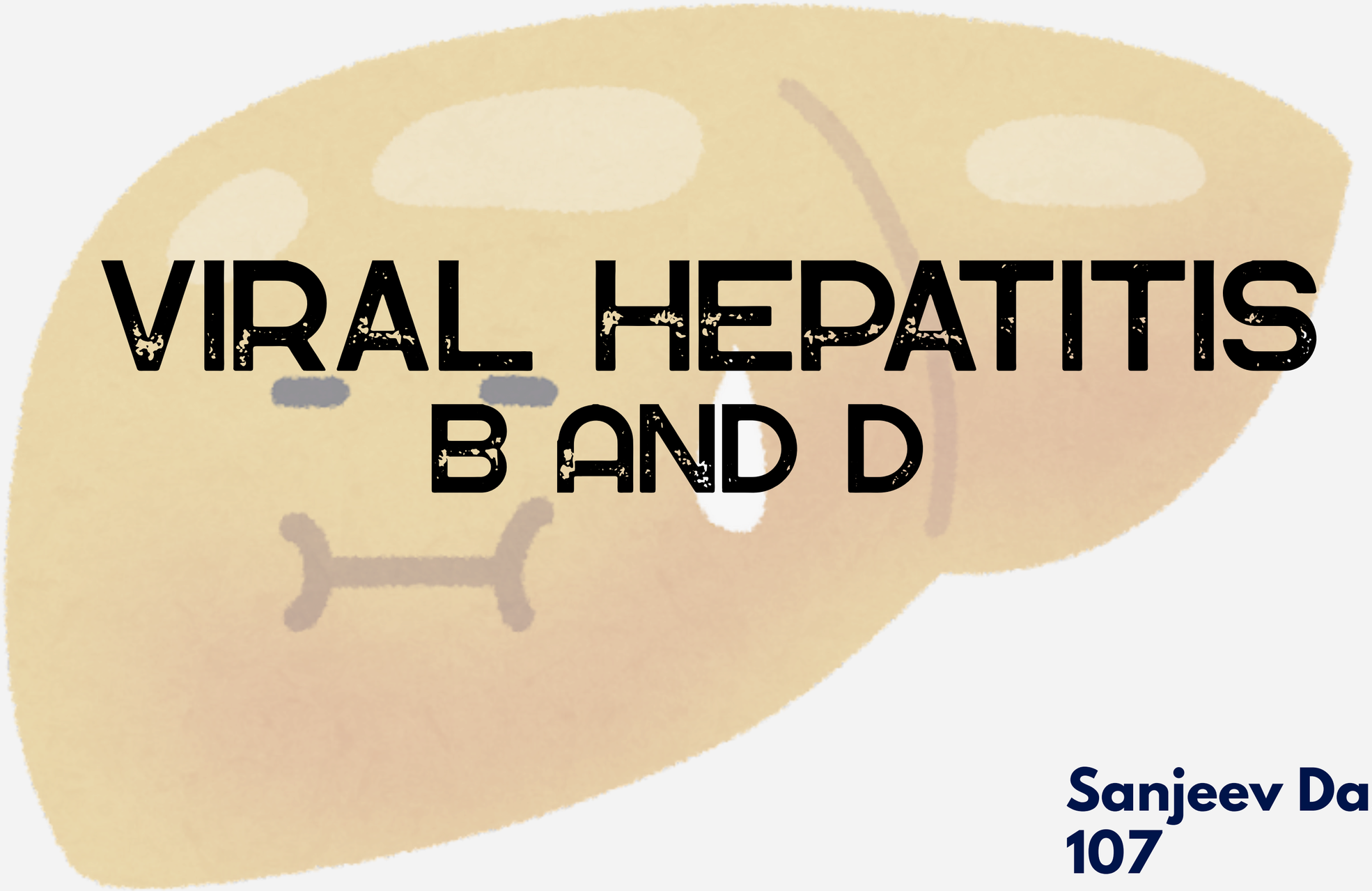

VIRAL HEPATITIS
B AND D

Sanjeev Das S
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HEPATITIS B

- Hepatitis B is one of the most common causes of chronic liver disease and hepatocellular carcinoma worldwide
- Caused by Hepatitis B virus
- It is a DNA virus , belongs to Hepadnaviridae family
- Incubation period: 30 - 180 days

Mode of transmission

Vertical transmission :

- From mother (who is a carrier) to child may occur in utero, during parturition, or soon after birth. Usually not transmitted by breastfeeding

