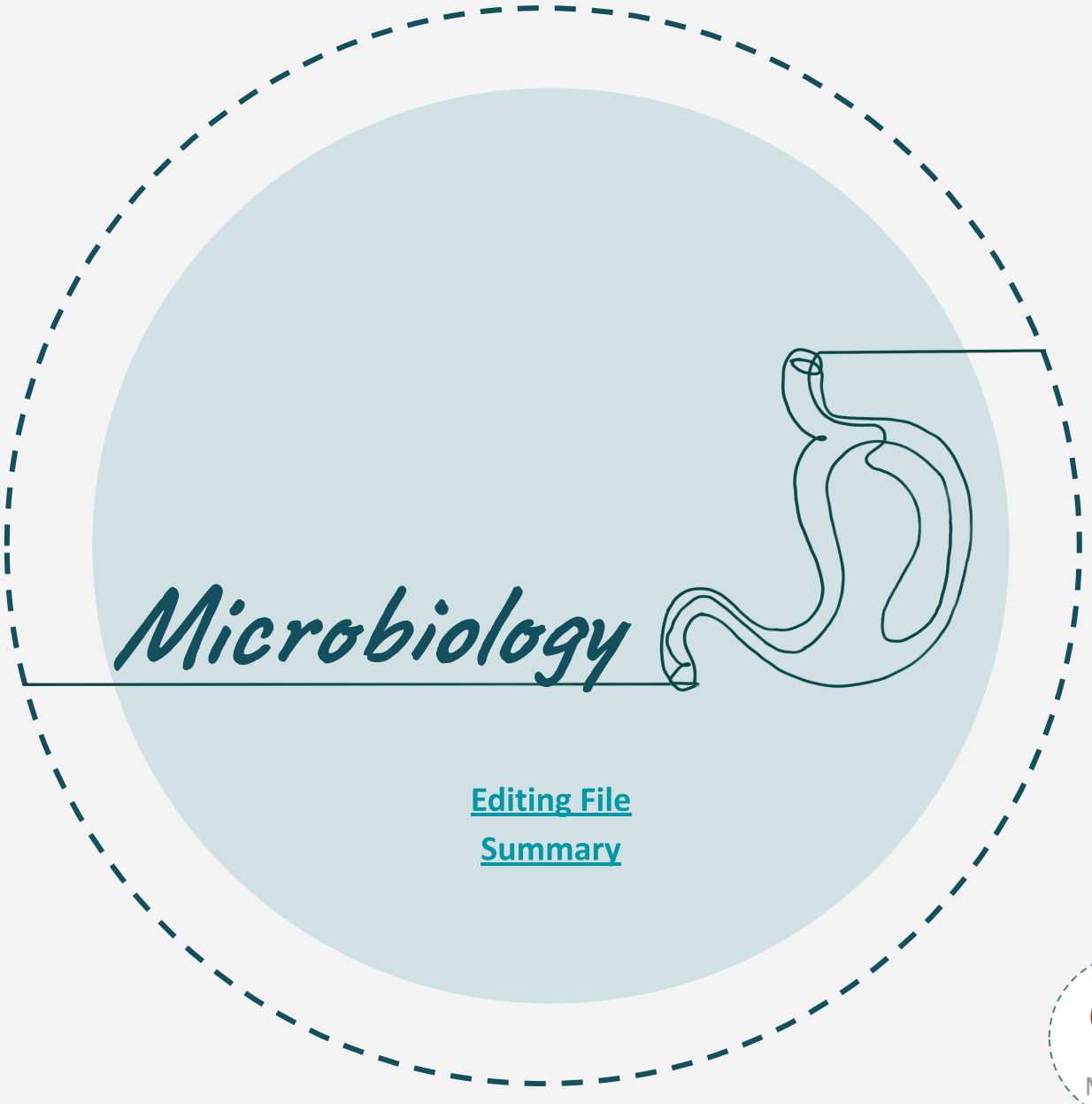
Viral Hepatitis B, C, D and G



Editing File

Summary

MED439
KING SAUD UNIVERSITY

MICROBIOLOGY
Team 439

Revised & Approved
Bassam Alasmari
Rania Almutiri

Color index

- Girls' slides
- Main content
- Important
- Boys' slides
- Extra
- Drs' notes

Objectives:

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

Hepatitis

Introduction

- Hepatitis is inflammation of the liver cells.
- Hepatitis is feature of many diseases usually as a part of a generalized infection. However, some viruses primarily targeting the liver to cause viral Hepatitis.
- Viral hepatitis presents more or less similar clinical picture whatever the causative viruses and we have to determine the causative virus to know how to treat and to determine the prognosis
- Laboratory tests can differentiate between different.

Etiology

Primary infections

- 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 a part of generalized infection

- Cytomegalovirus (CMV).
- Epstein-Barr virus (EBV).
- Yellow fever virus.

