SNS COLLEGE OF ALLIED HEALTH SCIENCES

SNS Kalvi Nagar, Coimbatore - 35

Affiliated to Dr MGR Medical University, Chennai

DEPARTMENT OF CARDIOPULMONARY PERFUSION CARE TECHNOLOGY

COURSE NAME: GENERAL PATHOLOGY

I YEAR

UNIT IV: INFECTIOUS DISEASES

TOPIC 5: HEPATITIS B VIRUS

Viral Hepatitis Alphabet

- Hepatitis A
- Hepatitis B
- Hepatitis C
- Hepatitis D
- Hepatitis E

Viral Hepatitis

By ways of transmission

Hepatitis A
Hepatitis E

Enteral route of transmission

Hepatitis B
Hepatitis C
Hepatitis D

Parenteral rout of transmission

Hepatitis B

- Is a Viral infection of the liver caused by the hepatitis B virus
- Hepatitis means “liver inflammation.”

Epidemiology

Epidemiology

- About 2 billion people are infected with HBV infection worldwide
- Around 400 million persons are living with chronic HBV infection
- From 5 to 20% of Asian population is infected with HBV
- 58% of HIV infected patients have coinfection with HBV (AntiHBc(total)

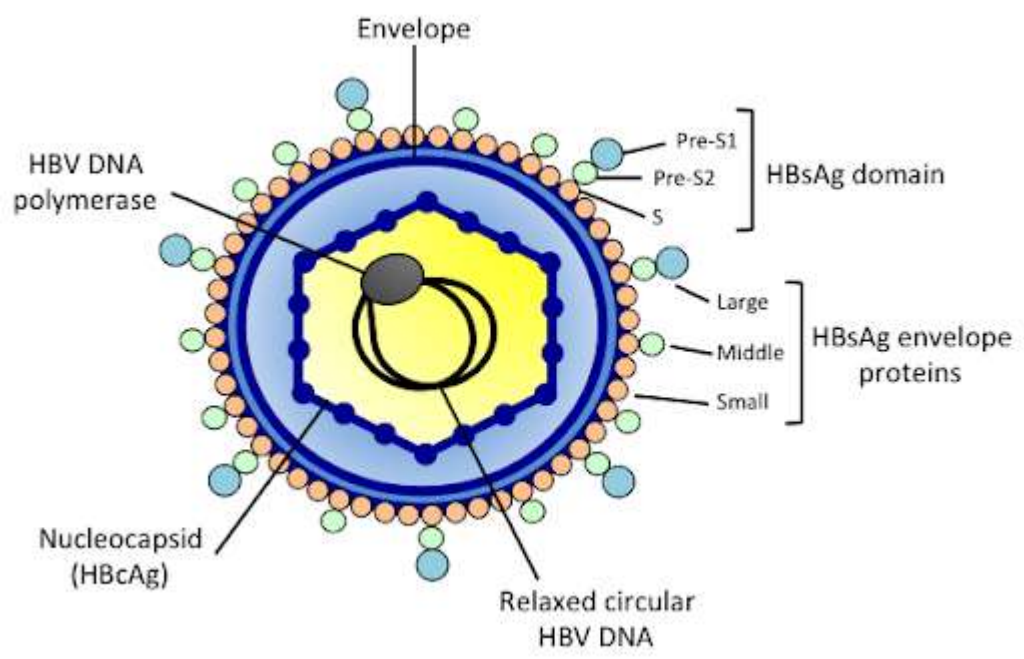
Epidemiology

- Around 1 000 000 patients die due to end stage liver disease caused by HBV
- About 550 000 persons die due to liver cancer caused by chronic HBV infection annually
- This accounts 2 800 deaths everyday
- This is 1-2 deaths every minute
- Annually tens of thousand persons with chronic HBV infection undergo liver transplantation

Etiology

Structure

- DNA virus
- Family- Hepadnaviridae
- Genus – Ortho-hepadnavirus
- Hepatitis B virus is 30-42 nm in diameter.



Transmission

Parenteral Route

- Transfusion of infected blood or its products, using non-sterile syringes, needles and medical instruments, transplantation of infected donor organs or tissues, Occupational exposure with infected blood

Sexual Transmission

- Sexual transmission of HBV is high (40-45%)
- The risk is much higher among persons having multiple sexual partners

Transmission

Mother to child

- Chance of Vertical transmission of HBV is about 10%.
- The risk is increased if HBV viral load in mother's blood is high.