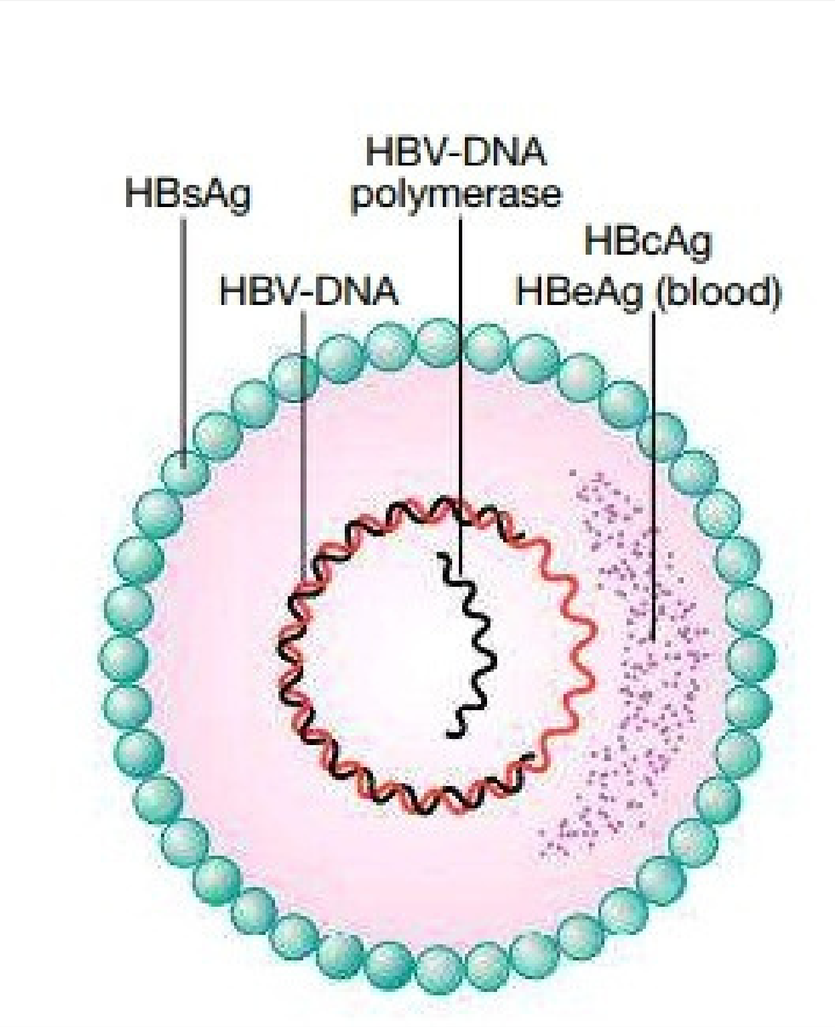
Horizontal transmission :

- Sexual transmission
- Intravenous drug use
- Infected unscreened blood products
- Tattoos/acupuncture needles
- Needlestick injury
- Sharing toothbrush/razor

CLINICAL FEATURES

- Usually asymptomatic
- Nausea , Vomiting, poor apetite, fatigue, malaise
- Fever , arthralgia, rashes
- Upper vague abdominal pain
- Jaundice
- Hepatomegaly

