Viral hepatitis B, C, D and G

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Male Slides

Objectives

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

Better for your eye:
●○ = Male slides
●○ = Female slides

Any future corrections will be in the editing file, so please check it frequently

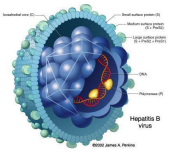
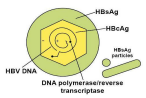
Color Index:
Main text
Important
Doctor Notes
Males slide
Females slide
Extra

Viral Hepatitis

Introduction	● Is inflammation of the liver. ● Hepatitis feature of many diseases usually as a part of a generalized infection e.g. cytomegalovirus, yellow fever, Epstein-Barr virus. ● However, some viruses primarily **target** the liver to cause viral hepatitis. ● Viral Hepatitis presents a similar clinical picture. Whatever the causative viruses. ● Laboratory tests can differentiate between different viruses. ● We have to determine the causative virus to know how to treat and what the prognosis.
Etiology	◎ **Primary infection:** (viruses mainly targeting the liver) ○ 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), has been reported in the literature but not confirmed ○ Hepatitis G virus (HGV) Male Slides ◎ **As a part of generalized infection:** (viruses which may include haptisis or may not. liver it's not the target) ○ Cytomegalovirus (CMV) ○ Epstein-Barr virus (EBV) ○ Yellow fever virus
Groups	**Viral hepatitis is divided into two large groups, based on the mode of transmission** A. **Enterically** transmitted hepatitis or water born hepatitis (by food)**:** hepatitis A & E viruses. B. **Parenterally** transmitted hepatitis or blood born hepatitis**:** hepatitis **B**, **C**, D (**defective virus**) C. G viruses. (mainly by blood, very important for physicians due to needle prick)

Hepatitis B virus

Parenterally transmitted				**Enterically transmitted**	
Hepatitis **B** virus	Hepatitis **C** virus	Hepatitis **D** virus	Hepatitis **G** virus	Hepatitis **A** virus	Hepatitis **E** virus

Characteristics * When we put capital letters it's mean we talk about the virus. but, if small letters it's mean the antigen. e.g: HB → Hepatitis B virus Hb → Hepatitis B antigen	 ○ Family of hepadnaviridae. ○ Virion consists of: - Outer envelope containing hepatitis B surface antigen (HBsAg)*. marker of infection (1) - Internal core (nucleocapsid) composed of hepatitis B core antigen (HBcAg)*. - The viral genome which is small partially circular ds-DNA. - HBeAg is also a part of the inner core, is a secretory protein, marker of active viral replication - The virus contains the enzyme reverse transcriptase & protease enzyme ○ ★There are 8 known genotype (A-H), **genotype D is dominant in Saudi Arabia.**
Types of HBV particles	◎ **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 ○ In addition to the complete HBV particles (Dane particles). 

Hepatitis B Virus

Parenterally transmitted				Enterically transmitted	
Hepatitis **B** virus	Hepatitis **C** virus	Hepatitis **D** virus	Hepatitis **G** virus	Hepatitis **A** virus	Hepatitis **E** virus

Very Important

Transmision

(**Highly virulent virus**) (2)

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.

Sexually (unprotected sex)

- The virus is present in blood and body fluids by having sexual contacts with infected person, virus is present in semen and vaginal secretion, more dominant in **homosexual**.

From mother to the newborn (Perinatally)

- Infected mothers can transmit HBV to their babies mostly (perinatal) during or around delivery (60%) and less likely through placenta (vertical transmission) 10% only if mother have acute HB infection.
- No teratogenic effect
- breastfeeding is also way of perinatal transmission (there is no evidence that transmission of HBV occurs during breastfeeding.)

High Risk Groups

- Intravenously drug users.
- Hemodialysis patients. If the machine isn't clean
- Patients receiving clotting factors.
- Individuals with multiple sexual partners, homosexuals.
- Recipient of blood transfusion , before 1992.
- **Health care workers with frequent blood contact.**
- Individuals exposed to risk factors such as tattooing, body piercing and cupping.

Female Slides

Pathogenesis

- Both innate and adaptive immune response have the main role in pathogenesis of HBV infection. **(cell mediated immunity)** (3)
- Antigen-antibody complexes cause some of the early symptoms e.g. arthralgia's, arthritis, urticaria. and some complications in chronic hepatitis e.g., glomerulonephritis and vasculitis.
- The main determinant of whether a person clears the infection or becomes a chronic carrier is the adequacy of the cytotoxic T- cells response.
- There is no evidence for a virus- induced cytopathic effect on the liver cells.

