Viral hepatitis
Blood Born hepatitis

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Outline

- Introduction to hepatitis
- Characteristics of viral hepatitis
- Mode of transmission
- Markers of hepatitis infections
- Serological profile
- Stages of hepatitis infection
- Lab diagnosis
- Management & treatment

Hepatitis

- Is inflammation of the liver.

Etiology

❑ Primary infection:

- Hepatitis A virus (HAV)
- Hepatitis B virus (HBV).
- Hepatitis C virus (HCV), was known as non-A non-B hepatitis,
- Hepatitis D virus (HDV) or delta virus.
- Hepatitis E virus (HEV).
- Hepatitis F virus (HFV).
- Hepatitis G virus (HGV).

❑ As part of generalized infection:

- (CMV, EBV, Yellow fever virus)

Continued ….

- Hepatitis F has been reported in the literature but not confirmed.
- Viral hepatitis is divided into two large groups, based on the mode of transmission:

1– Enterically transmitted hepatitis or water born hepatitis. This group includes hepatitis A and E viruses.

2– Parenterally transmitted hepatitis or blood born hepatitis. This group includes hepatitis B, C, D & G viruses.

Characteristics of HBV

- Family of *hepadnaviridae.*

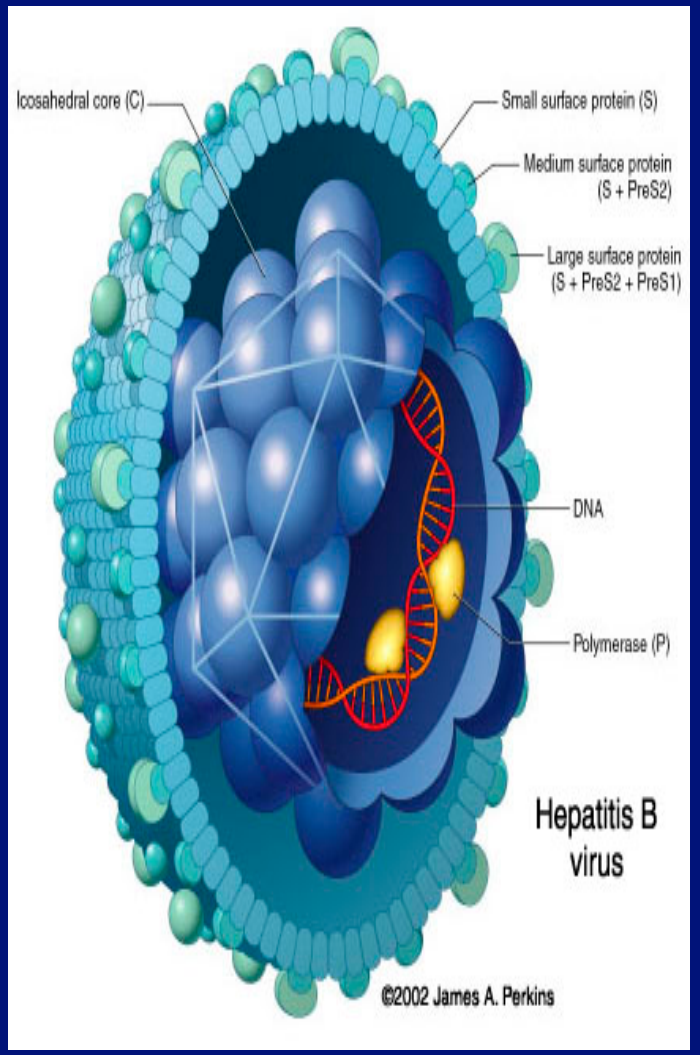
Virion consists of:

➢ Outer envelope containing hepatitis B surface antigen (HBsAg).

➢ Internal core (nucleocapsid) composed of hepatitis B core antigen (HBcAg).

➢ The viral genome which is small partially circular ds-DNA.

➢ The virus contains the enzyme reverse transcriptase.



The size is 42-nm in diameter.

Characteristics of HBV

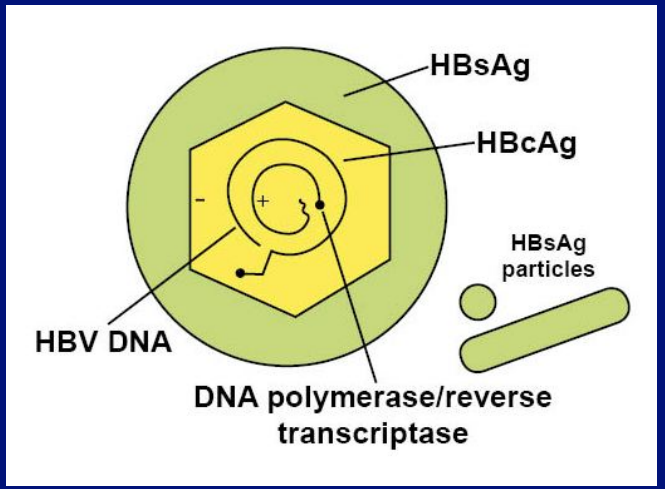
❑ The serum of infected individual contains three types of hepatitis B particles:

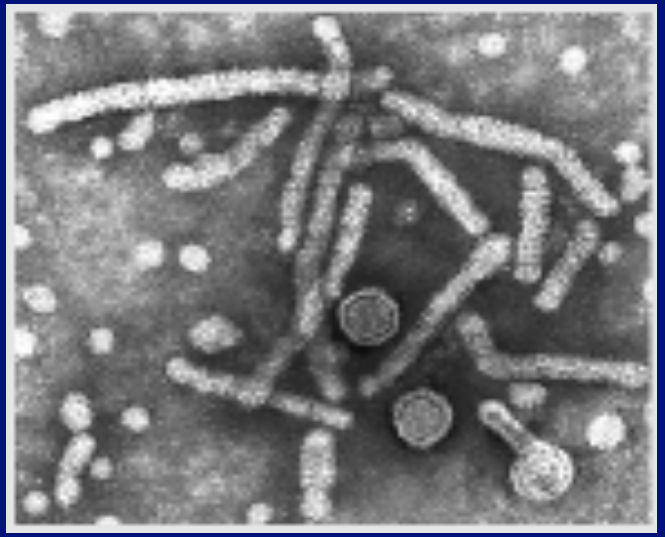
➢ Large number of small spherical free HBsAg particles.

➢ Some of these HBsAg particles are linked together to form filaments.

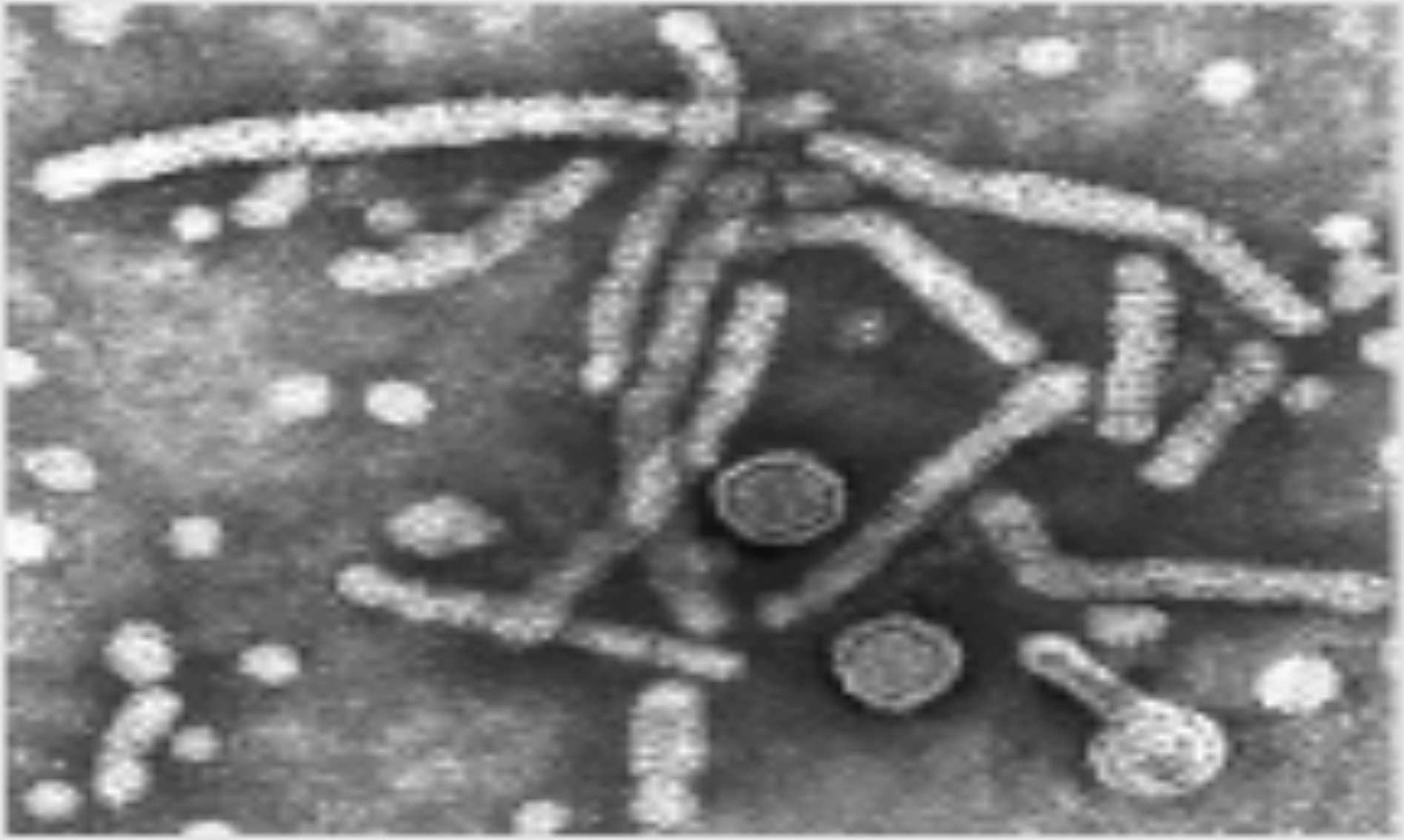
➢ The complete HBV particles (Dane particles).

