

Virology

Hepatitis viruses

Hepatitis refers to a systemic disease with an inflammatory of the liver caused by any one of heterogeneous group of viruses, but there are other possible noninfectious causes of hepatitis. These include autoimmune hepatitis (in some cases, the immune system mistakes the liver as a harmful object and begins to attack it, by makes antibodies against your liver tissue), drugs, toxins and alcohol. A different virus is responsible for each type of virally transmitted hepatitis.

Viral hepatitis is an infection that causes liver inflammation and damage. There are five medically important viruses are commonly described as “hepatitis viruses” because their main site of infection is the liver, these five are:

1. hepatitis A virus (HAV)
 2. hepatitis B virus (HBV)
 3. hepatitis C virus (HCV)
 4. hepatitis D virus (HDV, delta virus)
 5. hepatitis E virus (HEV)
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Hepatitis symptoms: the clinical manifestations of hepatitis are the same, regardless of which hepatitis virus is the cause, its include:

fever, anorexia, nausea, vomiting, and jaundice are typical , dark urine and pale feces.

- 1. Hepatitis A virus (HAV):** a member of picornavirus family, non-enveloped RNA virus with icosahedral nucleocapsid.

Disease: hepatitis A.

Transmission: HAV is transmitted by the **fecal–oral** route. 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.

Pathogenesis and clinical findings: the virus 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.

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.

****Cell culture** is the process by which cells are grown under controlled conditions, generally outside their natural environment. After the cells of interest have been isolated from living tissue, they can be maintained under carefully controlled conditions. These conditions vary for each cell type, but generally consist of a suitable vessel with a substrate or medium that supplies the essential nutrients (amino acids, carbohydrates, vitamins, minerals), growth factors, hormones, and gases (CO₂, O₂), and regulates the physio-chemical environment (pH buffer, osmotic pressure, temperature). Most cells require a surface or an artificial substrate to form an adherent culture as a monolayer (one single-cell thick), whereas others can be grown free floating in a medium as a suspension culture.

Treatment and Prevention: no antiviral therapy is available. Active immunization with a vaccine containing inactivated HAV is available.

- 2. Hepatitis B virus (HBV):** a member of hepadnavirus family, enveloped virion, with an icosahedral nucleocapsid, core containing a double-stranded circular DNA genome.

Disease: hepatitis B.

There is a high incidence of **hepatocellular carcinoma (hepatoma)** in many Asian countries—that indicates that HBV is a human tumor virus.

Transmission: three main modes of transmission are via blood, the observation that needle-stick injuries can transmit the virus indicates that only very small amounts of blood are necessary. HBV infection is especially prevalent in addicts who use intravenous drugs.

During sexual intercourse, HBV is found in semen and vaginal fluids, so it is likely that sexual transmission is important, and perinatally transmission from mother to newborn during birth is another important natural route.

Pathogenicity: after entering the blood, the virus infects hepatocytes, and viral antigens are displayed on the surface of the cells. Cytotoxic T cells mediate an

immune attack against the viral antigens, and inflammation and necrosis occur. **Immune attack** against viral antigens on infected hepatocytes is mediated by cytotoxic T cells. The pathogenesis of hepatitis B is probably the result of this cell-mediated immune injury because HBV itself does not cause a cytopathic effect. Antigen–antibody complexes cause some of the early symptoms and some of the complications in chronic hepatitis. A high rate of hepatocellular carcinoma (HCC) occurs in chronic carriers.

Laboratory Diagnosis: the two important serologic tests for the diagnosis of early hepatitis B are the tests for **HBsAg** and for **IgM antibody**. Both appear in the serum early in the disease.

Treatment and prevention: immunization against HBV has reduced the incidence of hepatoma in children. It appears that the HBV vaccine is the first vaccine to prevent a human cancer.

3. Hepatitis C virus (HCV): a member of flavivirus family (enveloped RNA virus)

Disease: hepatitis C

Transmission: humans are the reservoir for HCV. It is transmitted primarily via **blood**. At present, injection drug use accounts for almost all new HCV infections. Transmission from mother to child during birth is another very common mode of transmission.

Pathogenesis: HCV infects hepatocytes primarily, but there is no evidence for a virus-induced cytopathic effect on the liver cells. Rather, death of the hepatocytes is probably caused by immune attack by cytotoxic T cells. **HCV infection strongly predisposes to hepatocellular carcinoma**, but there is no evidence for an oncogene in the viral genome or for insertion of a copy of the viral genome into the DNA of the cancer cells. Alcoholism greatly enhances the rate of hepatocellular carcinoma in HCV-infected individuals. This supports the idea that the cancer is caused by prolonged liver damage and the consequent rapid growth rate of hepatocytes as the cells attempt to regenerate rather than by a direct oncogenic effect of HCV.

Laboratory Diagnosis: HCV infection is diagnosed by detecting antibodies to HCV in patients serum.

Treatment: There is no vaccine, the treatment of choice for **chronic** hepatitis C is a combination of drugs from three classes: RNA polymerase inhibitors (Sofosbuvir), NS5A inhibitors (Ledipasvir), and protease inhibitors (Boceprevir).

4. Hepatitis D virus (HDV): small enveloped RNA virus.

Disease: hepatitis D (hepatitis delta)

Transmission: HDV is transmitted by the same means as is HBV (sexually, by blood, and perinatally).

Pathogenesis: the virus-infected hepatocytes are damaged by cytotoxic T cells). There is some evidence that delta antigen is cytopathic for hepatocytes.

Laboratory Diagnosis: the diagnosis of HDV infection in the laboratory is made by detecting either delta antigen or IgM antibody to delta antigen in the patient's serum.

Treatment and prevention: interferon alpha can offer some of the effects of the chronic hepatitis caused by HDV but does not eradicate the chronic carrier state. No available vaccine against HDV.

5. Hepatitis E virus (HEV): member of the hepevirus family, is a non-enveloped, single-stranded RNA virus.

Disease: hepatitis E

Transmission: transmitted by the fecal– oral route.

Pathogenicity: clinically the disease resembles hepatitis A, with the exception of a high mortality rate in pregnant women. Chronic infection resulting in chronic hepatitis and cirrhosis but not hepatocellular carcinoma, occurs in immunocompromised individuals such as HIV-infected patients, those who are receiving cancer chemotherapy, and patients who are receiving immunosuppressive drugs to prevent rejection of solid-organ transplants.

Laboratory diagnosis: the diagnosis is typically made by detecting IgM antibody to HEV. PCR assay that detects HEV RNA in patient specimens is available.

Treatment and prevention: there is no antiviral drug available for acute infection in immunocompetent patients. In immunocompromised patients, ribavirin cleared HEV viremia in solid organ transplant recipients. There is no vaccine.

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