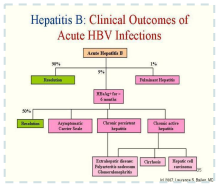
All is Very Very Important

★Clinical Outcomes (4)

★ About 90% of infected adults will develop acute hepatitis B infection & recover completely.

★ < 9% of the infected adult, 90% of infected infants & 20% - 50% of infected children from 1-5 years old may progress to chronic hepatitis B.

- always any type hepatitis < 1% may develop fulminant hepatitis B*, characterized by massive liver necrosis, liver failure and death.



*__Fulminant hepatitis__ is a rare syndrome of rapid (usually within days or weeks), massive necrosis of liver parenchyma and a decrease in liver size

Hepatitis B Virus

Parenterally transmitted				Enterically transmitted	
Hepatitis B virus	Hepatitis C virus	Hepatitis D virus	Hepatitis G virus	Hepatitis A virus	Hepatitis E virus

Acute Hepatitis B infection

Acute hepatitis B infection

- Incubation period varies from 2-4 months (10-12 weeks).
- Acute viral hepatitis usually lasts for several weeks or < 6 months.
- Approximately 70% of the patients with acute HBV infection have subclinical or anicteric (without jaundice) hepatitis, while only 30% of the patients develop icteric (with jaundice) hepatitis.
- Most acute hepatitis B & C are asymptomatic or anicteric.
- The disease may be more severe in patients coinfected with other hepatitis virus as HDV or with underlying liver disease.

Phases

is it different in prognosis? no

Anicteric phase (70%) No jaundice	○ Low grade fever, anorexia, malaise, nausea, vomiting ○ Pain at the right upper quadrant of the abdomen ○ Raised liver enzyme.
Icteric phase (30%)	○ Characterized by jaundice ○ Raised bilirubin leading, dark urine & pale stool & all of the above symptoms

Convalescent phase

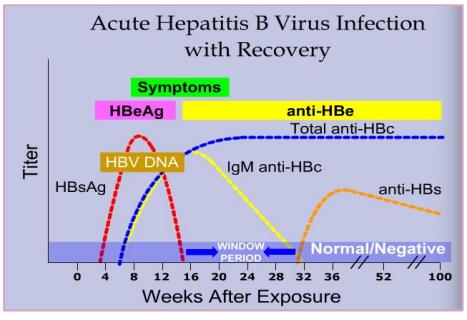
Serological Profile

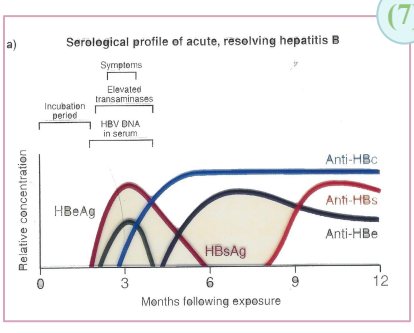
(5 , 6, 7)

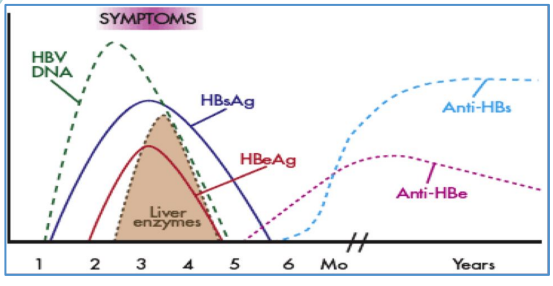
Very Important

- ○ Hepatitis **B- DNA:** is the 1st marker that appears in circulation, 3-4 weeks after infection (contiguous).معدي
- ○ **HBsAg:** is the 2nd marker that appears in the blood and persists only for < 6 months then disappears ,(contiguous) .معدى
- ○ **HBeAg:** is the 3rd maker that appears in circulation, it means active multiplication of the virus, and disappear before HBsAg (highly contiguous) .معدى جدا جدا
- ○ **Anti-HBc Ab(IgM):** is the 1st antibody that appears in the **blood** ***window period** and followed by **Anti-HBc(IgG)** which persists for whole life* (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 HBs-Ag and persists for whole life (several years). It indicates **★★immunity to hepatitis B infection.** غير معدى محصن

