Viral Hepatitis

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Viral Hepatitis

Viral hepatitis – liver (main target tissue)

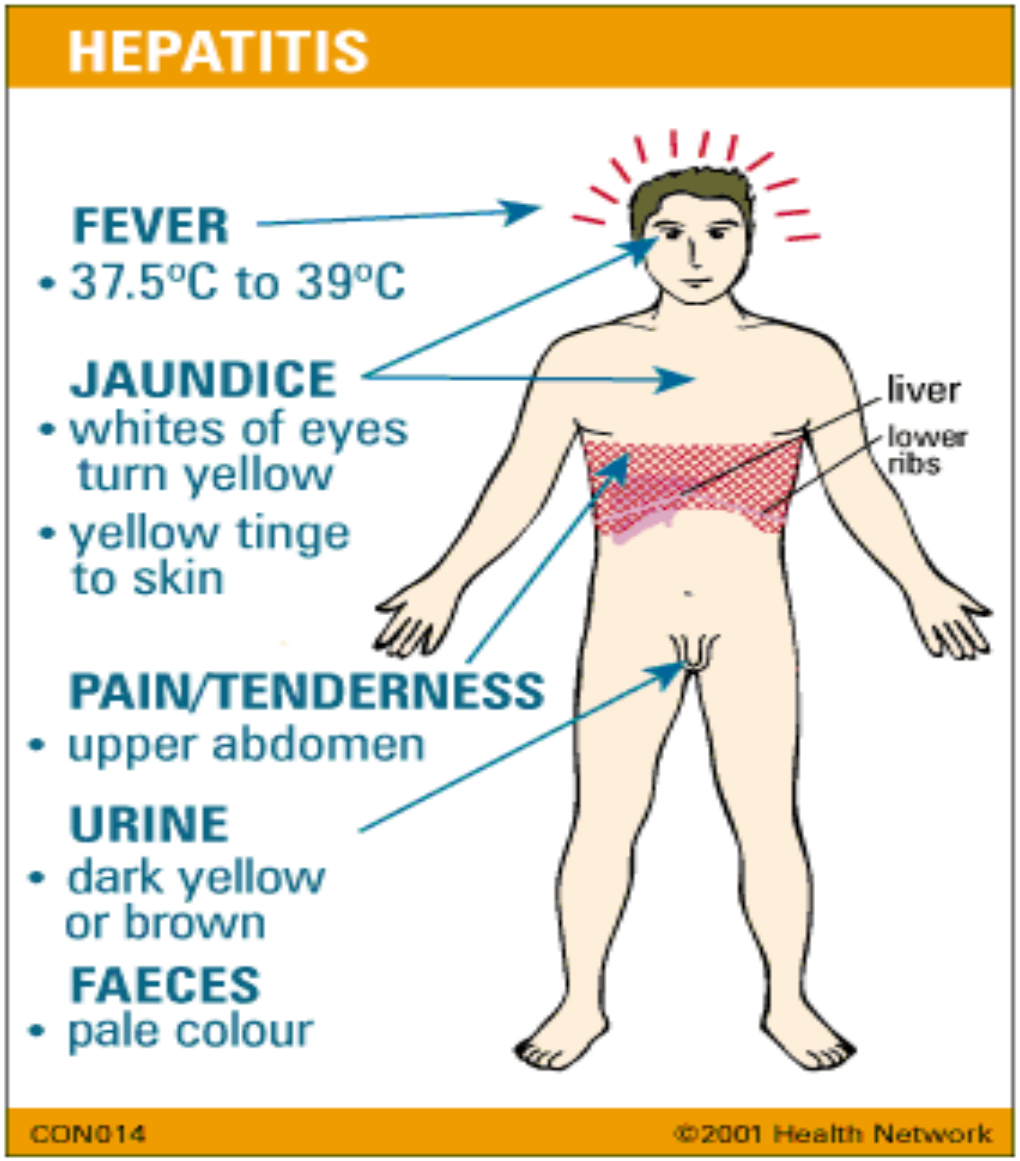
- **At least 6 hepatitis viruses**

  Enteric[A and E] and Serum[B, C, D and G].

