

# Hepatitis Virus

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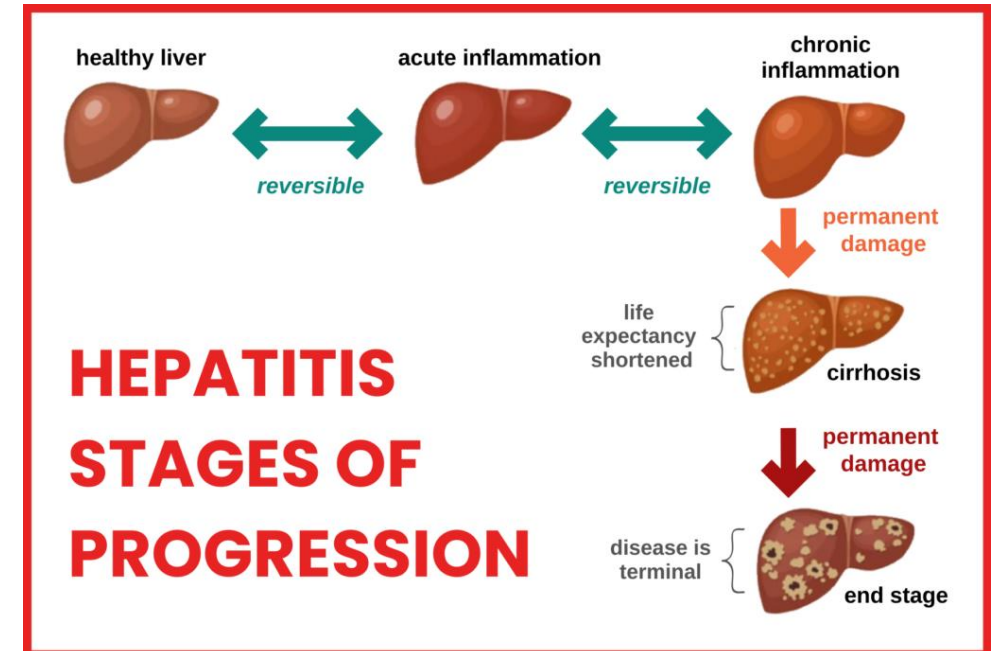
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# Introduction

- Viral hepatitis is an infection that causes liver inflammation and damage. Several different viruses cause hepatitis, including hepatitis A, B, C, D, and E.
- **Hepatitis is acute if it resolves within six months,** and chronic if it lasts longer than six months.
- Common symptoms of infectious hepatitis include:
  - fatigue
  - flu-like symptoms
  - dark urine
  - pale stool
  - abdominal pain
  - loss of appetite
  - unexplained weight loss
  - yellow skin and eyes, which may be signs of jaundice