Structure of HBV



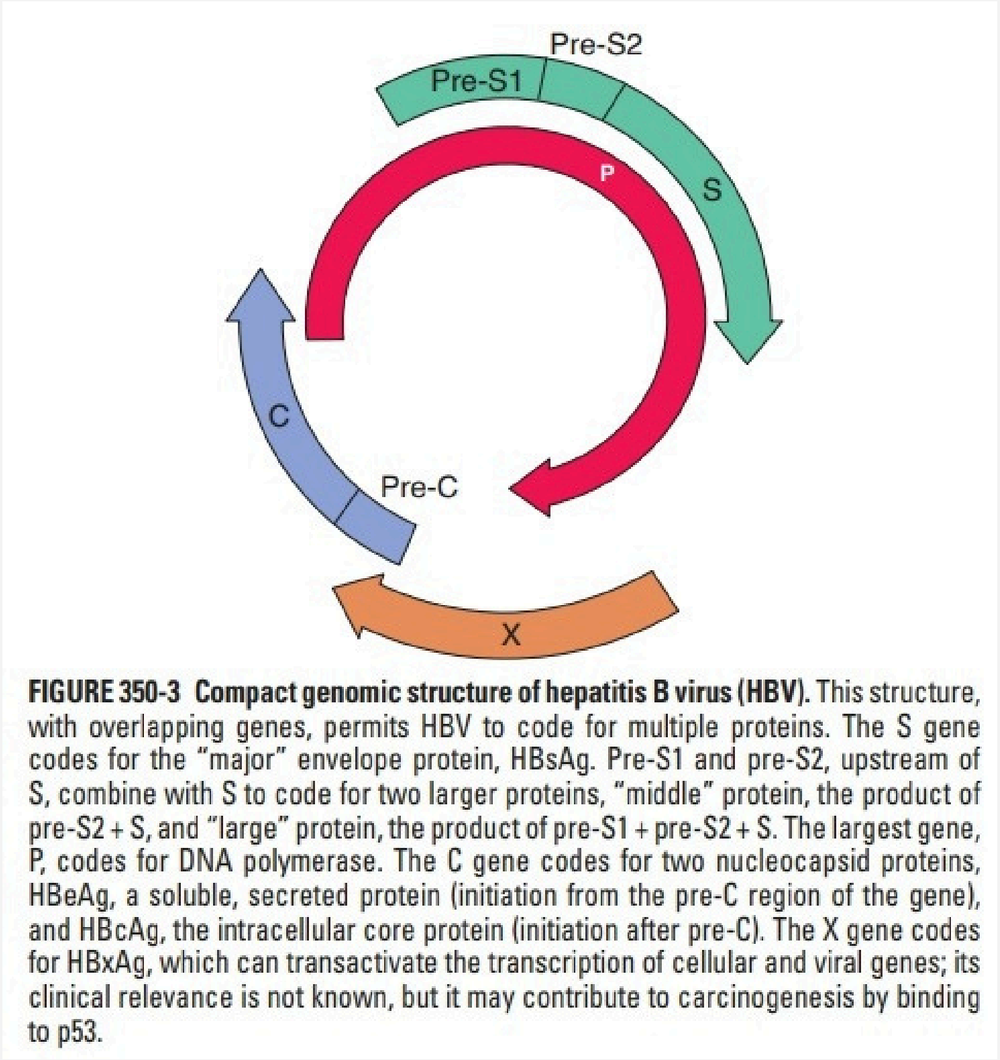


FIGURE 350-3 Compact genomic structure of hepatitis B virus (HBV). This structure, with overlapping genes, permits HBV to code for multiple proteins. The S gene codes for the "major" envelope protein, HBsAg. Pre-S1 and pre-S2, upstream of S, combine with S to code for two larger proteins, "middle" protein, the product of pre-S2 + S, and "large" protein, the product of pre-S1 + pre-S2 + S. The largest gene, P, codes for DNA polymerase. The C gene codes for two nucleocapsid proteins, HBeAg, a soluble, secreted protein (initiation from the pre-C region of the gene), and HBcAg, the intracellular core protein (initiation after pre-C). The X gene codes for HBxAg, which can transactivate the transcription of cellular and viral genes; its clinical relevance is not known, but it may contribute to carcinogenesis by binding to p53.

