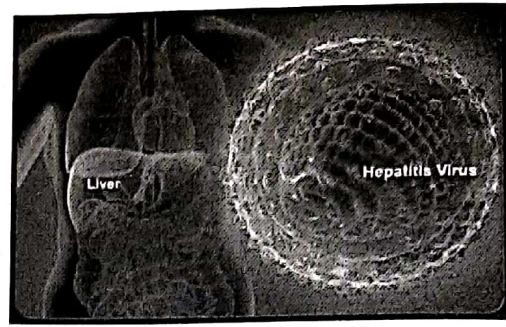


# Viral Hepatitis



By

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Helaly

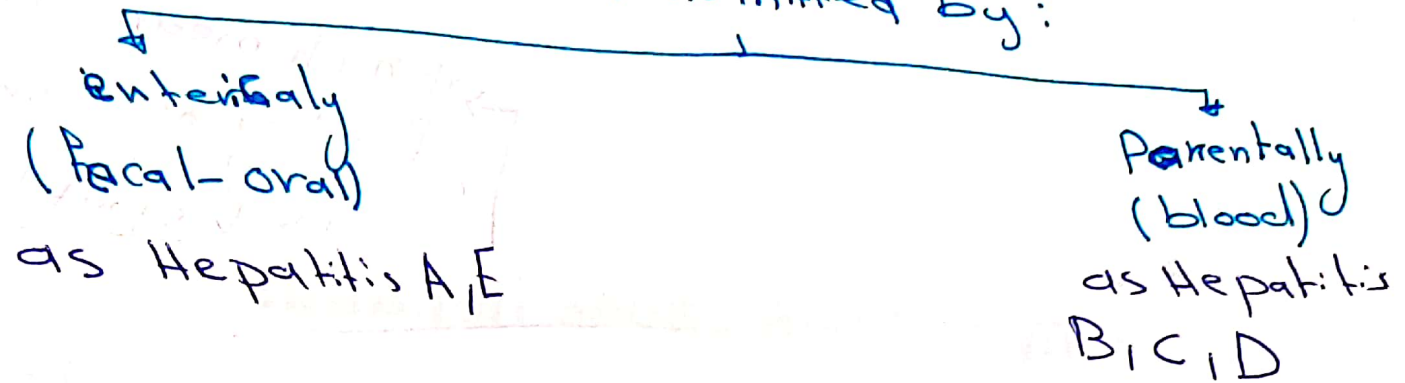
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\*Which means the main finding or clinical feature is hepatitis \*

- Many viruses cause hepatitis.
- Medically important "hepatitis viruses":
  - Hepatitis A virus (HAV),
  - Hepatitis B virus (HBV),
  - Hepatitis C virus (HCV),
  - Hepatitis D virus (HDV, delta virus),
  - Hepatitis E virus (HEV)

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\* The viruses causing infectious disease transmitted by:



\* symptom (mild-sever) according to the type or may be asymptomatic

\* Acute infection of All Hepatitis viruses can't be distinguish, They are manifestation of hepatitis.

\* لا يمكن التمييز بسهولة فرصية بيننا من طريق serological  
لكن التمييز وذلك بعد serology في هذا النوع  
من الفيروسات صعب جدًا

\* Some types of hepatitis have vaccine  
\* The management maybe vaccine or Anti-viruses or by Immune



\* The viruses which transmitted by fecal-oral route or enterically called → infectious hepatitis  
 Whereas another which transmitted through blood parentally → serum hepatitis