❑ There are 8 known genotypes (A-H), Genotype D is the dominant in Saudi patients.





Electron micrograph of particles in the blood of a patient infected with HBV



Hepatitis B virus (HBV)

- Hepatitis B viruses is an enveloped, dsDNA virus, and is the major member of the *Hepadanavirus*
- Hepatitis B virus, resist either, low pH, moderate heating
- HBV consists of an outer envelope lipoprotein ***(HBsAg)*** which surrounds an inner core of nucleocapsid protein ***HBcAg*** which surrounds the viral DNA and DNA polymerase and Reverse Transcriptase enzyme.
- ***HBeAg*** is a component of core gene product and *indicate ACTIVE VIRAL REPLICATION* .
- The integrated viral DNA been found in **hepatocellular carcinoma**

Transmission of HBV

1- Parentally:

- Direct exposure to infected blood or body fluids (e.g. receiving blood from infected donor).
- Using contaminated or not adequately sterilized tools in surgical or cosmetic practice (dental, tattooing, body piercing).
- Sharing contaminated needles, razors, or tooth brushes.

2- Sexually :

- The virus is present in blood and body fluids. By having sexual contacts with infected person ,virus is present in semen and vaginal secretion **(homosexual)**

Continued..

3- Perinatally (from mother to baby):

- Infected mothers can transmit HBV to their babies mostly during delivery.
- Breastfeeding is also way of perinatal transmission.
  through placenta (vertical transmission)

➢ **High risk groups INCULDES:**

- Intravenously drug users.
- Hemodialysis patients.
- Patients receiving clotting factors.
- Individuals with multiple sexual partners and homosexuals.
- Health care workers with frequent blood contact.
- Individuals who exposed to tattooing, body piercing or cupping.

Hepatitis B markers

Types	Description
HBV DNA	Marker of infection.
Hepatitis B surface antigen (HBsAg)	Marker of infection.
Hepatitis B e antigen (HBeAg)	Marker of active virus replication, the patient is highly infectious, the virus is present in all body fluids.
Antibody to hepatitis B e antigen (Anti-HBe)	Marker of low infectivity, the patient is less infectious.
Antibody to hepatitis B core (Anti-HBc)	Marker of exposure to hepatitis B infection.
Antibody to hepatitis B surface antigen (Anti-HBs)	Marker of immunity.

Hepatitis B virus

Acute hepatitis B infection;

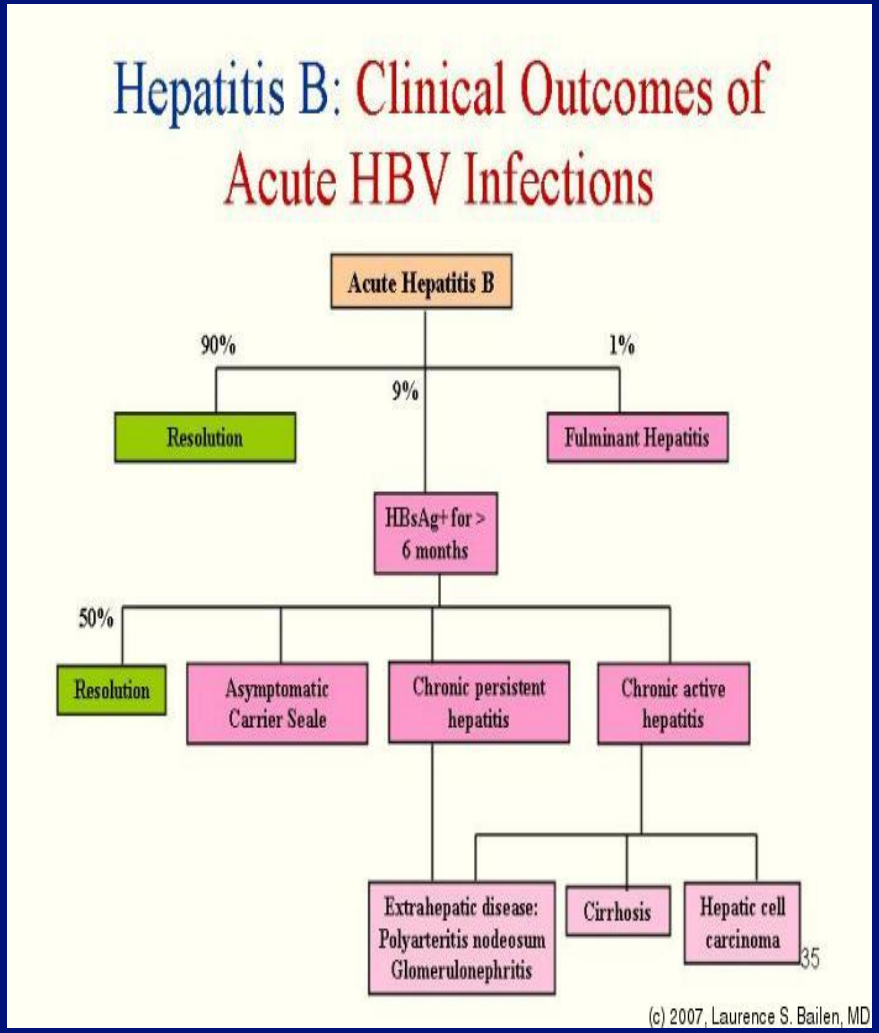
- Incubation period varies from 2 to 4 months.
- Many HBV infection are asymptomatic.
- If symptomatic hepatitis as:
- ***An-icteric hepatitis: (no jaundice)*** fever, malaise , anorexia, rash, nausea, vomiting and high upper quadrant abdominal pain with raised liver enzyme.
- ***Icteric hepatitis:*** **(with jaundice)** about 25% of the patient become icteric Jaundice with raised bilirubin, dark bile containing urine and pale stools .

The clinical outcome of HBV infection

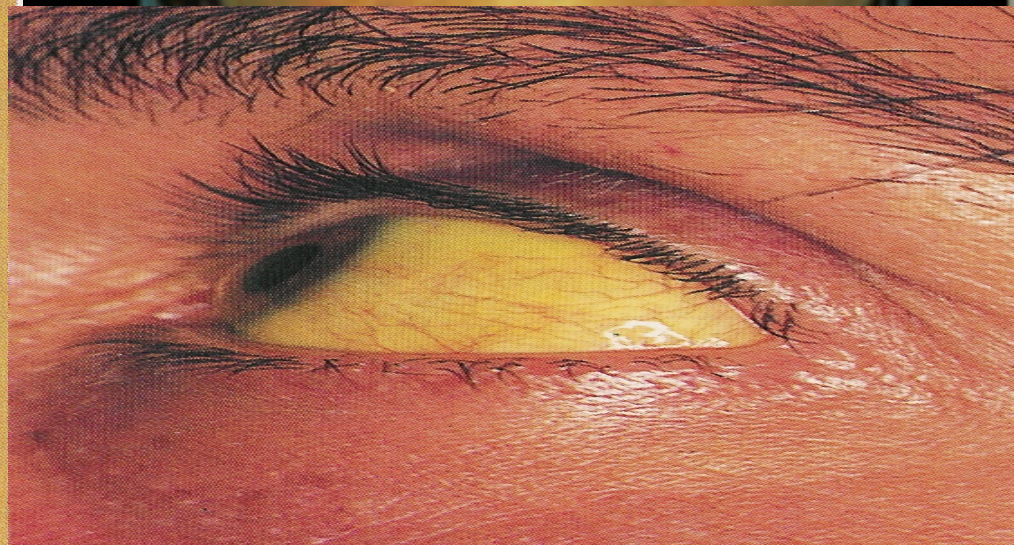
- **About 90 % of infected adults** will develop acute hepatitis B infection and **recover completely.**

- **< 9 % of the infected adult 90% of infected infants** and **20% of infected children** may progress to chronic hepatitis B.

