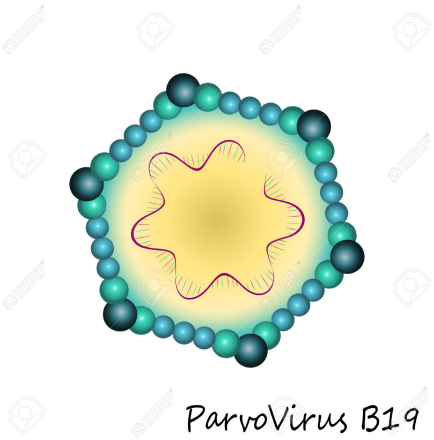
DNA Viruses

1- Parvoviridae Family:

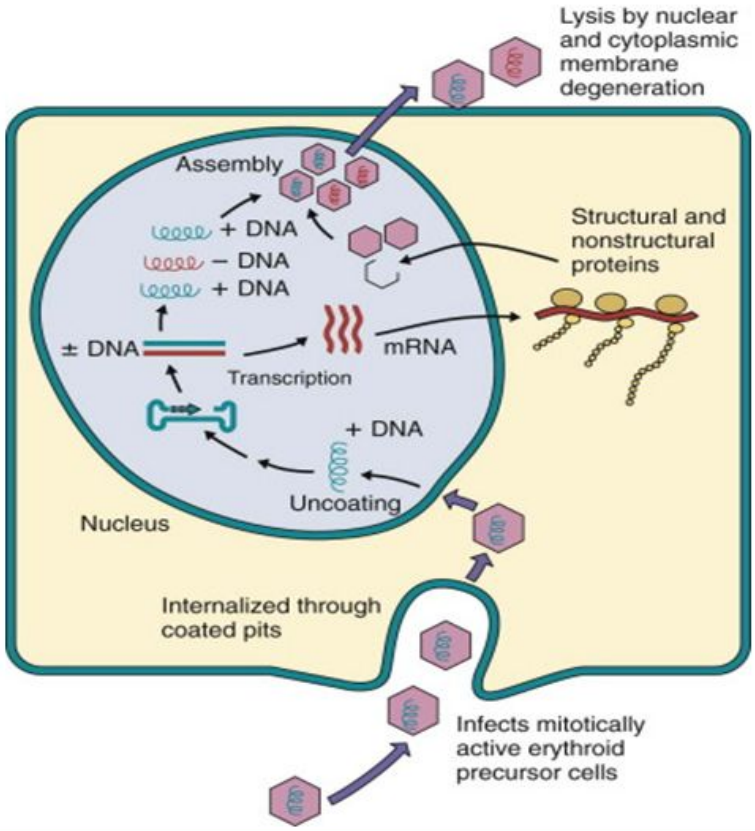
Are small (18-30nm - *parvum* = small), naked icosahedral DNA viruses with a single DNA strand of about 5kB. The packaged DNA may be either sense (same as the mRNA) or anti-sense. Replication of the virus requires that the host cell be undergoing DNA replication (that is, in S phase) yet unlike many other viruses, they cannot initiate cell DNA synthesis. This means that parvoviruses are restricted to the dividing cells of the body such as the erythropoietic and immune systems.
After infection the single strand DNA enters the nucleus where host cell repair enzymes convert it to double stranded DNA. The virus makes a replication enzyme but this is not a polymerase. It cleaves the DNA closed circle to make the single strand genomic DNA.



Human parvovirus B-19 replicates in dividing cells primerily in erythrocyte progenitors in the bone marrow and causes fifth disease-erythrema infectiosum (Fifth in a series of rash: Measles, Scarlet fever, German measles(Rubella), Duck disease, Erythrema infectiosum). This is usually amild disease but the decreased production of RBC can be problem in people with various types of sever hemolytic anemia.
Fifth disease is common in children, is usually mild and quickly resolves without intervention. It does not require treatment but it can cause serious problems in some members of the population. A child with fifth disease shows symptoms from a few days to as long as two weeks after infection but usually they resolve after about a week. The rash can look like the redness of a slapped face, intensely red on the cheeks with a pale ring around the mouth (circumoral pallor). It may extend to the rest of the body as a lacy rash. Sometimes there is itching. Before the manifestation of the rash, the child may have cold-like symptoms and perhaps a low fever. Most people are infected early in life and become immune but adults can be infected.