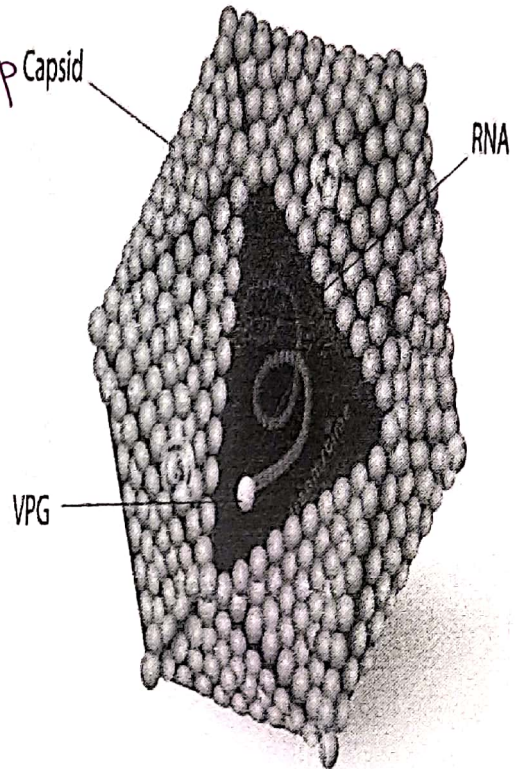
# HEPATITIS A VIRUS (infectious)

## Characteristics:

→ from (Picornavirus) group

Q A typical enterovirus, also known as enterovirus 72.

Q Naked icosahedral nucleocapsid virus with a single stranded, positive-polarity RNA. No virion polymerase. Virus has a single serotype. → which mean have (vaccine)



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## Transmission & Epidemiology

\* this virus need close personal contact

- Fecal-oral route.

- Virus in the feces ~ 2 weeks before symptoms. and the person which infect can be transmit the virus during these period

- Children are the most frequently infected group.

↳ They usually have a symptomatic

- Outbreaks arise from fecally contaminated water or food. esp. in areas which eat sea food as shell fish/oyster

\* This virus is found in large amount in developing countries

# Pathogenesis & Immunity

- Replicates in the GI tract → liver.
- Not cytopathic for the hepatocyte. → but the injury caused by
- Hepatocellular injury by (immune attack by cytotoxic T cells) ←
- No chronic infection. *only acute*
- Initially IgM antibody → IgG antibody, lifelong protection.  
which give

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## Clinical Findings:

- IP 3 – 4 weeks. → incubation period
- Most HAV infections are asymptomatic.
- Fever, anorexia, nausea, vomiting, and jaundice. Dark urine, pale stool, and elevated transaminase levels.
- Resolve spontaneously in 2 to 4 weeks.



## Laboratory Diagnosis:

- IgM antibody.

## Treatment:

- No antiviral drug. ( all treatment  $\rightarrow$  supportive)

## Prevention:

- ① Vaccine contains killed virus. Two doses, an initial dose followed by a booster 6 to 12 months later.
- ② Proper hygiene. (is very important) because it transmit

by oral-fecal route  
 $\rightarrow$  mean hand washing (personal)  
or  $\rightarrow$  proper ~~sewage~~ disposal ( الصرف الصحي)

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Transmit by fecal-oral ← \* بقال انتقاله كد و باني جنبه يكون  
Hepatitis B ← انتقاله كد فميه

# HEPATITIS B VIRUS

$\rightarrow$  cause serum hepatitis.



## Important Properties:

QR Hepadnavirus family.

its character QR 42-nm enveloped, icosahedral nucleocapsid.

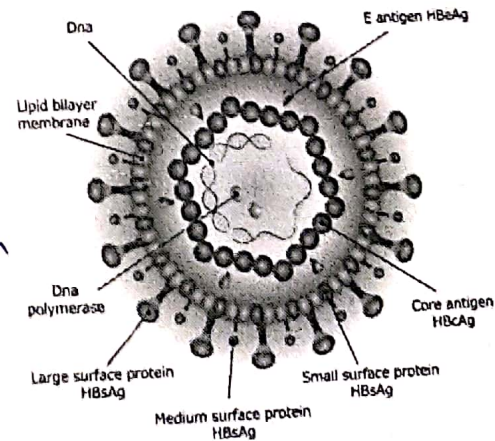
QR Partially double-stranded circular DNA genome.