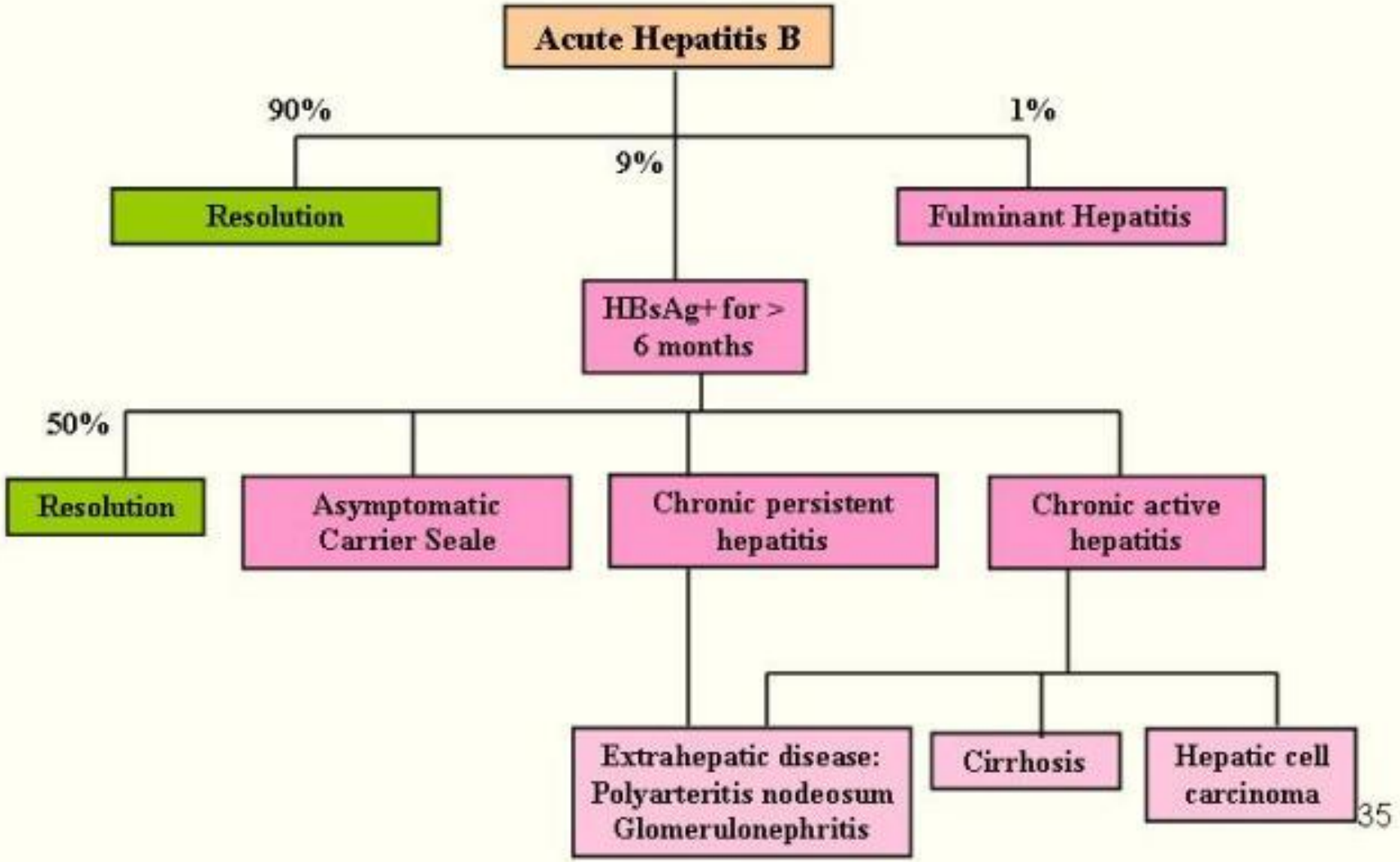
- < 1 % may develop fulminant hepatitis B, characterized by massive liver necrosis, liver failure and death.



Jaundice



Hepatitis B: Clinical Outcomes of Acute HBV Infections

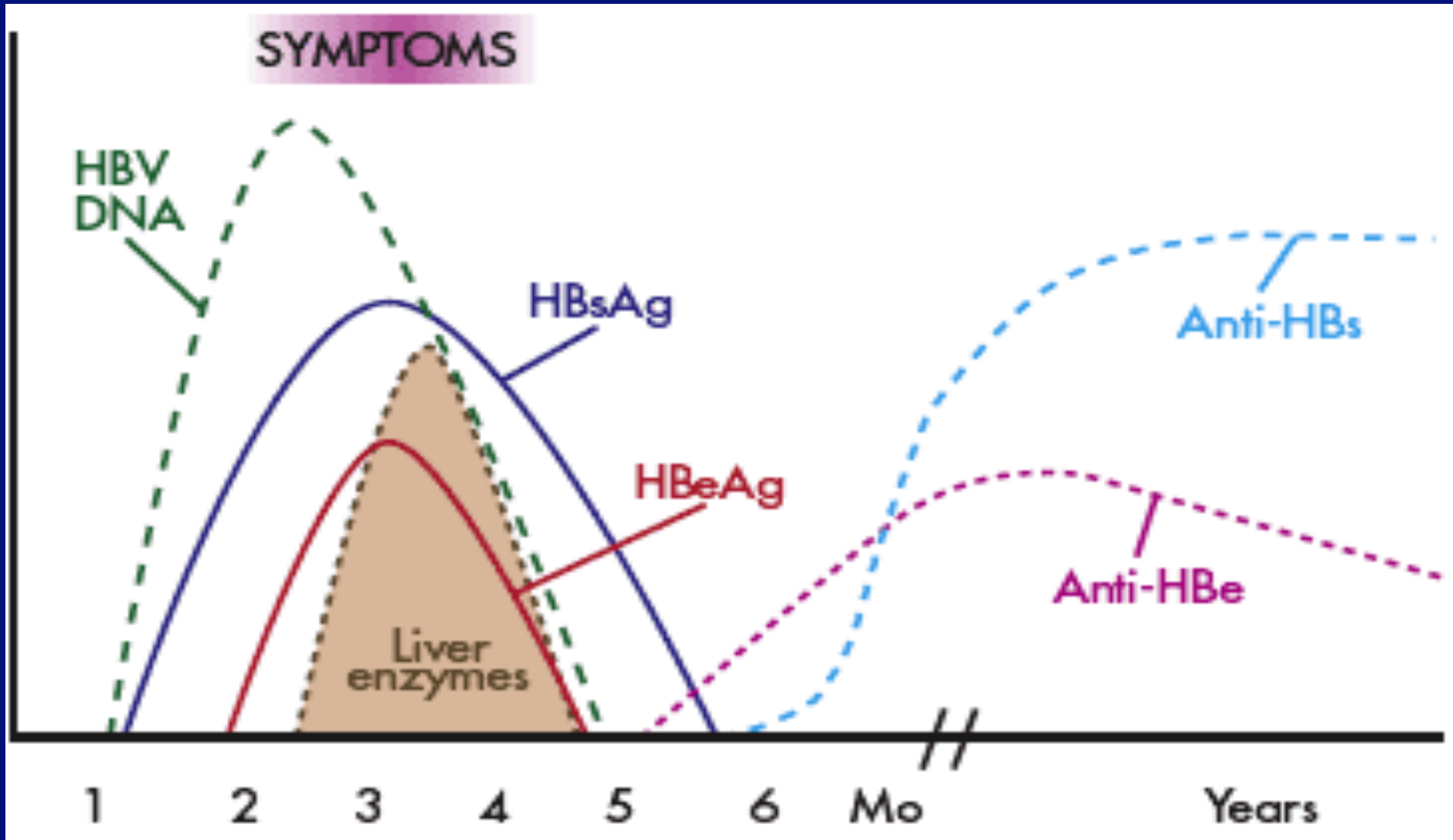


Serological profile of acute HBV infection

- Hepatitis **B DNA** is the 1st marker that appears in circulation, 3-4 weeks after infection.
- **HBsAg** is the 2nd marker that appears in the blood and persists for < 6 months, then disappears.
- **HBeAg** is the 3rd maker that appears in circulation and disappears before HBsAg, it indicate active viral replication.
- **Anti-HBc Ab** is the 1st antibody that appears in the blood and usually persists for several years.
- with the disappearance of **HBeAg** and appearance of **anti-HBe Ab** whish usually persists for several weeks to several months.
- **Anti-HBs Ab** is the last marker that appears in the blood, It appears few weeks after disappearance of HBsAg and persists for several years,

It is the marker of immunity to hepatitis B infection.

Serological profile of acute HBV infection



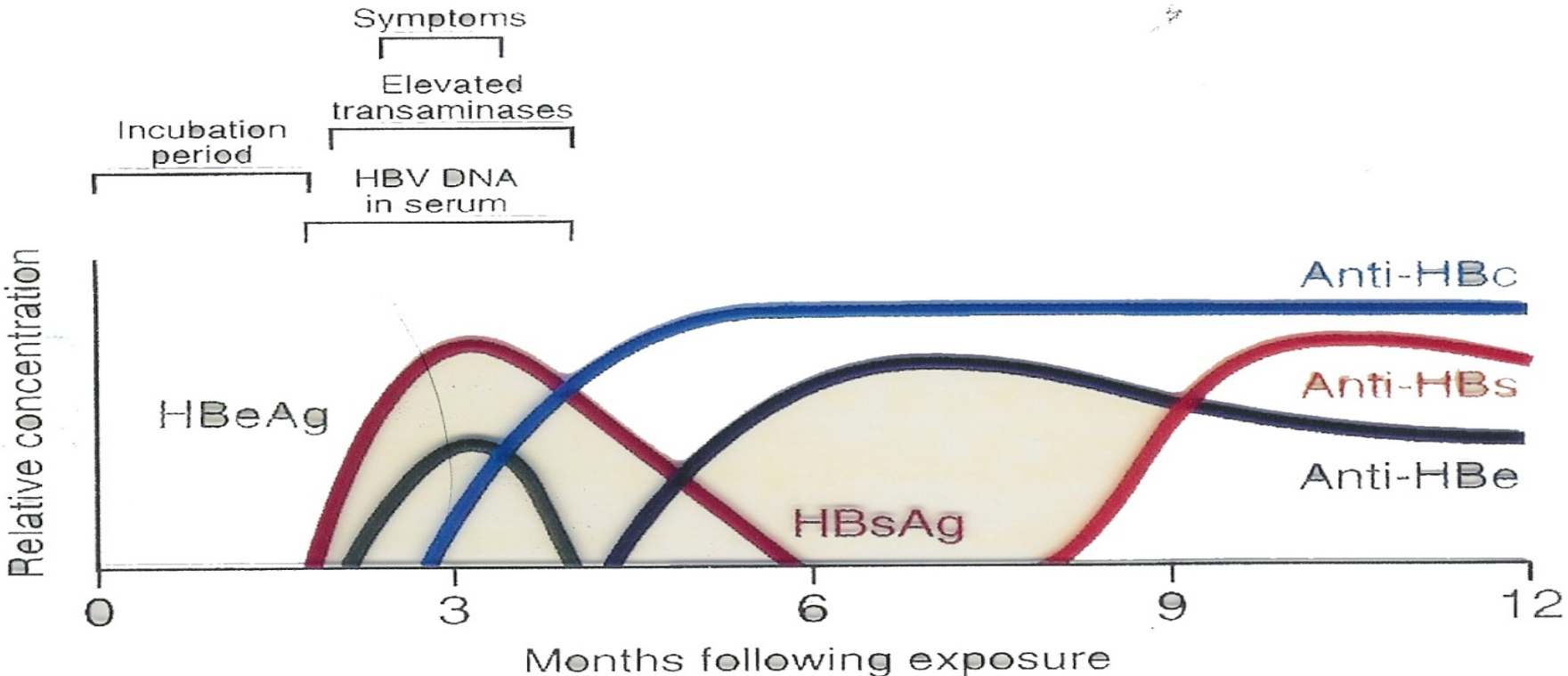
Important information

Notice here the **Anti –HB cAg** is found before any ANTI BODIES either **Anti -HBsAg** or **Anti –HB eAg.**