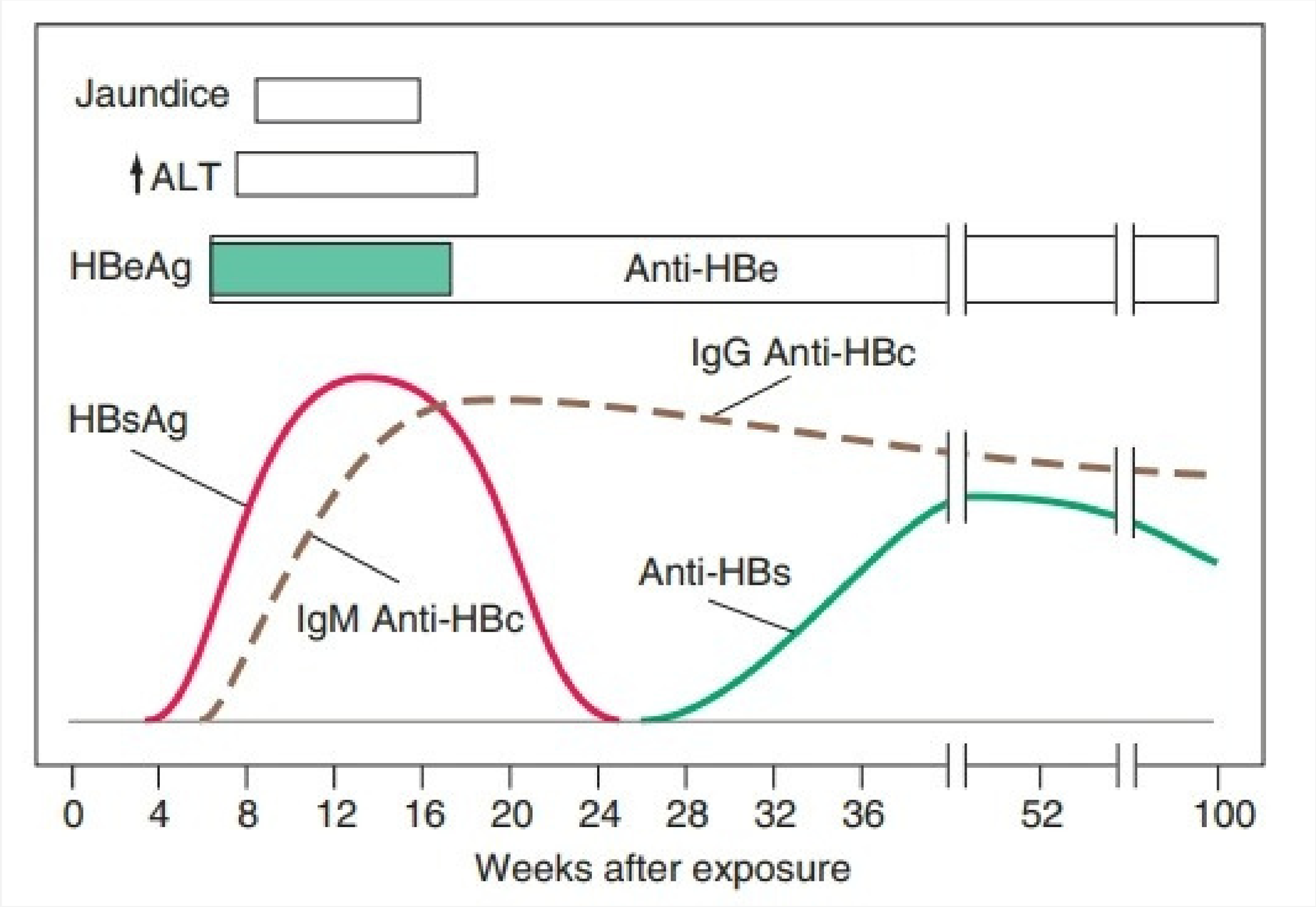
HBV	42	Double-shelled virion (surface and core) spherical	3.2-kb DNA, circular, ss/ds	Hepadnavirus	HBsAg HBcAg HBeAg	Anti-HBs Anti-HBc Anti-HBe
	27	Nucleocapsid core			HBcAg HBeAg	Anti-HBc Anti-HBe
	22	Spherical and filamentous; represents excess virus coat material			HBsAg	Anti-HBs

INVESTIGATIONS

1. **Liver function test :**
   - AST , ALT : Raised & Maximum level are seen during prodromal phase (400 - 4000 U/L)
   - ALP : Raised , less than 2x normal
   - Bilirubin : Both unconjugated & conjugated raised
   - Serum protein : Normal

2. **Hematology** :
   - Leucopenia with relative lymphocytosis
   - PT prolonged (indices for prognosis)
   - ESR raised

3. **Serological test** : Confirms the diagnosis


Jaundice
ALT
HBeAg
Anti-HBe
IgG Anti-HBc
HBsAg
IgM Anti-HBc
Anti-HBs
0
4
8
12
16
20
24
28
32
36
52
100
Weeks after exposure

Serological markers

- **HBsAg** :

Main indicator of active infection
First marker to elevate in blood before the onset of symptoms
Peaks during the disease and becomes undetectable within 3-6 months.

- **Anti HBs** :

It is antibody to HBsAg and appears after the disappearance of HBsAg.
Significance: Anti-HBs is a protective antibody and may persist for life providing protection.

