Anbar University

Science College

Biotechnology Department

Hepatitis viruses

Lecturer.D.Al-Moghira Khairi Al-Qaysi

Virology, Stephen N.J. Korsman, Gert U. van Zyl, ... Wolfgang Preiser 2012

Jawetz Melnick & Adelbergs Medical Microbiology, Stefan Riedel (Author), Stephen Morse (Author), Timothy Mietzner (Author), Steve Miller.

Viruses, Pandemics, and Immunity, By Arup K. Chakraborty and Andrey S. Shaw

Hepatitis Viruses

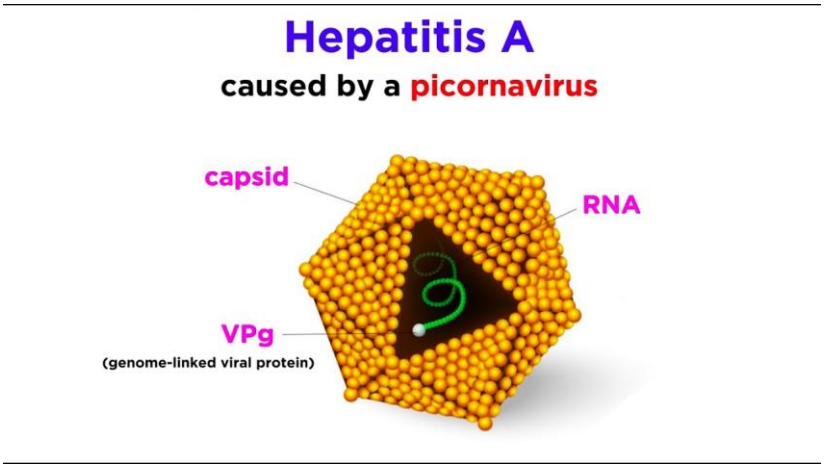
Several viruses cause Hepatitis, these five viruses are commonly describe as Hepatitis Virus

1- Hepatitis (A) viruses(HAV)
2- Hepatitis(B) Viruses (HBV)
3- Hepatitis(C) Viruses (HCV)
4- Hepatitis(D) Viruses (HDV)
5- Hepatitis(E) Viruses (HEV)

Additional wellcharacterized viruses that can cause sporadic hepatitis, such as cytomegalovirus, Epstein-Barr virus, and herpes simplex virus are discussed. Hepatitis viruses produce acute inflammation of the liver, resulting in a clinical illness characterized by fever, gastrointestinal symptoms such as nausea and vomiting, and jaundice. Regardless of the virus type, identical histopathologic lesions are observed in the liver during acute disease.

Hepatitis Type A

HAV is a distinct member of the picornavirus family. HAV is a 27- to 32-nm icosahedral symmetry containing a linear positive single stranded RNA genome. HAV is stable to treatment with 20% ether, acid (pH 1.0 for 2 hours), and heat (60°C for 1 hour), and its infectivity can be preserved for at least 1 month after being dried and stored at 25°C or for years at −20°C. Replication in cytoplasm of the host cell and it is non-envelop.



Transmission of epidemiology

1- Cause Hepatitis A disease
2- HAV unlike HBV , it is rarely transmitted via blood because level of viraemia is low
3- Chronic infection does not occur.
4- Transmitted by fecooral route
5- Children are most frequently infected group
6- Chronic infection does not occur
7- No CPE in tissue culture infected by HAV

Pathogenicity

HAV Probably replicate in GIT and spread via blood to the liver, then hepatocyte is infected. IgM antibodies early detected at the first time of jaundice, then IgG remain and produce for long time.

Clinical finding

Clinical manifestation of hepatitis is same regardless of which hepatitis virus cause fever, anorexia, nausea, vomiting, and jaundice. Short incubation period is 3-4 weeks whereas in HBV it 10-12 weeks. Most of cases are asymptomatic.

