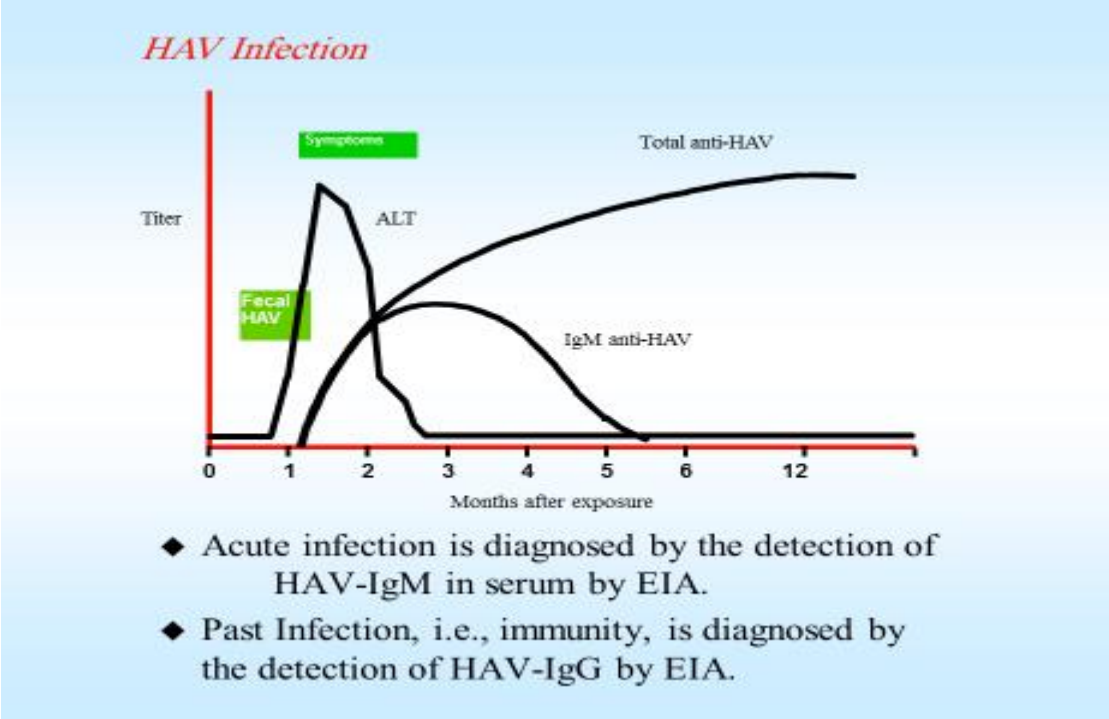
Transmission & Epidemiology; HAV is transmitted by the **fecal–oral** route. Humans are the reservoir for HAV. Virus appears in the feces roughly 2 weeks before the appearance of symptoms, so quarantine of patients is ineffective. **Children are the most frequently infected** group, and outbreaks occur in special living situations such as summer camps and boarding schools. Common-source outbreaks arise from fecally contaminated water or food such as oysters grown in polluted water and eaten raw. Unlike HBV, HAV is **rarely transmitted via the blood,** because the level of viremia is low and chronic infection does not occur.

Pathogenesis & Immunity;. The virus probably replicates in the gastrointestinal tract and spreads to the liver via the blood. Hepatocytes are infected, but the mechanism by which cell damage occurs is unclear. HAV infection of cultured cells produces no cytopathic effect. It is likely that attack by cytotoxic T cells causes the damage to the hepatocytes. The infection is cleared, the damage is repaired, and no chronic infection ensues. Hepatitis caused by the different viruses cannot be distinguished pathologically.

The immune response consists initially of IgM antibody, which is detectable at the time jaundice appears. It is therefore important in the laboratory diagnosis of hepatitis A. The appearance of IgM is followed 1 to 3 weeks later by the production of IgG antibody, which provides lifelong protection.

Clinical Findings; The clinical manifestations of hepatitis are virtually the same, regardless of which hepatitis virus is the cause. Fever, anorexia, nausea, vomiting, and jaundice are typical. Dark urine, pale feces, and elevated transaminase levels are seen. Most cases resolve spontaneously in 2 to 4 weeks. Hepatitis A has a short incubation period (3–4 weeks), in contrast to that of hepatitis B, which is 10 to 12 weeks. Most HAV infections are asymptomatic and are detected solely by the presence of IgG antibody. No chronic hepatitis or chronic carrier state occurs, and there is no predisposition to hepatocellular carcinoma.