◎**Window period:** when HBs-Ag has been disappeared and anti-HBsAg is not yet detectable, at that time only anti-HBc Ag- IgM antibody is detected & can be used to confirm the diagnosis







Hepatitis B Virus

Parenterally transmitted				Enterically transmitted	
Hepatitis **B** virus	Hepatitis **C** virus	Hepatitis **D** virus	Hepatitis **G** virus	Hepatitis **A** virus	Hepatitis **E** virus

Chronic Hepatitis B infection

Overview

- chronic hepatitis is limited to hepatitis B, C, D and G.
- Chronic hepatitis B is defined by the presence of HBsAg and/or HBV-DNA in the blood for more than 6 months (8)
- Chronicity may persists for life or some of the chronic patients may clear HB-sAg after several years or months and develop Anti-HBsAg, they become immune .
- The majority of patients with chronic hepatitis B and C are asymptomatic or have mild fatigue only. may only be detected by ↑ liver enzyme (ALT,AST) on a routine blood chemistry profile
- Symptoms include: some have mild fatigue, right upper quadrant abdominal pain or enlarged liver & spleen, jaundice may or may not developed.
- The major long term risk (complication) of chronic HBV infection are **cirrhosis** with hepatic failure and **hepatocellular carcinoma** ,when HBV genome integrates into hepatocytes DNA.

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Phases

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.
Inflammatory phase	○ HBsAg positive for > 6 months, HBeAg positive, Decline in HBV-DNA in the blood ○ VL is > 10^5copies/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 ○ VL < 10^5 copies/ml with Normal ALT.

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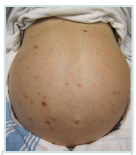
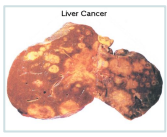
Prognosis

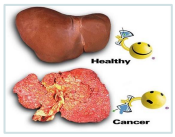
Cirrhosis


ascites

- ○ 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 and swelling, weight loss, anorexia, vomiting, jaundice.
- ○ Physical examination reveals 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.

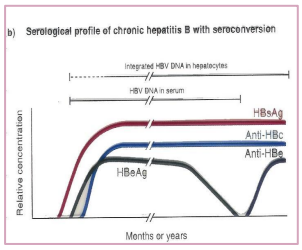
Hepatitis B Virus

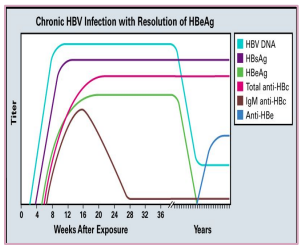
Parenterally transmitted				Enterically transmitted	
Hepatitis B virus	Hepatitis **C** virus	Hepatitis **D** virus	Hepatitis **G** virus	Hepatitis **A** virus	Hepatitis **E** virus

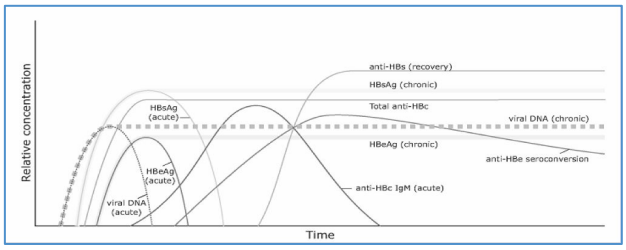
Chronic Hepatitis B infection

Serological Profile

- Chronic hepatitis B infection is defined by the presence of HBsAg or HBV-DNA in the blood for more than 6-months, some of them will also continue to have HbeAg these are with **bad prognosis,** until develop Anti-HBeAg.
- HBsAg may persists in the blood for life
- After disappearance of / Some patients may clear HBsAg after several months or years, then anti hepatitis surface antigen (Anti-HBs) will develop which persist for several years, means they become immune.