This antibodies (Anti-HBcAg) indicate viral infection in the past if we detected in immune patient = having both(Anti –HB SAg + Anti-HBc Ag)

Vaccinated patients= having only Anti- HB sAg.

a) Serological profile of acute, resolving hepatitis B



Chronic asymptomatic hepatitis B infection

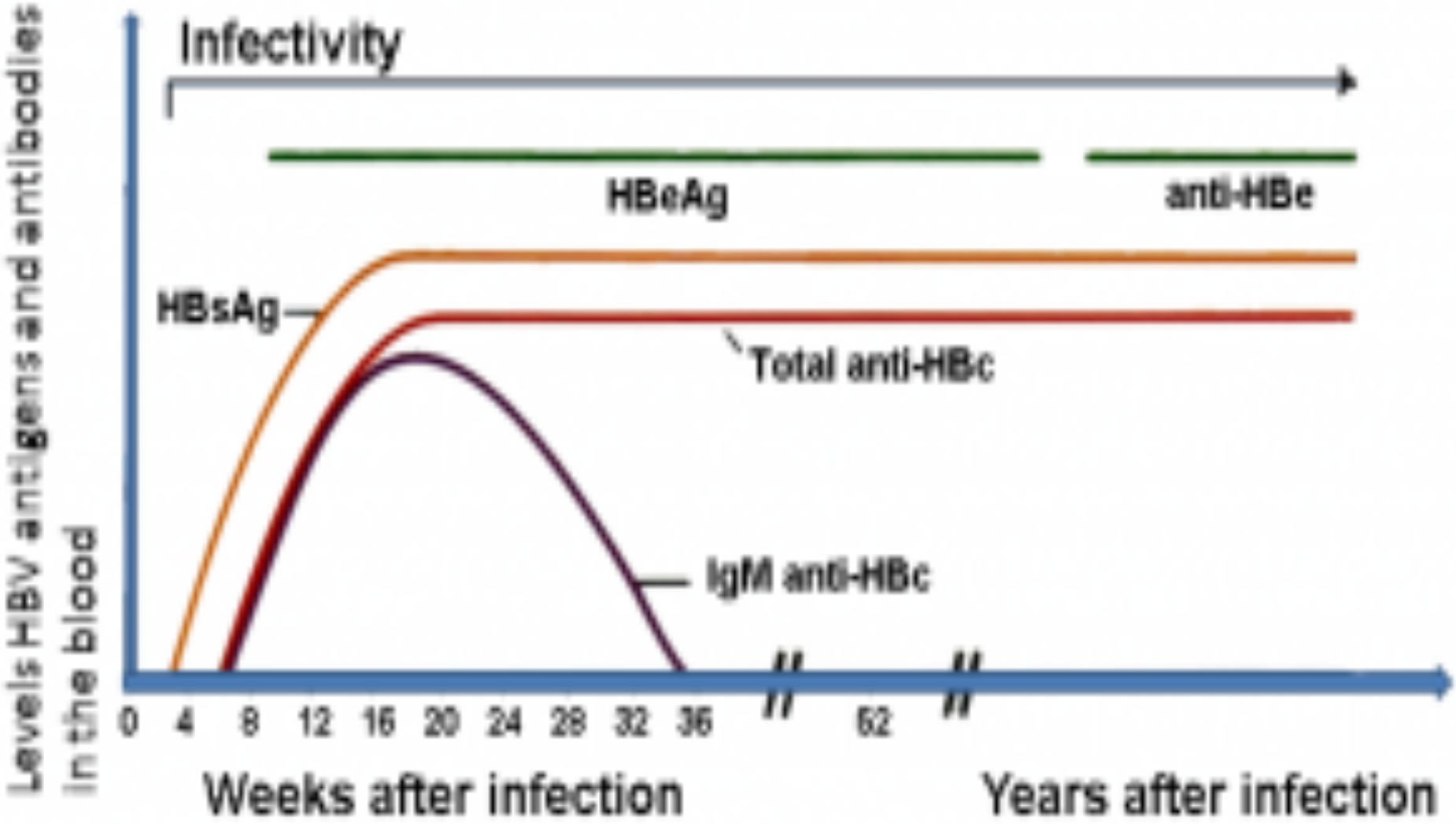
- **Chronic hepatitis B is defined by the presence of HBsAg and HBV-DNA in the blood for > 6 months.**

- The majority of patients with chronic hepatitis B are **asymptomatic** may only be detected by elevated liver enzyme(ALT,AST) on a routine blood chemistry profile , some have mild fatigue, RT upper quadrant abdominal pain or enlarged liver & spleen.

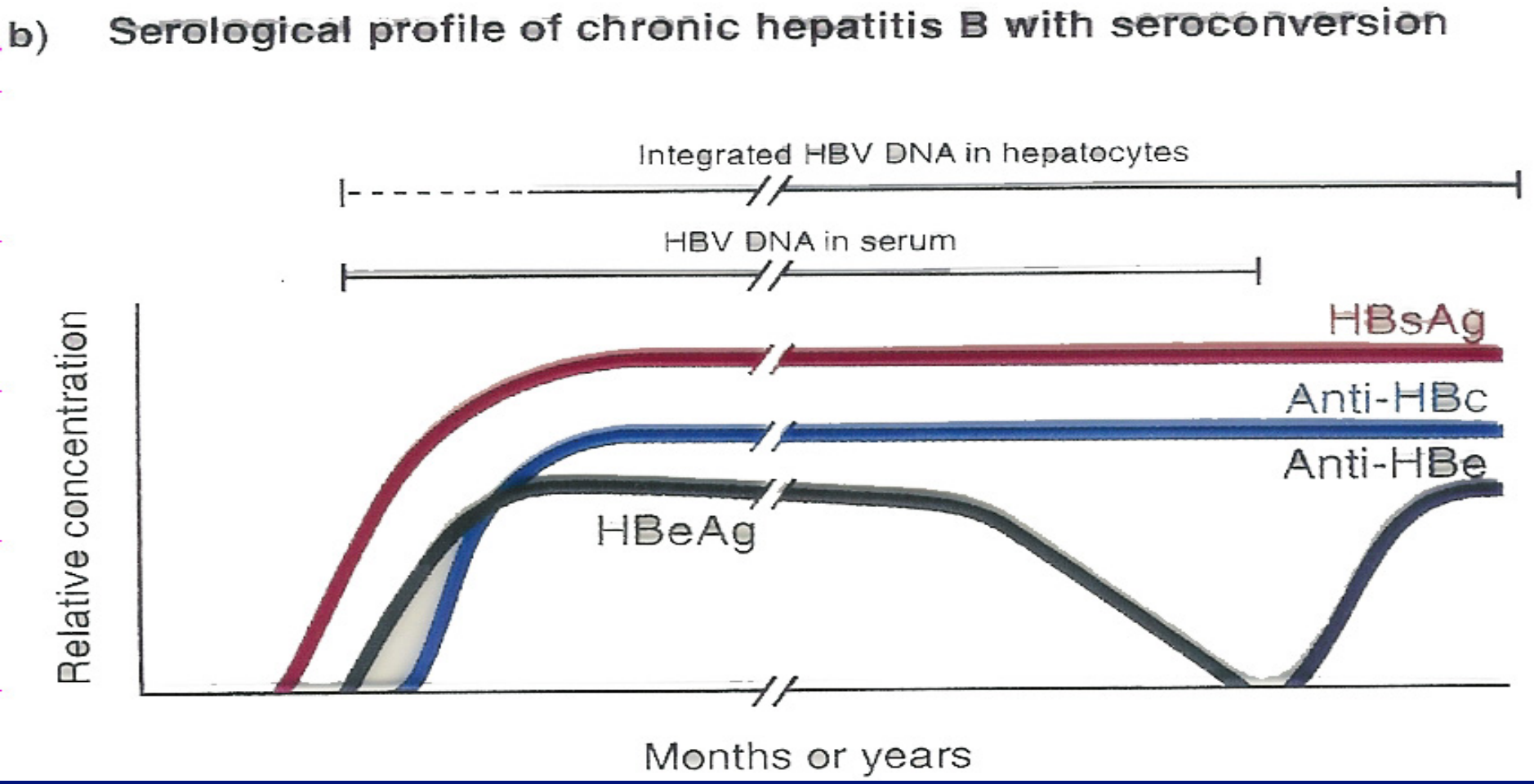
Serological profile of chronic HBV infection

- Chronic hepatitis B infection is defined by the presence of HBV-DNA and HBsAg in the blood for > 6 months.
- **HBsAg** may persist in the blood for life OR
- Some patients will become immune after years and the **HBsAg** disappeared and **anti-HBs Ab** detected in the serum and persists for life.

Serological profile of chronic HBV infection



Notice the Anti- HB cAg founded in the chronic HBV infected patient



Chronic active hepatitis

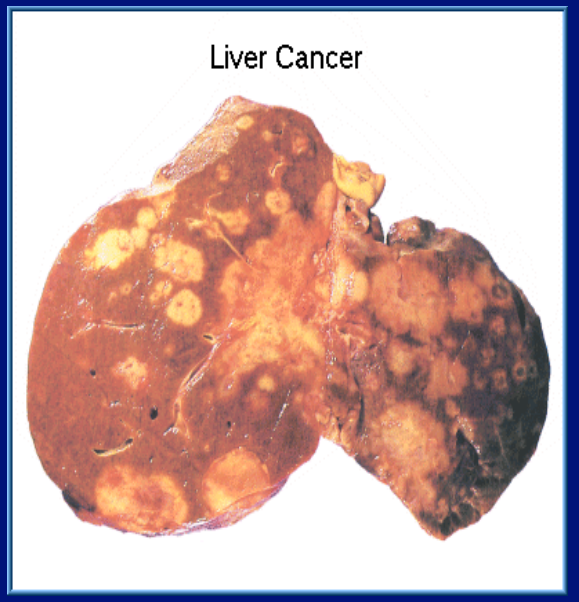
- The major long term risk of chronic HBV infection are cirrhosis with hepatic failure and hepatocellular carcinoma.