Laboratory Diagnosis; The detection of **IgM antibody** is the most important test. A fourfold rise in IgG antibody titer can also be used. Isolation of the virus in cell culture is possible but not available in the clinical laboratory.



Treatment & Prevention; No antiviral therapy is available. **Active immunization** with a vaccine containing inactivated HAV is available. The virus is grown in human cell culture and inactivated with formalin.

Two doses, an initial dose followed by a booster 6 to 12 months later, should be given. No subsequent booster dose is recommended.

The vaccine is recommended for **travelers to developing countries**, **for children ages 2 to 18 years,** and for **men who have sex with men** and **Persons with clotting-factor disorders (e.g. hemophilia)**

If an unimmunized person must travel to an endemic area within 4 weeks, then passive immunization (see below) should be given to provide immediate protection and the vaccine given to provide long-term protection. This is an example of **passive–active immunization.**

Because many adults have antibodies to HAV, it may be cost-effective to determine whether antibodies are present before giving the vaccine. The vaccine is also effective in postexposure prophylaxis if given within 2 weeks of exposure. A combination vaccine that immunizes against both HAV and HBV called Twinrix is available. Twinrix contains the same immunogens as the individual HAV and HBV vaccines.

Passive immunization with immune serum globulin prior to infection or within 14 days after exposure can prevent or mitigate the disease.

Observation of proper hygiene, e.g., sewage disposal and handwashing after bowel movements, is of prime importance.

Hepatitis E Virus

HEV is a major cause of enterically transmitted hepatitis (feco-oral). It is a common cause of waterborne epidemics of hepatitis in Asia, Africa, India, and Mexico but is uncommon in the United States. HEV is a non-enveloped, single-stranded RNA virus classified as a member of the hepevirus family. Clinically the disease resembles hepatitis A, with the exception of a **high mortality rate in pregnant women**. Chronic liver disease does not occur, and there is no prolonged carrier state.

the diagnosis is therefore typically made by

1:HEV Ab

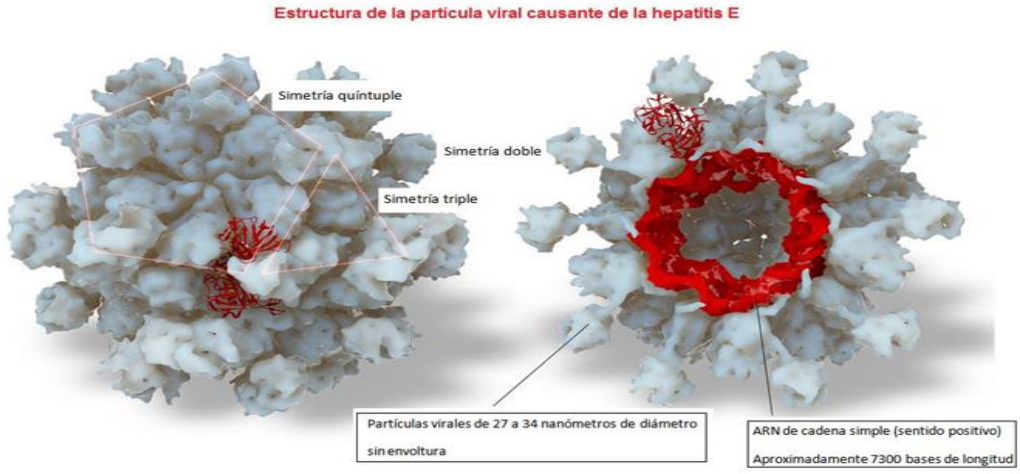
2.HEV RNA in serum or feces

There is no antiviral treatment and no vaccine. Most outbreaks associated with faecally contaminated drinking water.

Several other large epidemics have occurred since in the Indian subcontinent and the USSR, China, Africa and Mexico.

Minimal person-to-person transmission.

Prevention and Control Measures for Travelers to HEV-Endemic Regions :Avoid drinking water (and beverages with ice) of unknown purity, uncooked shellfish, and uncooked fruit/vegetables not peeled or prepared by traveler.



Hepatitis E - Clinical Features

- Incubation period: Average 40 days
- Case-fatality rate: Overall, 1%-3%
  Pregnant women, 15%-25%
- Illness severity: Increased with age
- Chronic sequelae: None identified