

Viral hepatitis (B, C, D, G)

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Objectives

The students should know the following:

- 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)

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- 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.

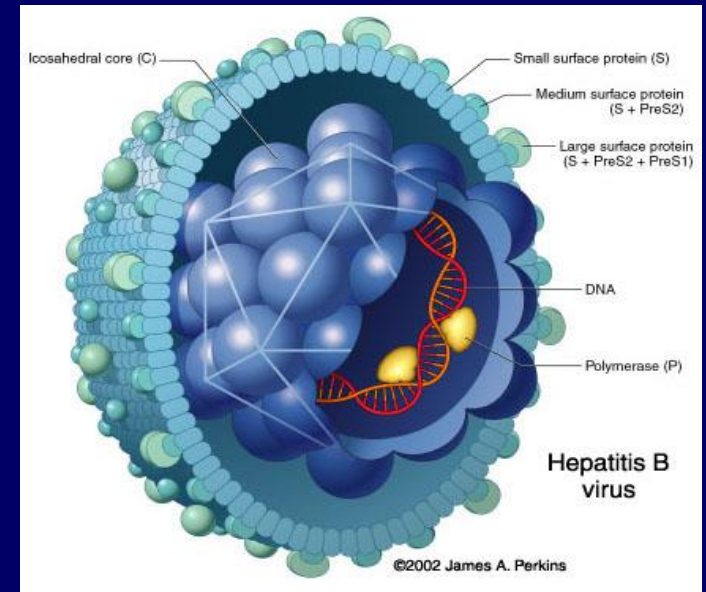
2– *Parenterally transmitted hepatitis or blood born hepatitis.* This group includes hepatitis B, C, D & G viruses.

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.

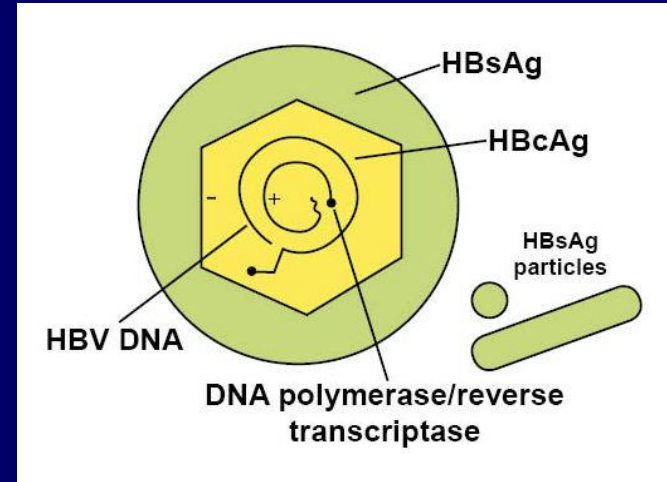


The size is 42-nm in diameter.

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.



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 (unprotected sex):

- The virus is present in blood and body fluids.

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3- Perinatally (from mother to baby):

