# GIS 10

## MICROBIOLOGY


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This sheet contains two parts:
quick revision of sheet 9 and then we'll continue talking about the remaining three types of HV; C, D and E.

Main points of last lecture:

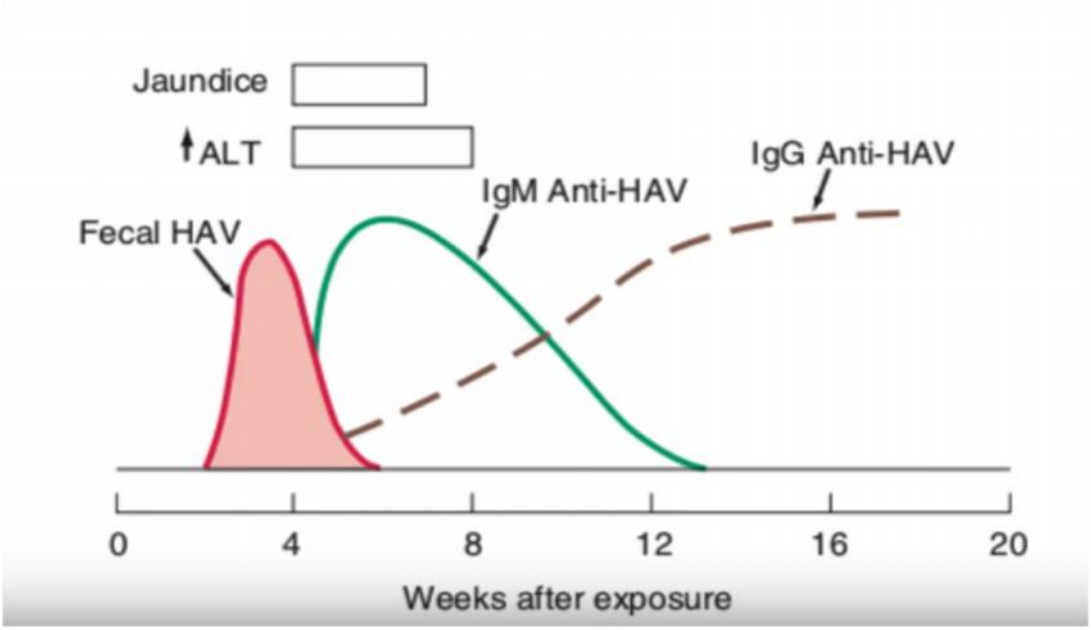
- How to diagnose hepatitis?
- How to know if there's hepatitis?
- How to tell if it's infectious or non-infectious hepatitis?

We'll cover some main ideas from last lecture briefly:

- ✓ **Any hepatitis is characterized by hepatocytes damage and elevation in serum AST and ALT.**
- ✓ Infectious cause → history (contaminated food, needle-stick injury, blood transfusion, sexual activity, etc.)
- ✓ Among infectious causes we'll focus on viral hepatitis, mainly hepatitis viruses (A, B, C, D and E).

## HEPATITIS "A" VIRUS:

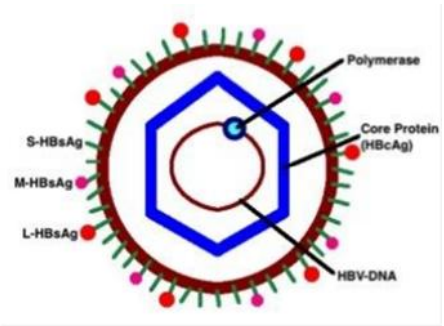
- **Route of transmission:** feco-oral.
- Four genotypes have been identified; all belong to the same serotype.
- **Main risk groups:** occur among homosexuals, IV abusers, and homeless people.
  Other risk groups are patients and staff in mental health institutions.
- **Clinical features:**
  Subclinical infection—common in children (>90% if <5 years of age).
  Acute hepatitis—this occurs more frequently with increasing age.
- **Diagnosis:** Anti-HAV (IgM) antibodies can be detected during acute illness while stool shedding is still present and ALT is high (we don't care about chronic forms, but we care about shedding and confirmation of the presence of the virus), most likely the patient will come between 3-4 months as the onset of symptoms occur, you'll be able to detect anti-HAV IgM in his serology test.
- This chart (next page) shows that shedding of the virus is prior to symptoms (transmission more likely). Symptoms and Anti HAV (IgM) detection in serum appear simultaneously which is perfect for the diagnosis to be straight forward.
- **Treatment:**
  - Acute hepatitis symptoms → Avoid paracetamol or any liver clearance drug and alcohol.
  - Fulminant hepatitis → Patients should be treated with supportive therapy and referred for consideration of liver transplantation.
- Fatalities are more common with advancing age and in those with hepatitis "C" co-infection