Lab diagnosis

1- Detection of IgM
2- 4 fold rise of IgG Ab titer
3- Isolation of the virus

Treatment & control

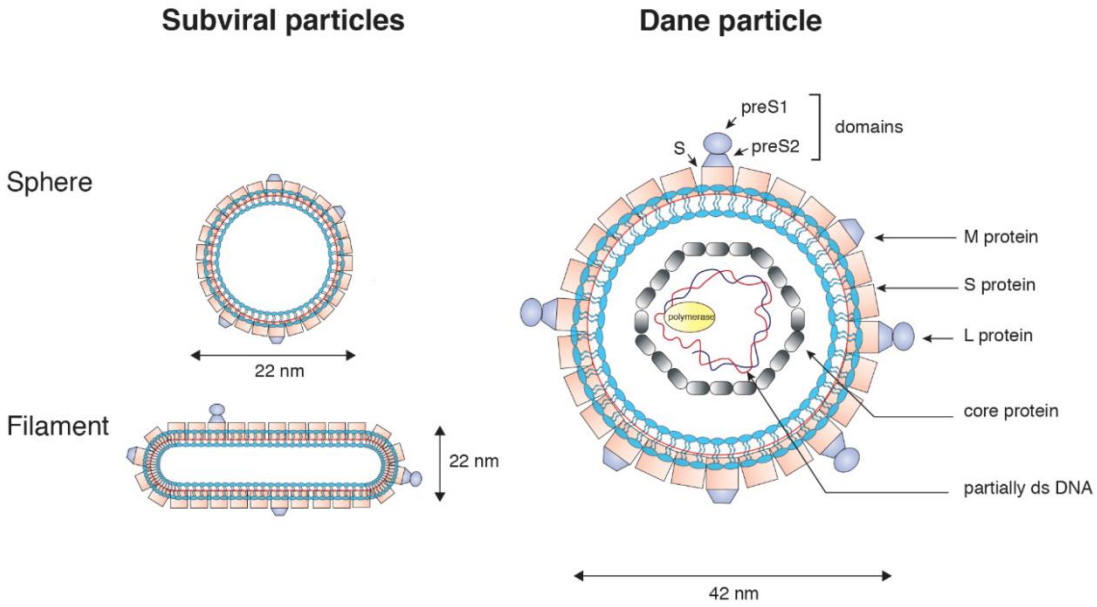
No antiviral drugs and no vaccine

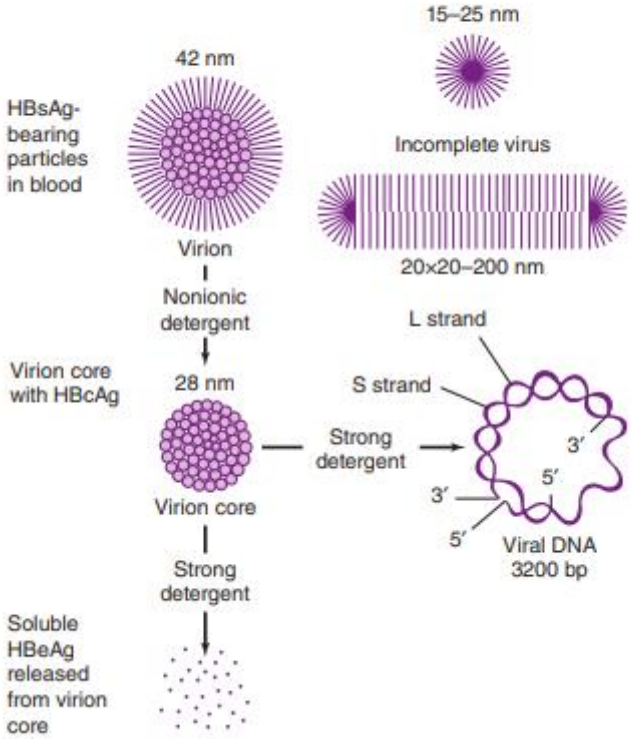
Hepatitis B virus (HBV)

HBV is classified as a hepadnavirus. HBV establishes chronic infections, especially in those infected as infants; it is a major factor in the eventual development of liver disease and hepatocellular carcinoma in those individuals.

Structure and Composition

- Electron microscopy of hepatitis B surface antigen (HBsAg)- positive serum reveals three morphologic forms. The most numerous are spherical particles measuring 22 nm in diameter. These small particles are made up exclusively of HBsAg—as are tubular or filamentous forms, which have the same diameter but may be more than 200 nm long—and result from overproduction of HBsAg. Larger, 42-nm spherical virions (originally referred to as Dane particles) are less frequently observed. The outer surface, or envelope, contains HBsAg and surrounds a 27-nm inner nucleocapsid core that contains hepatitis B core antigen (HBcAg).





- The viral genome consists of partially double-stranded circular DNA, The particles containing HBsAg are antigenically complex. Each contains a group-specific antigen, a, in addition to two pairs of mutually exclusive sub determinants, d/y and w/r. Thus, four phenotypes of HBsAg:

adw, adr, ayw, and ayr

- Enveloped
- The stability of HBsAg does not always coincide with that of the infectious agent. However, both are stable at −20°C for more than 20 years and stable to repeated freezing and thawing. The virus also is stable at 37°C for 60 minutes and remains viable after being dried and stored at 25°C for at least 1 week. HBV (but not HBsAg) is sensitive to higher temperatures (100°C for 1 minute) or to longer incubation periods (60°C for 10 hours). HBsAg is stable at a pH of 2.4 for up to 6 hours.