- Specific diagnosis: only in lab
- Most infections: asymptomatic
- Acute hepatitis may also be induced by:

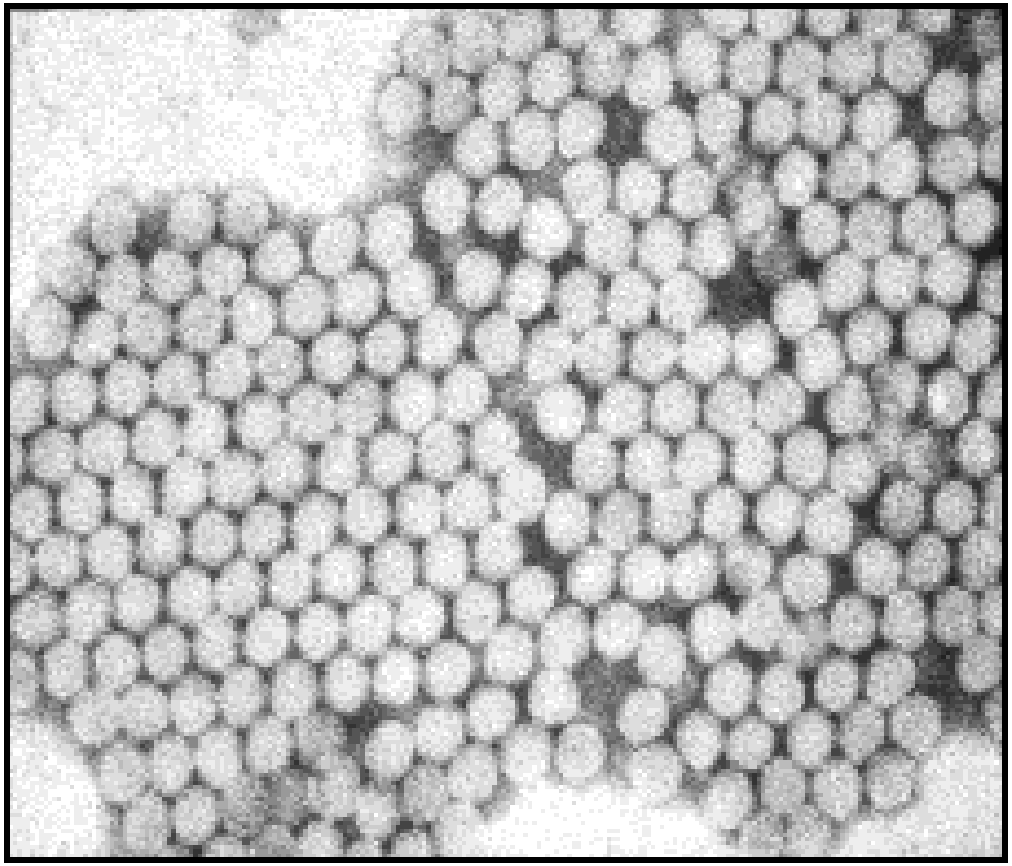
  CMV, EBV, HSV, YFV, and rubella**.**

Typical hepatitis symptoms



HEPATITIS A VIRUS(HAV)

Virology



- Family: Picornaviridae
- Enterovirus 72
- ssRNA genome.
- Replication is in the cytoplasm.

Hepatitis A Virus Transmission

- Fecal-oral
- Close personal contact(household contact, child day care centers).
- Contaminated food, water (infected food handlers, raw shellfish)

Hepatitis A – Clinical features

- Incubation period 14-28 days
- **<u>Clinical symptoms</u>**:

  Fever, malaise, loss of appetite, diarrhea, nausea, abdominal discomfort, dark-colored urine and jaundice.