- **Prevention:** vaccination for children given in two doses to reduce the shedding of HAV. (more details in the previous sheet)

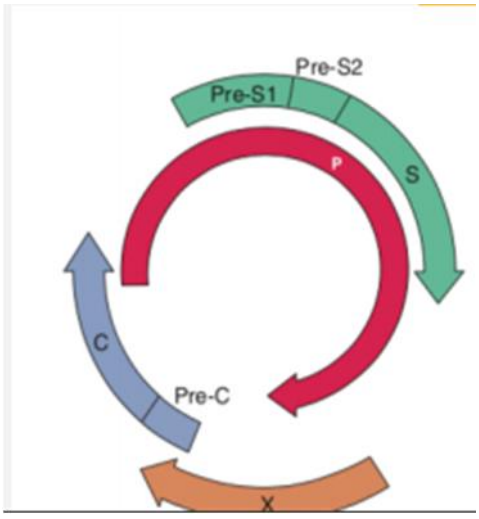
## HEPATITIS "B" VIRUS:

- The only DNA hepatitis virus, it can cause both acute and chronic hepatitis.
- HBV has a unique genome, with a wide replicative capacity that gives different proteins (antigens) while replicating.
  - Replicate in liver, but exists extrahepatically
  - The risk of chronicity is greatest in the very young (90%).
  - Beneath the **envelope** is the **internal core** or nucleocapsid, which contains hepatitis B core antigen (HBcAg).




- ✓ HBV has a small compact circular DNA genome with eight genotypes (A–H) and **four long ORFs (Open Reading Frames)**:

- ✓ **C (core) gene** encodes **HBcAg** and **HBeAg**.
- ✓ **S (surface) gene** encodes **HBsAg**.
- ✓ **P (polymerase) gene** encompasses 3/4 of the viral genome, encodes a polypeptide (**DNA polymerase** with ribonuclease H activity)
- ✓ **X gene** encodes a polypeptide with several functions.




IMPORTANT NOTE:
The incomplete reading of **C (core) gene** will result in **HbcAg** and it's **intracellular**.

**HBV** may be transmitted **vertically** (high-prevalence areas), **sexually, blood**, by **IV drug use**, by **needle-stick injury**, and **horizontally** (especially between children in intermediate prevalence areas).
In **HBV,** after **acute infection,** there'll be **anti-HBe detected** in the serum, preventing the development of the **chronic** form.

**- Phases of chronic hepatitis:** Refer to the previous sheet for more details

**1- Replicative immune – tolerant phase:** HBeAg is active with high HBV DNA loads and normal ALT.
**2- Replicative immune – clearance phase:** HBeAg seroconversion into Anti-HBe at the end.
**3- Inactive carrier state:** HBeAg becomes absent (negative) with low DNA loads and normal ALT levels. In 10% of patient, a peak of ALT level may occur as shown.

**- Complications of chronic HBV:**
**1- End-stage liver disease** (15-40 % of cases) and **hepatocellular carcinoma** (HCC).
**2- Disease progression** in patients with prolonged replicative phase, alcoholic, and in co-infections with HCV or HDV. It is associated with high DNA levels and HBeAg +ve.
Remember:
1) The presence of **HBeAg** is a **qualitative** measure for **chronic form and viral replication.**
2) The presence of **HBV DNA** is a **quantitative** measure for **chronicity.**

**- Antigens used for diagnosis:**
**1) HbsAg** The most important and the first to appear**.**
**2) HBcAg** An intracellular antigen and **not detectable in serum**, may be the **only indicator** of infection in the **window** between **HBsAg** loss and **anti-HBs** production.
**3) HBeAg** A secretory protein and a marker of HBV **replication** and **infectivity**.