- **HBV is not transmitted HBV is not transmitted by air, droplets, vectors or from animals.**

Risk factors

- Have unprotected sex or with someone who's infected with HBV
- Share needles during intravenous (IV) drug use
- Live with someone who has a chronic HBV infection
- Are an infant born to an infected mother
- Have a job that exposes you to human blood
- Travel to regions with high infection rates of HBV, such as Africa, Central and Southeast Asia, and Eastern Europe Risk Factors

Pathogenesis

- Hepatitis B virus is not directly cytopathic to hepatocytes.

- The fact that patients with defects in cellular immune competence are more likely to remain chronically infected.

- The virus causes persistent infection, chronic hepatitis, liver cirrhosis, hepatocellular carcinoma, and immune complex disease.

- Because hepatocytes are continually proliferating, the virus is constantly being shed into the blood which contributes to chronic infection

HBV Replication

- **Attachment:** The virus enters the cell using endocytosis by binding to a receptor on the surface of the cell.

- **Penetration:** The viral membrane merges with the host cell membrane then sends its DNA and several proteins into the host cell's cytoplasm.

HBV Replication

Uncoating:

- Unlike other viruses, HBV uses RNA to replicate. HBV has partially double stranded DNA that must be made into fully double stranded DNA first.
- Core proteins separate from the partially double stranded viral DNA and make covalently closed circular DNA (cccDNA).
- The cccDNA becomes the transcription template for four mRNAs.