★VERY Important

Hepatitis B Markers

Type	description
HBV DNA	First appear in circulation, marker of infection, contiguous. معدي
Hepatitis B surface antigen (HBsAg)	Marker of infection, contiguous .معدي
Hepatitis B e antigen (HBeAg)	Marker of active virus replication, the patient is highly infectious, the virus is present in all body fluids, highly contiguous معدي جدا جدا
Antibody to hepatitis B e antigen (Anti-HBe)	Marker of low infectivity, the patient is less infectious, contiguous.معدي
Antibody to hepatitis B core (Anti-HBc)	Marker of exposure to hepatitis B infection, contiguous.معدي
Antibody to hepatitis B surface antigen (Anti-HBs)	The only Marker of immunity, NOT Contiguous.غير معدي,محصن

Marker	Result	Interpretation
- HBsAg - anti-HBc - anti-HBs	- Negative - Negative - Negative	Susceptible, need vaccination
-HBsAg - anti-HBc - anti-HBs	- Negative - Positive - positive	Immune due to natural infection
-HBsAg - anti-HBc - anti-HBs	- Negative - Negative - positive	Immune due to hepatitis B vaccination
-HBsAg - anti-HBc - IgM anti-HBc - anti-HBs	- Positive - Positive - Positive - Negative	Acutely infected
-HBsAg - anti-HBc - IgM anti-HBc - anti-HBs	- Positive - Positive - Negative - Negative	Chronically infected
- HBsAg - anti-HBc - anti-HBs (Window period)	- Negative - Positive - Negative	Interpretation unclear, 4 possibilities: 1. resolved infection (most common) 2. false-positive anti-HBc, thus susceptible 3. "low level" chronic infection 4. resolving acute infection

Female Slides

Hepatitis B Virus

Parenterally transmitted				Enterically transmitted	
Hepatitis **B** virus	Hepatitis **C** virus	Hepatitis **D** virus	Hepatitis **G** virus	Hepatitis **A** virus	Hepatitis **E** virus

Lab diagnosis (9)	★ Hepatitis B infection is diagnosed by detection of HBsAg in the blood (serum) *by ELISA* - Positive result must be repeated in duplicate (twice) - Repeatedly reactive result must be confirmed by **neutralization test** ★ • Serum HBV-DNA assay: Qualitative & quantitative tests for HBV-DNA in serum have been developed to assess HBV replication. Currently, most HBV-DNA assays use real time PCR techniques. The major clinical role of serum HBV-DNA assays in patients with chronic HBV infection is to assess the response of antiviral therapy. ○ **Additional lab investigations:** liver function tests (LFT), Ultrasound of the liver & liver biopsy to determine the severity of the disease.
Prevention	◎★**Recombinant yeast vaccine:** ○ It contains highly purified preparation of HBs-Ag particles, produced by genetic engineering in yeast, It is a recombinant and subunit vaccine. ★ *It is not live attenuated and not killed vaccine* مصنع, the vaccine is administered in three doses IM injection at 0,1 & 6 months. • the seroconversion rate is about 95% in healthy adults, If antibody titers have declined in immunized patients who are at high risk, such as dialysis patients, then a booster dose should be considered. • Booster doses may be reacquired after 5 years. ○ The vaccine is safe and protective, vaccine is recommended to all medical staff and to all newborn. ◎**Hepatitis B immune globulin (HB-IgM):** • ★It contain high titer of HBs-Ab (HB-IgM), it is used to provide immediate, **passive protection** to individuals known to be exposed to HBsAg positive blood (after accidental needle-stick injury). This type of individuals both the vaccine & **HBI-gM** should also be given to them and to a newborn whose mother is HBsAg -positive, this regimen effective in reducing the infection rate of newborns whose mothers are chronic carriers.
	All is Very Very Important Female Slides ★★**Based on what we will choose to give vaccine or HB-IgM?** ◎ In case of **Pre-exposure prophylaxis:** recombinant hepatitis B vaccine is given to all new born baby and adult not vaccinated. (★**Active immunity**) ◎ In case of **Post-exposure prophylaxis:** Persons exposed to needle prick or infant born to +ve HBsAg mother should immediately receive both Active vaccine (Recombinant hepatitis B vaccine) & hepatitis B specific immunoglobulin passive immunity. (★**Active immunity & Passive immunity**)
Treatment	There are several approved antiviral drugs: 1. Pegylated alpha interferon (used in HCV as well), one injection per week, for 6-12 months. ★(Lamivudine, Adefovir, Entecavir, & Tenofovir)★: antiviral drug, nucleoside analogue. One tablet a day for at least one year.