**NOMENCLATURE AND FEATURES OF HEPATITIS VIRUSES**

| HEPATITIS TYPE | VIRUS PARTICLE, nm | MORPHOLOGY | GENOME[a] | CLASSIFICATION | ANTIGEN(S) | ANTIBODIES | REMARKS |
|---|---|---|---|---|---|---|---|
| HAV | 27 | Icosahedral nonenveloped | 7.5-kb RNA, linear, ss, + | Hepatovirus | HAV | Anti-HAV | Early fecal shedding<br>Diagnosis: IgM anti-HAV<br>Previous infection: IgG anti-HAV |
| HBV | 42 | Double-shelled virion (surface and core), spherical | 3.2-kb DNA, circular, ss/ds | Hepadnavirus | HBsAg<br>HBcAg<br>HBeAg | Anti-HBs<br>Anti-HBc<br>Anti-HBe | Bloodborne virus; carrier state<br>Acute diagnosis: HBsAg, IgM anti-HBc<br>Chronic diagnosis: IgG anti-HBc, HBsAg<br>Markers of replication: HBeAg, HBV DNA<br>Liver, lymphocytes, other organs |
| | 27 | Nucleocapsid core | | | HBcAg<br>HBeAg | Anti-HBc<br>Anti-HBe | Nucleocapsid contains DNA and DNA polymerase; present in hepatocyte nucleus; HBcAg does not circulate; HBeAg (soluble, nonparticulate) and HBV DNA circulate—correlate with infectivity and complete virions |
| | 22 | Spherical and filamentous; represents excess virus coat material | | | HBsAg | Anti-HBs | HBsAg detectable in >95% of patients with acute hepatitis B; found in serum, body fluids, hepatocyte cytoplasm; anti-HBs appears following infection—protective antibody |

**- Diagnosis:**

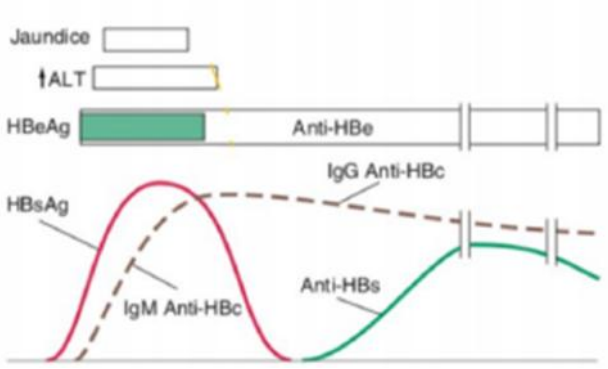
- Briefly, we look first for the presence of **HbsAg** (most important) and then **Anti HBc** (IgG&IgM):
  1-If **HbsAg** and **Anti HBc (IgM)** positive → **acute** HBV.
  2-If **HbsAg** and **Anti HBc (IgG)** positive→ **chronic** HBV.
- HBsAg +ve, and HBeAg +ve is highly infectious.
- A mother with **HBsAg +ve** and **HBeAg +ve** will >90% **transmit** HBV to her child, **HBeAg-ve** mothers have 10-15% chance only.
- **HBsAg** detected in serum before symptoms show up.

**In acute infection, the window period** starts once **HBeAg** is converted into **Anti-HBe**, it is dependent on the time taken for seroconversion from **HBsAg** into **Anti-HBs**.

Only marker at the **window period** → **IgG Anti-HBc.**

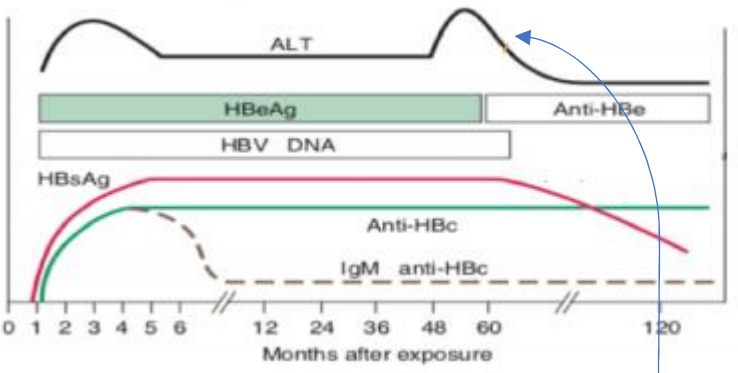
Once **HBeAg** disappear and **HBsAg** starts to decline, that indicates the clearance of infection and reduction of **HBV** replication → the patient had beaten the infection.

The **Anti-HBs** appears, which is **protective**.




If after 6 months the HBsAg persists, then it's **chronic infection** (either high or low infectivity chronic hepatitis).

Briefly, in this diagram, during the first 6 months is the acute phase of hepatitis. Since **HBsAg** remained beyond 6 months, this indicates chronicity where **HBsAg** is present with **Anti-HBc** IgG.




10% of cases per year go from replicative high infectivity phase **(HBeAg** positive) to inactive carrier phase**, Anti-HBe** positive, **HBeAg** negative, where another exacerbation in **ALT levels** occurs.
So, what you detect in an **inactive carrier** is **Anti-HBe and Anti-HBc**. (notice the declining **HBsAg** levels).