QR The envelope contains HBsAg.

QR DNA-dependent DNA polymerase

$\rightarrow$  (revers transcriptase)

Hepatitis B Virus  
Baltimore Group VII (dsDNA-RT)

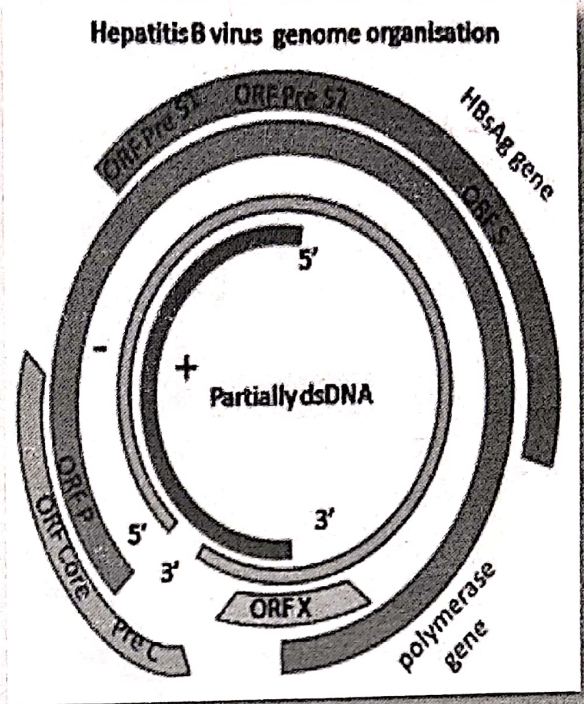


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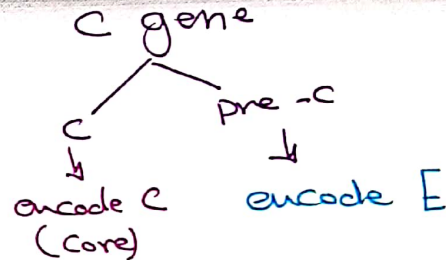
\* These genome read by overlapping reading

because of these  
 → encode 2 protein

Four open reading frames encode five proteins, namely, the S gene encodes the surface antigen, the C gene encodes the core antigen and the e antigen, the P gene encodes the polymerase, and the X gene encodes the X protein → play role in oncogenesis



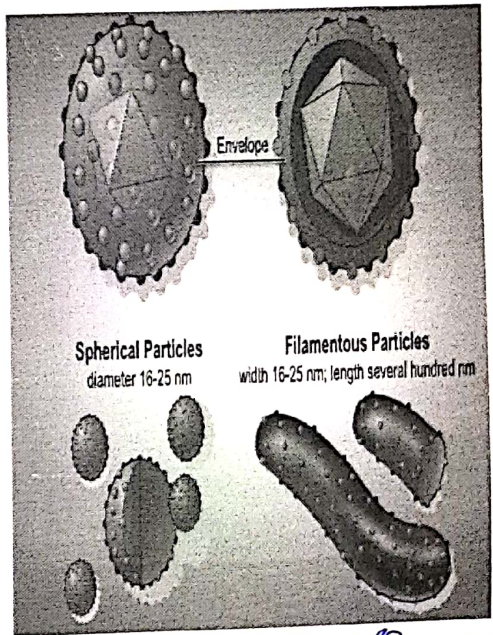
replication Prof. Dr. Ghada Fahmy Helaly  
 \* Dump ~~production~~ → occur production of excessive surface antigen → do virus particle spheres



Three different types of particles:

- 42-nm virions (virus particle diameter)
- 22-nm spheres and long filaments 22 nm wide → surface antigen.

- Vaccine: One serotype.
- Epidemiology: Four serologic subtypes of HBsAg: Group-specific antigen, "a" and two sets of mutually exclusive epitopes, d or y and w or r.