- **HBcAg** :

Not seen in serum

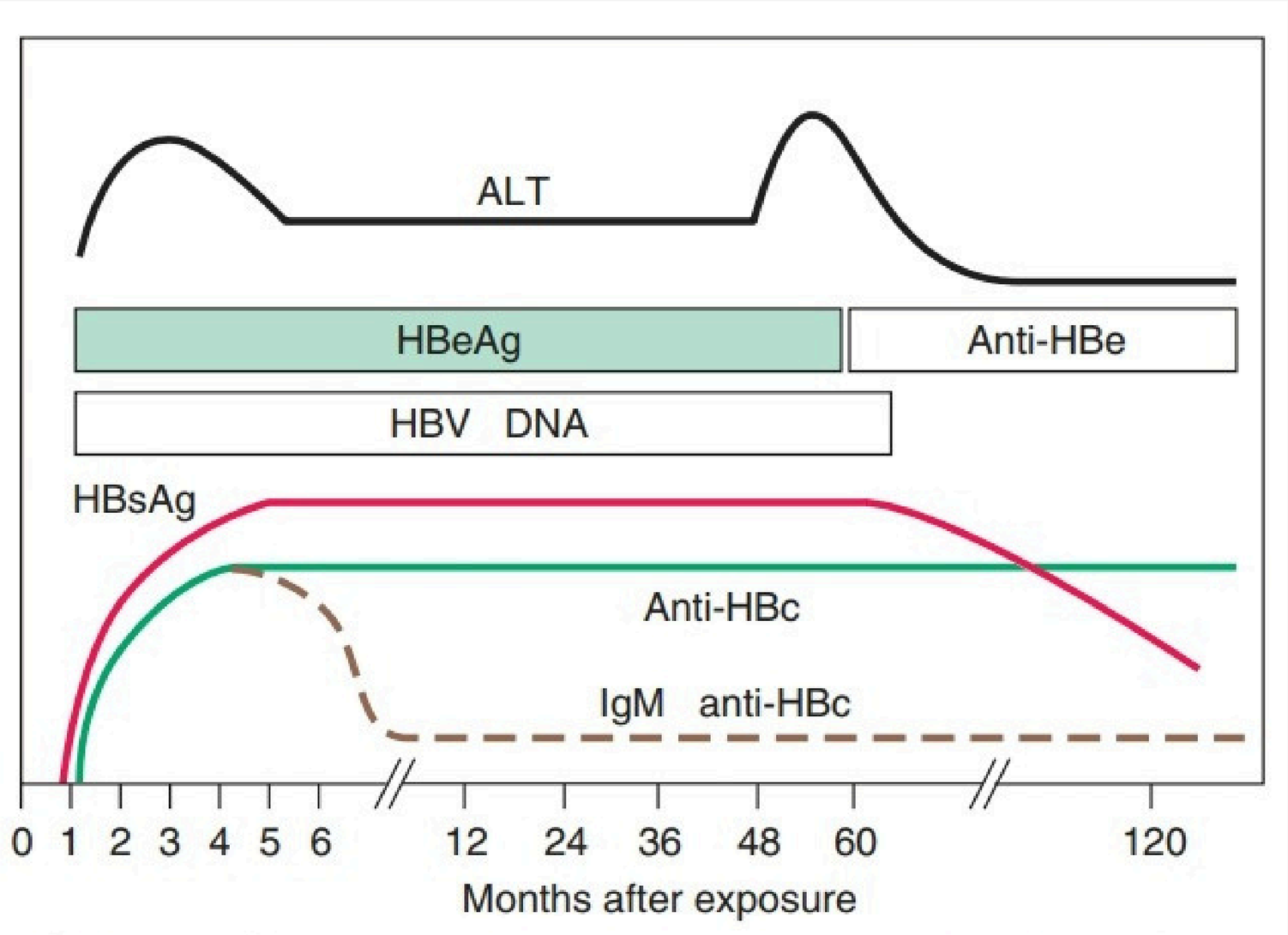
- **Anti HBc IgM :**

Appears in serum a week or two after the appearance of HBsAg,
Significance : IgM anti-HBc is the earliest antibody marker and indicates recent infection (first six months)

- **Anti HbC IgG** :

After about 6 months,the IgM anti-HBc antibody is replaced by IgG anti-HBc
Significance: IgG anti-HBC indicates remote infection (beyond 6 months).
Its presence indicates previous infection with HBV even when all the other viral markers are not detectable

- **HBeAg** : Detectable in the blood and can be used as an indicator of viral replication
- **Anti-HBe** : Present in the serum in the recovery phase



- 4. **PCR**

HBV DNA Detection

Table 11.11: Interpretation of serological findings and its significance in HBV.