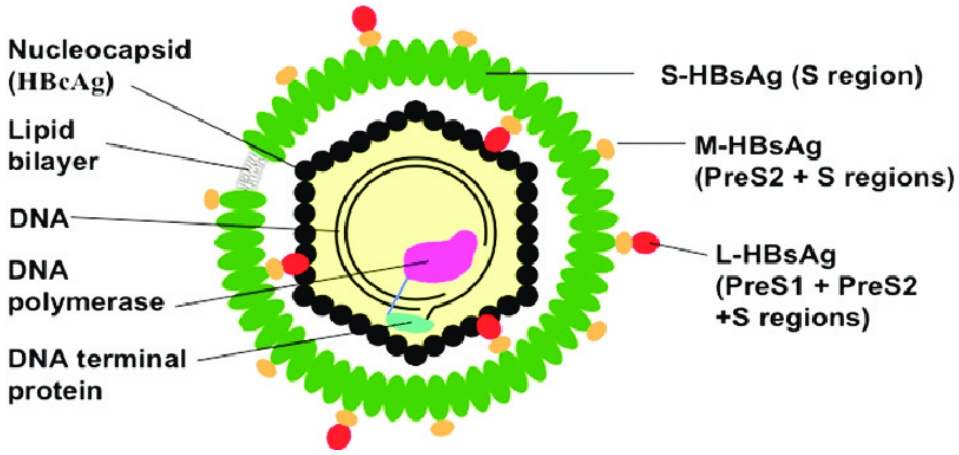
Life cycle of B-19 Parvovirus.

1- Binding to erythrocyte P antigen and entry.
2-Translocation of viral DNA to the nucleus.
3-Transcription of non structural RNA and later capsid protein RNA, followed by
4- protein translation
5- Capsid self-assembly,
6- Non structural protein action on viral DNA
7- Capsid translocation to nucleus
8- DNA replication
9- Insertion of DNA into intact capsids, and
10- Virus release and cell lyses.



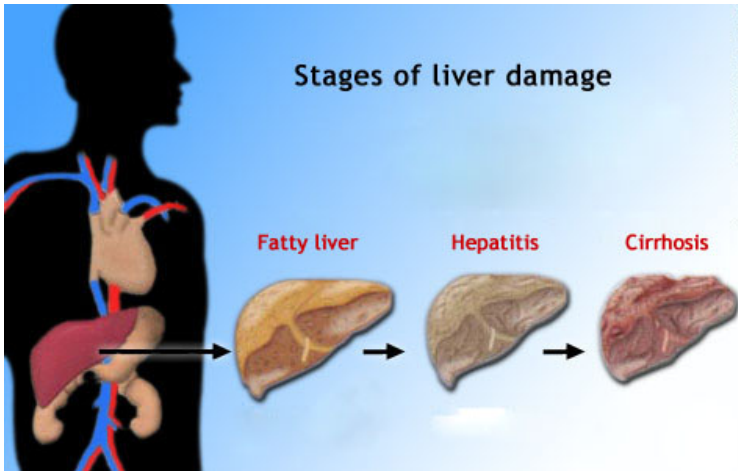
2- Hepadanaviridae Family:

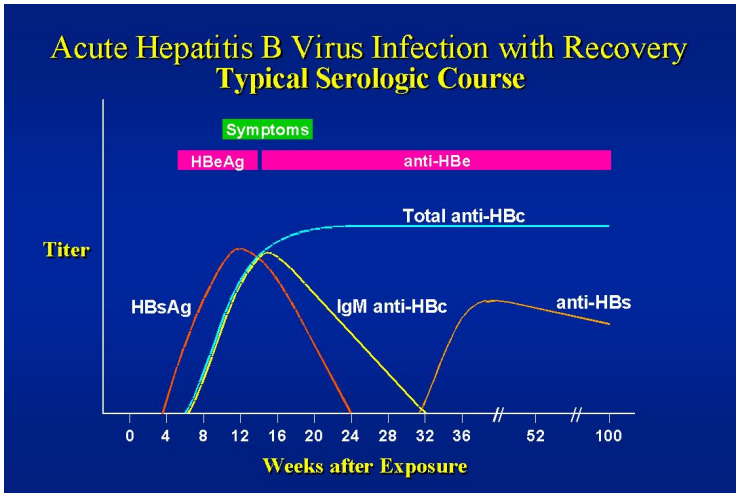
Small (42 nm), circular dsDNA, with lipid contain envelope with glycoprotein spikes. Replicate in the nucleus. Includes hepatitis B virus which may increase risk of hepatocarcinoma.
HBV (serum hepatitis) is stable to organic solvents and its also heat and pH resistant.