Viral hepatitis is divided into two large groups, based on the mode of transmission:

Enterically transmitted hepatitis or water borne hepatitis.

Hepatitis A & E viruses.
Non-enveloped viruses

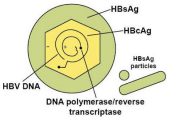
Parenterally transmitted hepatitis or blood borne hepatitis.

Hepatitis B, C, D & G viruses.
Enveloped viruses

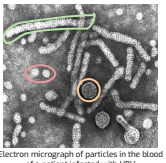
Hepatitis B Virus

Characteristics:

- Family of **Hepadnaviridae.**
- There are **8** known **genotypes** (A-H), genotype **D** is the dominant in Saudi Patients.
- **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.**
  - **HBeAg** is a component of core gene product and indicate **active viral replication**.
  - **The virus contains the enzymes reverse transcriptase and protease enzyme.**
  - Hepatitis B virus can resist low pH and moderate heating.



- **The serum of infected individual contains three types of hepatitis B particles:**
  - Dr. Mona: important in OSPE
  - 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) and they are 42-nm in diameter.


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

Hepatitis B

Transmission

- Hepatitis B virus (HBV) is transmitted from patients who are infected to those who are not immune.
- Hepatitis B vaccination has significantly reduced the risk of transmission worldwide.
- The predominant mode of HBV transmission varies in different geographical areas.

Parentally (blood) (Mainly)

- Direct exposure to infected blood Mainly 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 toothbrushes.

Sexually (unprotected sex)

- Sexual transmission remains as one of the common source of **HBV** transmission.
- Homosexual men & heterosexual persons who have multiple sex partners are at particularly high risk.

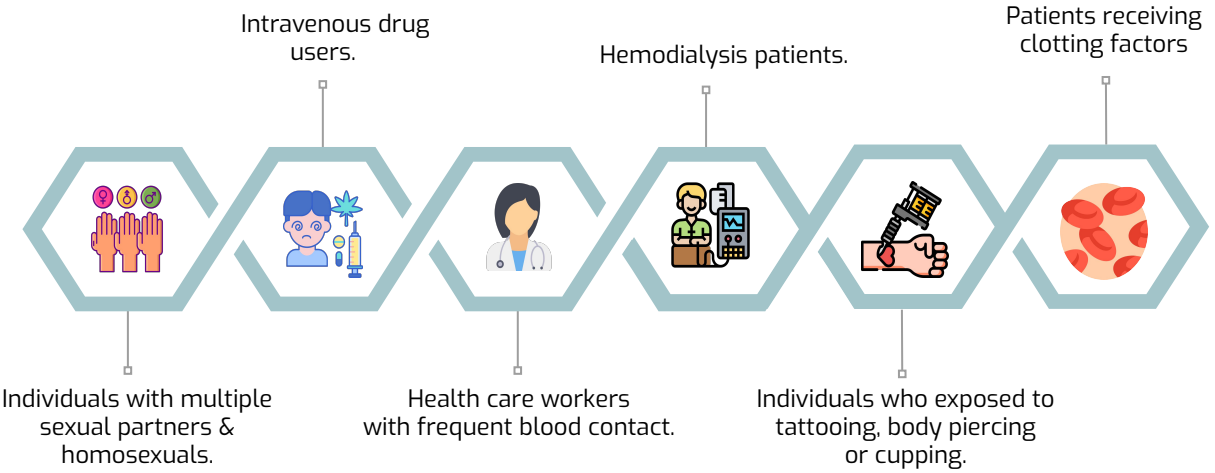
Mother-to-child transmission

- Mother-to-child transmission may occur in utero (**vertical** transmission), but more % of transmission are reported at the time of birth, or after birth (perinatal transmission) .
- **Passive** and **active** immunization of the newborn within 12 hours of delivery has reduced the risk of **HBV** transmission by more than 95%. However, despite the proper use of prophylaxis, transmission can still occur. The risk appears to be greatest if the mother is positive for (HBeAg) and/or has a high **HBV viral load**.
- There is no evidence that transmission of **HBV** occurs during breastfeeding.

Transplant recipients

- Infection can be transmitted from HBsAg-positive donors to HBsAg-negative recipients, with severe clinical consequences when the recipient is non-immune. Transmission of **HBV** infection has been reported after hematopoietic stem cell and solid organ transplantation.