# Hepatitis Virus

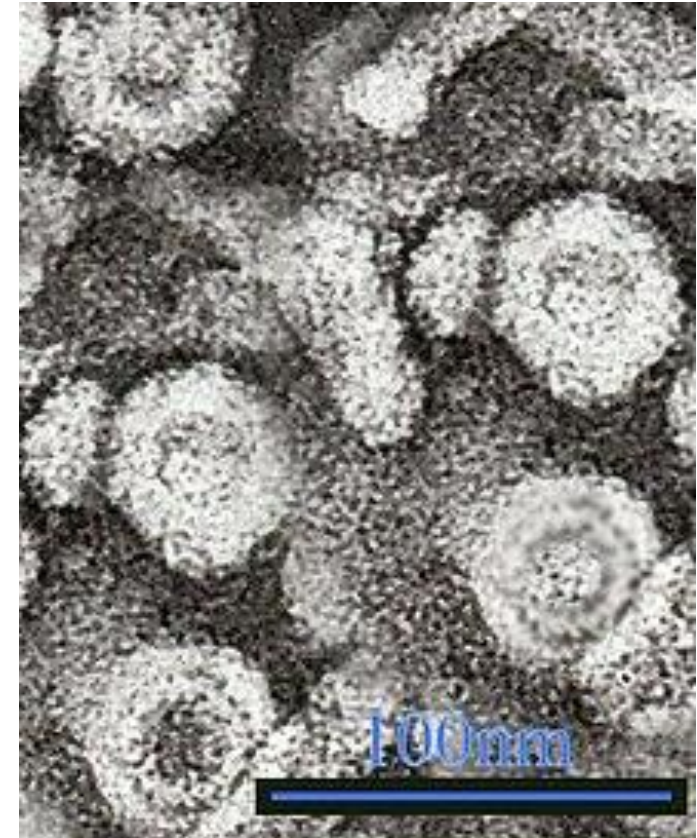
	<b>HAV</b>	<b>HBV</b>	<b>HCV</b>	<b>HDV</b>	<b>HEV</b>
Virus family, genus	<i>Picornaviridae</i> , <i>Hepatitis virus</i>	<i>Hepadnaviridae</i> , <i>Orthohepadnavirus</i>	<i>Flaviviridae</i> , <i>Hepacivirus</i>	Unassigned, <i>Deltavirus</i>	<i>Hepeviridae</i> , <i>Orthohepevirus</i>
Genome type	Positive-sense linear ssRNA	Circular, partially dsDNA (full length negative-sense, partial positive-sense), replication via reverse transcription	Positive-sense linear ssRNA	Viroid-like, negative-sense circular ssRNA	Positive-sense linear ssRNA
Approx. genome length (nt)	7,500	3,200	9,600	1,700	7,200
Virion diameter (nm)	27–32	42	55–65	36–43	30–34
Envelope	No/quasi- enveloped	Yes	Yes	Yes	No/quasi-enveloped
Course of infection	Acute <sup>61</sup>	Acute/chronic (children 30–90%; adults <5%) <sup>62</sup>	Acute/chronic (80–85%) <sup>63</sup>	Acute/chronic (>80% if superinfection) <sup>64</sup>	Acute/chronic (<1%) <sup>65</sup>
Predominant transmission routes	Mainly faecal-oral, parenteral	Vertical, parenteral, sexual	Parenteral	Parenteral, sexual	Faecal-oral, food- borne, parenteral
Cellular receptor	Unknown <sup>66</sup>	NTCP, heparan sulfate proteoglycans <sup>67,68</sup>	CD81, SR-B1, LDL receptor, claudin-1, occludin <sup>69–71</sup>	NTCP, heparan sulfate proteoglycans <sup>67,72</sup>	Unknown

dsDNA, double-stranded DNA; nt, nucleotide; NTCP, sodium taurocholate co-transporting polypeptide; ssRNA, single-stranded RNA.

<https://www.lsbio.com/research-areas/infectious-disease/hepatitis>

# Classification

- Group: VII partial ds DNA
  - Realm: Riboviria
  - Kingdom: Pararnavirae
  - Phylum: Artverviricota
  - Class: Revtraviricetes
  - Order: Blubervirales
  - Family: Hepadnaviridae
  - Genus: Orthohepadnavirus
  - Species: Hepatitis B virus



[https://en.wikipedia.org/wiki/Hepatitis\\_B\\_virus](https://en.wikipedia.org/wiki/Hepatitis_B_virus)

# Hepatitis B Virus

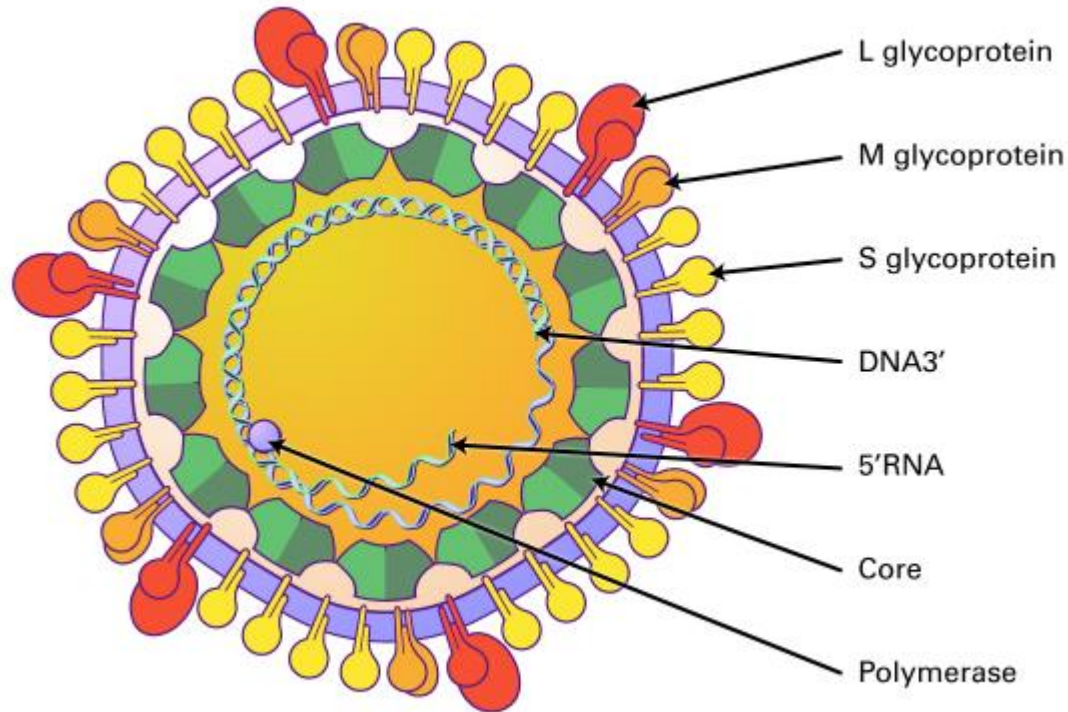
Hepatitis B virus (HBV) is a member of the Hepadnaviridae family of partially double stranded, enveloped DNA viruses with a circular genome and an icosahedral capsid. The family includes Orthohepadnaviruses and Avihepadnaviruses.