Hepatitis C Virus

Parenterally transmitted				Enterically transmitted	
Hepatitis B virus	Hepatitis C virus	Hepatitis D virus	Hepatitis G virus	Hepatitis A virus	Hepatitis E virus

Overview 	○ Family of **Flaviviridae,** Genus: **hepacivirus** ○ The virus is small, 60–80 nm in diameter, consists of an outer envelope, icosahedral core ○ linear positive **polarity ss-RNA genome**, It has no polymerase. ○ There are 6/7 major genotypes (1-6/7), genotype 4 is the dominant in Saudi patients. This genetic variation results in high mutation rate in the envelope gene لذلك يصعب تحديده, as a result multiple subspecies often occur in the blood of an infected individual at the same time.
Epidemiology	Global distribution The World Health Organization (WHO) estimated that in 2015, approximately 100 million people globally had serologic evidence of HCV exposure and 71 million people had chronic HCV infection Female Slides
Transmission	**Similar to HBV:** **Parentally:** ● Direct exposure to infected blood, using contaminated needles, surgical instruments ● Using contaminate instruments in the practice of tattooing, ear piercing & cupping. ● Sharing contaminated razors & toothbrushes. زي بالحج، الناس الي جايه من دول ناميه تستخدم شفرات مستخدمه من ناس ثانيه ● Intravenous drug user. **Sexually (household contact):** ● The efficiency of HCV transmission by sexual or household contact is low **From mother to child perinatal:** ● HCV occurs at the time of birth in about 5% of infants born to anti-HCV +ve women & having HCV-RNA, the risk of infection is higher in infants born to women coinfected with HCV & HIV.
Female Slides **Pathogenesis & immunity**	○ HCV infects hepatocytes primarily, but there is no evidence for a virus- induced cytopathic effect on the liver cells ○ Death of hepatocytes is probably caused by immune attack by cytotoxic T cells ○ HCV infection strongly predisposes to hepatocellular carcinoma HCC & Liver cirrhosis. ○ HCV infection also leads to significant autoimmune reactions including vasculitis, arthralgia, purpura and membranoproliferative glomerulonephritis.
Clinical Outcome	○ About 20 % of the infected individuals will develop self-limiting acute hepatitis C and recover completely. ○ About ★ **80 -*85%** of the infected will progress to chronic hepatitis C (about 10-30% of them can develop cirrhosis and liver cancer within 30 years) ○ Less than 1% will develop acute fulminant hepatitis C, liver failure and death

Hepatitis C Markers (important)★ (10)		
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)	○ Is the *last/only antibody marker that appears in the blood, usually appear 50 days after exposure (long window period). ● it is not marker of immunity, can be detected in completely recovered patient, and in chronic and acute patients.	★**NOTE:** there is no specific marker for developing immunity. but if the Ab exist without RNA it indicate immunity against HCV

Hepatitis C Virus

Parenterally transmitted				Enterically transmitted	
Hepatitis **B** virus	Hepatitis **C** virus	Hepatitis **D** virus	Hepatitis **G** virus	Hepatitis **A** virus	Hepatitis **E** virus

Clinical Picture

Important note:
If there is jaundice with virus B & C there will be dark urine and light stool due to excretion albumin in urine

as what we say in the beginning, all hepatitis viruses have similar clinical picture

Acute HCV

- Most patients who are acutely infected with HCV are asymptomatic
- Symptomatic patients may have jaundice, nausea, dark urine & right upper quadrant pain
- Patients with acute HCV infection typically have moderate to high serum aminotransferase elevation
- The acute illness usually lasts for 2-12 weeks.
- Fulminant hepatic failure due to acute HCV infection is very rare but may be more common in patients with underlying chronic hepatitis B virus infection.

Chronic HCV

- Chronic infection with hepatitis C virus (HCV) is often asymptomatic, screening is necessary to identify most patients with infection.
- The diagnosis of HCV infection is based on detection of antibodies to HCV as well as viral RNA.
- Chronic infection typically occurs, with approximately 85% of cases developing chronic hepatitis. However, chronic HCV infection is usually slowly progressive, Approximately 5-30% of chronically infected individuals develop cirrhosis over a 20-30 year period of time & hepatocellular carcinoma.

Lab diagnosis

Importance

◎**By detection of both:** ★

★ Antibody to HCV in the blood by ELISA, if positive *we have to repeat it in duplicate, then*, the result must be confirmed by **RIBA** (Recombinant ImmunoBlot Assay) or RT-PCR

★ HCV-RNA in the blood using RT-PCR .