Table 8.3 Diagnosis of hepatitis B virus

| | HBsAg | Anti-HBs | HBeAg | Anti-HBe | Anti-HBc IgM | Anti-HBc IgG | HBV DNA |
|---|---|---|---|---|---|---|---|
| Acute infection | ✓ | | ✓ | | | | +++ |
| Window | | | | | ✓ | | + |
| Prior infection | | ✓ | | | | ✓ | |
| Vaccinated | | ✓ | | | | | |
| Chronic (high infectivity) | ✓ | | ✓ | | | ✓ | +++ |
| Chronic (low infectivity) | ✓ | | | ✓ | | ✓ | ± |
| Pre-core mutant | ✓ | | | ✓ | | ✓ | ++ |

This table should make things crystal clear for you

NOW LET'S GET INTO OUR LECTURE, SHALL WE?

## HEPATITIS "C" VIRUS:

• **HCV** is a spherical, enveloped **RNA** flavivirus.
• Its genome is a positive ssRNA molecule, which codes for a single gene of a large polyprotein (3k aa), cleaved to yield **10** proteins.
• 4 structural proteins, a nucleocapsid protein (C), two envelope glycoproteins (E1, E2), membrane protein (P7).
• **Envelope** proteins are coded in **hypervariable regions**, **core is conserved**.
(The outer **envelope** is more likely to be more **variable** in its composition, the **core** is not changed. That will help me if I want to detect HCV, I'll look in the **conserved areas**).
• At least seven major genotypes (genotypes 1–7) exist, and these may be further grouped into subtypes (e.g. 1a, 1b, 1c).
• Different subtypes predominate in different geographical locations.
• The high replication rate and absence of proofreading by NS5b polymerase result in the rapid accumulation of mutations (multiple quasi-species exist at any one time).

### EPIDEMIOLOGY:

✓ HCV infects an estimated **170 million** people worldwide.
✓ In **developed** countries, HCV prevalence is **low** (0.5–2%), injecting drug users.
✓ HCV is **more common** in certain areas (**Egypt, Japan, Italy**) and may be related to the **reuse** of **needles** for injection, acupuncture, or folk remedies.
✓ **Transmission routes**: **transfusion, injecting drug use, nosocomial** (**needle- sticks**, dialysis, inadequate sterilization of colonoscopes).
✓ **Vertical or sexual** transmission is **rare**.

### PATHOGENESIS:

*the usual clinical picture is someone with needle-stick injury*

✓ **15%** of people with acute infection clear the virus in 3–24 months
✓ **85%** develop **chronic** infection.
✓ **HCV-specific cytotoxic T- lymphocyte (cellular) responses** play an important role in suppressing HCV RNA levels.
✓ There is a broad **humoral response** to HCV epitopes, but these are **not sufficient** to clear the virus.

- ✓ **Infection results in hepatic inflammation**, steatosis, hepatic **fibrosis** and **HCC** (estimated risk 5–25% after 10–20 years).
- ✓ Factors associated with **cirrhosis** include **alcohol**, **HBV** or **HIV** co-infection, HLA B54, HCV genotype 1b, and high levels of HCV viremia. (**Quasi species** –high variance in subtypes within the same host) (**remember the outer envelope variance**)

❖ **CLINICAL FEATURES:**

- ✓ **Acute hepatitis C** → **75%** of infections are anicteric **(non-jaundice)**.
- ✓ **Symptomatic infection** is similar to acute HAV and HBV, but with **lower transaminases**. Presents 7– 8 weeks (range 2–26) after exposure. If diagnosed early, treatment is appropriate.
- ✓ **Fulminant hepatitis C** → unusual in the **Western countries**. More common in HBV co-infection. And in **40–60%** of cases in **Japan**.
- ✓ **Chronic hepatitis C** → 85% of patients, associated with fatigue, malaise, and reduced quality of life indice, **ALT levels fluctuate independently of symptoms, whereas HCV RNA levels remain fairly constant**, and **this is what helps you in diagnosis (HCV RNA level)** **Eventually** progresses to cirrhosis, decompensated liver disease, and HCC.
- ✓ **Extrahepatic manifestations** → essential mixed cryoglobulinemia, membranoproliferative glomerulonephritis, sporadic porphyria cutaneatarda, Mooren's corneal ulcers, Sjögren's syndrome, lichen planus, pulmonary fibrosis, thyroid hormone abnormalities. (hallmark: autoimmune syndromes) "note: those weren't mentioned by the doctor in the lecture, read them please ☺"

❖ **DIAGNOSIS:**

- ✓ **Serology** → Detection of antibody to recombinant HCV peptides.
  Third-generation enzyme linked assays have **a sensitivity** of ~97% and can detect HCV antibody within 6–8 weeks. The positive predictive value is ~95%, but much lower in low-prevalence populations such as blood donors; thus, **confirmatory testing by HCV RNA detection is essential.**
  Immunocompromised patients (including HIV) may have false-negative serology.