Cirrhosis

- Characterized by fibrosis and nodular formation.
- Results from liver cell necrosis and the collapse of hepatic lobules.
- Symptoms includes: ascites, coagulopathy (bleeding disorder), portal hypertension, hepatic encephalopathy, vomiting blood, weakness, weight loss.

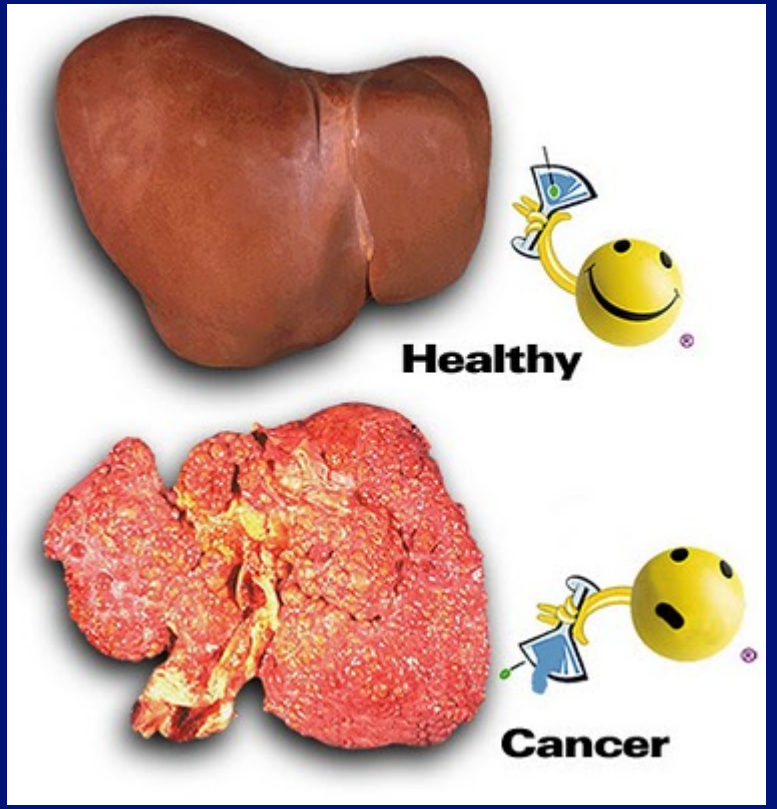
Hepatocellular carcinoma (HCC)

- One of the most common cancer in the world. Also, one of the most deadly cancer if not treated.
- Hepatitis B and C viruses are the leading cause of chronic liver diseases.
- Symptoms include: abdominal pain, abdominal swelling, weight loss, anorexia, vomiting, jaundice.
- Physical examination reveals hepatomegaly, splenomegaly and ascites.



Hepatocellular carcinoma

- Prognosis: without liver transplantation, the prognosis is poor and one year survival is rare.
- Diagnosis: alpha-fetoprotein measurement with multiple CT-abdominal scan are the most sensitive method for diagnosis of HCC.
- Treatment: surgical resection and liver transplant.



Lab diagnosis of hepatitis B infection

- Hepatitis B infection is diagnosed by detection of HBsAg in the blood.
  - Positive results must be repeated in duplicate.
  - Repeatedly reactive results must be confirmed by **neutralization test**.
  - Detection of HB-DNA by PCR.

- Additional lab investigations:

1- Liver function tests (LFT).

2- Ultrasound of the liver.

3- Liver biopsy to determine the severity of the diseases.

Hepatitis B vaccine

- It contains highly purified preparation of HBsAg particles, produced by genetic engineering in yeast.
- It is a recombinant and subunit vaccine.
- The vaccine is administered in three doses at 0,1, & 6 months.
- The vaccine is safe and protective.

Hepatitis B virus

Prevention and Control:

- **Pre-exposure prophylaxis:**
  - Active vaccination given to all newborn, children or adult.

Recombinant hepatitis B vaccine:

It is prepared by cloning HBsAg in yeast cells. The vaccine is given in 3 IM injection at 0-1-6 months and booster dose after 5 years.

- **Post exposure prophylaxis:**
- Persons exposed to needle prick or infant born to +ve HBsAg mother should immediately receive both: Active vaccine and hepatitis B specific immunoglobulin.

Treatment of hepatitis B infection

- There are several approved antiviral drugs:

1- Pegylated alpha interferon, one injection per week, for 6- 12 months.

2- Lamivudine, antiviral drug, nucleoside analogue. One tablet a day for at least one year.

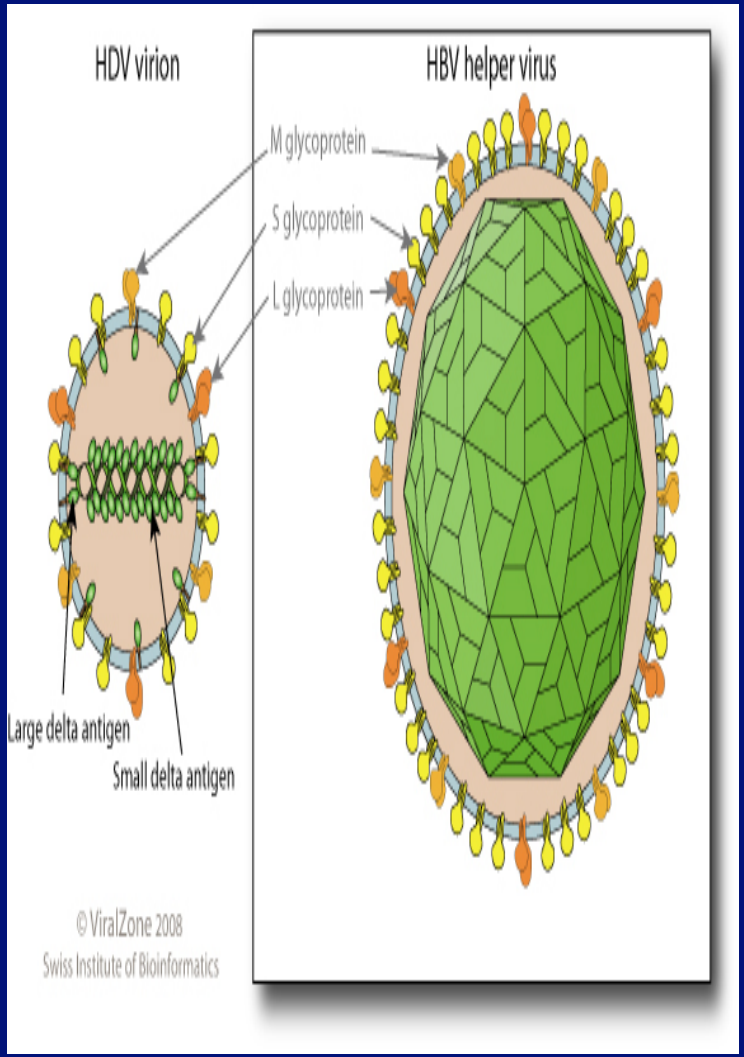
3- Adefovir, antiviral drug, nucleoside analogue. One tablet a day for at least one year.

- Treatment is limited to patients having chronic hepatitis B based on liver biopsy.

- Criteria for treatment:
- Positive for HBsAg
- Positive for HBV-DNA > 20,000 IU/ml.
- ALT > twice the upper normal limit .
- Moderate liver damage.
- Age > 18 years.

Hepatitis D virus (delta virus): Structure

- It is a defective virus, that cannot replicates by its own.
- It requires a helper virus.
- The helper virus is HBV.
- HBV provides the free HBsAg particles to be used as an envelope.
- HDV is small 30-40 nm in diameter.
- Composed of small ss-RNA genome, surrounded by delta antigen that form the nucleocapsid.