Explanation from the female slides:

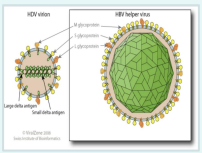
- HCV (acute or chronic) infection is diagnosed by detecting antibodies by ELISA to HCV. The test does not distinguish between IgM & IgG, and does not distinguish between an acute, chronic or resolved infection. So, If the result of ELISA antibody test is positive, a PCR-based test that detect the presence 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.

Treatment

- The currently used treatment is the combined therapy using: ★Pegylated alpha interferon and ribavirin. ★
  - The dose for pegylated alpha interferon: one injection per week
  - The does for ribavirin: two capsules a day.
- Protease inhibitor such as boceprevir or telaprevir has increased the effectiveness of the treatment to about 70%.
- RNA-dependent RNA polymerase inhibitors such as ledipasvir and sofosbuvir.
- New treatment for hepatitis C name SOVALDI (sofosbuvir).
- At the present time, there is no vaccine available to hepatitis C.

Hepatitis D Virus

Parenterally transmitted				Enterically transmitted	
Hepatitis **B** virus	Hepatitis **C** virus	Hepatitis **D** virus	Hepatitis **G** virus	Hepatitis **A** virus	Hepatitis **E** virus

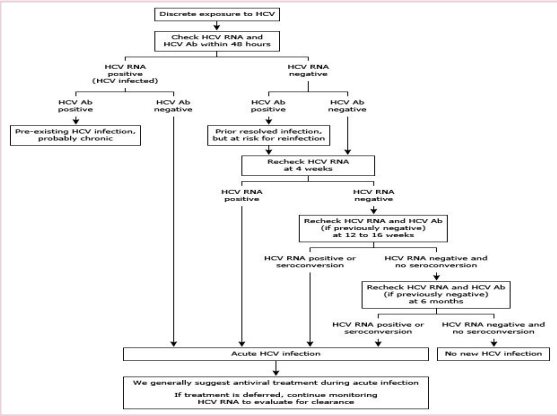
Structure 	○ It is a **defective virus** (weak), that cannot replicates by its own so it requires a **helper virus**. ○ The helper virus is HBV which provides the free HBsAg particles to be used as an envelope. (HDV needs the HBsAg to replicate) ○ HDV is small 30-40 nm in diameter. ○ Composed of **small ss-RNA genome**, surrounded by delta Ag 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.
Clinical findings (Type of infection)	○ **Co-infection**: The patient is infected with HBV & HDV **at the same** time leading to severe acute hepatitis (Prognosis: recovery is usual.) ○ **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**.

Hepatitis G Virus

Parenterally transmitted				Enterically transmitted	
Hepatitis **B** virus	Hepatitis **C** virus	Hepatitis **D** virus	Hepatitis **G** virus	Hepatitis **A** virus	Hepatitis **E** virus

All is Male Slides

Family & Genus	○ Family: Flaviviridae (similar to HCV), 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, and From mother to child transmission have been reported.
Clinical findings	○ Causes mild acute and chronic hepatitis infection. ○ Usually occurs as co-infection with HCV, HBV and HIV.