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

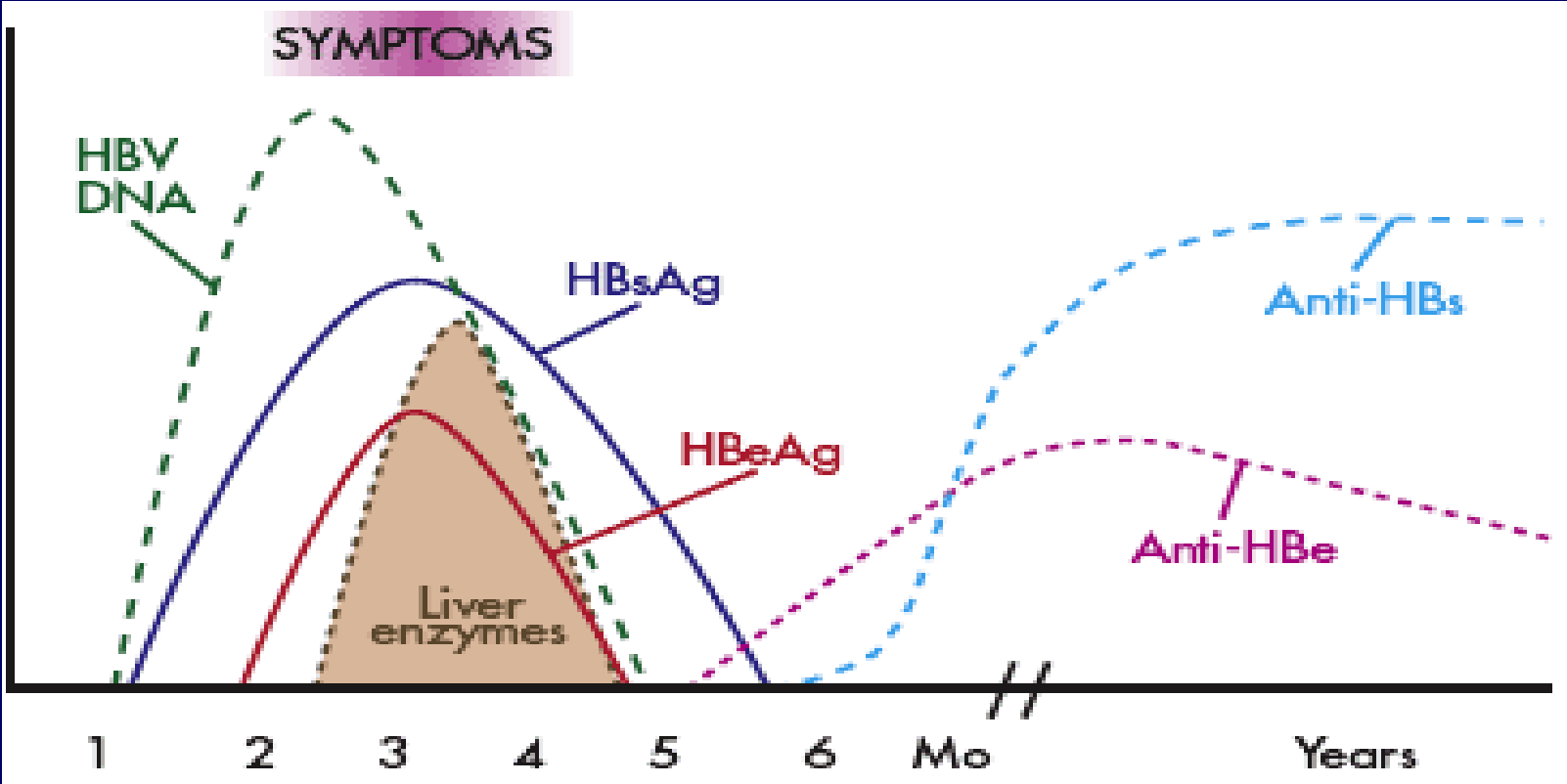
➤ **High risk groups INCULDES:**

- Intravenously drug users.
- Hemodialysis patients.
- Patients receiving clotting factors.
- Individuals with multiple sexual partners.
- 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.