\* The surface antigen → has 3 epitopes → its movement (different) epidemiology



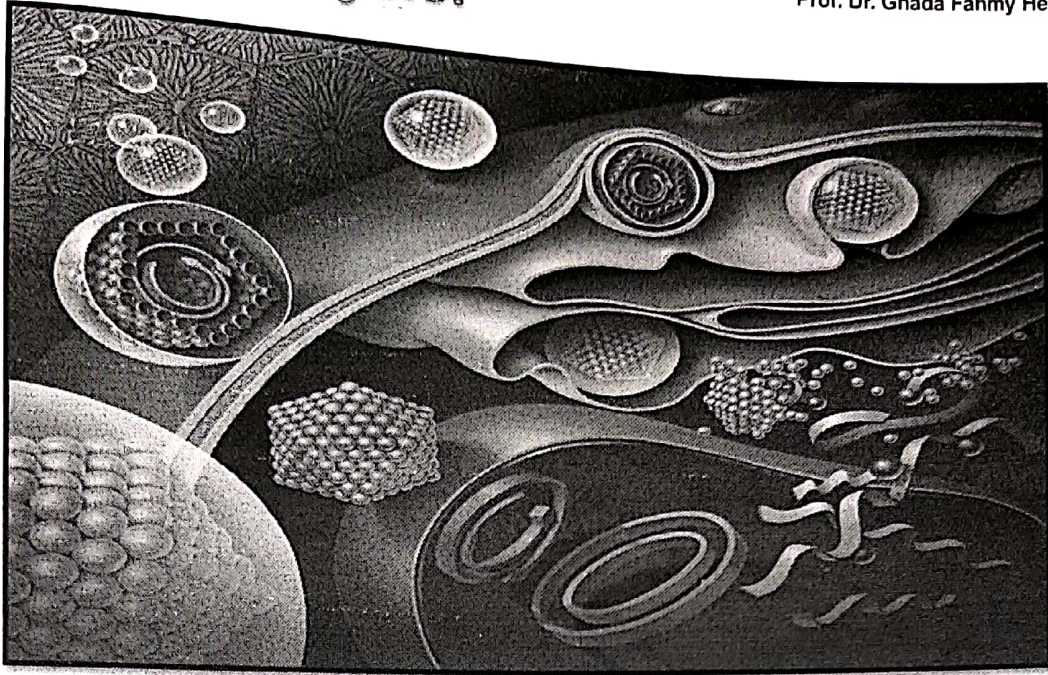
\* 3 epitopes of surface antigen one of them is common to all serotype  $\Rightarrow$  so vaccine is effective which is (a)

\* another epitopes cause sets of mutually exclusive epitopes (d or y) and (w or r)

that mean  $\rightarrow$  someone who infected have in his surface antigen  $\rightarrow$  (a, d, w) or (a, y, w) or (a, d, r) or (a, w, r)

# Replicative Cycle:

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\* Some of the progeny DNA integrates into the host cell genome → the carrier state.

\* these integration cause → carcinogenesis

\* Found all over the world up to 300 million person chronically infected

## Transmission:

❖ Worldwide ... Asia.

❖ > 300 million people are chronically infected.

➤ Blood.

➤ Perinatally during birth or breast feeding.

➤ Sexual intercourse.

➤ Needle-stick injuries.

➤ IVDU.

\* Which viruses is the most susceptible to do infection by needle-stick injury?