Risk Factors

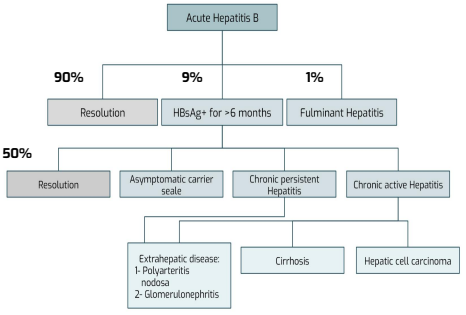


Hepatitis B

Acute hepatitis B infection		
Pathogenesis	• HBV infected hepatocytes, and viral antigens are displayed on the **surface** of hepatocytes cells. • Cytotoxic T cells mediate an immune attack against the viral antigens, causing inflammation and necrosis (cell mediated immunity), **HBV itself does not cause a cytopathic effect** (The effect on the surface of the cell NOT inside the cell)	
Other Info	• Incubation period varies from 1 to 4 months (10 to 12 weeks). • ***Most*** of the **HBV** infections are asymptomatic. • The clinical appearance of acute hepatitis **B** is similar to that of hepatitis **A**. However, with hepatitis **B** symptoms tend to be more severe.	
Phases	Anicteric phase No jaundice	• An means = without and icteric means = jaundice. • Low grade fever, anorexia, malaise, nausea, vomiting and pain at the right upper quadrant of the abdomen, raised liver enzyme
	Icteric phase (25%) Jaundice	• Which is characterized by jaundice, raised bilirubin leading, dark urine and pale stool (whitish).
	Convalescent Recovery	• Symptoms and icteric phase resolve, liver enzymes return to normal but malaise and fatigue may persist for weeks

Clinical Outcomes

- Adults: **About 90 %** of them will develop acute hepatitis B infection and recover completely and may develop immunity* "*Dr. Mona: add this to your slides". **less than 9 %** of adult may progress to chronic hepatitis B. And **less than 1 %** of adult may develop fulminant hepatitis B.
- Children: **About 20%-50%** of them age 1 to 5 years may
- progress to chronic hepatitis B. (More chronicity)
- Infants: **About 90%** of infected infants may progress to chronic hepatitis B. (Most chronicity)
- **Fulminant hepatitis B** characterized by massive liver necrosis, liver failure and death and is believed to be due to massive immune-mediated lysis of infected hepatocytes. (very fatal)



Hepatitis B

Chronic Hepatitis B Infection

About		• Chronic hepatitis is limited to hepatitis B, C , D and may be G viruses. • Characterized by the presence of HBsAg or HBV-DNA in the blood for **more than 6 months**. • The majority of patients with chronic Hepatitis B are asymptomatic or have mild fatigue only, may only be detected by elevated liver enzyme on a routine blood chemistry profile. • Symptoms include right upper quadrant abdominal pain, enlarged liver & spleen, Jaundice may or may not developed and fatigue. • Some of these chronic patient will become immune after years and they develop anti-HBsAb in the serum with disappearance of HBeAg "develop immunity" • Some other chronic patient will develop active hepatitis, which can lead to **cirrhosis** and **death**.
Phases	The replicative phase	• The patient is positive for HBsAg, HBeAg and HBV-DNA. • High viral load more than 105 copies/ml -ALT is normal or nearly normal. • Liver biopsy shows minimal damage.
	Inflammatory phase	• HBsAg positive for more than 6 months, HBeAg positive, Decline in HBV-DNA in the blood. • Viral load is more than 105 copies/ml. • ALT is elevated. • The immune system attacks hepatocytes harboring the virus. • Liver biopsy shows damage to hepatocytes.
	Inactive phase	• Negative for HBeAg, Positive for anti-HBe, HBV-DNA. • Viral load less than 105 copies/ml. • Normal ALT. (it is a liver enzyme)

Factors predictive of disease progression

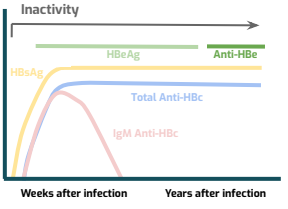
- Both virologic and non-virologic factors influence disease progression and survival in patients with chronic HBV infection.

1. **HBeAg:** Patients with a prolonged replication phase (ie, HBeAg positive) have a **worse prognosis**, mostly due to the development of cirrhosis and hepatocellular carcinoma.
2. **HBV DNA:** High HBV DNA levels are associated with an increased incidence of cirrhosis, hepatocellular carcinoma, and liver-related mortality.
3. **HBsAg levels:** In patients with HBeAg negative chronic HBV with a low viral load, HBsAg levels more than 1000 IU/mL have been associated with an increased risk of disease progression and hepatocellular carcinoma .

- Host related factors as (gender[1], age[2], diabetes) and environment (alcohol, smoking, carcinogens) as well as co-infection with other viruses (eg, HCV, HDV, HIV) can play a role in prognosis.

Serological profile of chronic HBV infection

- In patients with **chronic hepatitis** the HBsAg will be present throughout the period of infection.
- If HbeAg is present for a long time it indicates a bad prognosis for the infection and sometimes will disappear and get replaced by Anti-HBe.
- In early weeks of infection we will find raised IgM Anti-HBc then it will start to decline.
- Total Anti-HBc (IgG) will be detected in early weeks after infection then will remain elevated throughout the period of infection.