These viruses infect hepatocytes and cause liver injury and hepatocellular carcinomas in mammals and birds.

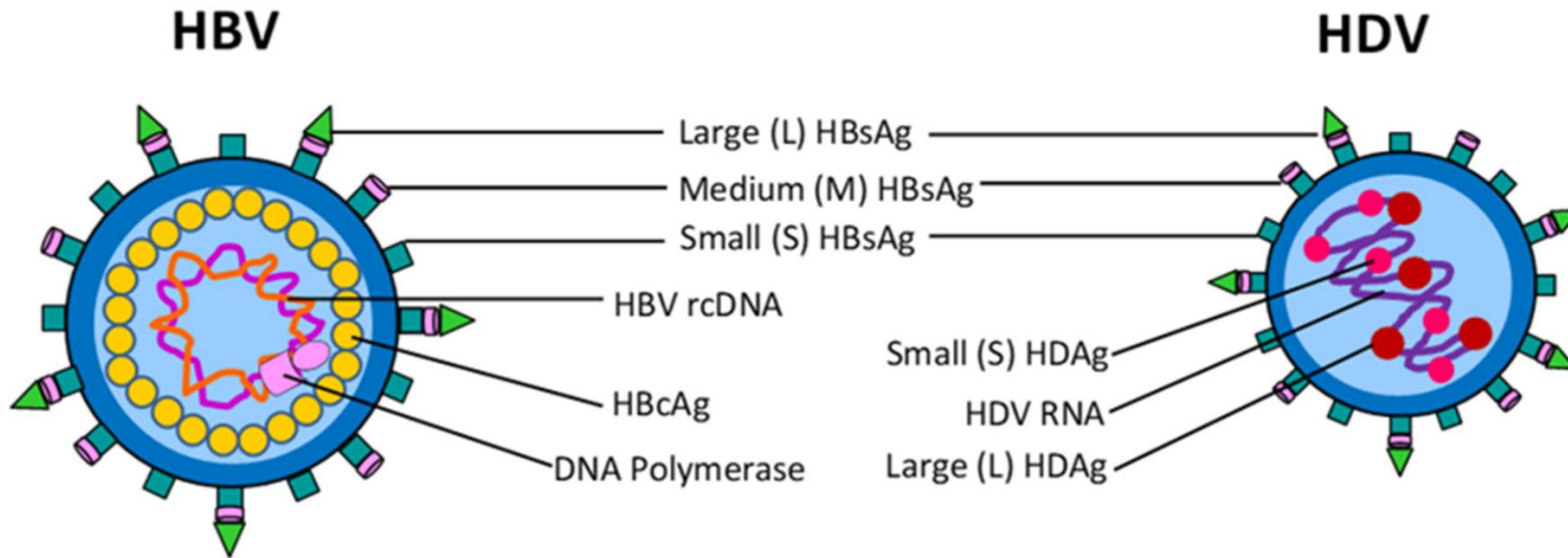
## STRUCTURE

Enveloped, spherical. Diameter from about 42nm. Icosahedric capsid with a T=4 symmetry. The hepatitis B virus contains an outer envelope and an inner core. The outer envelope of the virus is composed of a surface protein called the hepatitis B surface antigen or "HBsAg". The HBsAg can be detected by a simple blood test and a positive test result indicates a person is infected with the hepatitis B virus.

The inner core of the virus is a protein shell referred to as the hepatitis B core antigen or "HBcAg," which contains the hepatitis B virus DNA and enzymes used in viral replication.