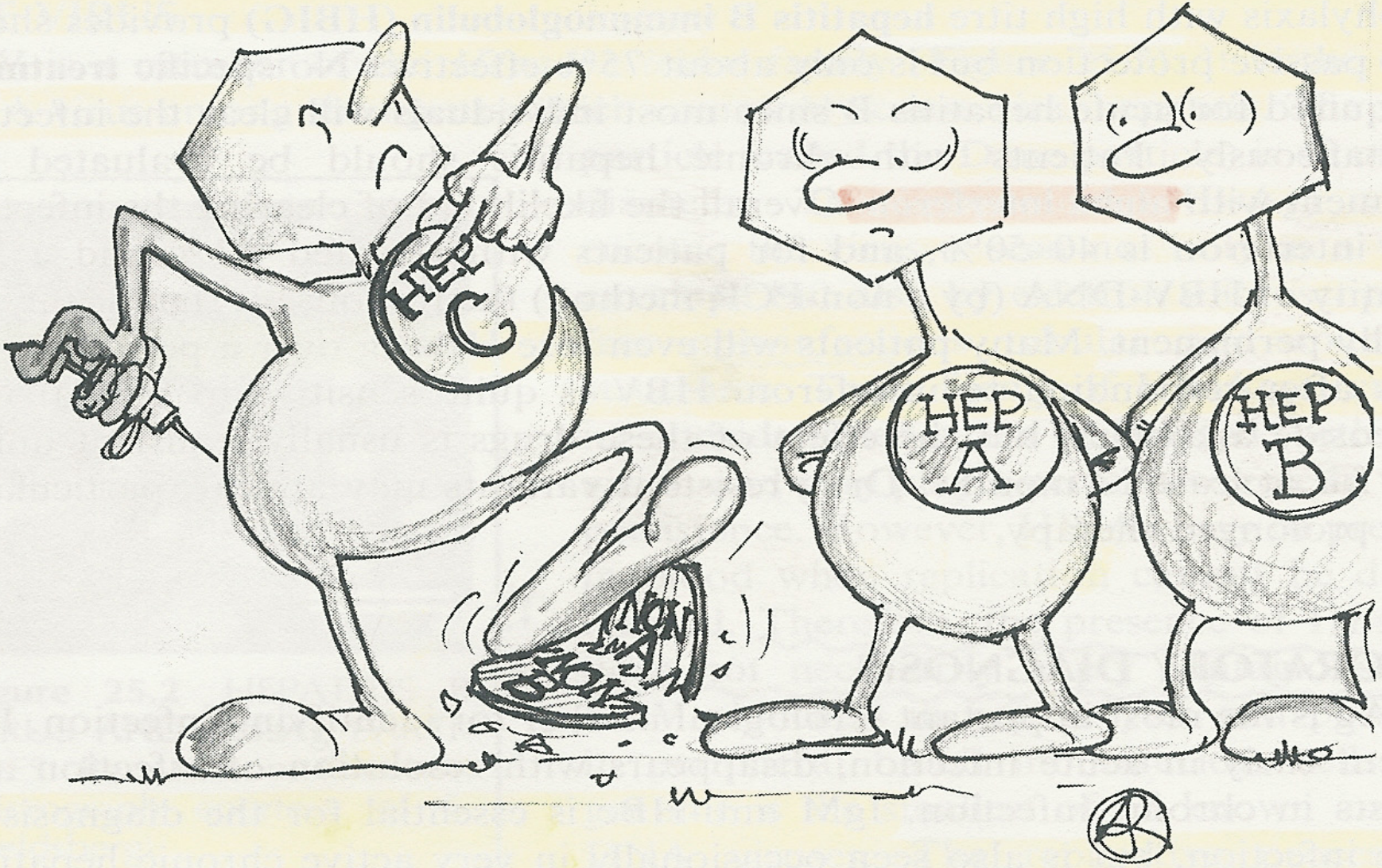
Types of HDV infections

➢ *1- Co-infection:*

- ❖ The patient is infected with HBV and HDV at the same time leading to severe acute hepatitis .
- ❖ Prognosis: recovery is usual.

➢ *2- Super infection:*

- ❖ In this case, delta virus infects those who are already have chronic hepatitis B leading to severe chronic hepatitis.



FINALLY NAMED, SEE?!

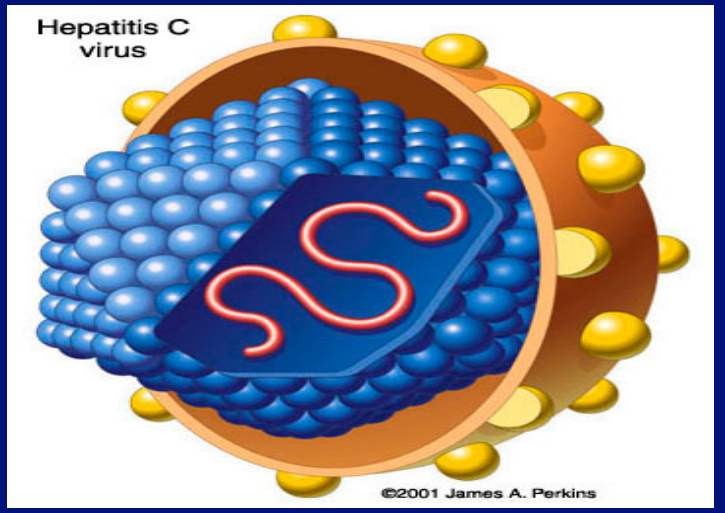
Hepatitis C virus: Classification & structure

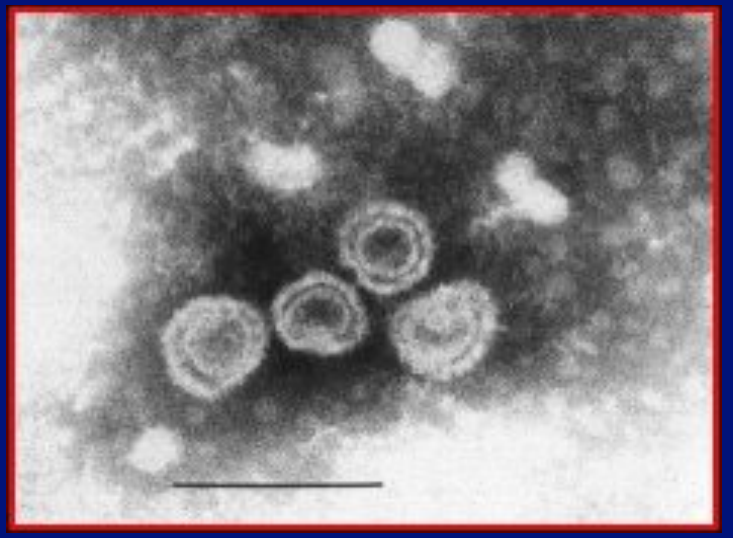
- Family: *Flaviviridae.*
- Genus: *hepacivirus.*

- The virus is small, 60 – 80 nm in diameter.

- Consists of an outer envelope, icosahedral core and linear positive polarity ss-RNA gemone.

- There are 6 major genotypes (1 – 6), genotype 4 is the dominant in Saudi patients.





Transmission of HCV

Similar to HBV:

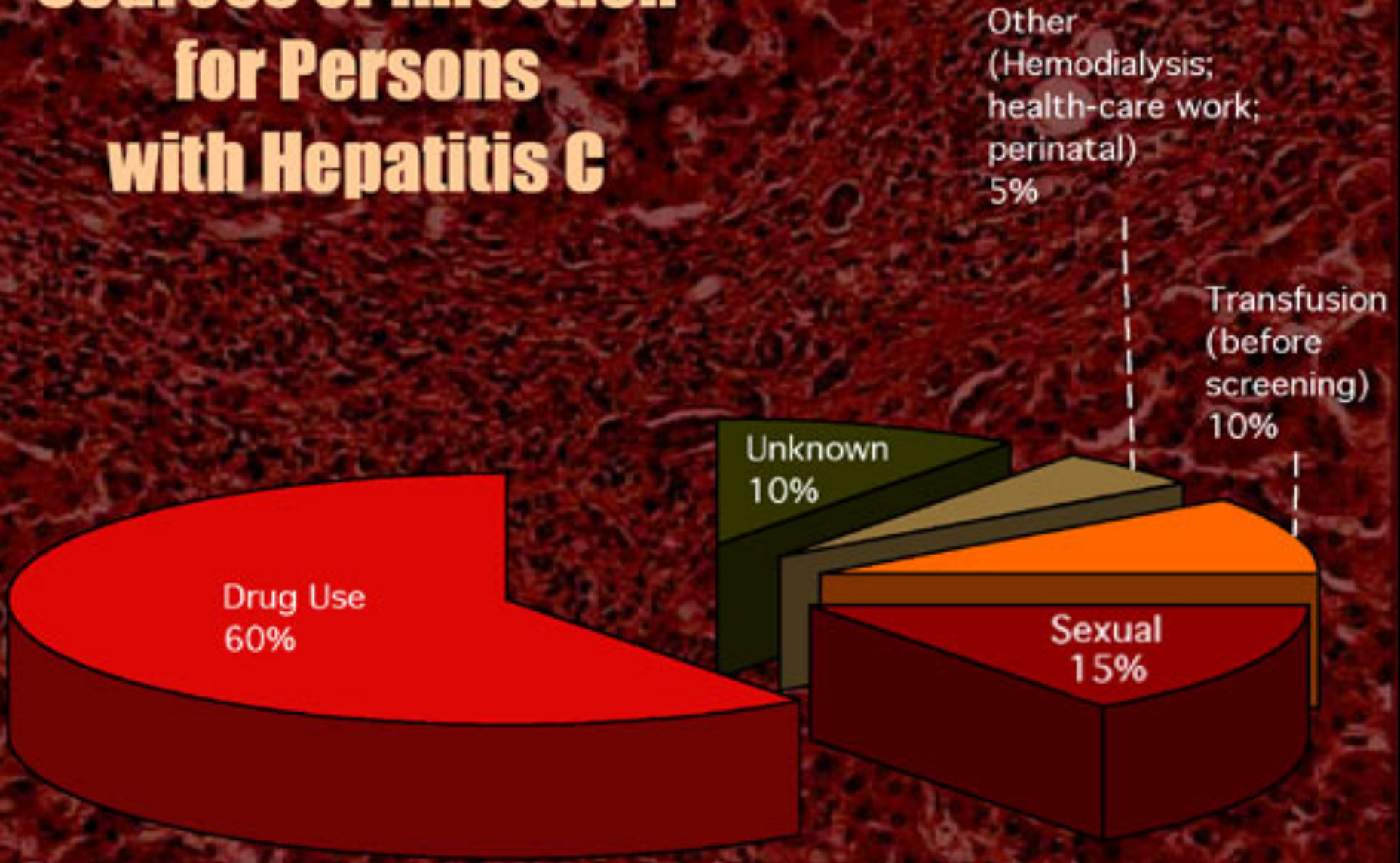
1- Parenterally:

- Direct exposure to infected blood.
- Using contaminate needles, surgical instruments.
- Using contaminate instruments in the practice of tattooing, ear piercing & cupping.
- Sharing contaminated razors 7 tooth brushes.

2- Sexually.

3- From mother to child perinatally.

Sources of Infection for Persons with Hepatitis C



Hepatitis C markers

- ***Hepatitis C virus – RNA .***
- Is the first marker that appears in the serum, it appears as early as 2-3 weeks after exposure , **It is a *marker of infection***
  Ig G Antibody to hepatitis C.

❖ **Antibodies to hepatitis C virus is the last marker that appears in the serum , usually appear 50 days after exposure**
long window period.
This Ab present in both
Acute or chronic patient.