[1] Males tend to develop chronicity more than females

[2] Higher likelihood of chronicity in infants and decrease as child grows up

Hepatitis B

Complications of Chronic Hepatitis

The whole slide was skipped by Dr. Mona
- **just** know that chronic HBV can lead to cirrhosis and hepatocellular carcinoma

Hepatocellular carcinoma	
Definition	• One of the most common cancers in the world. • Also, one of the most deadly cancers if not treated.
Cause of chronic liver diseases	• Hepatitis B and C viruses
Symptoms	• Abdominal pain. • Abdominal swelling. • Weight loss. • Anorexia. • Vomiting. • Jaundice.
Physical examination	• Hepatomegaly, splenomegaly and ascites.
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.
Cirrhosis[1]	
Definition	• It is a chronic diffuse liver disease.
Characterized by	• Fibrosis and nodular formation.
Results from	• Liver cell necrosis and the collapse of hepatic lobules.
Symptoms	• Ascites. • Coagulopathy (bleeding disorder). • Portal hypertension. • Hepatic encephalopathy. • Vomiting blood. • Weakness. • Weight loss.

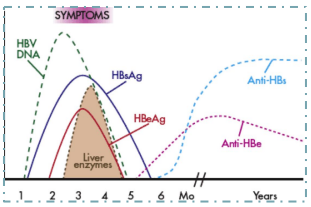
[1] Not everyone develop Cirrhosis From Hepatitis.

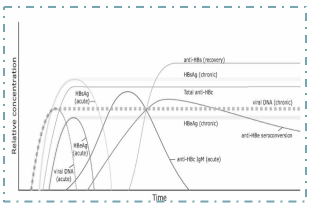
Hepatitis B

Hepatitis B Serological Markers

Dr. Mona: the markers are **VERY IMPORTANT**.

Antigen/Antibody	About	Indicative of
HBV-DNA	○ **Serum HBV DNA assays:** Qualitative and quantitative tests for HBV DNA in serum have been developed to assess HBV replication. ○ Currently, most HBV DNA assays use **real-time PCR techniques**, report results in international units/mL, Recovery from acute hepatitis B is usually accompanied by the disappearance of HBV DNA in serum. ○ Is the 1st marker that appears in circulation, 3-4 weeks after infection	**- Marker of infection**
Hepatitis B surface antigen (HBsAg)	○ HBsAg (HBsAg) is the serologic **hallmark of HBV infection**. It can be detected using an (EIA), HBsAg appears in serum 1 to 12 weeks (I.P) after an acute exposure to HBV prior to the onset of hepatitis symptoms or elevation of serum alanine aminotransferase (ALT). ○ Is the **2nd marker** that appears in the **blood** with patient having acute HBV infection and persists for less than 6 months, then disappears if patient not become chronic.	**- Marker of infection**
Antibody to Hepatitis B core (HBcAb) or (Anti-HBc)	○ Anti-HBc can be detected throughout the course of HBV infection. ○ IgM Anti-HBc is the **sole** marker of HBV infection during the window period "the period in infection when neither hepatitis B surface antigen (HBsAg) nor its antibodies (Anti-HBsAg) can be detected in the serum of the patient will be explained later.." and it is the 1st antibody that appears in the blood and usually persists for 2 years. ○ Anti-HBc IgG (Total Anti-HBc) persists along with Anti-HBsAg in patients who recover from acute hepatitis B (immune), It also persists in association with HBsAg in those who progress to **chronic HBV** infection and it indicate natural infection.	- Marker of exposure to hepatitis B infection. - **Not** found in vaccinated person only if exposed to natural infection which means we find it only in patients who exposed to HBV "natural immunity"[1] - **Not immune.**
Hepatitis B e antigen (HBeAg)	○ Is a secretory protein that is processed from the pre-core protein. ○ It is generally considered to be a marker of HBV replication and infectivity. The presence of **HBeAg** is usually associated with high levels of **HBV DNA** in serum and higher rates of transmission of HBV infection from carrier mothers to their babies and from patients to another person. ○ In such patients, the presence of HBeAg is usually associated with the detection of high levels of HBV DNA in serum and active liver disease. ○ is the **3rd maker** that appears in **circulation** and disappears before HBsAg, it indicates active viral replication.	- Marker of active virus replication, the patient is **highly infectious**, the virus is present in all body fluids even in his tears.
Hepatitis B e Antibody (HBeAb) or (Anti-HBeAg)	○ Is HBeAg to Anti-HBeAg seroconversion occurs early in patients with acute infection, However, HBeAg seroconversion may be delayed for years to decades in patients with chronic HBV infection. ○ With the disappearance of HBeAg and appearance of Anti-HBe, Ab usually persists for several weeks to several months.	- Marker of low infectivity, the patient is **less infectious**. - **Not immune.**
Hepatitis B surface antibody (HBsAb) or (Anti-HBsAg)	○ 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 **only marker of immunity** to hepatitis B infection which means we find it in vaccinated person[2]





[1] If there was Anti-HBs and Anti-HBc in patients makers, it means immunity was gained after a natural infection of hepatitis B virus.