Extra

Summary

Hepatitis B virus (HBV)	
Overview	○ There are 8 genotype (A-H), genotype D is dominant in Saudi Arabia. ○ Pathogenesis: cell mediated immunity (so if the patient has strong immunity he will kill the virus, otherwise, the immunity will react with the virus and cause liver damage)
Transmission	○ Parentally ○ Sexually (unprotected sex) ○ From mother to the newborn (Perinatally)
Clinical Outcome	○ 70% will be without jaundice (Anicteric phase). while 30% will be with jaundice (Icteric phase) ○ **9%** of the infected adults, **90%** of infected infants, **20-50%** of infected children → develop **chronic** hepatitis. While the rest will develop acute hepatitis & recover completely. ○ The time difference that takes us from the acute stage to chronic stage is: 6 months
Diagnosis	○ Previously: by detection of HBsAg in the blood by ELISA (if +ve then repeated twice) → confirm the diagnosis by neutralization test ○ Nowaday: detection of the genome (HBV-DNA) by PCR (qualitative & quantitative tests)
Prevention	○ Pre-exposure prophylaxis: recombinant (not live attenuated and not killed vaccine) hepatitis B vaccine, is given to all people (Active immunity) ○ Post-exposure prophylaxis: Persons exposed to the disease should immediately receive both Active vaccine (Recombinant hepatitis B vaccine) & hepatitis B specific immunoglobulin passive immunity. (Active immunity & Passive immunity)
Treatment	Lamivudine, Adefovir, Entecavir, & Tenofovir ★
Serological Profile ★	○ Hepatitis **B- DNA:** is the 1st marker that appears in circulation, 3-4 weeks after infection. معدي ○ **HBsAg:** is the 2nd marker that appears in the blood. Persists for < 6 months in acute, but > 6 months in chronic. معدي ○ **HBeAg:** is the 3rd maker that appears in circulation, indicate active multiplication of the virus. معدي جدا جدا ○ **Anti-HBcAb (IgM):** is the 1st antibody that appears in the **blood,** the **ONLY marker** that appear in **window period** and followed by **Anti-HBc (IgG)** which persists for whole life. It indicate that the patient have the disease either know or in the past, it does NOT indicate immunity ○ With the disappearance of HBeAg, anti-HBe appears and usually persists for several weeks to several months. ○ **Anti-HBsAb:** is the last marker that appears in the blood, It appears few weeks after disappearance of HBs-Ag and persists for whole life. It indicates ★★**immunity to hepatitis B infection.** غير معدي محصن ○ The immunized person due to exposure to the disease will have Anti HBc & Anti HBs. While immunization due to vaccine will have Anti HBs ONLY ◎**Window period**: when HBs-Ag has been disappeared and anti-HBsAg is not yet detectable, at that time only anti-HBc Ag- IgM antibody is detected & can be used to confirm the diagnosis
Hepatitis C virus (HCV)	
Overview	○ ss-RNA ○ Transmission, Pathogenesis, and clinical picture: all are similar to HBV
Clinical Outcome	About **80 - 85%** of the infected will progress to chronic HCV (the chonicity is more higher than HBV). While the rest of the infected individuals will develop self-limiting acute HCV & recover completely.
Diagnosis	Completely identical to HBV but here we look for anti-HCV, and the confirmed test is RIBA
Treatment	Pegylated alpha interferon and ribavirin ★
Serological Profile ★	○ HCV-RNA: marker of infection (Acute if < 6 months, chronic if > 6 months) ○ Anti-HCV: the *only* antibody marker that appear in the blood ○ There is no specific marker of immunity, but if we found Anti-HCV alone without the HCV-RNA → indicates having the disease in the past (recover & develop immunity against it)

Hepatitis D virus (HDV): it's a defective virus, and it requires a **helper virus** (HBV)

Differentiation between different types of hepatitis viruses is by laboratory tests, NOT by clinical picture (they are similar)

Dr Notes

1. Nowadays, we can catch the virus DNA (genome) by PCR. But before we had the PCR, we were checking for the presence of the virus by catching the HBsAg which is the envelope of the virus, we will find it free in the serum.

2. مدى قوته؟ قوي جدًا لدرجة نقطة دم صغيرة جدًا يعني ٠.٠٠٠١ من الدم و كان الواحد مجروح ودخلت على دمه ممكن انها تسوي المرض! وانجرح وجاء دمه على الطاولة وما نظفها كويس، الفايروس راح يبقى Hepatitis B وبرضو من قوته ان لو مثلا فيه شخص (أ) كان عنده بالطاولة حتى لو انه ناشف لمدة اسبوعين تقريبا، ف إذا جاء شخص (ب) وكانت يده مجروحة وحط يده على الطاولة ممكن أن الفايروس يدخل اذا انجرح الشخص المصاب فيه وطلع الدم HIV ويسبب له المرض. فهذا الفيروس **قادر على انه يعيش خارج جسم الإنسان** على عكس مثلا خارج جسم الإنسان الفايروس يموت.