- ✓ **HCV RNA** → Detectable within days to 2 months after exposure (varies with inoculum size). Qualitative tests can detect <50 IU/mL HCV RNA and are used to confirm diagnosis and achievement of a sustained virological response (SVR). Quantitative tests report a viral titer and are used to assess response to treatment. New real-time PCR assays detect <10–15 IU/mL and may be sensitive enough for both purposes.
- ✓ **Genotype testing** → essential before treatment.
  The line probe assay reports the genotype and subtype, currently only the genotype is used in planning therapy.
- ✓ **Liver disease severity** → assessed prior to therapy.
  Important to identify **cirrhosis**, as prognosis and treatment selection are altered.
  **Fibrosis** can be assessed non-invasively (elastography), with liver biopsy reserved for those cases in which there is uncertainty.

✓ **Acute hepatitis C** → diagnosis is **confirmed by** newly positive **HCV RNA PCR (mainly)**, and conversion to HCV antibody-positive within 12 weeks.

**In the absence of a documented initial negative test**, distinguishing acute from chronic is problematic. **Circumstantial evidence**, **clinical features**, timing of **aminotransferase changes**, and presence of **liver fibrosis** may help.

✓ **Chronic hepatitis C** → positive **ELISAs** should be confirmed **with** a HCV **RNA test**.
**High-risk patients** with negative PCRs should be **retested** a few months later, in case of false-negative results.

**most sensitive** indicator of HCV infection is the presence of HCV **RNA**, by **PCR** or transcription-mediated amplification **(TMA)**.

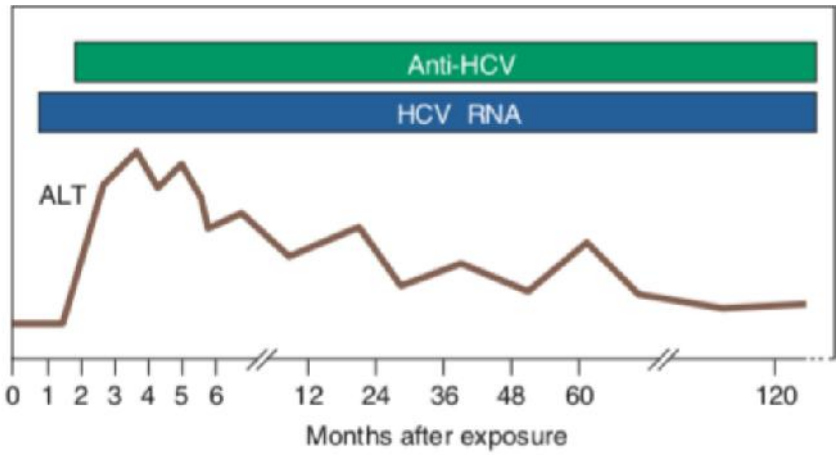



**FIGURE 95-7**
**Scheme of typical laboratory features during acute hepatitis C progressing to chronicity.** HCV RNA is the first detectable event, preceding alanine aminotransferase (ALT) elevation and the appearance of anti-HCV.

**RNA** is the **first** detectable event, then the **ALT** levels increase right before **symptoms** appear.

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| HCV | Approx. 40–60 | Enveloped | 9.4-kb RNA, linear, ss, + | Hepacivirus | HCV C100-3 C33c C22-3 NS5 | Anti-HCV | Bloodborne agent, formerly labeled non-A, non-B hepatitis Acute diagnosis: anti-HCV (C33c, C22-3, NS5), HCV RNA Chronic diagnosis: anti-HCV (C100-3, C33c, C22-3, NS5) and HCV RNA; cytoplasmic location in hepatocytes |

**Acute diagnosis: anti-HCV test**
**Chronic diagnosis: anti-HCV and RNA PCR tests**

❖ **TREATMENT:**

✓ **The aim** is to achieve a **'sustained virological response'** (**SVR**, the **absence of HCV RNA by PCR** at 6 months after finishing treatment). An SVR is associated with 98–100% chance of being RNA-negative in the longer term and reduces all-cause mortality.

✓ **Treatment** has been revolutionized by direct-acting antivirals such as **sofosbuvir**.

✓ **Response** is affected by the **genotype**, **race**, baseline **viral load**, and certain host **genetics.** **Cirrhotic patients achieving an SVR should continue to be monitored**, as they remain at risk of **HCC**.