Replication

The infectious virion attaches to cells and becomes uncoated. In the nucleus, the partially double-stranded viral genome is converted to covalently closed circular double-stranded DNA (cccDNA). The cccDNA serves as template for all viral transcripts. Within the cores, the viral polymerase synthesizes by reverse transcription a negative-strand DNA copy. The polymerase starts to synthesize the positive DNA strand, but the process is not completed. Cores bud from the pre-Golgi membranes, acquiring HBsAg-containing envelopes, and may exit the cell.

Transmission

1- Sexual Transmission
2- From mother to children
3- The most important mode of Transmission is via blood Needle stick injuries can transmit the virus indicated that only very small amount of blood in necessary to produce disease as in case of drug users.

Pathogenesis & immunity of HBV

Many get infection through the blood, Infection of hepatocyte cause Necrosis and inflammation. Immune response against viral Ag on infected hepatocyte plays a very important role in pathogenesis because:

1- Ag — Ab complexes cause some early serum sickle like reaction symptoms. Some complication in chronic hepatitis (Vasculitis and immuncomplex glomeralonehphritis) and Arthralgia.
2- HBV-DNA are exist primarily as episome in the cytoplasm of persistently infected cells, but small amount of HBV – DNA is integrated into host cell, So high rate of hepatocellular carcinoma occur in chronic carrier.

Immunity

Long life Immunity mediated Ab against HBV

Incubation period

10 – 12 weeks this is longer than that of HA 3 – 4 weeks.

Note1: Many HBV infections are asymptomatic & detected only by presence of HBS Ab.

Note2: All blood for transfusion should be screened for HBS Ag

Note2: In activated vaccine consisting of HBs — Ag prepare from spherical particles purified from the serum of infected individual was used

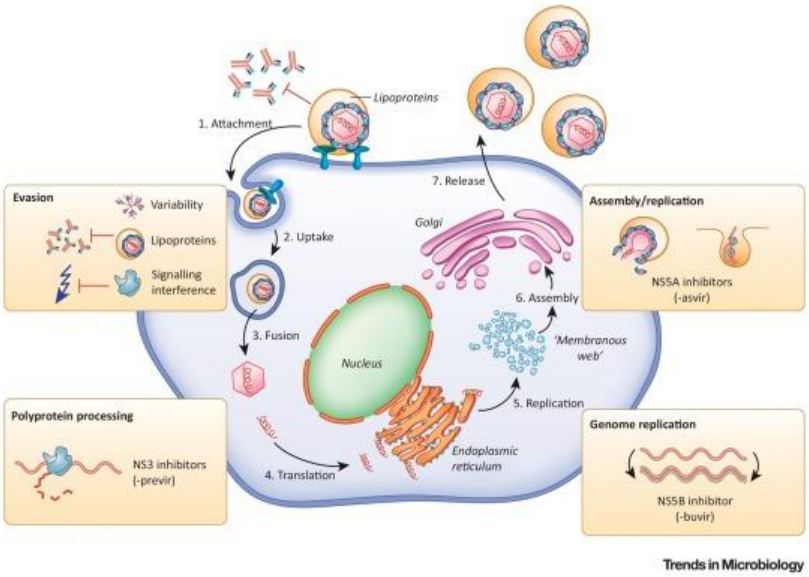
Treatment

Alfa interferon is clinical important for Treatment of chronic hepatitis B infection.

Hepatitis C Viruses (HCV)

There are several non-A, non-B (NANB) hepatitis agents that, based on serologic tests, were not related to HAV or HBV. The major agent was identified as HCV. HCV is a single positive stranded RNA virus, classified as family Flaviviridae, genus Hepacivirus.

Most new infections with HCV are subclinical. The majority (70–90%) of HCV patients develops chronic hepatitis, and many are at risk of progressing to chronic active hepatitis and cirrhosis (10–20%). In 1–5% of infected individuals, HCV leads to hepatocellular carcinoma, which is the fifth most common cause of cancer worldwide.