- Jaundice Under 6 yrs (<10%)

  6-14yrs (40-50%)
- Chronic sequelae None

Diagnosis

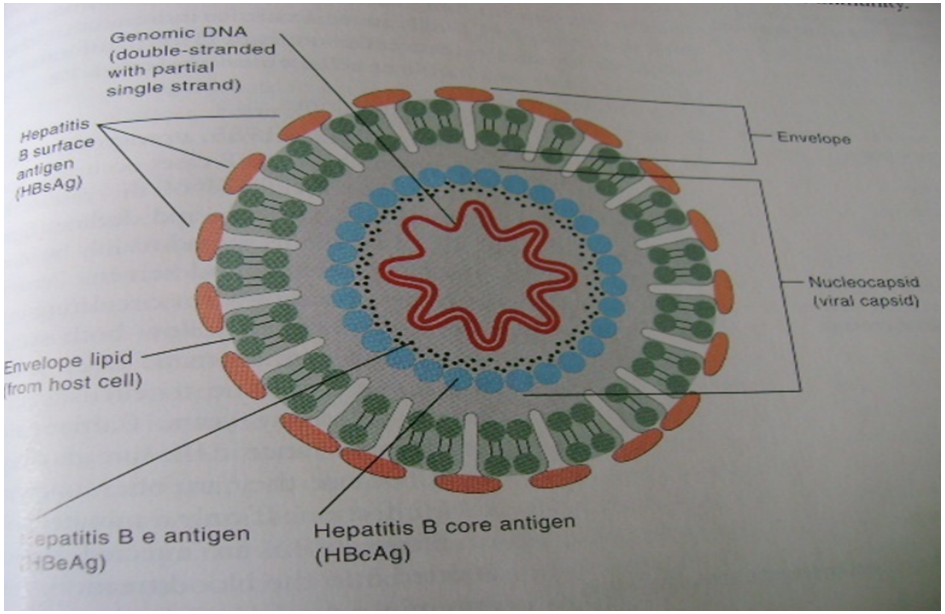
- Cases of hepatitis A are not clinically distinguishable from other types of acute viral hepatitis.
- Acute infection is diagnosed by the detection of HAV-IgM in blood by EIA.
- Past Infection: Immunity is determined by the detection of HAV-IgG by EIA.
- Direct Detection: RT-PCR of faeces. Can detect illness earlier than serology but rarely performed.

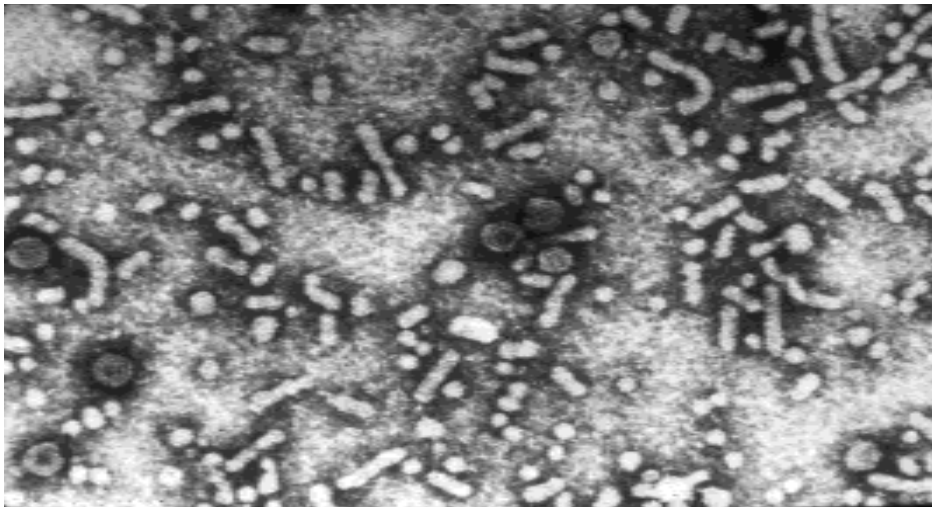
Hepatitis A Prevention

- Adequate supplies of safe drinking water.
- Proper disposal of sewage within communities
- Personal hygiene practices such as regular hand-washing with safe water.
- Health education
- Vaccination with HAV inactivated vaccine.