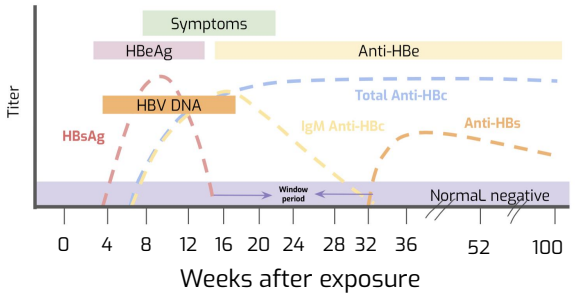
[2] If there was Anti-HBs BUT NO Anti-HBc in patients makers, it means immunity was gained after vaccination.

Hepatitis B

Window phase

* Only in female slides

Acute Hepatitis B virus infection with Recovery



- There is a period of several weeks when HBsAg has disappeared but HBsAb (Anti-HBsAg) is not yet detectable, at that time, HBcAb (IgM Anti-Hbc) is always positive and can be used to make the diagnosis.
- HBV-DNA will be detected before HBsAg and then HBsAg will be detected from 10-12 weeks after the exposure to the infection and they have to persist throughout the course of infection up to 6 months then they will disappear.
- After the disappearance of HBV-DNA and HBsAg , HBeAg and Anti-HBe will appear and as we know HBeAg indicates that there is **active virus replication** "the patient will be **highly infectious**"and then after few weeks HBeAg has to disappear and it will be replaced by IgM Anti-HBc and that is the window period which means that neither hepatitis B surface antigen (HBsAg) nor its antibodies (Anti-HBsAg "IgG") can be detected in the serum of the patient "the only marker that can be detected in this period is the serum is IgM Anti-HBc".
- After the disappearance of IgM Anti-HBc it will be replaced by Anti-HBsAg "IgG" and it will persists throughout the course of infection.

Summary

* Only in female slides

Interpretation	HBV DNA	Anti-HBe	Anti-HBs	IgG anti-HBc	IgM anti-HBc	HBeAg	HBsAg
Acute HBV Infection							
Early Phase[1]	+++				+	+	+
Window Phase[2]	+				+		
Recovery Phase[3]	+ or -	+	+	+			
Chronic HBV Infection							
HBeAg+ high replicative phase (immune tolerance or immune clearance)[4]	+++	-		+		+	+
HBeAg- low replicative or inactive phase[5]	+ or -	+		+		-	+
Flare of chronic HBV	+			+	+ or -	+	+ or -
HBeAg- replicative phase (HBeAg-chronic hepatitis precore/core promoter variants)	++	+		+		-	+
Occult HBV	+	+ or -	+ or -	+ or -		-	-

[1] Early phase is characterized by high levels of HBV-DNA and raised IgM Anti-Hbc, HBeAg and HBsAg.

[2] If only IgM Anti-HBc is present, it means that the patient is in window period and it doesn't mean that the patient is immune.

[3] Raised levels of IgG Anti-HBc, Anti-HBs and Anti-HBe means the patient is in recovery phase and is developing immunity.

[4] Raised levels of HBsAg and HBeAg after 6 months indicates a bad prognosis for the infection because HBeAg is elevated which will lead to HCC and cirrhosis (chronic complications)

[5] Raised levels of HBsAg after 6 months but NOT HBeAg indicates that the patient's prognosis is better than HBeAg+ high replicative phase (immune tolerance or immune clearance) and the patient will be less infectious and not developing immunity

Hepatitis B

Lab Diagnosis

Important

- Hepatitis B infection is diagnosed by detection of HBsAg in the blood by **ELISA***
  *Dr. Mona: add this to your slides".
- 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.

Prevention

- Prevention involve the use of either the vaccine or hyper immune globulin or both.

HBV Prevention	
HBV-Vaccine	• Vaccine is not live attenuated nor killed vaccine, It contains highly purified preparation of HBsAg particles , produced by **genetic engineering in yeast**. • The vaccine is highly effective and has few side effect. • The vaccine is administered in **three doses IM injection** at 0 &1 & 6 months. Thr seroconversion rate is about 95% in healthy adults. It is indicated for people who are frequently exposed to blood or blood products and to travelers who plan to visit endemic area, in our region it is given to all newborn. If antibody titers have declined in immunized patients who are at high risk, such as dialysis patients, then a booster dose should be considered.
Hepatitis B immunoglobulin (HBIG)	• It contain high titer of HBsAb, it is used to provide immediate, passive protection to individuals known to be exposed to HBsAg positive blood (after accidental needle-stick injury). Both the vaccine and HBIG should also be given to them and to a newborn whose mother is HBsAg–positive, this regimen is very effective in reducing the infection rate of newborns whose mothers are chronic carriers.
Pre-exposure prophylaxis "Skipped by Dr. Mona"	• Vaccine is prepared by cloning HBsAg in yeast cells. • Universal vaccination of newborns is recommended in most countries. • Vaccination should also be provided to individuals who are not immune to HBV and are at high risk of exposure (eg, healthcare personnel, injection drug users, household contacts of hepatitis B surface antigen [HBsAg]-positive patients, men who have sex with men, human immunodeficiency virus [HIV]-infected patients and hepatitis C virus [HCV]-infected patients) • Vaccine is given in **3 IM injection** at 0-1-6 months and lin booster dose after 5 years.
Post exposure prophylaxis "Skipped by Dr. Mona"	• Persons exposed to needle prick or infant born to +ve HBsAg mother should immediately receive both: Active vaccine and hepatitis B specific immunoglobulin.