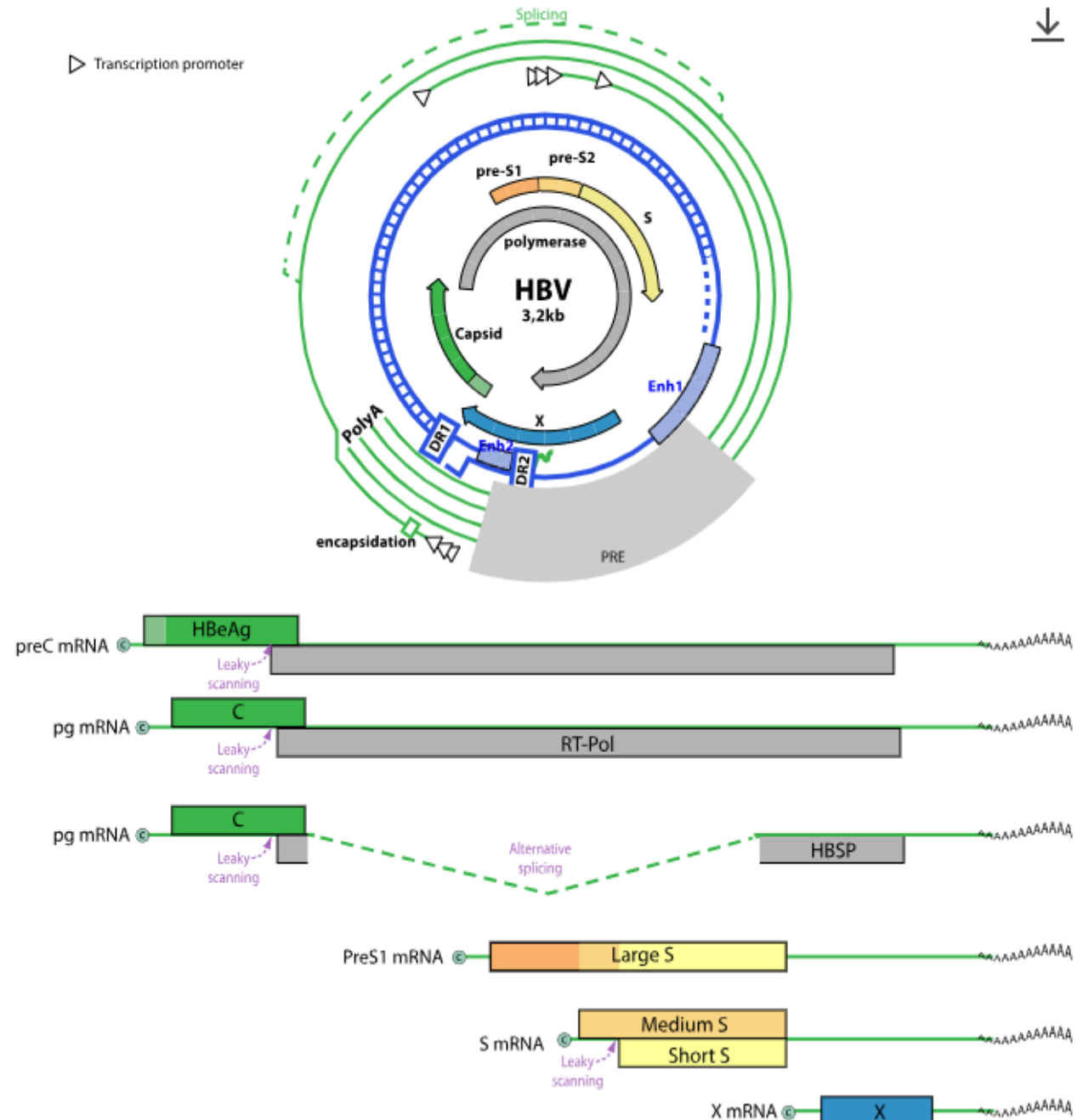


Hepatitis D virus (HDV, also known as hepatitis delta), a satellite virus of HBV, is highly pathogenic and requires HBsAg for its propagation and infectivity



# Genome

- Partially dsDNA circular genome, about 3.2 kb in size. Encodes for 7 proteins. that replicates by a reverse transcriptase via an RNA intermediate.
- On rare non-specific recombination, the viral genome can be integrated in host chromosome. This inactivates the integrated virus but can give the host cell a replicative advantage sometimes leading to hepatocarcinoma.
- The [minichromosome](#) is transcribed by cellular RNA polymerase II under the control of three to four promoters (the core, pre-S1, pre-S2/S promoters, and the X promoter in mammalian viruses) and two enhancer regions (ENH1 and ENH2).
- The pre-genomic RNA is [alternatively spliced](#). The unspliced form is [exported from the nucleus](#) through a PRE motif possibly by capsid protein.
- The Polymerase and short S proteins are expressed by [leaky scanning](#) from the pg mRNA and the S mRNA respectively.
- ENZYMES**
- Reverse transcriptase
  - RNA-dependent DNA polymerase [P]
  - DNA-dependent DNA polymerase [P]
  - Protein-primed terminal transferase [P]
- RNAse H [P]