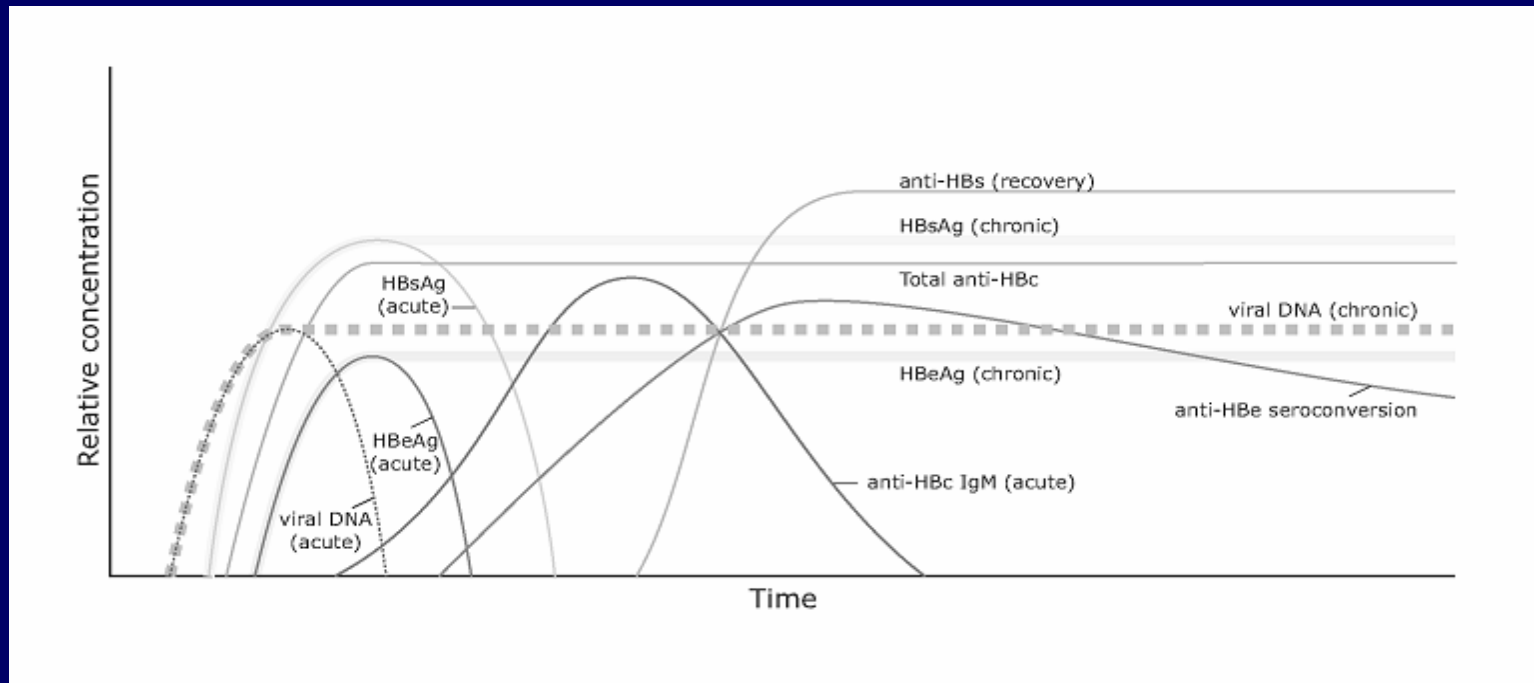
Serological profile of acute HBV infection



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 marker that appears in circulation and disappears before HBsAg.
- Anti-HBc Ab is the 1st antibody that appears in the blood and usually persists for several years.
- with the disappearance of HBeAg, anti-HBe appears and 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 indicates immunity to hepatitis B infection.

Serological profile of chronic HBV infection



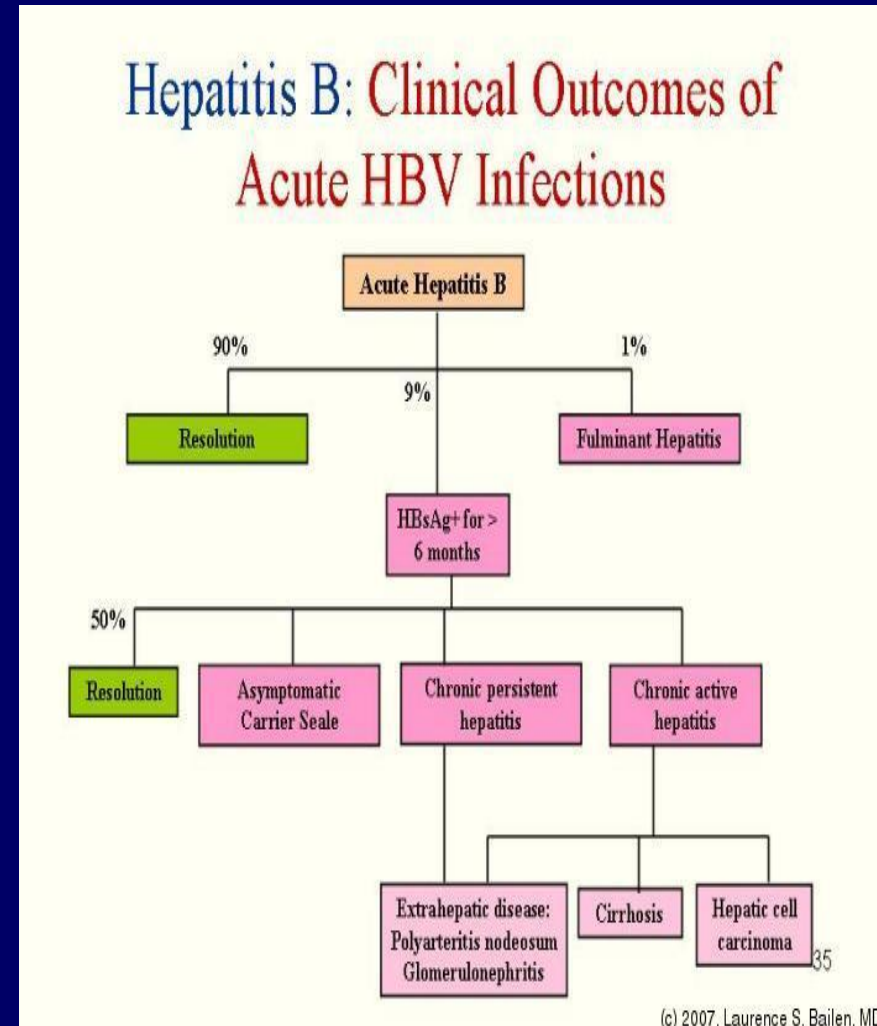
- Chronic hepatitis B infection is defined by the presence of HBV-DNA or HBsAg in the blood for > 6 months.
- HBsAg may persist in the blood for life.
- After disappearance of HBsAg, anti-HBs Ab appears and persists for several years.