- 1- Hepatitis B (the First)
- 2- Hepatitis C
- 3- HIV

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# Pathogenesis:

- Hepatocellular injury → immune attack by cytotoxic T cells.
- Ag-Ab complexes cause arthritis, vasculitis.
- About 5% → chronic carrier state. 10% of these have Serosis and permanent damage
- Approximately 90% of infected neonates → chronic carriers  
→ high risk of hepatocellular carcinoma. → الأكثر عرضة لأنه (chronic) سير
- HCC → integration of viral DNA.
- Lifelong immunity [HBsAb]
- progression to chronicity depend on Age → inverse proportional to Age (أقل عرضة في كبار السن)
- Antibodies against surface antigen only give long life immunity

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# Clinical Findings

- Many HBV infections are asymptomatic.
- IP is 10 to 12 weeks. (Long)
- Symptoms tend to be severe, and life-threatening.
- Most chronic carriers are asymptomatic but some have chronic active hepatitis → cirrhosis and death.  
→ person who has surface antigen more than 6 months in their blood.

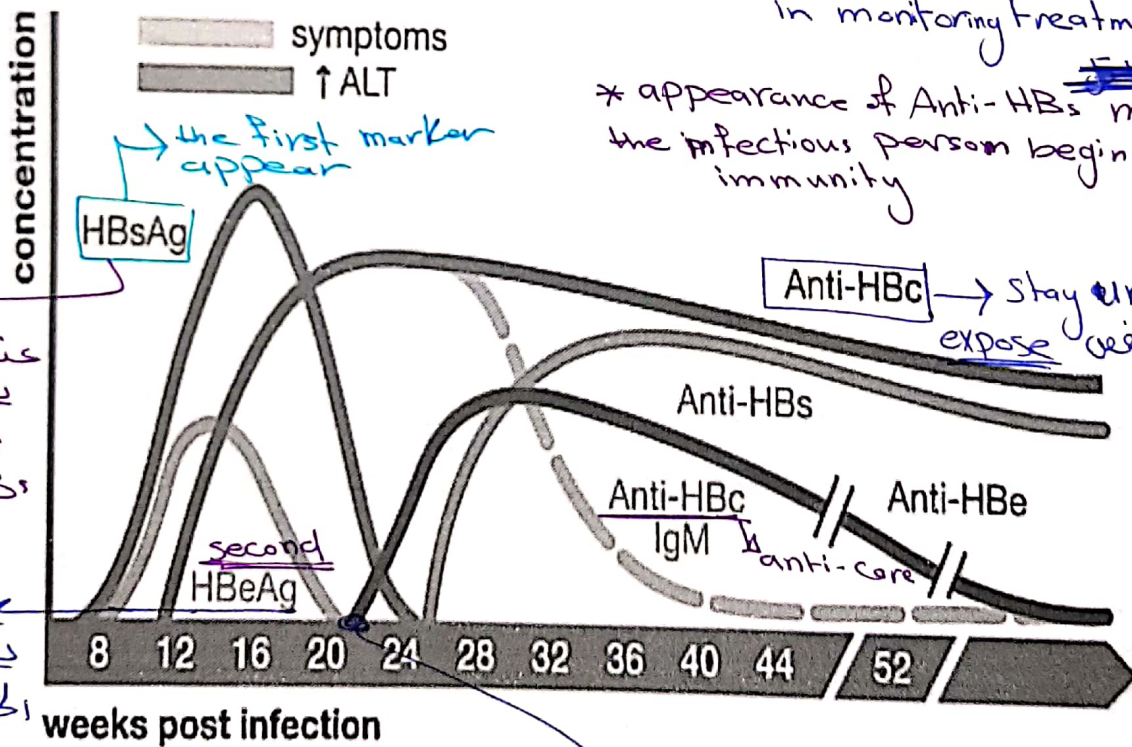
# Laboratory Diagnosis:

- HBsAg, anti-HBs, and anti-HBc. <sup>important in immunity</sup> → is a marker of exposure <sup>from core</sup>
- Detection of HBsAg for more than 6 months indicates a chronic carrier state.
- The presence of e antigen indicates a chronic carrier who is making infectious virus (transmissibility). <sup>(indicate that is the person highly infected)</sup>
- The detection of viral DNA (viral load) in the serum.   
<sup>↳ is important when the marker not appear</sup>  
<sup>if some one is infected and (surface antigen ⊕)</sup>  
<sup>e antigen ⊖</sup>