# Life Cycle

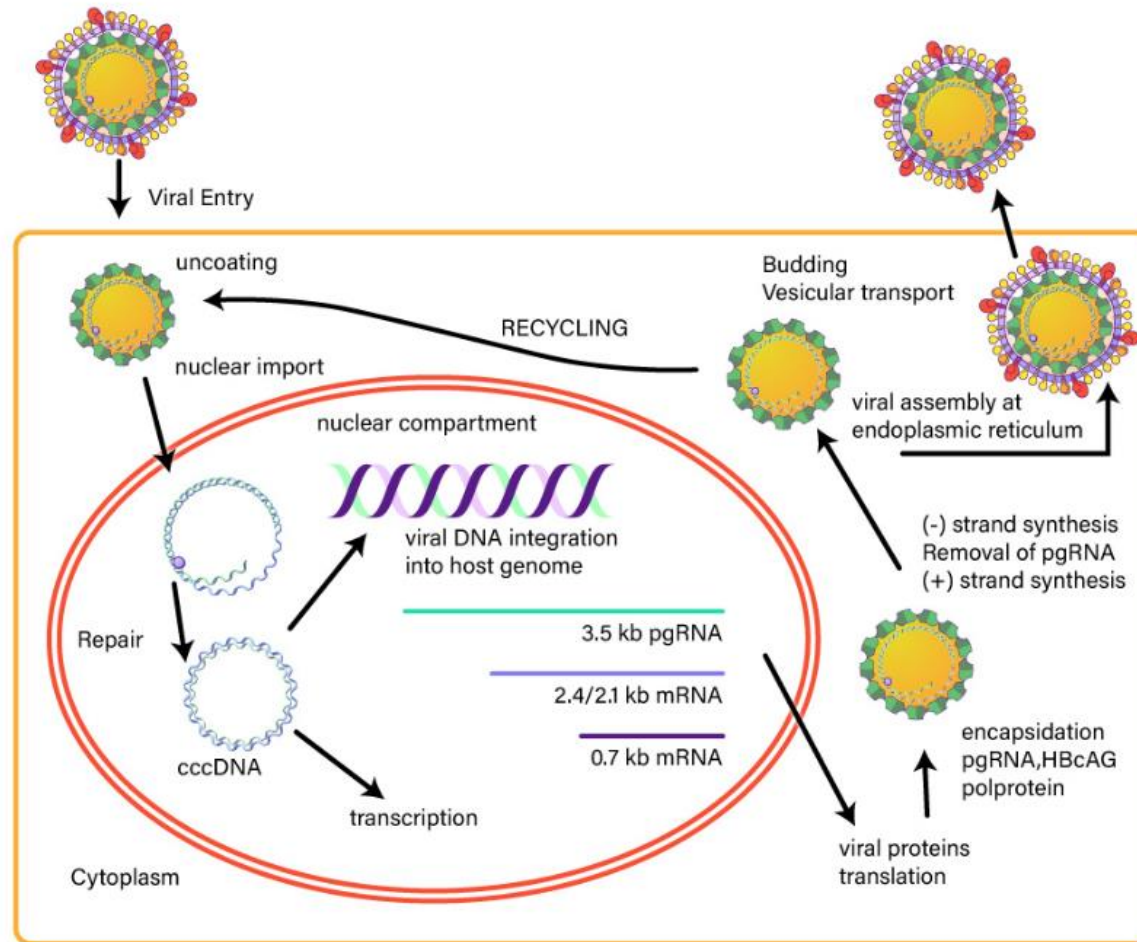


Figure 1: Hepatitis B Life Cycle

The hepatitis B virus (HBV) has a complex life cycle. The virus enters the host liver cell and is transported into the nucleus of the liver cell. Once inside the nucleus, the viral DNA is transformed into a covalently closed circular DNA (cccDNA), which serves as a template for viral replication (creation of new hepatitis B virus). New HBV virus is packaged and leaves the liver cell, with the stable viral cccDNA remaining in the nucleus where it can integrate into the DNA of the host liver cell, as well as continue to create new hepatitis B virus. Although the life cycle is not completely understood, parts of this replicative process are error prone, which accounts for different genotypes or “genetic codes” of the hepatitis B virus.