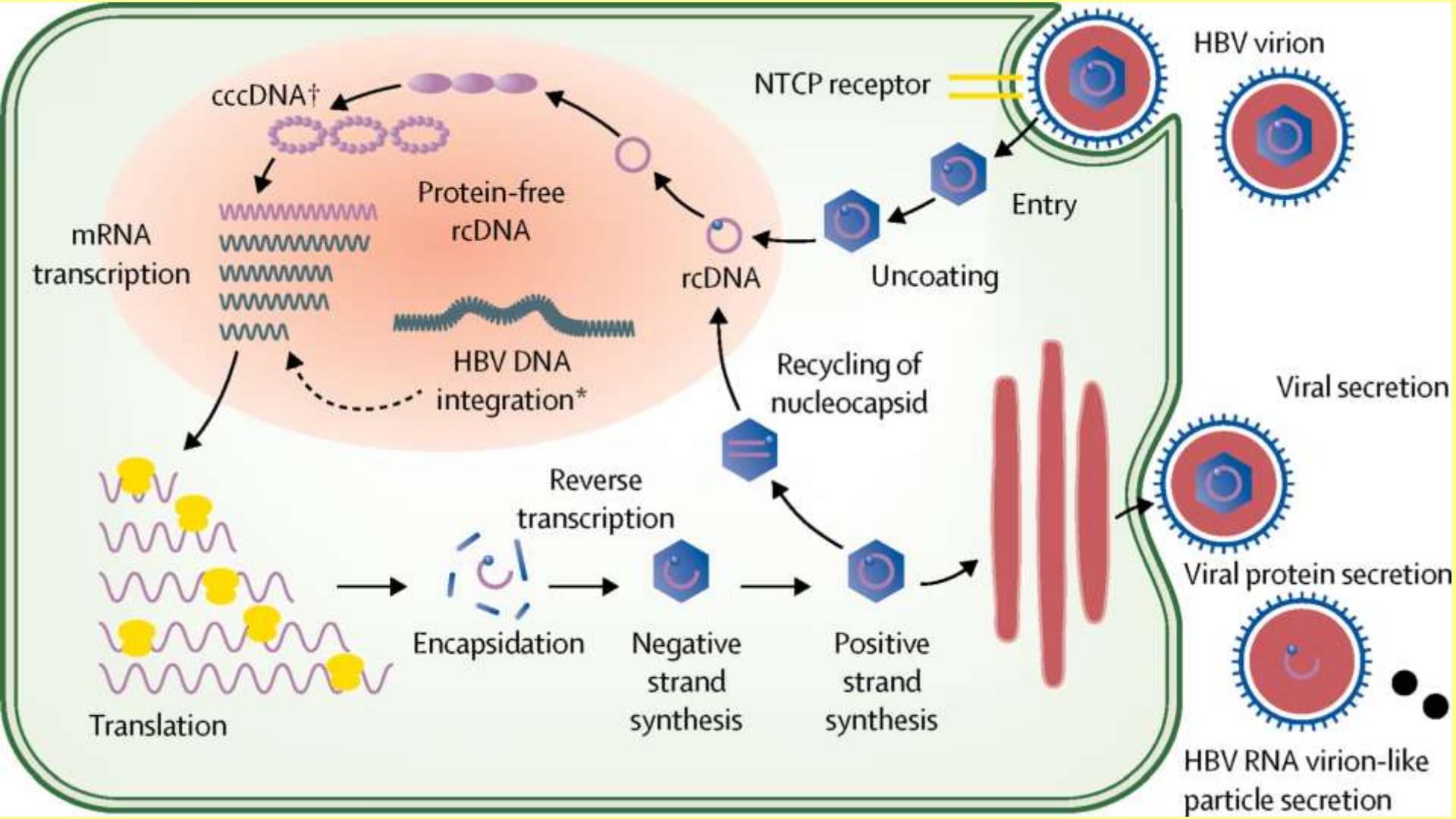
HBV Replication

- **Replication:** The largest of the four mRNA is used to make new copies of the genetic material.

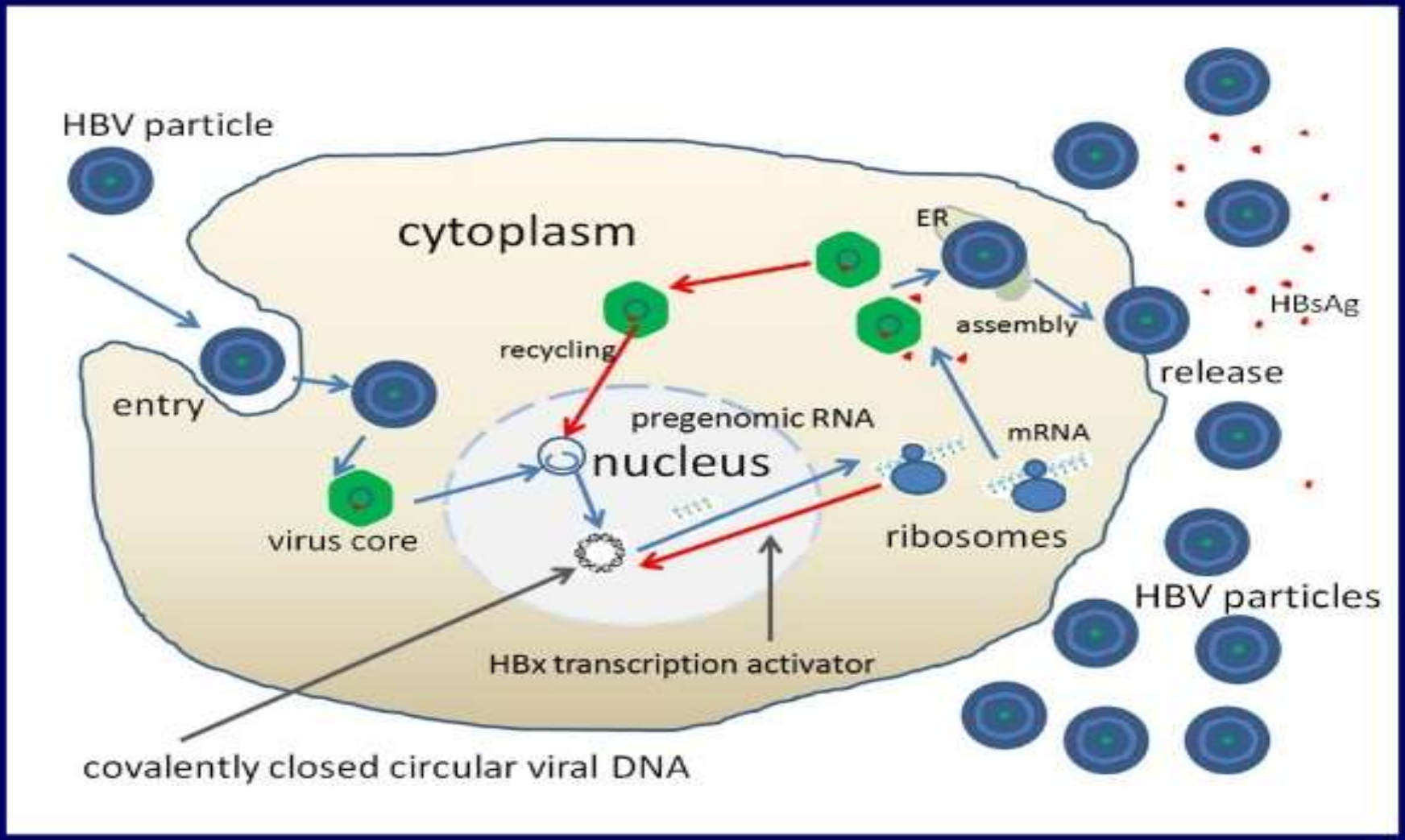
- **Assembly:** The four mRNA are reprocessed, forming progeny virions that are returned to the nucleus where they are recycled and make additional virions.