→ his capacity to transmit is less than another who (surface antigen ⊕) e antigen ⊖

\* viral load is important in monitoring treatment

\* appearance of Anti-HBs ~~mean~~ the infectious person begin develop immunity



\* if anti-antibody not found ⊕  
 Serum  $\bar{E}$   $\bar{L}$   $\bar{I}$   $\bar{H}$   $\bar{B}$   $\bar{c}$   $\bar{I}$   $\bar{g}$   $\bar{M}$   $\bar{A}$   $\bar{B}$   $\bar{s}$   
 We find → the only marker → Anti-Core (Anti-HBc) <sup>(early convalescence)</sup>

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this stage called window period



\* if HBsAg (+) only → so the person is vaccinated

## Serologic Test Results in Four Stages of HBV Infection.

Test	Acute Disease	Window Phase	Complete Recovery	Chronic Carrier State
HBsAg	Positive	Negative	Negative	Positive
HBsAb	Negative	Negative	Positive	Negative <sup>1</sup>
HBcAb	Positive <sup>2</sup>	Positive	Positive	Positive

→ all have (+) because exposed

Neither detectable HBsAg nor anti-HBs → "window" phase. Diagnosis of this patient is made by detecting HB core antibody (anti-HBc).

\* HBcAb not exposed job (+) US ←

\* if someone (Ant-HBs negative / Anti-Core negative) (Antibody surface positive) these person is → vaccinated

### Treatment:

- Tenofovir, .....
- Pegylated alpha interferon and lamivudine.

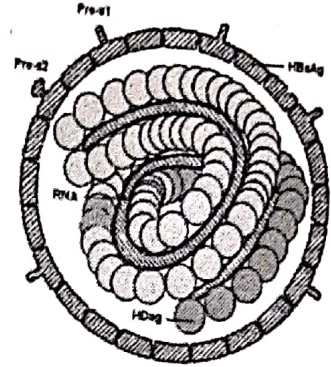
### Prevention:

- (1) Vaccine, contains HBsAg only three-dose regimen.
- (2) Hepatitis B immune globulin (HBIG). It is used to provide immediate, passive protection.
- (3) Both the vaccine and HBIG should also be given to a newborn whose mother is HBsAg-positive.
- (4) Education of chronic carriers regarding precautions.

# HEPATITIS D VIRUS

## Characteristics:

- ☞ Defective virus.
- ☞ Replicate only in cells infected with HBV.
- ☞ Single-stranded, negative, circular RNA, encodes delta antigen. diagnosis by D-Ab or D-Ag
- ☞ One serotype.
- ☞ Transmitted by blood, sexually, and from mother to child. as the same of HBV



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## Pathogenesis:

- Hepatocellular injury → cytotoxic T cells.
- Delta antigen is cytopathic.
- Chronic carriers of HBV could be either "co-infected" or "super-infected" with HDV.

\* super infection  
 → so bad  
 → HBV → damage to liver cell and give Surface antigen  
 (+) superly infected HDV and cause more damage very severe damage

D-Agent may enter the human body with HBV at same time

## Laboratory Diagnosis:

- ❖ Delta antigen or antibody to delta antigen.

## Treatment & Prevention:

- Pegylated alpha interferon.
- Prevention of HBV infection (very important)