Antigens		***Antibodies***			***Interpretation***
HBsAg	HBeAg	Anti-HBc	Anti-HBs	Anti-HBe	
–	–	–	–	–	Susceptible
–	–	–	+	–	Immunity to HBV caused by previous exposure or vaccination
+	+	IgM +ve and IgG –ve	–	–	**Acute hepatitis B**, highly infectious High titer in acute hepatitis B and low titer in chronic hepatitis B
–	–	IgM –ve and IgG +ve	+	+	**Resolved acute hepatitis B, seroconversion, low infectivity**
+	+	IgM –ve and IgG +ve	–	–	**Chronic infection** or carrier state, **high infectivity**
+	–	IgG +ve	–	+/–	**Chronic infection** or carrier state, **low infectivity**
–	–	–	+	–	**HBV vaccination**

MANAGEMENT

- Full spontaneous recovery occurs in 95% of adults following acute HBV infection. Remaining <5% develop a chronic infection
- Treatment is supportive with monitoring for acute liver failure
- Antiviral therapy is considered when there is severe liver injury with coagulopathy
- Recovery from acute infection occurs within 6 months.
- Persistence of HBeAg or HBsAg indicates chronic infection

Chronic hepatitis B - Treatment

Criteria for treatment :

- Serum HBV-DNA above 2000 iu/mL (about >10,000 copies/mL).
- Serum ALT level greater than two times normal.
- Moderate to severe active necroinflammation and/or fibrosis in the liver biopsy

Management is aimed at:

- HbeAg seroconversion
- Reduction in HBV DNA
- Normalization of LFTs

Direct-acting nucleoside/nucleotide antiviral agents

- Inhibits the reverse transcription of pre-genomic RNA to HBV-DNA by HBV-DNA polymerase
- Do not directly affect the covalently closed circular DNA (cccDNA) template for viral replication
- So relapse is common if treatment is withdrawn.
- Entecavir, tenofovir, lamivudine

Pegylated interferon-alfa (PEG-IFN) :

- augments host immune response
- This is most effective in patients with a low viral load and serum transaminases greater than twice the upper limit of normal
- Contraindicated in the presence of cirrhosis, as it may cause rise in serum transaminase and precipitate liver failure

Liver transplantation

- For patients with advanced liver disease or hepatocellular carcinoma

PREVENTION

- A recombinant hepatitis B vaccine containing HBsAg is available (Engerix)
- The vaccine should be offered to those at special risk of infection who are not already immune.
- The vaccine is ineffective in those already infected by HBV.
- After a known exposure, Infection can also be prevented or minimised by the intramuscular injection of specific hepatitis B immunoglobulin (HBIg) prepared from blood containing anti-HBs.
- Given within 48hrs, or at most a week of exposure
- Neonates born to hepatitis B-infected mothers should be immunised at birth

HIV COINFECTION

- Around 10% of HIV-infected population has concurrent HBV
- Co-infection increases morbidity and mortality
- There are greater levels of HBV viremia, faster progression to chronic infection and greater risk of cirrhosis and HCC
- The immunosuppression that is seen in HIV infection can lead to loss of anti-HBs antibodies, reactivation of infection and a poorer antibody response to HBV vaccination
- Managed by combination of antiviral agents
- Antiviral therapy should be considered for co-infected pregnant women, using drugs with dual activity, e.g. tenofovir with emtricitabine or lamivudine

HEPATITIS D

Etiology

- Caused by hepatitis D virus (HDV or delta virus), which is a defective/incomplete RNA virus and belongs to the Deltaviridae family
- The RNA genome is covered by an outer coat/shell of HBsAg
- It has no independent existence and requires HBV for its replication and expression.
- It can infect individuals simultaneously with HBV or can superinfect those who already have chronic HBV.
  Mode of spread: Parenteral route and sexual contact

INVESTIGATION

- HDV RNA: Detectable in the blood and liver before and in the early days of acute disease.
- Anti-HDV IgM : Most reliable indicator of recent HDV exposure

MANAGEMENT

- Effective management of hepatitis B prevents hepatitis D
- Active liver disease is treated with Pegylated interferon and adenofovir for 12months

THANK YOU

Reference :

Davidson’s principles and practice of medicine,24th edition
Harrisons principles of internal medicine 22nd edition
Archit boloor exam preparatory manual for undergraduates,4th edition