- **Release:** DNA is synthesized via reverse transcriptase and new virus is sent into the cytoplasm, then towards the cell membrane where it is released

HBV Replication



HBV Replication



Clinical Manifestations

Clinical Features

Two forms of Hepatitis B exists:

- **Acute Hepatitis B**
- **Chronic Hepatitis B**

Acute Hepatitis B

- Acute Hepatitis B is an infectious disease caused by hepatitis B virus, which develops within 6 months after entering virus to the organism.

- Disease has symptomatic (with jaundice and without jaundice) and asymptomatic course.

- In >90% of cases acute hepatitis B is self-limited disease.

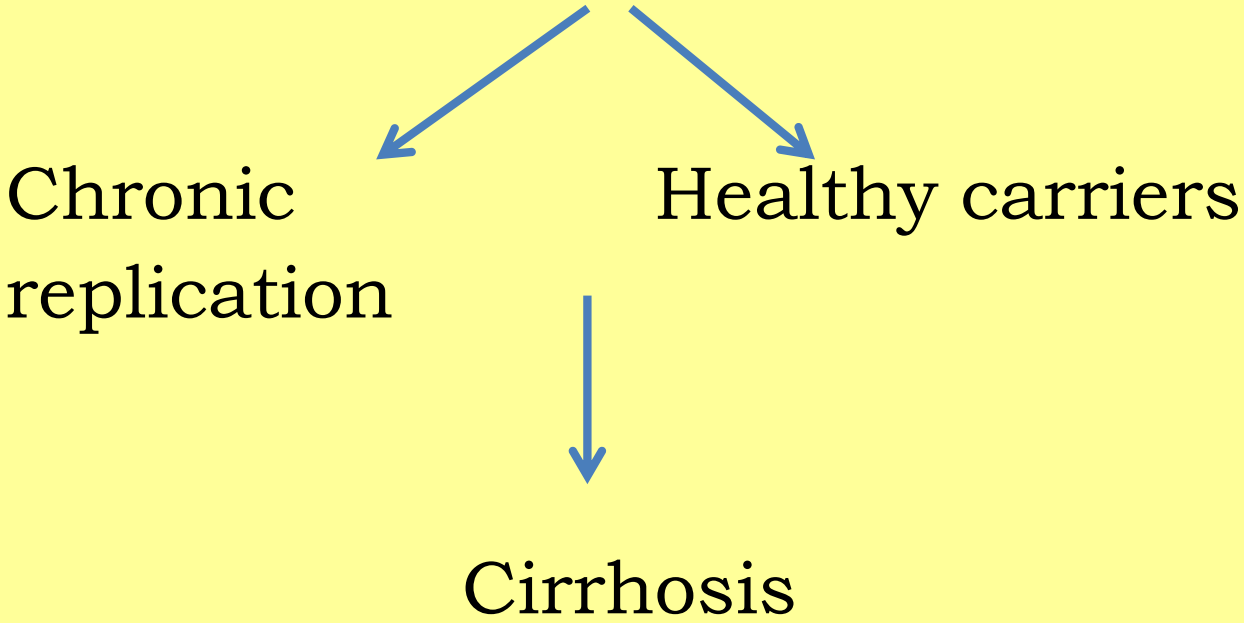
Main Symptoms

- Discomfort in Abdominal cavity
- Jaundices
- Dark urine
- clay-colored stools
- Fever
- Joint pain
- Loss of appetite
- Nausea and vomiting
- Weakness and fatigue

Natural history of Hepatitis B

Acute HBV Infection

- 90% Recovery
- < 10% Persistent infection



Incubation period

- Incubation period for hepatitis B is from 30–180 days (mean, 8–12 weeks)

The prodromal symptoms of acute viral hepatitis B are systemic and quite variable.

Constitutional symptoms:

- anorexia,
- nausea and vomiting,
- fatigue, malaise,
- arthralgia's, myalgia's
- headache, photophobia, pharyngitis

May precede the onset of jaundice by 1–2 weeks.