Hepatitis C markers

- *1- hepatitis C virus RNA.*
- Is the 1st marker that appears in circulation, it appears as early as 2-3 weeks after exposure. It is a *marker of infection.*

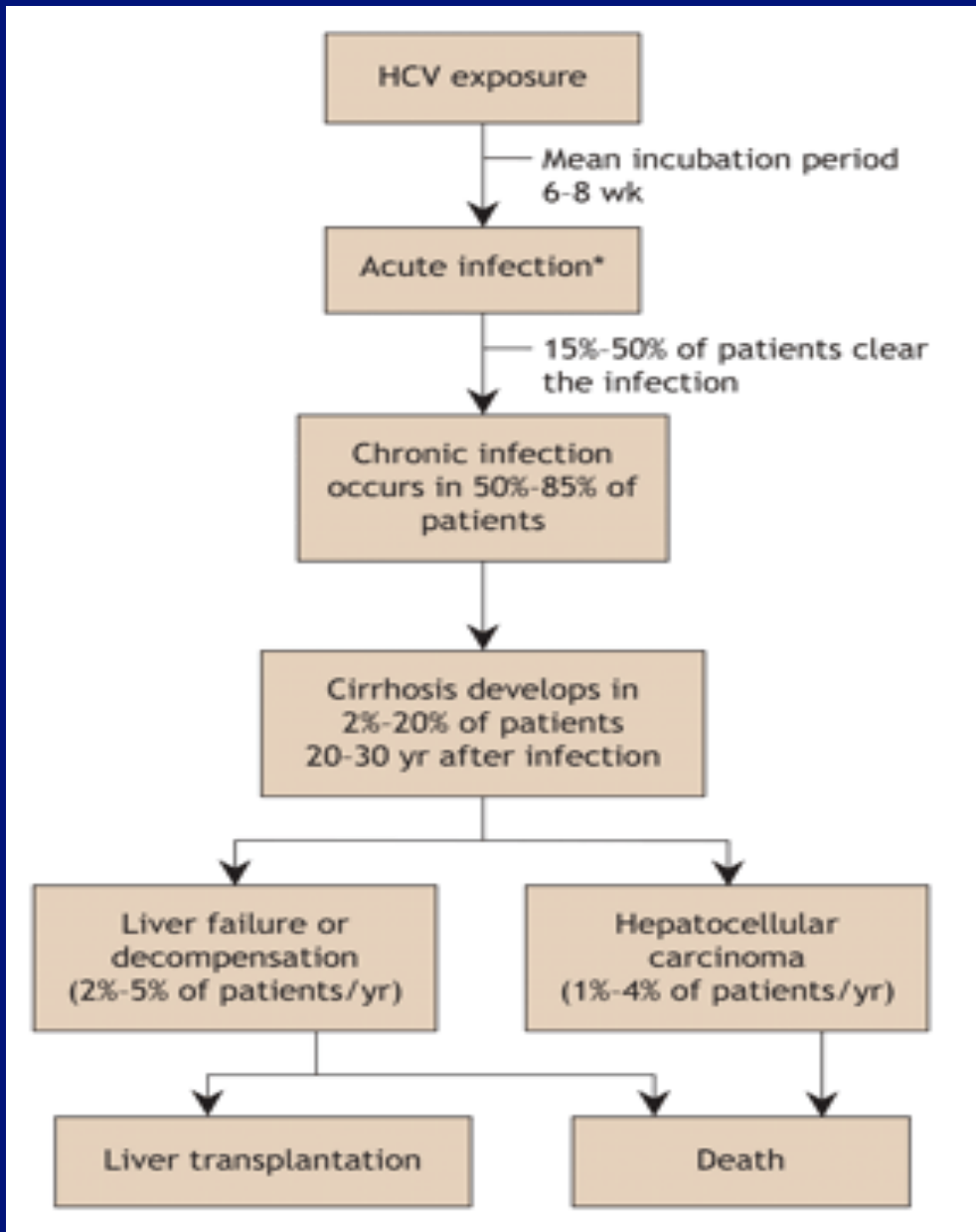
- *2- hepatitis C core antigen.*
- The 2nd marker that appears in the blood, usually 3-4 weeks after exposure. Marker of infection .

- *3- IgG antibody to hepatitis C.*
- Antibodies to hepatitis C virus is the last marker that appears in the blood, usually appear 50 days after exposure (long window period).

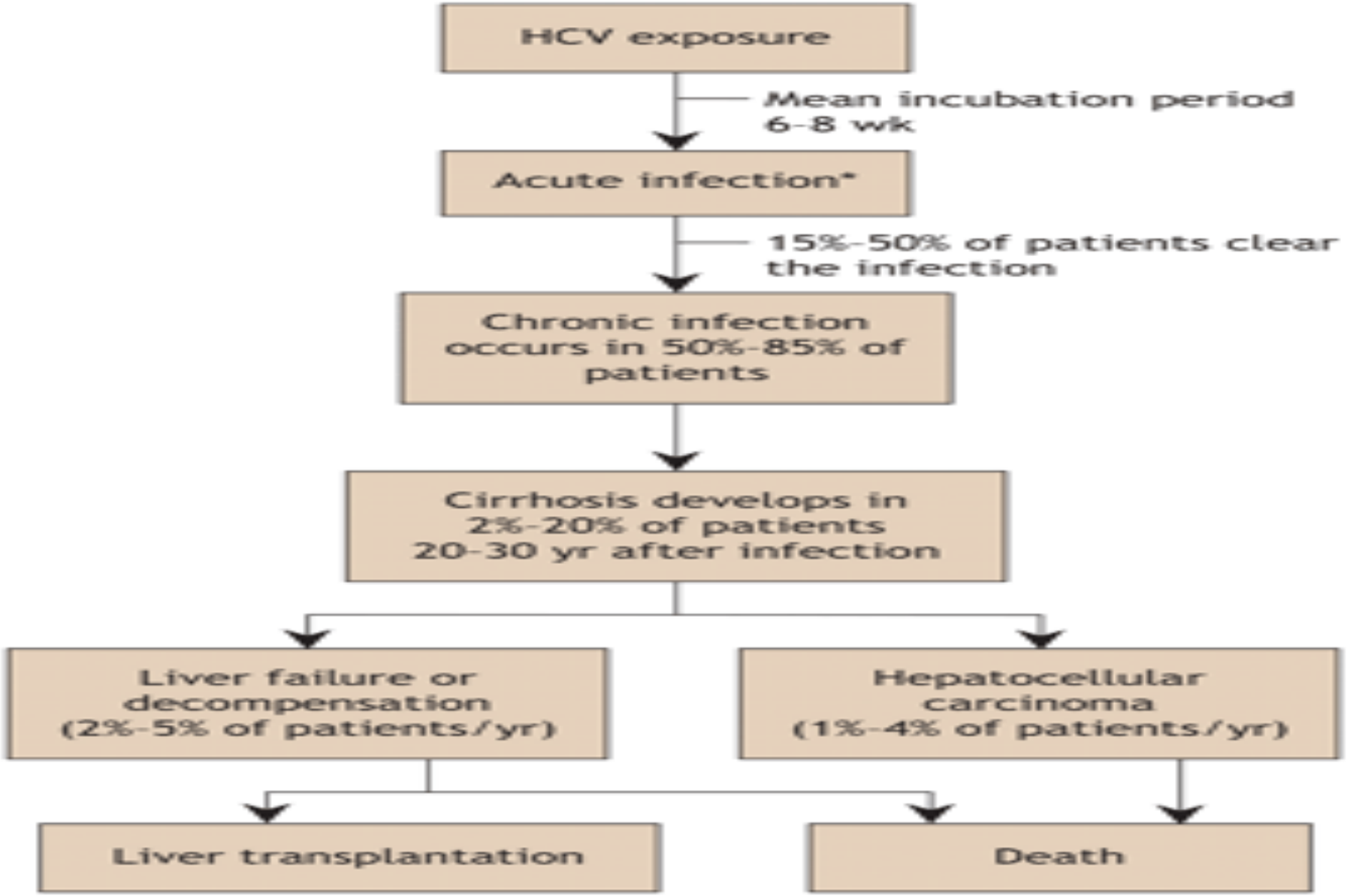
The clinical outcome of HCV infection

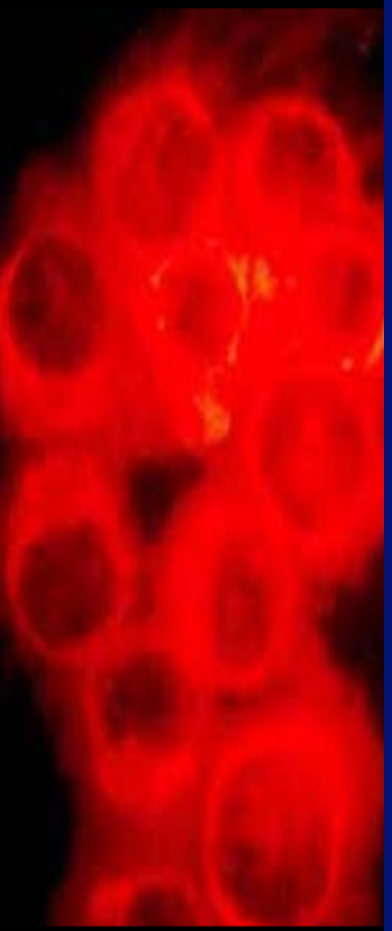
- **About 20 % of the infected individuals will develop self-limiting acute hepatitis C and recover completely.**

- **About 80 % of the infected will progress to chronic hepatitis C.** *about 10%-30% of them can develop cirrhosis within 30 years and liver cancer.* Less than 1 % will develop acute fulminant hepatitis C , liver failure and death.