Hepatitis B

Treatment

Skipped by Dr. Mona
Dr. Abdulkarim: Dosage and Time are not important, Just Names are Important

- There are several approved antiviral drugs:
  - Pegylated alpha interferon, one injection per week, for 6-12 months.
  - Lamivudine, antiviral drug, nucleoside analogue. One tablet a day for at least one year.
  - 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

Skipped by Dr. Mona

1. Positive for HBsAg
2. Positive for HBV-DNA more than 20,000 IU/ml.
3. ALT more than twice the upper normal limit.
4. Moderate liver damage.
5. Age more than 18 years.

Hepatitis C Virus

Characteristics:

- Family of **Flaviviridae**.
- Genus: **hepacivirus**.
- The virus is small, 60–80 nm in diameter.
- Consists of an outer envelope
- It has icosahedral core and linear positive **polarity ss-RNA genome**.
- It has no polymerase.
- There are **6** major **genotypes** (1–6), genotype **4** is the dominant in Saudi patients. This genetic variation results in high mutation rate in the envelope gene, as a result multiple subspecies often occur in the blood of an infected individual at the same time.

Hepatitis C

Stages	
Acute hepatitis	Chronic hepatitis
• **Mostly asymptomatic, if symptomatic:** - 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.	• Defined as the presence of anti-HCV & elevated serum level of ALT for more than 6 months. • Almost all patients with chronic hepatitis C have the genome HCV-RNA in serum. • Usually **asymptomatic**, but if symptomatic it's usually mild, non-specific & intermittent. • Lab finding: Elevated ALT & AST ranging from 3-20 times ALT more than AST.

Transmission

Parentally (blood) "Mainly"

- Direct exposure to infected blood.
- Using contaminated needles and surgical instruments.
- Using contaminate instruments in the practice of tattooing, ear piercing & cupping (High risk).
- Sharing contaminated razors & toothbrushes.

Sexually

- Is uncommon (unlike B), controversial.

Mother-to-child transmission

- No evidence for transplacental transmission.
- No evidence of breastfeeding transmission.

Clinical Features

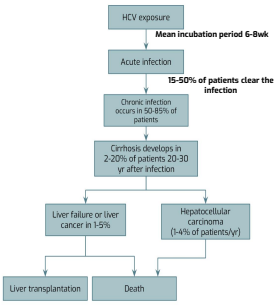
- It's very similar to HBV.
- The mean incubation period is 8 weeks.
- Acute infection is often **asymptomatic**.
- If symptomatic: malaise, nausea, and upper quadrant pain but symptoms in general are less severe than other viral hepatitis.
- Fever, anorexia, nausea, vomiting, and jaundice **are common**.
- Dark urine, pale feces, and elevated liver enzyme (transaminase) are seen.
- Chronic carrier state occur much more often with HCV (75%-85%) infection than with HBV(<9%).

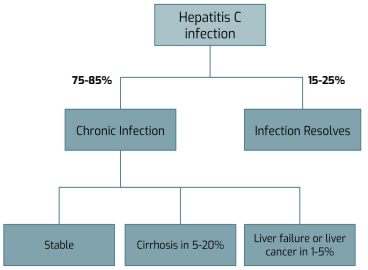
Hepatitis C

Clinical Outcomes

Important

- 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 fulminant hepatitis C, liver failure and death
- About the right pic: if we have 100 patients with Hepatitis C infection 75-85% of them will develop **chronic infection** and 15-25 of them will **recover completely** " **that means this virus has high chance of chronicity**. This virus is more **dangerous** because of high chronicity and **no vaccine is available until today.**

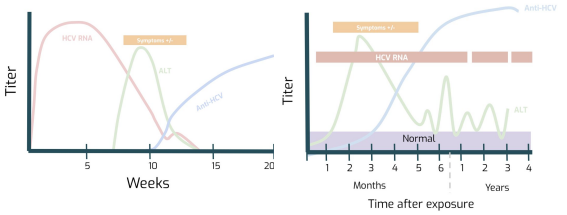




Hepatitis C Serological Markers

Observation:

- Acute: Very high HCV RNA, High Anti-HCV, High ALT
- Chronic: High Anti-HCV (IgG),decreasing HCV-RNA and Fluctuating ALT
- Recovered: High Anti-HCV (IgG), the rest are normal.
- Marker of immunity is to see Anti-HCV (IgG) and there's no HCV RNA.
- Marker of Active infection is to see high levels of HCV RNA.