- Dark urine and clay-coloured stools may be noticed by the patient from 1–5 days before the onset of clinical jaundice

Period of Jaundice

- Mild weight loss (2.5–5 kg) is common
- The liver becomes enlarged and may be associated with right upper quadrant pain and discomfort.
- Splenomegaly are present in 10–20% of patients with acute hepatitis B

Treatment

- In hepatitis B, among previously healthy adults who present with clinically apparent (visible) acute hepatitis, recovery occurs in > 90%

- Therefore, antiviral therapy is not likely to improve the rate of recovery and is not required.

- In rare cases of severe acute hepatitis B, treatment with a **nucleoside analogues (entecavir or tenofovir)** at oral doses is used.

Chronic hepatitis B

- Chronic hepatitis B is a chronic infection caused by HBV which develops after 6 months from acute phase of infection.

- Chronic hepatitis B usually progresses slowly and is characterised with non-specific clinical symptoms.

Serologic and virologic markers

- HBs Ag
- Anti-HBs
- HBe Ag
- Anti- HBe
- Anti-HBc (total)
- Anti-HBc IgM

Each serologic marker has its clinical significant

HBsAg

- After a person is infected with HBV, the **first virology marker** detectable in serum within 1–12 weeks, usually between 8–12 weeks, is HBsAg
- Clinical symptoms appears by 2–6 weeks
- Remains detectable during symptomatic phase of acute hepatitis B and beyond.
- After HBsAg disappears, **antibody to HBsAg (anti-HBs)** becomes detectable in serum (**protective antibody)**

Anti-HBc IgM Anti-HBc IgG

- Anti-HBc of the IgM class (IgM anti-HBc) predominates during the first six months after acute infection, whereas IgG anti-HBc is the predominant class of anti-HBc beyond six months.

- Therefore, patients with current or recent acute hepatitis B, have IgM anti-HBc in their serum.

- In patients who have recovered from hepatitis B, as well as those with chronic HBV infection, anti-HBc is predominantly of the IgG class

Generally, in persons who have recovered from hepatitis B, anti-HBs and anti-HBc persist indefinitely.

HBeAg

- The other readily detectable serologic marker of HBV infection, is HBeAg.
- HBeAg appears concomitantly with or shortly after HBsAg.
- Its appearance coincides temporally with high levels of virus replication and reflects the presence of circulating intact virions and detectable HBV DNA

HBV DNA

- During acute and early chronic HBV infection
- HBV DNA can be detected both in serum and in hepatocytes.
- This replicative stage of HBV infection is the time of maximal infectivity and liver injury
- HBeAg is a qualitative marker and HBV DNA a quantitative marker of this replicative phase.

Hepatitis B Vaccine

- The first vaccine for active immunization, introduced in 1982.
- The first vaccine was purified HBsAg derived from the plasma of healthy HBsAg carriers.
- In 1987, the plasma-derived vaccine was replaced by a **genetically engineered vaccine.**

Hepatitis B Vaccine

- Hepatitis B vaccine is Genetically Engineered recombinant vaccine

- The two available recombinant hepatitis B vaccines are comparable, one containing 10 µg of HBsAg **(Recombivax-HB)** and the other containing 20 µg of HBsAg **(Engerix-B)**, and recommended doses for each injection vary for the two preparations.

After vaccination

- HBs Ag (-) negative
- **Anti-HBs (+) positive**
- HBe Ag (-) negative
- Anti-HBe (-) negative
- Anti-HBc(total) (-) negative
- Anti-HBcIgM (-) negative
- HBV DNA (-) negative

The hepatitis B vaccine is recommended for:

- Newborns
- Children and adolescents not vaccinated at birth
- Anyone who has a sexually transmitted infection, including
- HIV
- Health care workers, emergency workers and other people
- who come into contact with blood
- People with chronic liver disease
- People who inject illicit drugs
- Sexual partners of someone who has hepatitis B
- Travellers planning to go to an area of the world with a high hepatitis B infection rate

Indications for treatment of chronic hepatitis B

This is based mainly on the combination of three criteria:

- Serum HBV DNA levels.
- Serum ALT levels.
- Severity of liver disease.

Treatment

- Entecavir
- Telbivudine
- Lamivudine

THANK YOU

Reference:

Infectious Diseases, AIDS & Clinical Immunology Research Center, Tbilisi. Georgia