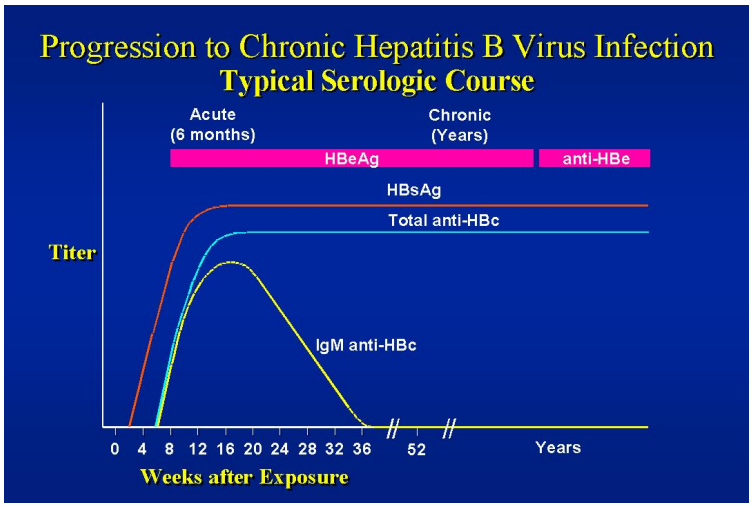


Infected hepatocytes are characteristically enlarged and their cytoplasm has a ground glass appearance. HBsAg is found associated with the endoplasmic reticulum; core particles containing HBcAg are present in the cell nuclei. Due to large antigenic load present in hepatocytes and in the serum it has been postulated that liver injury may result from immune mechanism. Necrosis of hepatocytes results in scattered focal inflammatory response with macrophage and lymphocyte infiltrations with portal inflammation of the central veins. In more severe cases, lines of necrosis extends from the portal tracts to the central veins and this often precedes chronic hepatitis and cirrhosis

Those who become asymptomatic carriers may either have normal liver histology or may show chronic liver inflammation that is recognized as chronic persistent hepatitis. This normally resolves within months or years of acute infection. Some may develop chronic periportal hepatitis which correlates clinically with chronic active hepatitis and continuing patchy necrosis with fibrosis is likely to lead to the major disruption in liver architecture characteristic of cirrhosis. It takes around 4 to 5 years for cirrhosis to develop. Some carriers may go on to develop hepatocellular carcinoma.


Stages of liver damage
Fatty liver
Hepatitis
Cirrhosis

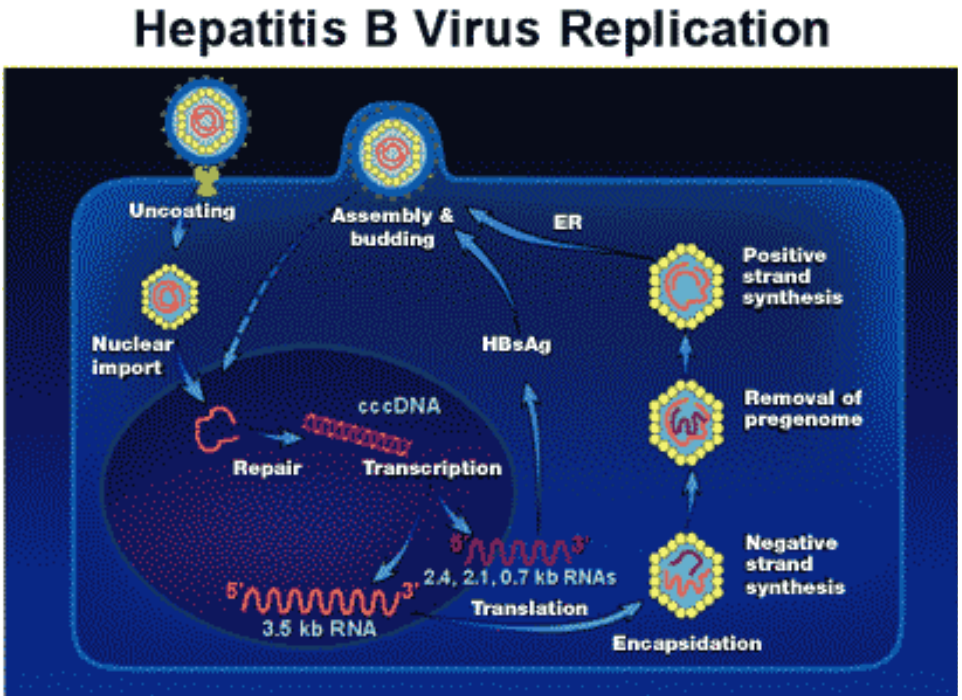

Acute Hepatitis B Virus Infection with Recovery
Typical Serologic Course
Symptoms
HBeAg
anti-HBe
Total anti-HBc
Titer
HBsAg
IgM anti-HBc
anti-HBs
0 4 8 12 16 20 24 28 32 36 52 100
Weeks after Exposure