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.



Acute hepatitis B infection

➤ Acute viral hepatitis usually lasts for several weeks or < 6 months.

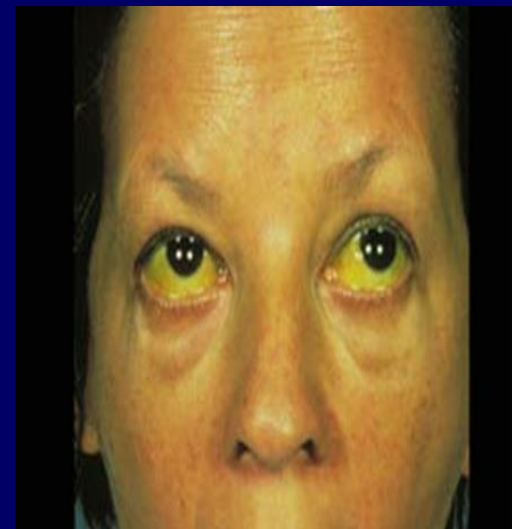
➤ Most acute hepatitis B & C are asymptomatic or anicteric.

➤ 1- *Anicteric phase*:

❖ Low grade fever, anorexia, malaise, nausea, vomiting and pain at the right upper quadrant of the abdomen.

➤ 2- *Icteric phase*: which is characterized by jaundice, dark urine and pale stool.

➤ 3- *Convalescent phase*.



Chronic hepatitis infection

- Chronic hepatitis is limited to hepatitis B, C , D and may be G viruses.
- The majority of patients with chronic hepatitis B and C are asymptomatic or have mild fatigue only.
- Symptoms include right upper quadrant abdominal pain, enlarged liver & spleen. Jaundice may or may not developed, fatigue.
- Chronic hepatitis B is defined by the presence of HBsAg or HBV-DNA in the blood for > 6 months.

Chronic hepatitis B infection

Chronic hepatitis B has three phases:

1- The replicative phase: The patient is positive for HBsAg, HBeAg and HBV-DNA, High viral load $> 10^5$ copies/ml, ALT is normal or nearly normal, Liver biopsy shows minimal damage.

2- Inflammatory phase: HBsAg positive for > 6 months, HBeAg positive, Decline in HBV-DNA in the blood but VL is $> 10^5$ copies/ml, ALT is elevated, The immune system attacks hepatocytes harboring the virus, Liver biopsy shows damage to hepatocytes.

3- Inactive phase: Negative for HBeAg, Positive for anti-HBe, HBV-DNA VL $< 10^5$ copies/ml, Normal ALT.