Hepatitis C Markers		
Antigen/Antibody	About	Indicative of
Hepatitis C virus RNA (HCV-RNA)	◦ Is the **1st marker** that appears in circulation, it appears as early as 2-3 weeks after exposure.	- **Marker of infection**.
Hepatitis C core antigen (HCcAg)	◦ The **2nd marker** that appears in the **blood**, usually 3-4 weeks after exposure.	- Marker of infection
IgG antibody to hepatitis C (Anti-HCV)	◦ Antibodies to hepatitis C virus is the **last marker** that appears in the blood, usually appear 50 days after exposure (long window period). ◦ This Ab present in both acute, chronic patient, **recovery** and immunity.	- Marker of **immunity** If we DON'T have HCV-RNA (we can't say that it's a marker for immunity alone)

Hepatitis C

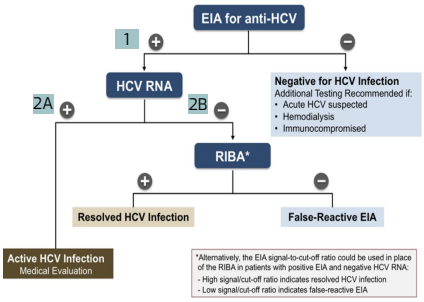
Lab diagnosis

Important

- **By detection of both:**

1. Antibody to HCV in the blood by **ELISA**, if positive result must be **confirmed by**: PCR then **Recombinant ImmunoBlot Assay (RIBA)**.
   - ELISA does not distinguish between IgM and IgG and does not distinguish between an **acute**, **chronic** or **resolved** infection.
2. HCV-RNA in the blood using PCR "polymerase chain reaction(PCR)" based test that detect the presence of **viral RNA** (viral load) in the serum should be performed to determine whether active disease exists.

- **A chronic infection** is characterized by elevated transaminase level, a positive ELISA antibody test and detectable viral RNA for at least 6 months.
- No vaccine available to hepatitis C.
- **(1)** the patient have or had the virus → if PCR is positive **(2A)** then the patient have the virus (Active infection).
- If PCR is negative, we do RIBA for confirmation **(2B)**:
  - → if positive then patient recovered.
  - → if negative then EIA was false positive.



Criteria for Treatment

1	Positive for HCV-RNA.
2	Positive for Anti-HCV.
3	Known for HCV genotype.
4	ALT exceeds twice the upper normal limit.
5	Moderate liver damage (based on liver biopsy).

Treatment

- **The currently used treatment is the combined therapy using:** (Dosage Not important)

1 Pegylated **Alpha interferon** one injection per week.

2 **Ribavirin** Two capsules a day.

- There are number of approved therapies as **Sovaldi** may be given together with or without **Ribavirin** & **Peg-interferon**, 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.
  "Only for your information (no need to memorize it)"

Hepatitis D & G

Virus	Hepatitis D virus
Description	• It is a **defective virus** (weak), that cannot replicates by its own so it requires a **helper virus**. • The helper virus is HBV which 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.
Transmission & Epidemiology	• HDV is transmitted by the same means as HBV. • HDV infections occur worldwide, with a similar distribution to that of HVB.
Pathogenesis & Immunity	• Same like pathogenicity of HBV, but there is some evidence that delta antigen **is cytopathic** (goes inside the cell NOT on the surface) for hepatocytes.
Clinical findings	1. **Co-infection**: - The patient is infected with HBV and HDV **at the same** time leading to severe acute hepatitis. 2. **Super infection**: - In This case, delta virus infects those **who are already have chronic hepatitis B** leading to severe chronic hepatitis, the incidence of fulminant, life threatening hepatitis and liver failure is significantly higher.
Diagnosis	• Detecting either delta antigen or **IgM Ab** to **delta antigen**.

Virus	Hepatitis G virus Dr. Mona: NOT important
Family & Genus	• Family: Flaviviridae. • Genus: Hepacivirus. • Hepatitis G virus or GB-virus was discovered in 1995.
Description	• Enveloped, **ss-RNA with positive polarity**. • Share about 80% sequence homology with HCV.
Transmission	• **Parenterally.** • Sexual. • From mother to child transmission.
Clinical findings	• Causes mild acute and chronic hepatitis infection. • Usually occurs as co-infection with HCV, HBV and HIV.