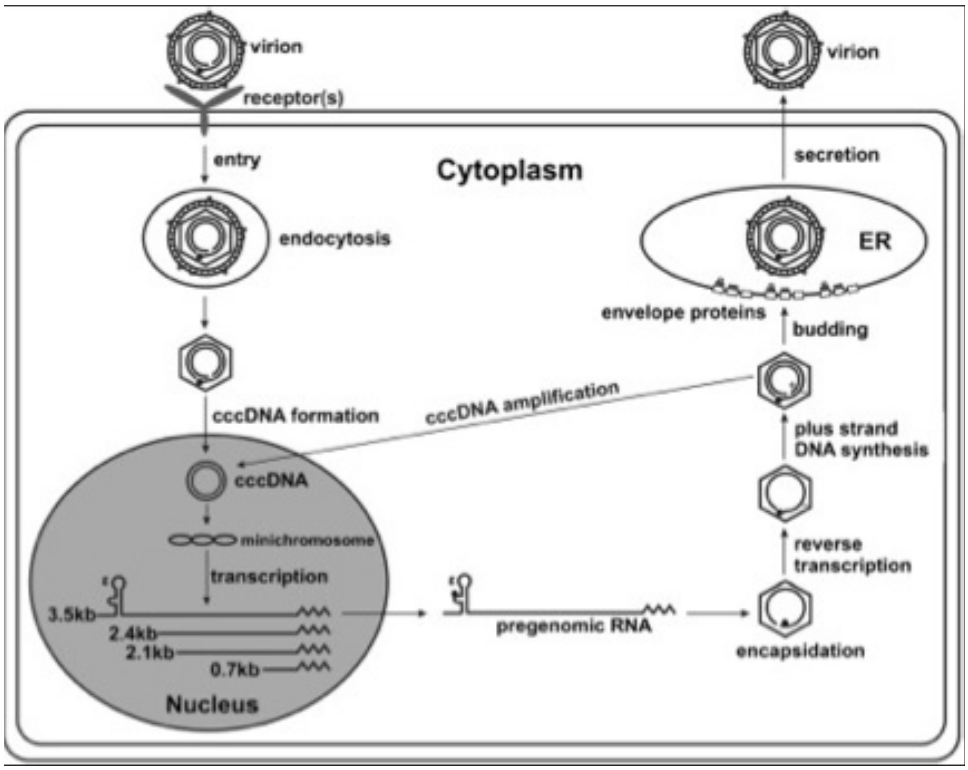

Progression to Chronic Hepatitis B Virus Infection
Typical Serologic Course
Acute
(6 months)
Chronic
(Years)
HBeAg
anti-HBe
HBsAg
Total anti-HBc
Titer
IgM anti-HBc
0 4 8 12 16 20 24 28 32 36 52
Years
Weeks after Exposure

The replicative process of the hepadnaviruses is unique among animal DNA viruses in that reverse transcription is involved. After absorption, the virus is uncoated and the single-stranded region of the genome is repaired by the viral polymerase. Viral RNAs are transcribed some of which act as mRNAs, others act as templates for the synthesis the progeny genomes where the process of reverse transcription is involved.

HBV Replication cycle

HBV attachment to a receptor on the surface of hepatocytes occurs via a portion of the pre-s region of HBsAg. After uncoating of the virus, unidentified cellular enzymes convert the partially double-strand DNA to covalent closed circular (ccc) DNA that can be detected in nucleus. The cccDNA serve as the template for the production of HBV mRNAs and the 3.5 Kb RNA pregenome. The pregenome is encapsidated by a packaging signal located near the 5 end of the RNA into newly synthesized core particles, where it serves as template for the HBV transcriptase encoded within the polymerase gene. An RNase H activity of the polymerase removes the RNA template as the negative-strand DNA is being synthesized. Positive- strand DNA synthesis dose not proceed to completion with the core, resulting in replicative intermediates consisting of full length minus-strand DNA plus variable-length (20-80%) positive-strand DNA. Core particles contain these DNA replicative intermediates bud from pre-Golgi membranes (acquiring HBsAg in the process) & may either exit the cell or reenter the intracellular infection cycle.




virion
receptor(s)
entry
Cytoplasm
endocytosis
cccDNA formation
cccDNA amplification
cccDNA
minichromosome
transcription
3.5kb
2.4kb
2.1kb
0.7kb
Nucleus
pregenomic RNA
encapsidation
reverse transcription
plus strand DNA synthesis
budding
envelope proteins
ER
secretion
virion