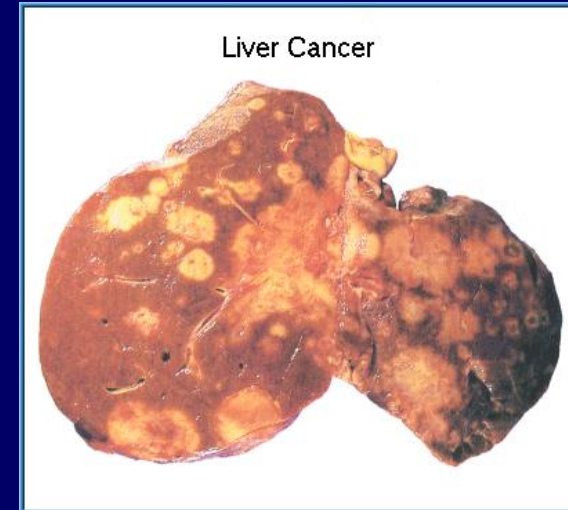
Cirrhosis

- ❖ Is a chronic diffuse liver disease.
- ❖ 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.



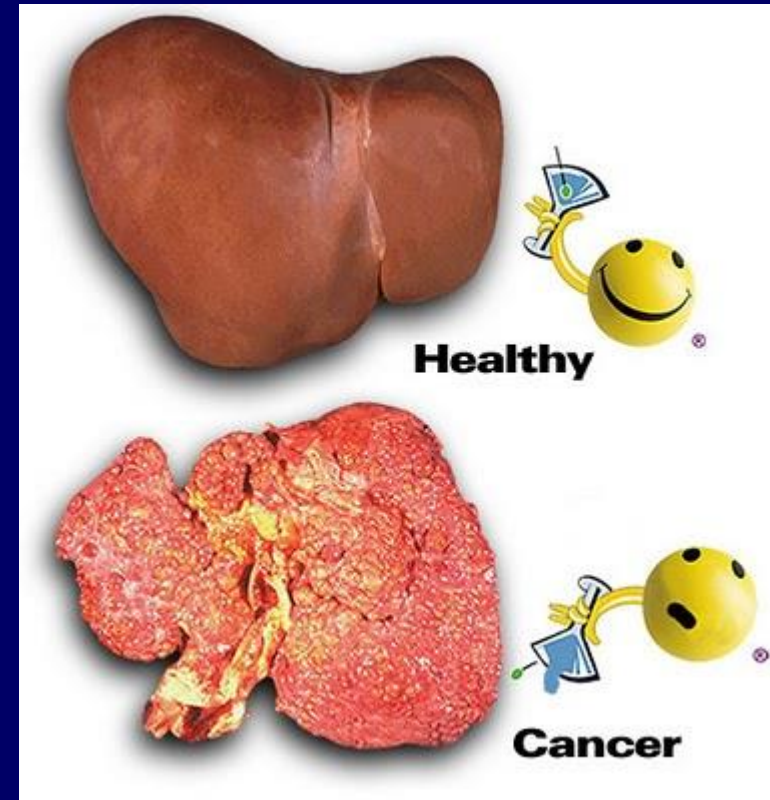
Hepatocellular carcinoma (HCC)

- ❖ 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.



HCC

- 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.
- 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.

Treatment of hepatitis B infection

➤ There are several approved antiviral drugs:

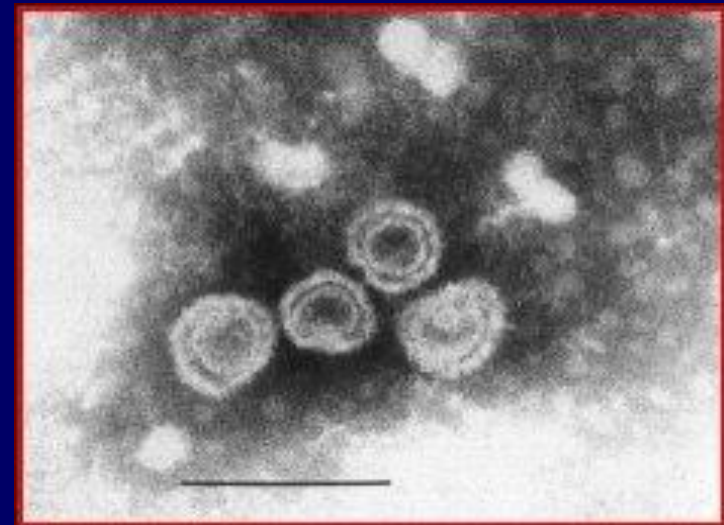
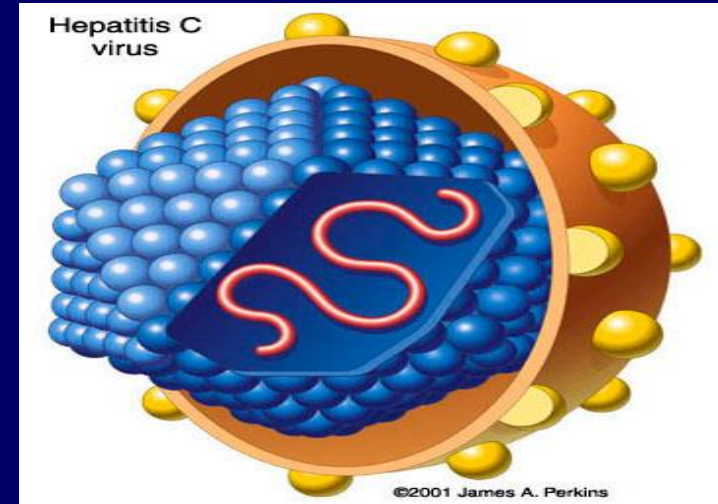
1- Pegylated alpha interferon, one injection per week, for 6- 12 months.