**TABLE 95-2**

**CLINICAL AND EPIDEMIOLOGIC FEATURES OF VIRAL HEPATITIS**

| FEATURE | HAV | HBV | HCV | HDV | HEV |
|---|---|---|---|---|---|
| Incubation (days) | 15–45, mean 30 | 30–180, mean 60–90 | 15–160, mean 50 | 30–180, mean 60–90 | 14–60, mean 40 |
| Onset | Acute | Insidious or acute | Insidious | Insidious or acute | Acute |
| Age preference | Children, young adults | Young adults (sexual and percutaneous), babies, toddlers | Any age, but more common in adults | Any age (similar to HBV) | Young adults (20–40 years) |
| Transmission | | | | | |
| Fecal-oral | +++ | – | – | – | +++ |
| Percutaneous | Unusual | +++ | +++ | +++ | – |
| Perinatal | – | +++ | ±[a] | + | – |
| Sexual | ± | ++ | ±[a] | ++ | – |
| Clinical | | | | | |
| Severity | Mild | Occasionally severe | Moderate | Occasionally severe | Mild |
| Fulminant | 0.1% | 0.1–1% | 0.1% | 5–20%[b] | 1–2%[e] |
| Progression to chronicity | None | Occasional (1–10%) (90% of neonates) | Common (85%) | Common[d] | None |
| Carrier | None | 0.1–30%[c] | 1.5–3.2% | Variable[f] | None |
| Cancer | None | +(Neonatal infection) | + | ± | None |
| Prognosis | Excellent | Worse with age, debility | Moderate | Acute, good Chronic, poor | Good |
| Prophylaxis | IG, inactivated vaccine | HBIG, recombinant vaccine | None | HBV vaccine (none for HBV carriers) | Vaccine |
| Therapy | None | Interferon Lamivudine Adefovir Pegylated interferon Entecavir Telbivudine Tenofovir | Pegylated interferon plus ribavirin, telaprevir, boceprevir | Interferon or pegylated interferon (efficacy moderate) | None |

## ❖ Some notes on the previous table:

™ **Incubation period →** HAV & HEV are approximately the same.
HBV & HDV are the same (30-180).
HCV is in between (15-160).

™ **Age →**
HAV **children.**
HEV **children** (young adults).
HBV & HCV **any age** will be at risk group (**HCV** people that might get **blood products**).

™ **Clinical severity →** HAV & HEV are **mild,** but we worry about HBV, HCV & HDV to **progress** to **fulminant hepatitis**.

™ **Carriers →** are present in HBV, HCV and HDV.

™ **Prognosis →** ***HAV, HEV have the best prognosis***. HEV has a worse prognosis than HAV, because it's more common in the third trimester of pregnancy and in older men, and it carries a high mortality (up to 20%).

HBV, HCV and HDV→ If the patient cleared it in the **acute** state → prognosis is **good**, but if the patient developed **chronic** → the prognosis is **poor** and **worsens with age**.

™ **Prophylaxis →**

HEV & HAV **vaccine is available**.

HDV & HBV **no vaccine**, you give **HBIG prophylactic** if got exposed.

HCV still has **no vaccine.**

## HEPATITIS "D" VIRUS:

™ **Hepatitis delta virus** (HDV) is a defective virus whose replication requires **HBV**.

™ Hence those with HDV are **always co-infected** with **HBV**.

™ Virions of HDV consist of a **core of delta antigen and single-stranded circular RNA enclosed in an envelope provided by HBV** (with **HBsAg**).

™ 8 genotypes.

™ Most patients with **delta antigen** in the liver have **anti-delta antibodies** in their serum.

™ **HDV superinfection** usually results in the ***suppression of HBV replication*** by mechanisms as yet unknown (**HBsAg and HBV DNA levels drop**).

### EPIDEMIOLOGY:

™ It is thought that **5% of chronic HBV carriers worldwide may be infected with HDV**. However, the prevalence of HDV in HBV carriers varies around the world.

™ It is endemic in Mediterranean countries (around 10% in Italy) and the Far East (90% in the Pacific islands, 5% in Japan), but largely confined to at-risk groups in other Western countries.

™ *There is a **higher** incidence of HDV infection in **HBsAg-positive** patients with **acute** and **chronic** hepatitis, compared with **asymptomatic**.*

### CLINICAL FEATURES:

✓ Symptoms range from **asymptomatic** to **fulminant liver failure** (rare, but still **ten times** more common than in **other** viral hepatitis).

✓ Clinical features seem to cluster in **geographical areas** that may relate to the prevailing genotype in that area, **Western countries see higher rates of fulminant disease that may relate to genotype 1 (which is dominant in these areas)**.

✓ Simultaneous **co-infection with HBV/HDV**—causes ***acute hepatitis*** indistinguishable from ***classical acute hepatitis B*** (maybe with higher rates of liver failure, especially in **IV drug abusers**).

✓ **5%** of people develop **chronic** HDV.