Hepatitis B virus (HBV)

- Double stranded DNA virus, the + strand not complete.
- Family: Hepadnaviridae - also known as "Dane particles"





FACTS ABOUT HBV

- An estimated 240 million people are chronically infected with HBV.
- More than 686 000 people die every year due to cirrhosis and liver cancer.
- Hepatitis B is an important occupational hazard for health workers.

HBV - Transmission

The virus can survive outside the body for at least 7 days

(1) Blood Transfusion.

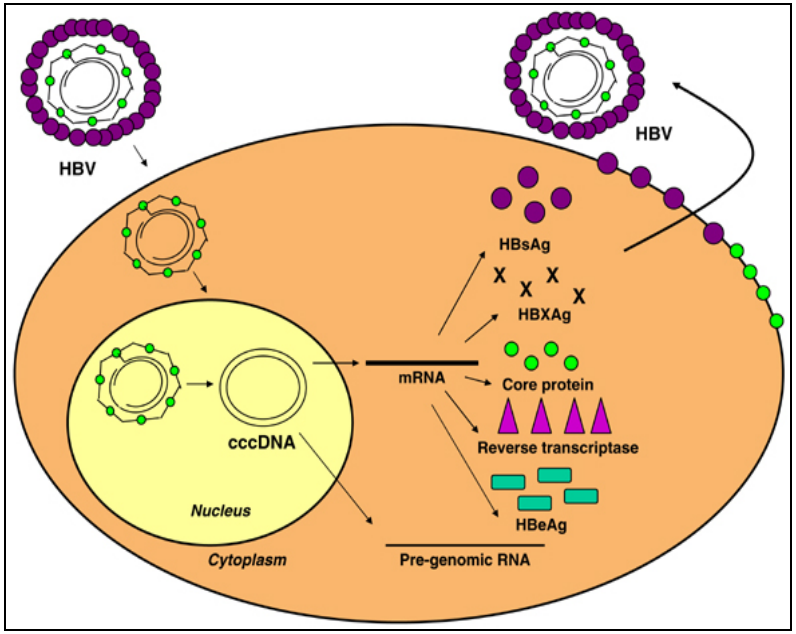
(2) Sexual intercourse.

(3) Vertical transmission

- transplacental (rare)
- during delivery
- post natal , ??breast feeding , ??

REPLICATION CYCLE: HBV

- Attachment and Virus entry into the cell.
- Uncoating of virion(in cytoplasm), Virion DNA polymerase synthesis of missing portion of DNA(ssDNA).
- A double-stranded closed-circular DNA is formed in the nucleus.
- This DNA acts as a template for mRNA synthesis by cellular RNA polymerase.