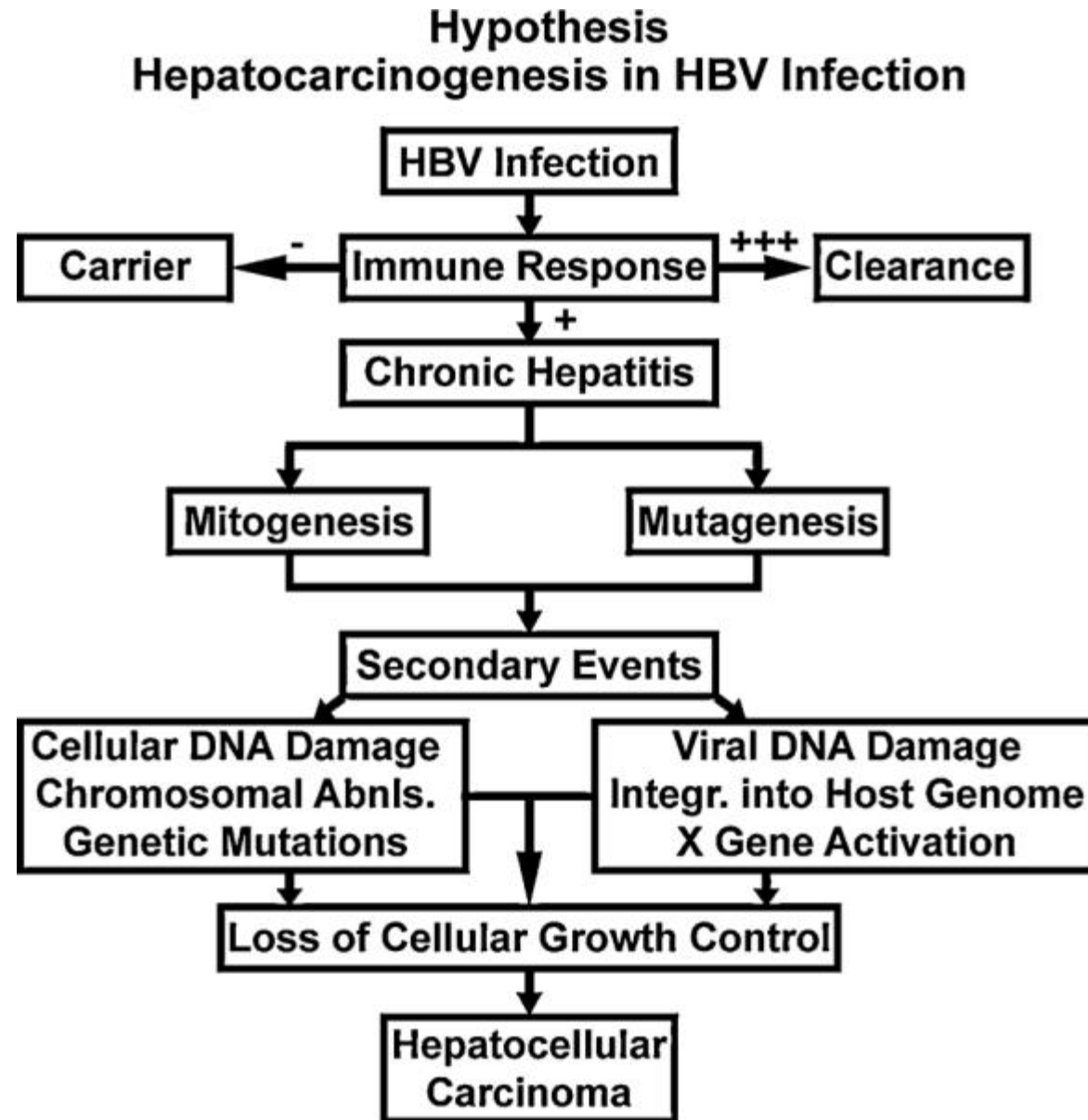


# REPLICATION

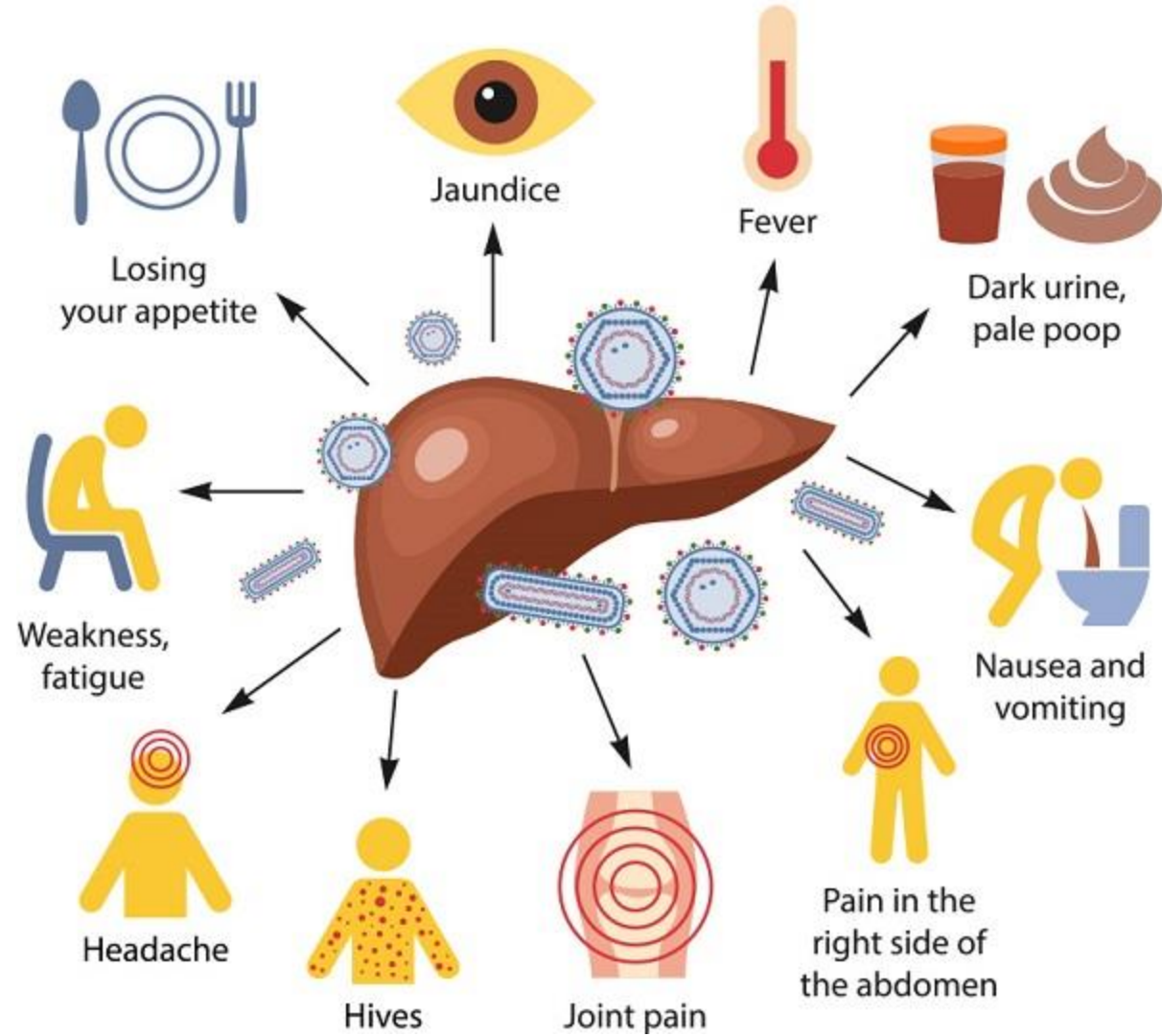
- CYTOPLASMIC/NUCLEAR
- Virus attaches to host receptors through major surface antigen and enters the cell by an unknown mechanism.
- Relaxed circular DNA (RC-DNA) and capsid are transported via microtubules to the nucleus where DNA is released through the nuclear pore, and repaired to form covalently closed circular DNA (cccDNA).
- Transcription by RNA polymerase II of the pregenomic RNA (pgRNA) and subgenomic mRNAs, inducing synthesis of all the viral proteins.
- pgRNA is encapsidated, together with the P protein, and reverse-transcribed inside the nucleocapsid in (-)DNA covalently linked to P protein.
- (+)DNA synthesis from the (-)DNA template generates new RC-DNA.
- Transport to the nucleus of new RC-DNA leads to cccDNA amplification; alternatively, the RC-DNA containing nucleocapsids are enveloped at the ER, and new virions are released by exocytosis.