✓ **HDV superinfection** of a carrier of HBV→ may cause liver flare (may present as severe acute hepatitis if HBV is undiagnosed), up to 80% of people become chronically infected.

✓ In the longer term, HDV seems to exacerbate the pre-existing liver disease due to HBV, with potentially rapid progression of cirrhosis (within 2 years).

✓

**DIAGNOSIS OF HDV HEPATITIS:**

- **First, diagnose HBV (HDV cannot exist without it)**. **Consider HDV** in those with **acute HBV** if they have HDV risk factors or experience particularly **severe hepatitis**, and in those with **established HBV** with severe **liver flare**.
- **HDV antibodies** → appear late (4 weeks) and may vanish after resolution of acute infection (Present in high titers in chronic infection).
- **HDV RNA** → can be detected in serum by hybridization or RT-PCR assays.
- Differentiating between **HBV/HDV co-infection** and **HDV superinfection** relies on the detection of **high levels of IgM anti-HBc** (in those co-infected).

## HEPATITIS "E" VIRUS:

• **Route of transmission:** feco-oral route.
• A member of the **family** Hepeviridae.
• It is the **commonest** cause of **acute hepatitis** in certain parts of Asia *(prevention for travelers)*.
• Infection with hepatitis E may be asymptomatic or range in severity from *mild* to *fulminant* hepatitis.
• Fulminant disease is more common in **pregnant women** and **elder men**.

**THE VIRUS:**

• An **icosahedral**, non-enveloped **RNA** virus (30–32nm in diameter).
• The genome is 7.2kb in length, encoding **three ORFs**→ORF1 encodes **non-structural** proteins, ORF2 encodes **the capsid**, ORF3 encodes an **immunogenic protein** of unknown function.
• There are **four genotypes** → **1 and 2** appear to be confined to **humans**, **3 and 4** infect **humans and animals** (pigs in the case of 3), genotype 3 may cause milder disease.

**EPIDEMIOLOGY** – Epidemiology similar to HAV

- ✓ Highest incidence is in Africa, Asia, Central America, and the Middle East, and rising in the west.
- ✓ HEV has a wide host range and has been shown experimentally to infect New and old World monkeys, swine, rodents, and sheep.
- ✓ **Transmission**: Many epidemics of HEV have been **waterborne** (contaminated water), some food-borne (maybe undercooked meats), and infection may follow blood transfusion in endemic areas.
- ✓ Transmission from animals (esp. swine) may occur (high seroprevalence amongst those with occupational exposure to animals). Person-to-person transmission (e.g. within a household) seems to be uncommon.
- ✓ Perinatal transmission has been reported, and severe neonatal disease can occur.
- ✓ the presence of anti-HEV antibodies is 15–60% in endemic countries, and higher than expected in non-endemic regions (overall US rate reported at 21%, higher in those consuming organ meat).
- ✓ In the US, UK: most cases are due to genotype 3 (may not have clinical manifestations).
- ✓ Peak incidence in 15–35 years old (males>females) low in infants and children.

**CLINICAL FEATURES:**

• Maybe asymptomatic or range in severity from mild to fulminant hepatitis.

• Acute cases of HEV are clinically indistinguishable from other viral hepatitis (more severe than HAV).

• Symptoms: fever, nausea, vomiting, jaundice, and abdominal tenderness. Cholestasis may be prolonged; arthralgia and urticarial rash may occur.

• **Fulminant hepatitis is more common in the third trimester of pregnancy and older men, and carries a high mortality (up to 20%)**. This accounts for the overall fatality rate of 0.5–3%.

• Outcome can be poor in those with chronic liver disease.

• **Chronic HEV infection occurs amongst organ transplant recipients**.

**DIAGNOSIS:** the professor just read the things in bold

❖ **Serology**

• **Anti-HEV IgM can be detected in up to 90% of cases 1–4 weeks after acute infection**, usually within the same period as symptoms occur.

• By 3 months, anti-HEV IgM is only detectable in 50% of patients.

• Anti-HEV IgG is detectable 2–4 weeks after the onset of symptoms (one high titer or rising current titer suggest infection).

❖ **PCR**

• HEV is detectable by RT-PCR in **blood** and **stool** (**viremia is short**, but may last up to 4 months in some patients).

• In stool, it appears around 1 week before illness onset, remaining until 2 weeks after.

**TREATMENT:**

• Supportive.

• Transplant for liver failure.

• Reductions in immunosuppressive therapy can help chronically infected patients.

**CLINICAL FEATURES** *of all types of Hepatitis Virus*

• There are **no clinical features** that distinguish the **various causes**.

• **Acute viral hepatitis** can be divided into four clinical stages: incubation period, pre-icteric phase, icteric phase, and convalescence.