HDV

سواءا كان

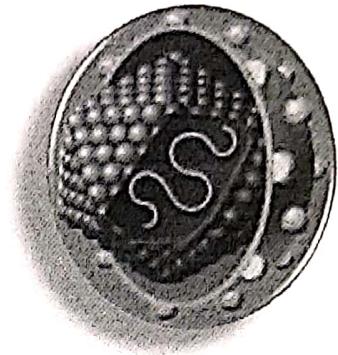
HBV اذا كان

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# HEPATITIS C VIRUS

## Important Properties:

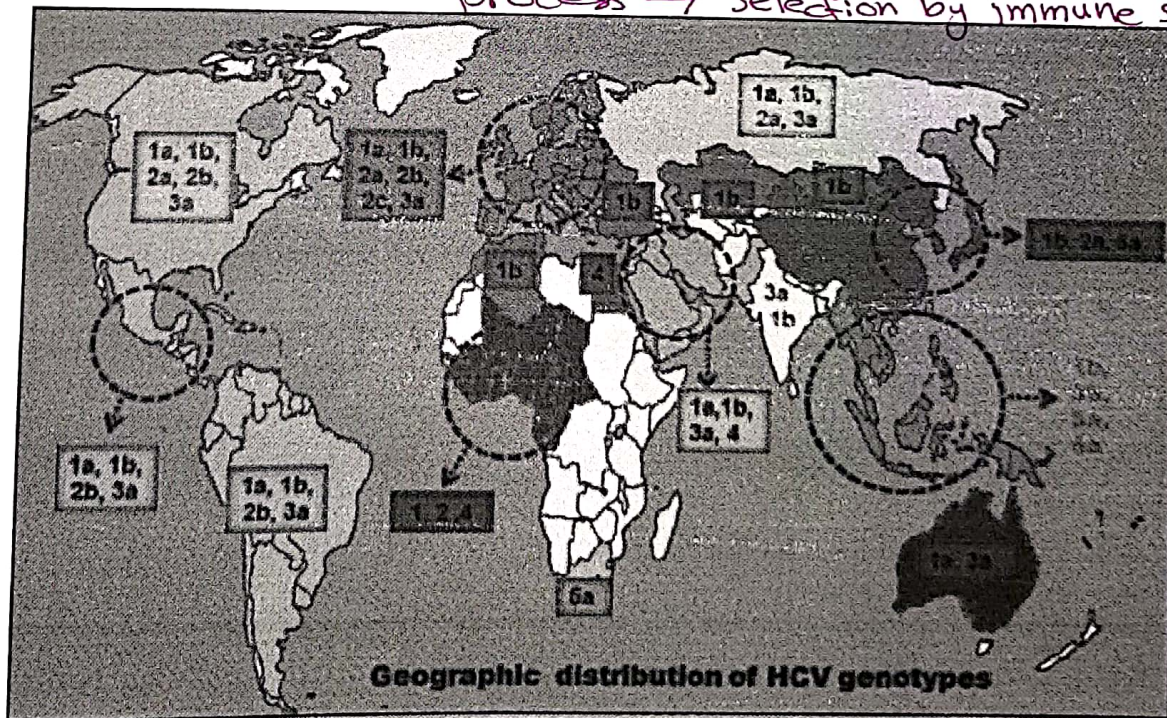


- ☞ Flavivirus family.
- ☞ Enveloped, single-stranded, positive-sense RNA.
- ☞ No polymerase in virion.
- ☞ HCV has at least six genotypes and multiple sub-genotypes → "hypervariable" region in the envelope glycoprotein

genotype → result from major genetic changes  
 - the similarity between different genotype  
 → 65% sequence similarity

☞ Quasispecies → result from minor genetic changes  
 \* it consider as most common cause of transfusion transplant associated hepatitis  
 → mutant generated by mutation selection ~~process~~  
 process → Selection by immune system