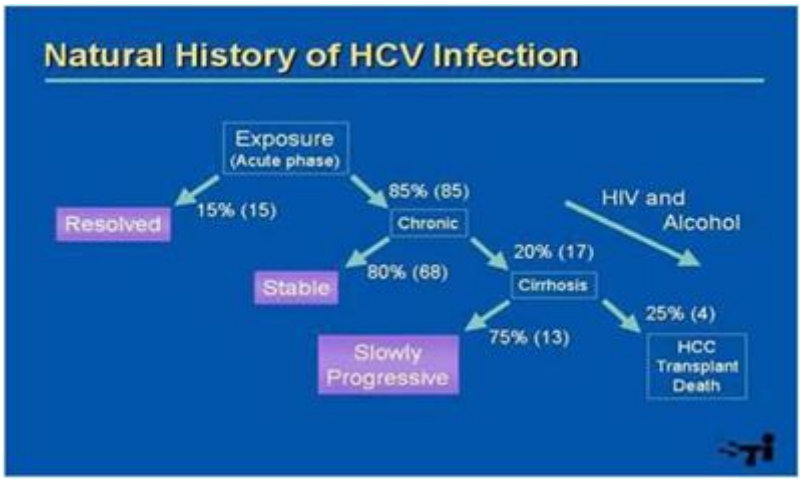


Transmission

Via blood and sexual contact

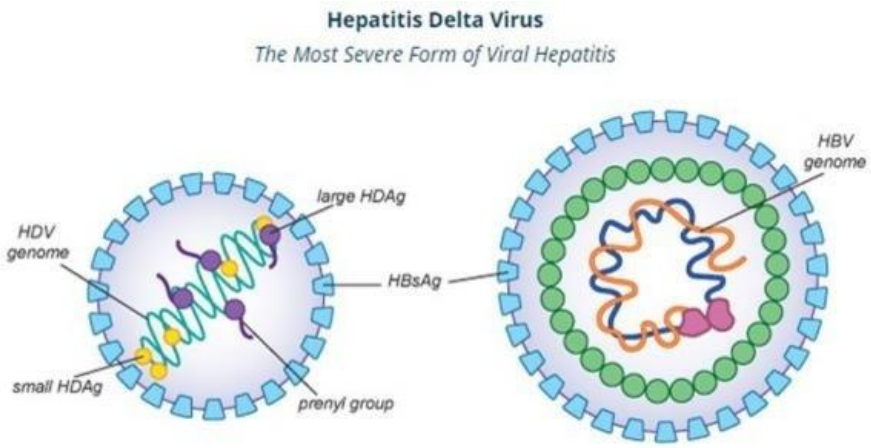
Treatment and prevention

No vaccine and no specific antiviral drugs but alpha IFN is provide for use in chronic active HCV.



Hepatitis D Viruses

An antigen–antibody system termed the delta antigen (delta-Ag) and antibody (anti-delta) is detected in some HBV infections. The antigen is found within certain HBsAg particles. In blood, HDV (delta agent) contains delta-Ag (HDAg) surrounded by an HBsAg envelope. The genome of HDV consists of single-stranded, circular, negative-sense RNA, 1.7 kb in size. HDAg is the only protein coded for by HDV RNA and is distinct from the antigenic determinants of HBV. HDV is a defective virus that requires the HBsAg coat for transmission. It is often associated with the most severe forms of hepatitis in HBsAg-positive patients. It is classified in the Deltavirus genus, which is not assigned to any virus family.



Hepatitis E Viruses (HEV)

1- Spherical non enveloped
2- Icosahedra particles
3- SS+ RNA
4- Burma subtype and Mexico subtype
5- Incubation period 10-70 d
6- Route of transmission: Fecooral route
7- Nausea, Diarrhea, Vomiting, and abnormal pain

Diagnosis

1- Anti HEIgG and Anti HEIgm
2- RT – PCR

TYPES OF HEPATITIS

	Viral Hepatitis A	Viral Hepatitis B	Viral Hepatitis C	Viral Hepatitis D	Viral Hepatitis E
Agent	Hepatitis A virus (HAV); ssRNA; No envelope	Hepatitis B virus (HBV); dsDNA; envelope	Hepatitis C virus (HCV); ssRNA; envelope	Hepatitis D virus (HDV); ssRNA; envelope from HBV	Hepatitis E virus (HEV); ssRNA; no envelope
Route of Transmission	Fecal-oral	Parenteral, Vertical, Sexual.	Parenteral	Parenteral	Fecal-oral
Age affected	Children	Any age	Adults	Any age	Young adults
Carrier state	Nil	Common	Present	Nil (only with HBV)	Nil
Incubation period	10-50 days (avg. 25-30)	50-180 days (avg. 60-90)	40-120 days	2-12 weeks	2-9 weeks
Chronic infection	No	Yes	Yes	Yes	No
Specific Prophylaxis	Ig and Vaccine	Ig and Vaccine	Nil	HBV vaccine	Nil