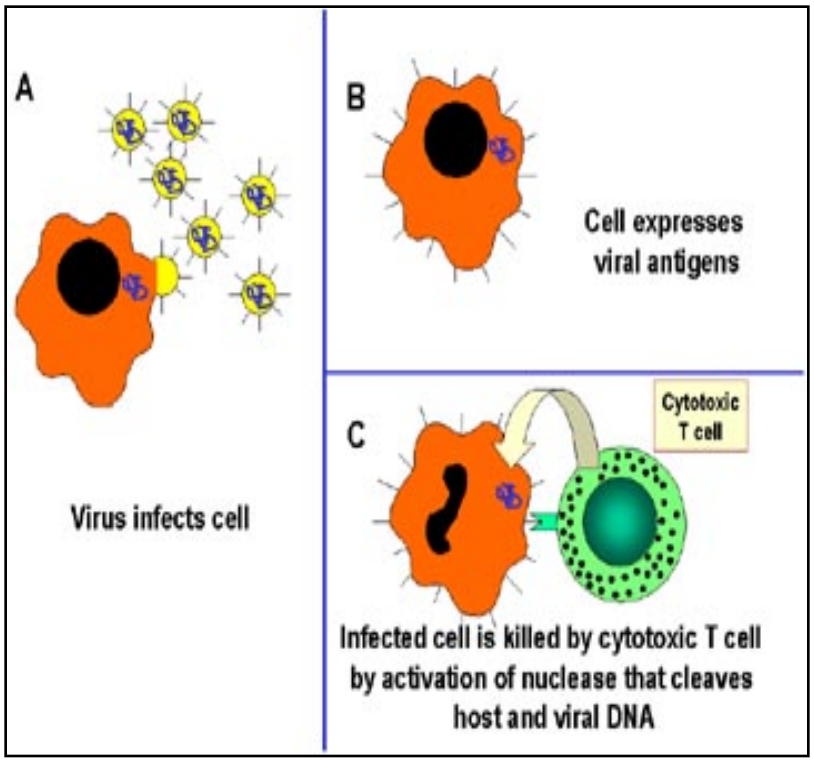


Hepatitis B – Clinical Features

▪ Incubation period:	Average 60-90 days Range 45-180 days
▪ Clinical illness (jaundice):	<5 yrs, <10% 5 yrs, 30%-50%
▪ Acute case-fatality rate:	0.5%-1%
▪ Chronic infection:	<5 yrs, 30%-90% 5 yrs, 2%-10%
▪ Premature mortality from chronic liver disease:	15%-25%

PATHOGENESIS & IMMUNITY

- Virus enters in the (blood)
- Infects hepatocytes (viral antigens displayed on hepatocytes)
- Cytotoxic T cells mediate an immune attack against the viral antigens
- Inflammation and necrosis occur.
- Therefore hepatitis B pathogenesis is probably due to immune attack.



Pathogenesis: 2

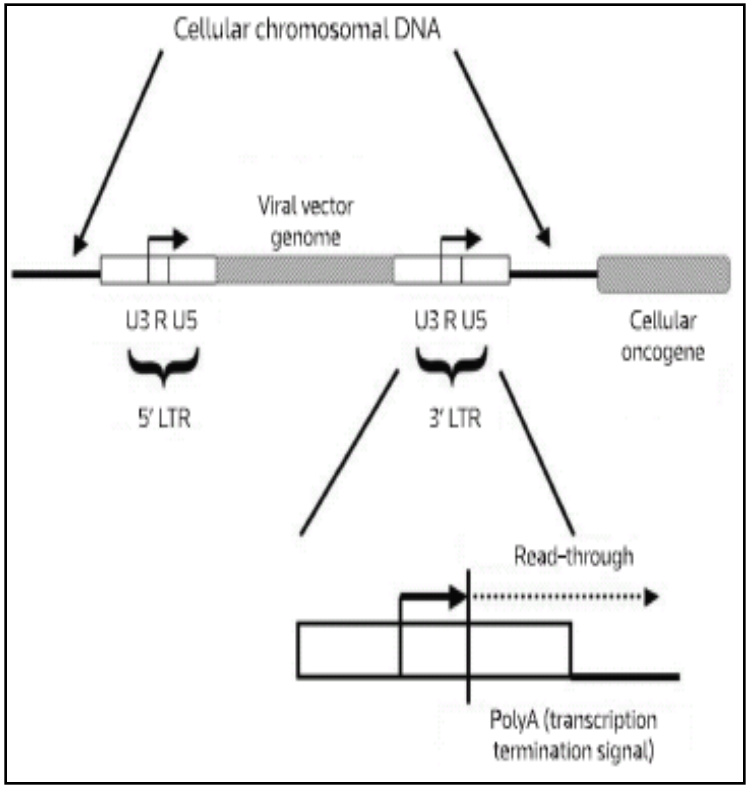
HCC due to:

Malignant transformation due to insertional mutagenesis as HBV genome integrate into hepatocyte DNA.

Integration can activate

cellular oncogene

loss of growth control (hence cancer)



HBV in Hepatocellular carcinoma [HCC]

a) 80% of patients with HCC are carriers of hepatitis B VIRUS

b) Virus DNA can integrate into the host chromosome.