which mean infected person may have many quasispecies



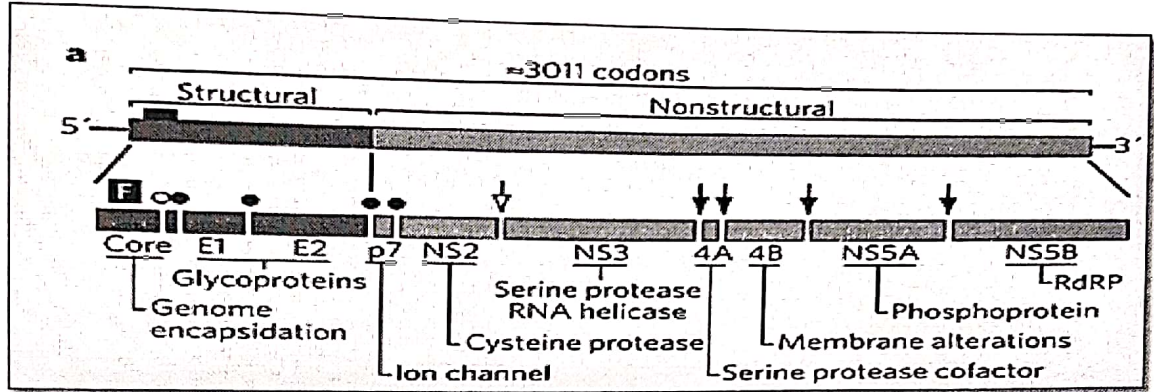
Geographic distribution of HCV genotypes and their subtypes

its importance in response to treatment, some genotype maybe response to treatment which mean treatment may be easy compared with another genotype and in severity infection



The HCV RNA, 9.6 kb. encodes a single polyprotein that is cleaved by a virion-encoded protease into three structural proteins (C, E1 and E2) and seven non-structural proteins (p7, NS2, NS3, NS4A, NS4B, NS5A, NS5B).

Core and envelop  
hypervariable region



## \*HCV GENOME

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## Transmission & Epidemiology:

- Worldwide, ~180 million people.
- Transmission:
  - ↳ *intra venous drug uses*
  - blood: IVDU, needle-stick injury
  - Sexual and from mother to child occur but are inefficient modes. (0-10%)



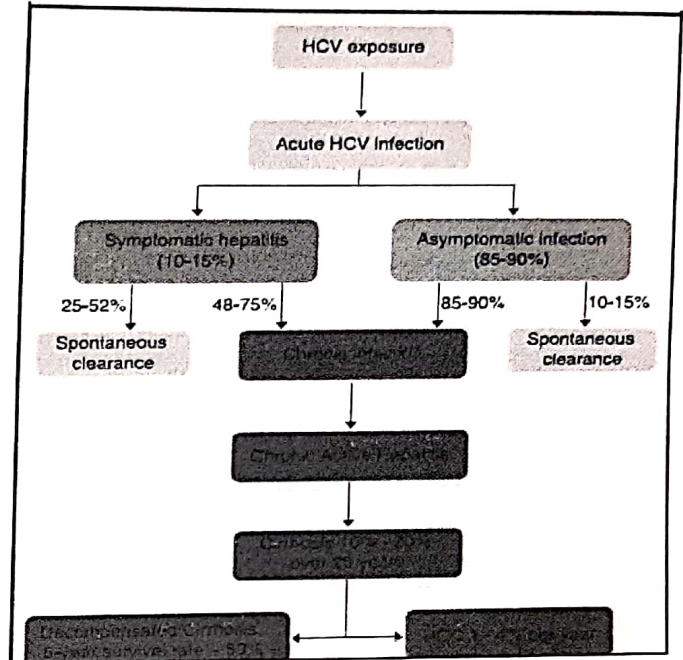
# Pathogenesis & Clinical Findings:

- Hepatocellular injury → cytotoxic T cells.
- HCV infection → HCC, no viral oncogene, no integration.
- The IP is 8 weeks.
- Acute HCV is milder than HBV.
- Cirrhosis is indication for liver transplantation.

\* because it has no integration in liver cell → the progression of

hepatocellular

carcinoma → depend on damage of liver cell that means liver cell change to cirrhosis



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## Laboratory Diagnosis

- Antibodies to HCV in ELISA → (+) إذا كانت النتيجة إيجابية فيض بها
- RIBA (recombinant immunoblot assay) → confirmatory test → define antibody against which Ag
- PCR: viral RNA (viral load).