Out come of HCV

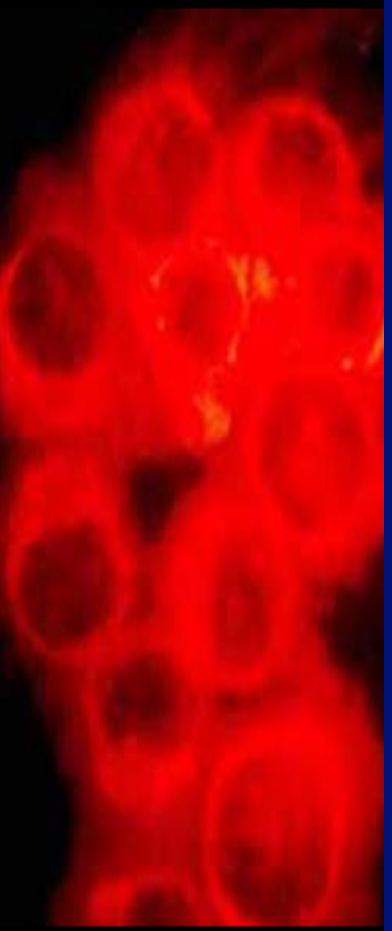




OUTCOMES

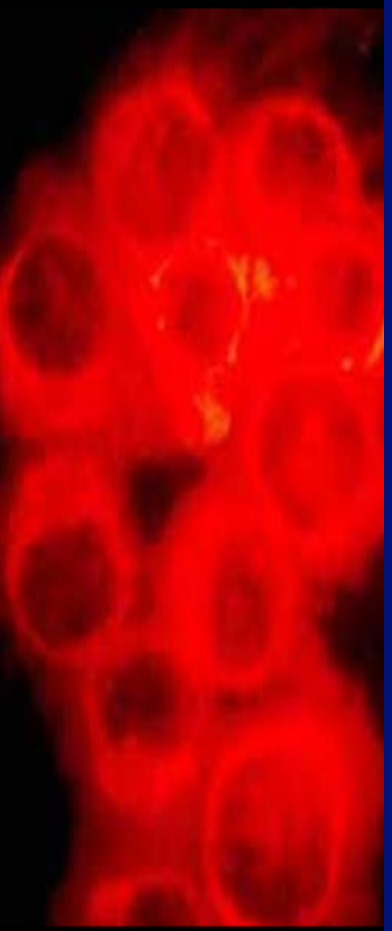
- At least 80% of acute HCV will develop chronic infection.
- Almost 20-40% of chronic hepatitis C develop cirrhosis within 10-20 years.
- Smaller percentage with chronic disease & cirrhosis develop cancer after 20-40 years.

- **Risk factor to develop cancer:**
  - Men.
  - Alcohol consumption.
  - Age above 40 years.
  - Patient with cirrhosis.
  - Infection with HCV for more than 20 to 40 years.



ACUTE HEPATITIS

- Symptom: jaundice, fatigue & nausea.
- Elevated serum ALT (usually greater than 10 folds).
- Presence of anti-HCV (-ve in 30-40%) in early stages of disease.
- HCV-RNA is +ve even before the onset of symptoms.



CHRONIC HEPATITS

- Defined as the presence of anti-HCV & elevated serum level of ALT for >6 ms.
- Almost all patients with chronic hepatitis C have the genome HC RNA in serum.
- Usually asymptomatic, but if symptom present it's usually mild, non-specific & intermittent.
- Lab finding:
  - Elevated ALT & AST ranging from 3-20 times
  - ALT >AST.

Lab diagnosis of hepatitis C infection

- **By detection of both:**

1- **Antibody to HCV in the blood by ELISA, if positive the result must be confirmed by RIBA or PCR.**

2- HCV-RNA in the blood using PCR.

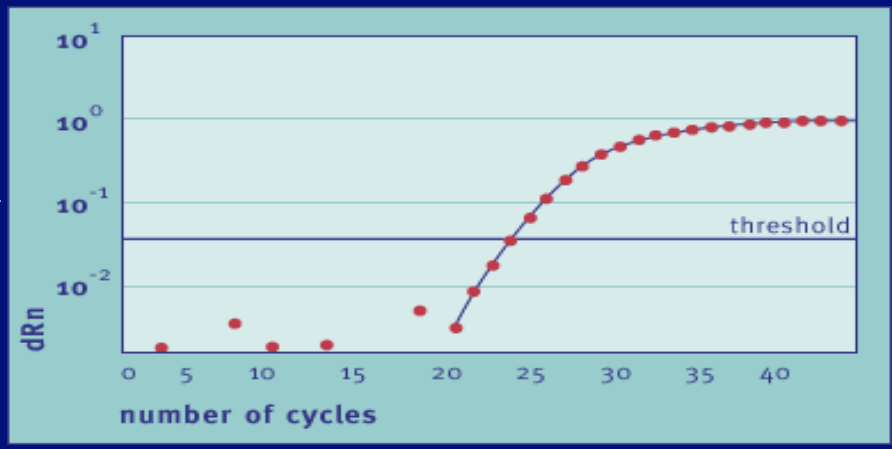
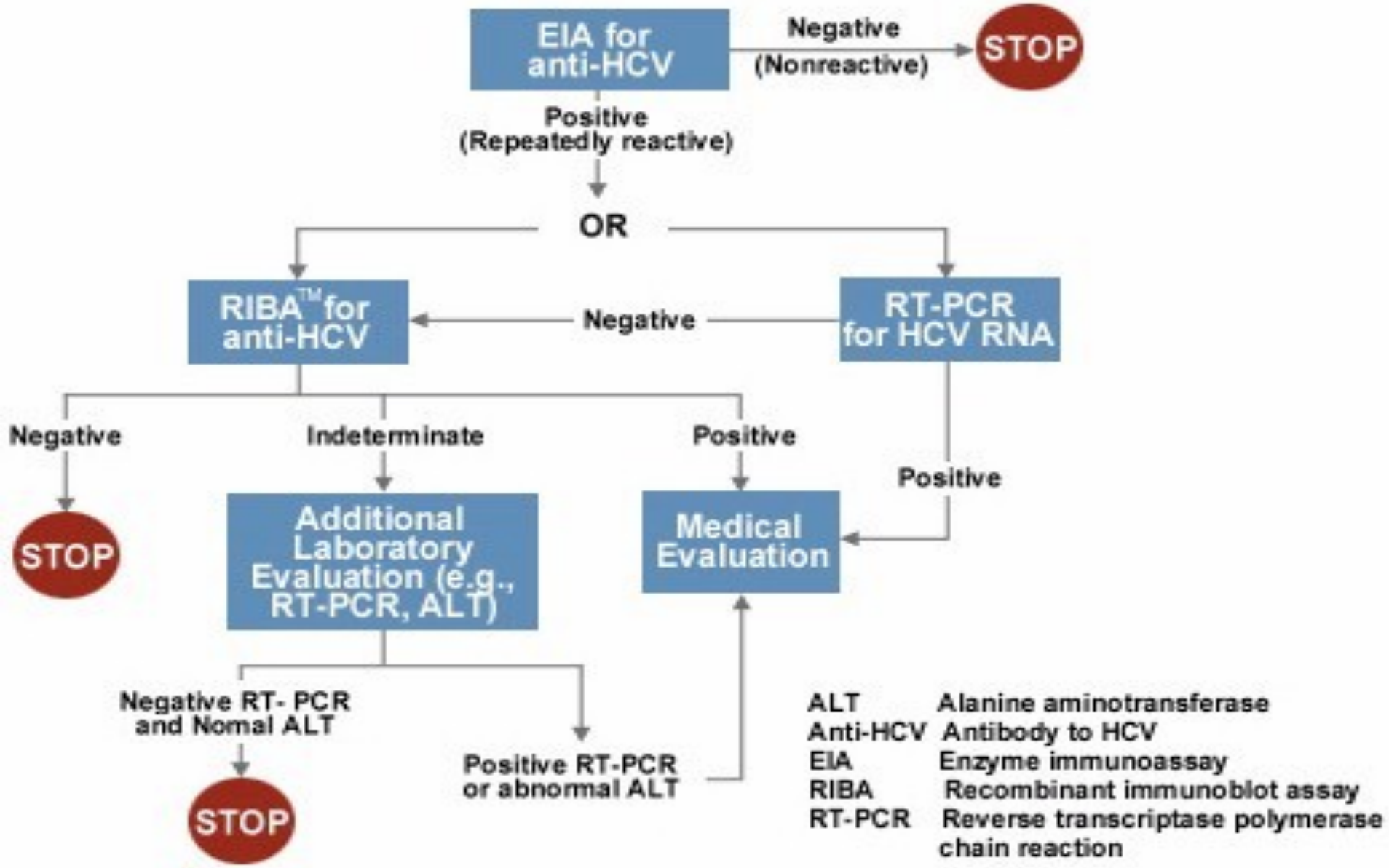


Figure 3. Hepatitis C virus (HCV)-infection-testing algorithm for asymptomatic persons



Treatment of hepatitis C infection & vaccine

- **The currently used treatment is the combined therapy using both :**
  Pegylated alpha interferon & ribavirin.***

- **Criteria for treatment:**
- **Positive for HCV-RNA.**
- **Positive for anti-HCV.**
- **Known HCV genotype.**
- **ALT > twice the upper normal limit.**
- **Moderate liver damage based on liver biopsy.**

there is no vaccine available to hepatitis C.

New Drugs

- There are number of approved therapies as SOVALDI may be given together with or without RIBAVIRIN &PEGINTERFERON , When hepatitis C treatment is working , the virus will become undetectable within 4 to 12 weeks and will remain that way throughout treatment .patients consider cured when virus remain undetectable for 12 to 24 weeks after completing therapy.

Hepatitis G virus

- Hepatitis G virus or GB-virus was discovered in 1995.
- Share about 80% sequence homology with HCV.
- Family: *Flaviviridae*, genus: *Hepacivirus.*
- Enveloped, ss-RNA with positive polarity.
- Parenterally, sexual and from mother to child transmission have been reported.
- Causes mild acute and chronic hepatitis infection.
- Usually occurs as co-infection with HCV, HBV and HIV.

Thank you for your attention !

THANK YOU