HBV Diagnosis

Based on serum markers

- HBsAg, Anti-HBs
- Anti-HBc
- HBeAg, Anti-Hbe
- HBV-DNA

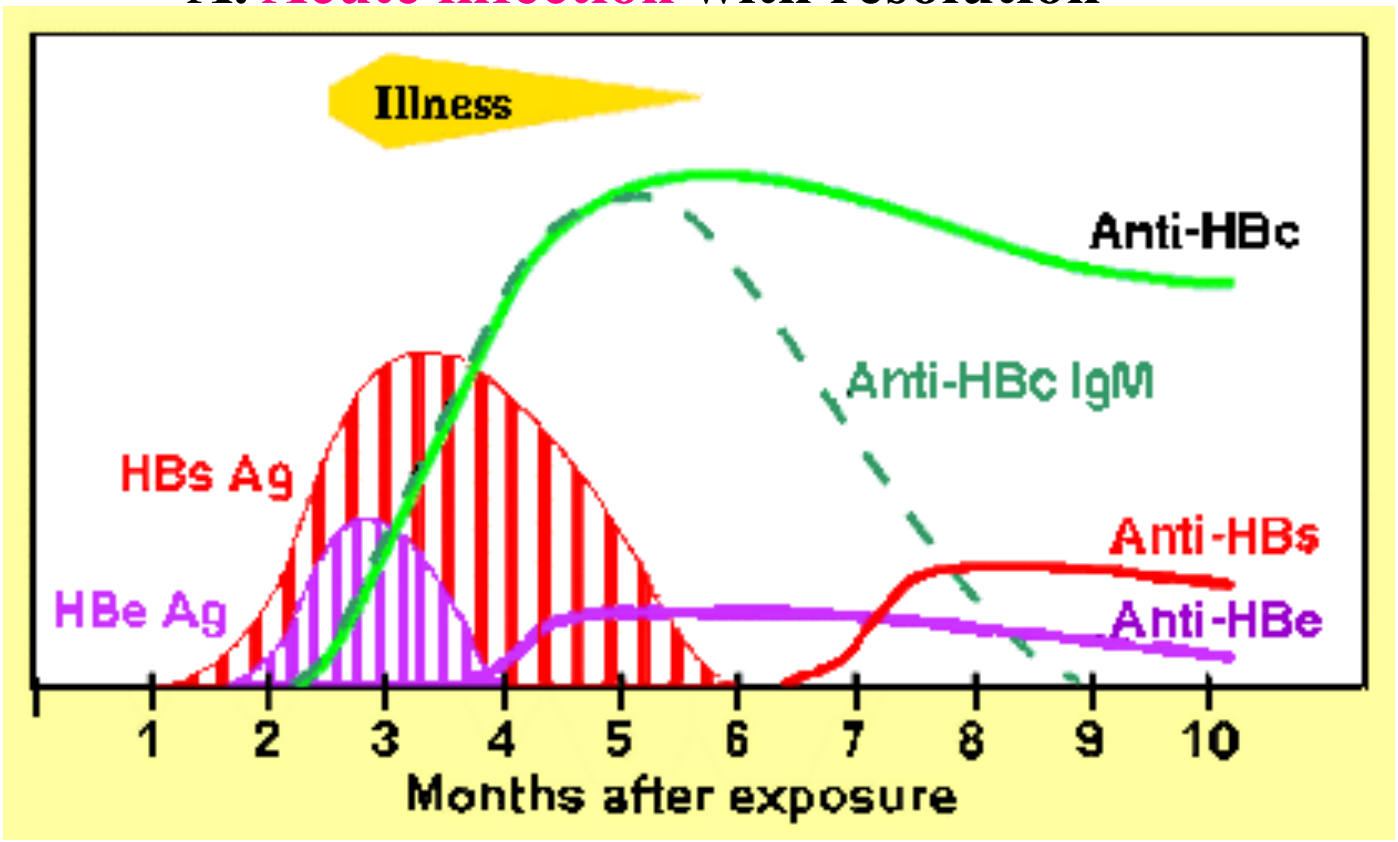
HBV: Serologic diagnosis

Acute infection with resolution

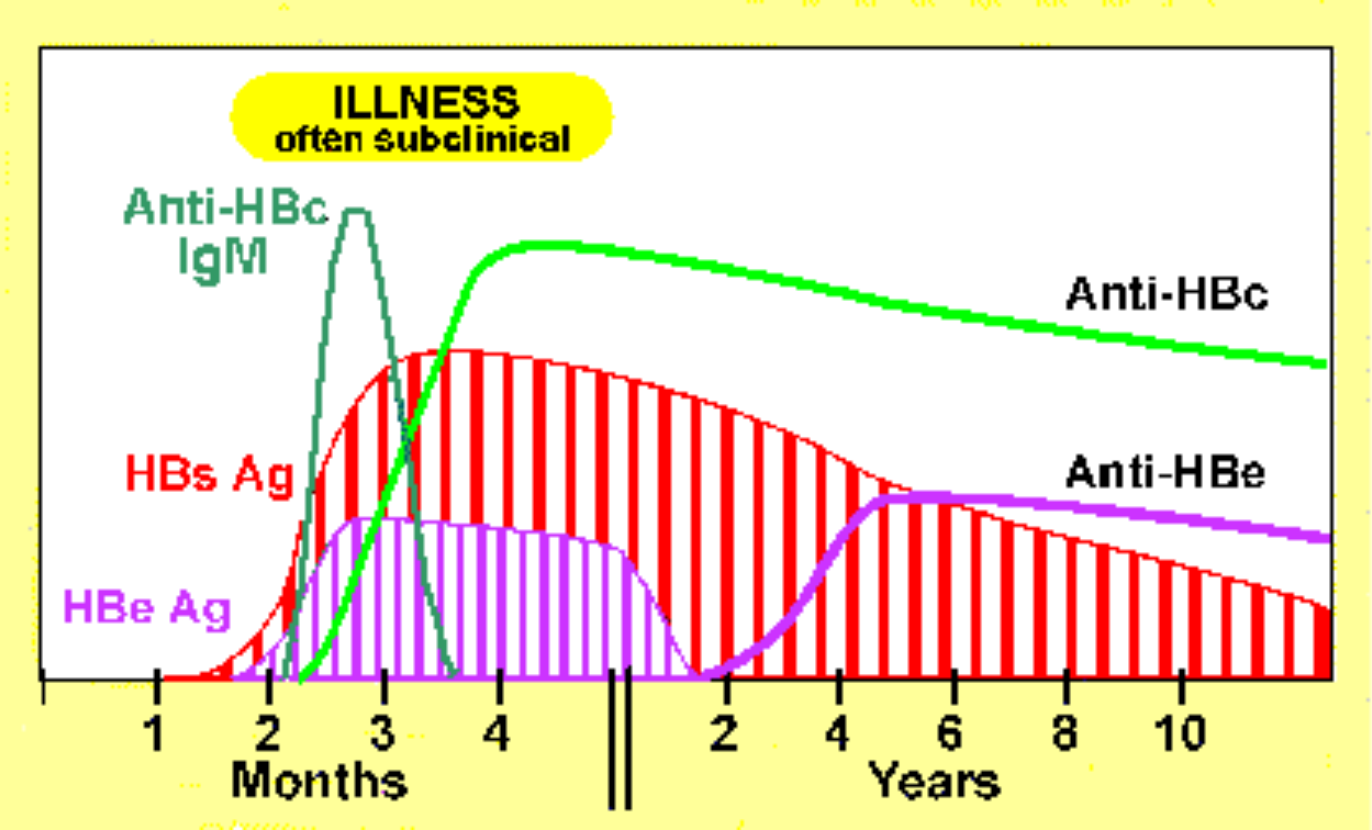
(a) Viral antigens

- **Surface antigen (HBsAg)** - secreted in excess into the blood. Presence in serum = virus replication in liver
- **'e' antigen (HBeAg)** - shed in small amounts into the blood. Presence in serum = high level of viral replication liver
- **core antigen (HBcAg)** core protein - not found in blood

A. Acute infection with resolution



B. Serology of the chronic carrier



Diagnosis.