# Pathogenesis

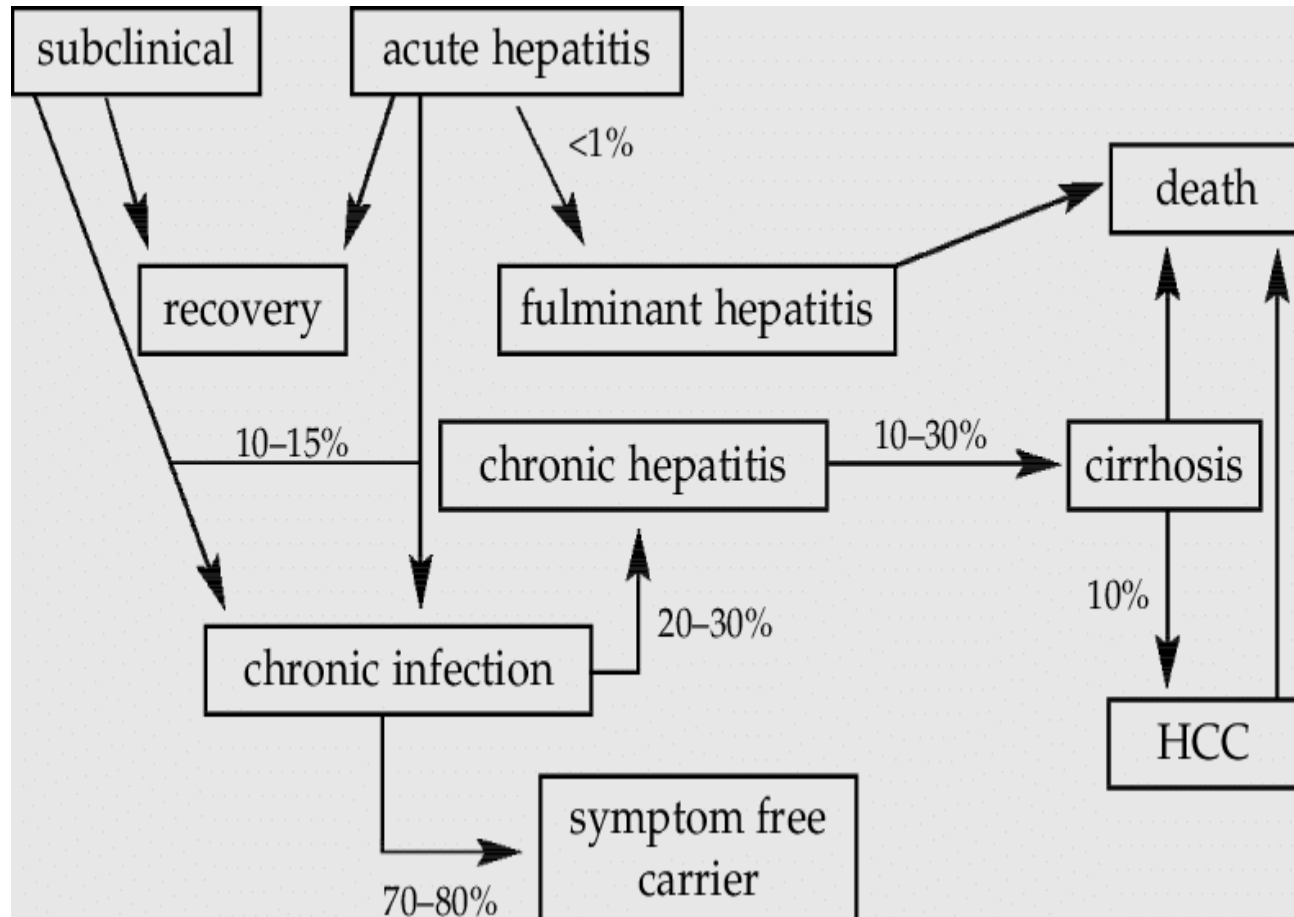
- Mode of Transmission:  
Sexual, Blood,  
Vertical



# SYMPTOMS OF HEPATITIS B



# Treatment



## Chronic Hepatitis B

Approved drugs

Interferons

- Conventional IFN- $\alpha$
- Peg-IFN  $\alpha$ -2a (*Pegasys*)

Combined antiviral and immunomodulatory effect

Nucleoside/nucleotide analogues

- Lamivudine (*Zeffix*)
- Adefovir (*Hepsera*)
- Entecavir (*Baraclude*)
- Telbivudine (*Sebivo*)
- Tenofovir (*Viread*)

Direct antiviral effect

<https://www.intechopen.com/chapters/44882>

# Vaccine (Wikipedia)

## Hepatitis B vaccine



Hepatitis B vaccine

### Vaccine description

**Target** Hepatitis B virus

**Vaccine type** Subunit

### Clinical data

**Trade names** Recombivax HB, Engerix-B, Henlisa-B, others

Hepatitis B vaccine is a vaccine that prevents hepatitis B. The first dose is recommended within 24 hours of birth with either two or three more doses

The vaccine contains one of the viral envelope proteins, Hepatitis B surface antigen (HBsAg). It is produced by yeast cells, into which the gene for HBsAg has been inserted.