Drs' notes

Dr. Mona

- Composition and antigens of hepatitis B are as following:
  - (HBsAg) from the envelope.
  - (HBcAg) from the core / capsid.
  - (HBeAg) from the core.
  - DS-DNA and enzymes.
- The only hepatitis virus with DNA genome is Hepatitis B virus.
- Hepatitis B can resist the outside environment (even after blood dries).
- Immunity to hepatitis B can either be acquired through vaccination or by previous infection.
- Main route of transmission of hepatitis B is by blood. Also, its transmission from mother to child mostly occur by direct contact (time of birth & after birth). In these cases, active (vaccine) and passive (antibodies) immunization of child is indicated.
- Pathogenesis of Hepatitis B is due to immune reaction, not due to cytopathic effect. To illustrate, hepatitis B virus does not kill the hepatocytes itself as it has no cytopathic effect. However, it causes the disease by staying on the surface of the cells and then attracting cytotoxic T cells to cause inflammation and destruction.
- Depending on patient's immunity, body reaction to HBV varies significantly. Some patients might be anicteric (have general symptoms but no jaundice) while others might have it in the icteric phase (with jaundice and pale stool).
- If there was Anti-HBs and Anti-HBc in patients makers, it means immunity was gained after a natural infection of hepatitis B virus.
- If there was Anti-HBs but NO Anti-HBc in patients makers, it means immunity was gained after vaccination.
- The longer HBeAg is present and the higher its levels in chronic infection. the worse the prognosis (patient is more likely to develop complications such as cirrhosis and hepatocellular carcinoma). In contrast, chronic patients who lack HBeAg have better prognosis due to reduced viral replication. (high HBeAg = high multiplication of the virus)
- Diagnosis of HBV is by:
  - Detecting HBsAg by ELISA
  - Confirmation by neutralization test.
- Only marker for immunity of HBV is Anti-HBs.
- Hepatitis C virus is more dangerous (1) because it has no vaccine, and (2) that its chronicity rates are high. (20 % of the infected individuals will recover and about 80 % of the infected will progress to chronic hepatitis C)
- The marker of immunity in HCV is lacking HCV-RNA along with presence of Anti-HCV. (Anti-HCV alone is NOT the a marker for immunity).
- If you were asked (how to diagnose HBC?)
  - 1- Antibody to HCV by ELISA → if positive confirm with RIBA.]
  - 2- PCR to look for HCV-RNA.
- HDV is a defective virus, meaning that it requires another virus to replicate which is HBV.

Dr. Alhetheel

- Free surface antigens of HBV are utilized by HDV to make an envelope.
- Core antigen (HBcAg) cannot be measured (no kits available for its screening), so we measure Anti-HBc instead.
- If hepatitis B markers test was requested from the lab, we do HBsAg and Anti-HBc. If HBsAg came positive, we investigate presence of HBeAg or Anti-HBe (only one of them will be present) to evaluate infectivity. (This will be further explained in practical session).

Quiz

MCQ

Q1: Which one of the following is the proper diagnostic approach to confirm HBV infection?.

A- RIBA
B- EIA
C- Neutralization test
D- PCR

Q2: Which of the following viruses cannot replicate on its own and requires a helper virus (defective)?

A- HGV
B- HCV
C- HDV
D- HBV

Q3: A 34 year-old patient who was HCV-infected 4 months ago came to the clinic for routine testing, blood work showed elevated Anti-HCV, normal ALT, nothing else is significant, what stage of disease does this patient have?

A- Acute
B- Chronic
C- Relapsed
D- Recovered

Q4: 1st marker that appears in circulation in HBV is?

A- Hepatitis B DNA
B- HBcAB
C- HBsAg
D- HBeAg

Q5: Which one of the following markers is specific to immunity to HBV?

A- Anti-HBs
B- Anti-HBc
C- HBsAg
D- HBeAg

Q6: Which one of the following HBV markers indicate that the patient is highly infectious?

A- Anti-HBs
B- Anti-HBc
C- HBsAg
D- HBeAg

Answers: Q1:C | Q2:C | Q3:D | Q4:A | Q5:A| Q6:D

SAQ

Case: A 24-year old man was asked to do routine tests required by his new firm he works at, clinical examination showed nonspecific symptoms of fever, nausea and vomiting. Patient was admitted and blood work revealed markedly elevated HCV-RNA, elevated Anti-HCV and an increase in ALT as well.

Q1: What is the most likely diagnosis?

Acute hepatitis C virus

Q2:Mention two routes of transmission?

Parentally and Sexually

Q3: What are the best diagnostic methods for this case?

ABs in blood by ELISA, confirmation by PCR and RIBA

Q4: What is the treatment in this case?

Pegylated alpha interferon and Ribavirin

Members Board

Team Leaders

Muneerah Alsadhan

Shuaa Khdary

Abdurahman Addweesh

Team Members

Sadeem Alhazmi

Raed Alnutaifi

Organizer

Meshal Althunian

Revisers

Mishal Alhamed

Note takers

Duaa Alhumoudi

Faisal Alomri