- **HBsAg:** used as a general marker of infection.
- **HBsAb**: used to document recovery and/or immunity to HBV infection.
- **anti-HBc IgM**: marker of acute infection.
- **anti-HBcIgG**: past or chronic infection.
- **HBeAg**: indicates active replication of virus and therefore infectiveness.
- **Anti-Hbe:** virus no longer replicating. However, the patient can still be positive for HBsAg which is made by integrated HBV.
- **HBV-DNA**: indicates active replication of virus, more accurate than HBeAg especially in cases of escape mutants. Used mainly for monitoring response to therapy.

TREATMENT OF HBV

a) There is no specific treatment for *acute* hepatitis B.

b) *Chronic* hepatitis B infection can be treated with antiviral drugs, but treatment only slow the progression of cirrhosis, reduce incidence of liver cancer and improve long term survival.

WHO recommends the use of oral treatments - tenofovir or entecavir, because they are most potent drugs to suppress hepatitis B virus and rarely lead to drug resistance as compared with other drugs.

Treatment using interferon injections may be considered in some people in certain high-income settings, as this may shorten treatment duration, but its use is less feasible in low-resource settings due to high cost.

HBV - Prevention

Active Immunization

- Two types of **vaccine** (safe & effective)

  (a) **Serum derived** - prepared from HBsAg purified from the serum of HBV carriers

  (b) **Recombinant** HBsAg: made by genetic engineering in yeast.

- Vaccine should be administered to people at high risk of infection with HBV:

  1) Health care workers

  2) Sexual partners of chronic carriers

  3) Infants of HBV carrier mothers

Hepatitis C (HCV)

- Discovered in 1989
- Family: Togaviridae
- ss(+)RNA (approx. 10,000 bases)
- Enveloped virus
- Does not grow in cell culture

  - Can infect Chimpanzees

FACTS ABOUT HCV

- HCV cause both acute and chronic hepatitis infection.
- Globally, between 130–150 million people globally have chronic HCV infection.
- A significant number of those chronically infected will develop liver cirrhosis or liver cancer.
- Approximately 700 000 people die each year from hepatitis C-related liver diseases.
- Antiviral medicines can cure approximately 90% of persons with hepatitis C infection.
- There is currently no vaccine for hepatitis C.

HCV

Transmission

- Blood
- Organ donation
- Intravenous drug abusers
- sexual intercourse

Hepatits C virus (HCV)

a) Clinical Features

- Incubation period 6-8 wks
- milder form of acute hepatitis than hepatitis B
- 50% individuals develop chronic infection, following exposure.

b) Complications

1) Chronic liver disease

2) Hepatocellular carcinoma

Hepatitis C: Clinical Features

Incubation period:	Average 6-7 wks Range 2-26 wks
Clinical illness (jaundice):	30-40%
Chronic hepatitis:	70%
Persistent infection:	85-100%
Immunity:	No protective antibody response identified

HCV: Diagnosis

1. Screening for anti-HCV antibodies with a serological test identifies people who have been infected with the virus.
2. If the test is positive for anti-HCV antibodies, a nucleic acid test for HCV ribonucleic acid (RNA) is needed to confirm chronic infection because about 15–45% of people infected with HCV spontaneously clear the infection without the need for treatment. Although no longer infected, they will still test positive for anti-HCV antibodies.

Treatment

- **Interferon and Ribavirin-[old methods tx]**
  - Required weekly injections for 48 weeks,
  - cured approximately half of treated patients
  - caused frequent and sometimes life-threatening adverse reactions.

- **<u>Direct antiviral agents (DAA)-[Recent]:</u>**
  - are much more effective.
  - safer and better-tolerated.
  - can cure most persons with HCV infection and
  - treatment is shorter (usually 12 weeks) and safer.

Prevention of Hepatitis C

- Screening of blood, organ, tissue donors
- High-risk behavior modification

Other hepatitis viruses

Hepatitis E virus(HEV).

Hepatitis D virus(HDV).

Hepatitis G virus(HGV).