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.

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 genome.
- 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 & tooth brushes.

2- Sexually.

3- From mother to child perinatally.



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*.

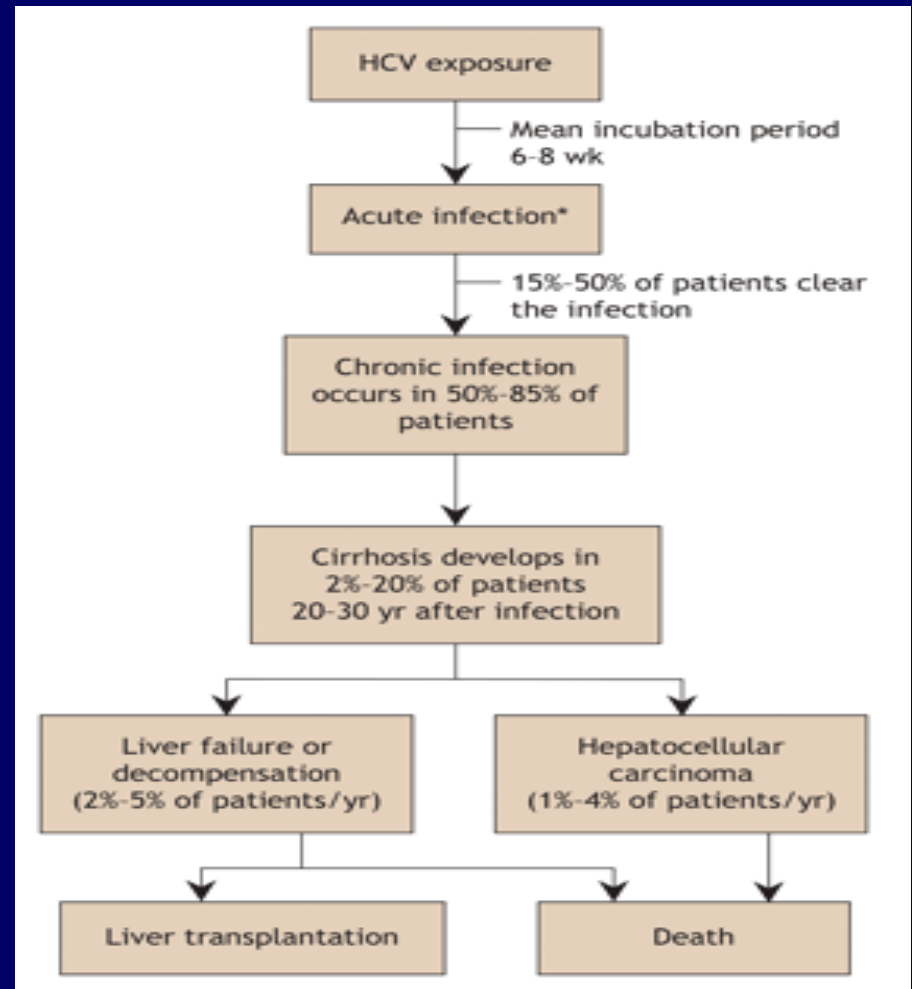
❖ The 2nd marker that appears in the blood, usually 3-4 weeks after exposure. Marker of infection.