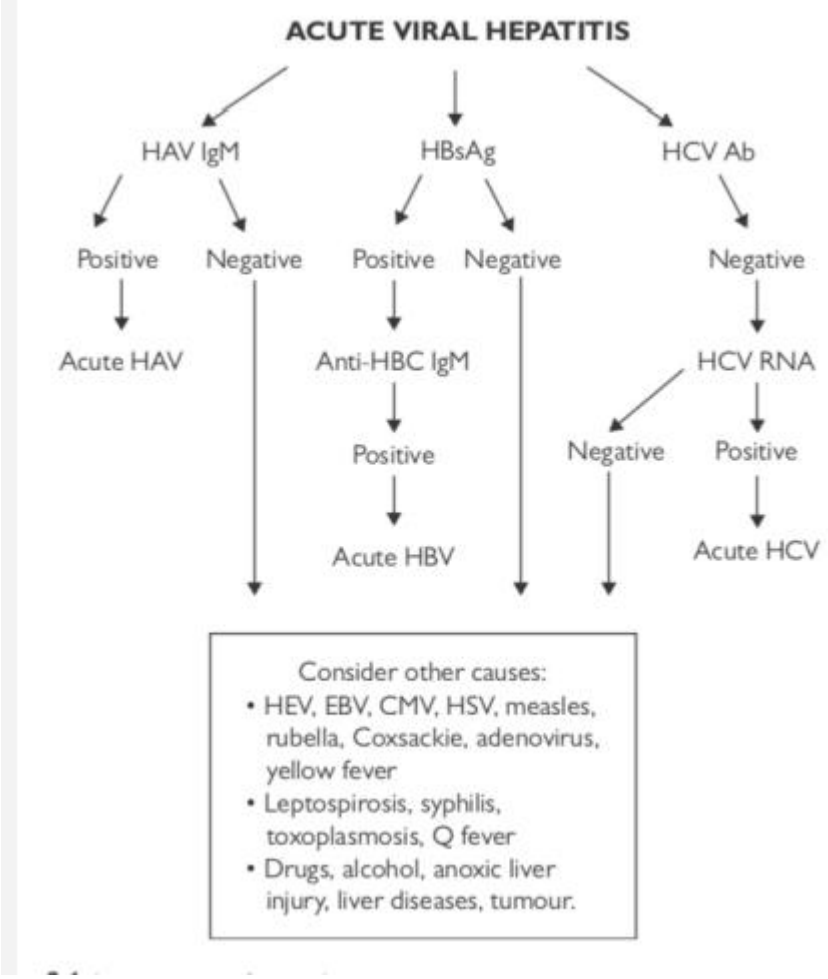
• **Clinical features** may range from asymptomatic disease to anorexia, malaise, abdominal pain, and jaundice to fulminant hepatic failure.

• **hepatitis B and C** may cause immune complex-mediated diseases, e.g. serum sickness, polyarteritis nodosa (hBV), glomerulonephritis, mixed cryoglobulinaemia.

• **Fulminant viral hepatitis**, characterized by liver failure and hepatic encephalopathy, occurs within 8 weeks after onset of symptoms.

**DIAGNOSIS**:

- Routine blood tests.
- **AST** and **ALT** are usually **very high**, with **bilirubin levels** variably **increased**.
- A prolonged PT is rare and suggests severe hepatic necrosis.
- Serology → anti-hAV IgM, HBsAg and anti-HBc IgM, and anti-HCV should be performed initially (**see the scheme**).
- If these are negative, other diagnosis should be considered.
- Liver ultrasound is usually normal in acute viral hepatitis.
- Other abnormalities such as hepatic lesions, cirrhosis, portal hypertension, or ascites suggest alternative diagnoses.
- Liver biopsy may be performed to establish the diagnosis in acute hepatitis with negative serology.




Notice this scheme is for acute viral hepatitis so we detect IgM Not IgG.

As we come to end, here are some clinical features to help you in diagnosis

**CLINICAL FEATURES OF CHRONIC HEPATITIS:**

- There are **no specific clinical features**, and many patients remain **asymptomatic**, until they develop **end-stage liver disease**.
- **Non-specific features** (e.g. fatigue and right upper quadrant discomfort) are common.
- **Symptoms**, such as **jaundice**, **weight loss**, **abdominal distension**, or **confusion**, suggest **decompensation**.
- Examination may show signs of chronic liver disease (e.g. palmar erythema, Dupuytren's contractures, jaundice, spider naevi, hepatosplenomegaly, caput medusae, ascites).

™ **Clinical features of hepatic encephalopathy** include confusion, drowsiness, asterixis, ophthalmoplegia, and ataxia.