➤ 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

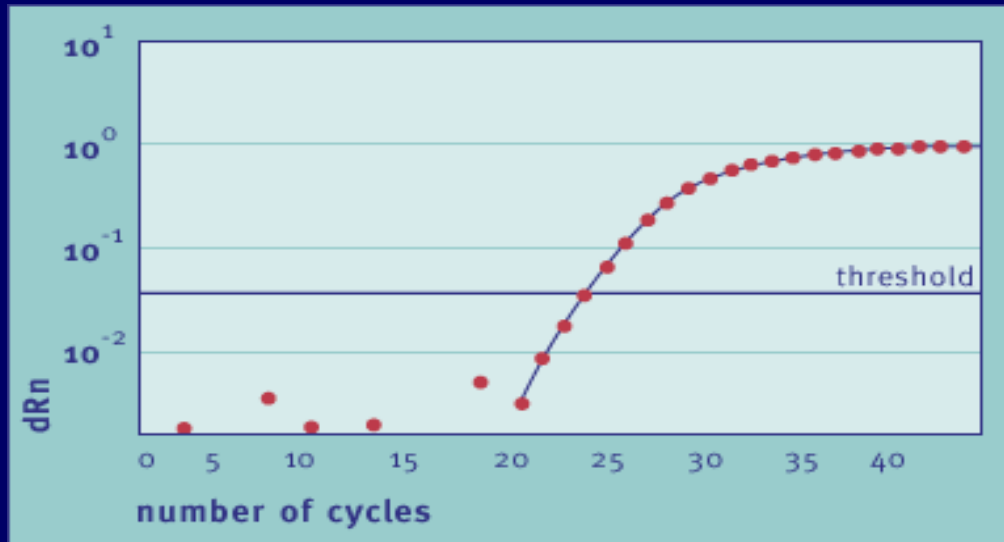
- About 20 % of the infected individuals will develop self-limiting acute hepatitis C and recover completely.
- About 80 % of the infected will progress to chronic hepatitis C.
- < 1 % will develop fulminant hepatitis C, liver failure and death.



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.

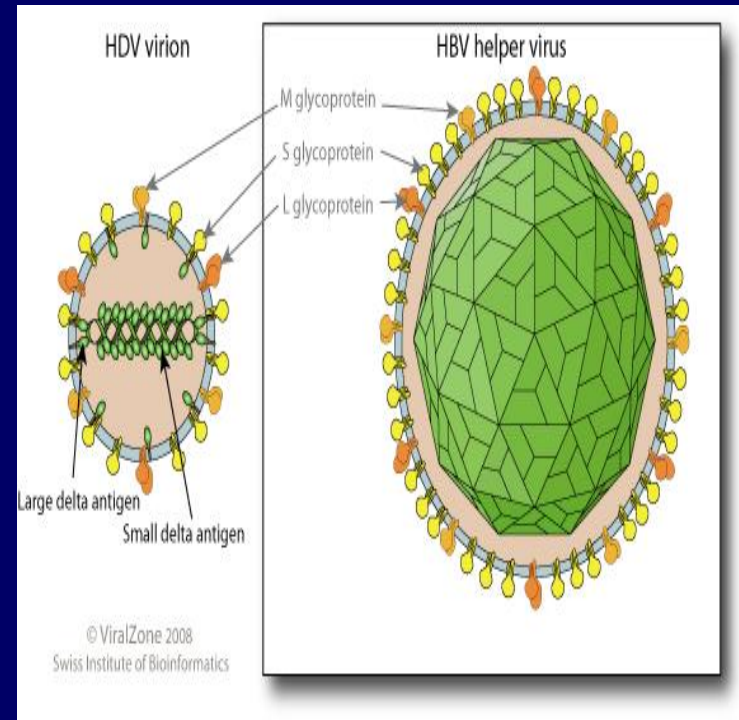


Treatment of hepatitis C infection & vaccine

- The currently used treatment is the combined therapy using: Pegylated alpha interferon and ribavirin.
- The dose: for pegylated alpha interferon, one injection per week.
- For ribavirine two capsules a day.
- Hepatitis C vaccine:
At the present time, there is no vaccine available to hepatitis C.

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.

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 !