3. That is important, because unlike HIV it doesn't directly injures the hepatocyte, the body immune response what causes the damage. So if the patient has strong immunity he will kill the virus, otherwise, the immunity will react with the virus and cause liver damage

4. » لو جبنا ١٠٠ شخص كبار وعطيناهم الفايروس ب ابره بنفس الجرعة وش راح يصير فيهم؟ لقوا انه ٩٠٪ منهم راح ياخذون المرض ثم تصير عندهم مناعة و ٩٪ راح يتحولوا ل chronic والمرض يقعد معهم لفترة طويلة .
» لو جبنا ١٠٠ رضيع كانوا مولودين لأم عندها الفايروس وكلهم جاهم المرض، ٩٠٪ منهم راح يتحولوا ل chronic حامل للمرض وماراح يتعافون ليه؟ لان ماعندهم مناعة و ١٠٪ راح يتعافون.
» لو جبنا ١٠٠ طفل فوق سنتين راح نشوف ٢٠-٥٠٪ راح يتحولوا ل chronic.
so to summarized **imp thing ** The chronicity in adult 9% , in infant 90% and in children 20-50%.

5. if it was acute it will be ↑ for lease then six months, if it exceeds that then it is chronic.

6. DNA → HBs → HBe → Anti HBc → Anti HBs (after 6M)
   (DNA → HBe: Acute; Anti HBc → Anti HBs: from disease; Anti HBs: Vaccine)

7. ○ المرض إذا جاء راح نلقى اول شيء ال DNA طلعت بتحليل الدم بعدين ال HBsAg ثم HBeAg و هذا في acute stage و ما نعرف اذا المرض بيكمل أو يتعافى.
○ لو المريض بيتعافى ويصير محصن ال HBeAg تنزل و بعدها HBsAg & HB DNA ينزلون وخلال هالفتره يطلع Anti HBc للكل سواء راح يتعافى أو يكمل chronic وبعد فتره من طلوع Anti HBc تقريبا بعد ٦ شهور بتطلع Anti HBs واللي معناها ان الشخص محصن
○ طيب عشان انا اعرف اذا الشخص محصن من التطعيم او انه جاه المرض وراح منه الفرق الوحيد اللي يحدد لي ان اللي مرض و خف راح يكون عنده Anti HBc وهذا يجي بس للي خذوا المرض وما يجي للي ماخذين تطعيم وطبعا بكل الحالتين سواء أخذ المرض وصار محصن أو أنه محصن بسبب التطعيم راح يكون عندهم Anti HBs.
○ يعني ال Anti HBc ليست دلالة على كون الشخص اكتسب مناعة ضد المرض، هي فقط دلالة على أن الشخص أصابه المرض، طيب كيف أعرف إذا إصابته بالمرض للحين نشطة أو تعافى منها؟ من خلال ال Anti HBs هي اللي وجودها يشير إلى تكون مناعة ضد المرض.

8. the distinguishing mark is the **6 months**. usually after 6 months the Ag (HBsAg, HBeAg) will decrease & disappear and Ab will develop. But, if they did **not** decrease even after 6 months it mean chronic hepatitis.
9. in the **past** (but you should know because still there is some hospitals use this method) when we had blood sample to check for HBV, first we check by ELISA, if the result came +ve then we check again twice (now the total number of the performed test is 3), if the test result still +ve, then we will check again (4th test) but this time by confirmed test which called **neutralization test.** Nowadays we just use PCR.
10. - If we found HCV-RNA & Anti-HCV: it indicates that the patient have the disease. but acute or chronic? if the RNA stay in the sample for short period = acute, but if it stay long time = chronic
    - If we found Anti-HCV alone without the HCV-RNA:it indicates that the patient have the disease but he/she recover & develop immunity against it

MCQs

Q1 - Which virus is defective virus?			
A- virus B	B- virus C	C-visus D	D-virus A
Q2 - Which virus is more chronicity?			
A-virus C	B- virus D	C-virus B	D-virus A
Q3 - Which genotype is dominant in Saudi Arabia?			
A. Genotype A	B. Genotype B	C. Genotype C	D. Genotype D
Q4 - which of the following is the type of immunity response exhibited in HBV infection?			
A. adaptive immune response	B. Cell mediated	C. innate immune response	D. none
Q5 - What is the clinical outcome in patients with hepatitis C virus?			
A.9% will progress to chronic	B. 20% will progress to chronic	C. 80% will progress to chronic	D.1% will progress to chronic
Q6 - Which of the following is type of hepatitis B vaccine?			
A. Recombinant	B. live attenuated	C. killed	D. none
Q7 - A dentist documented a needle prick accident during treating a patient, he was concerned about acquiring HBV infection, a serological profile was done, and the results were the following: **HBe: -ve HBs: -ve Anti HBs: +ve Anti HBc: -ve**			
A. Needs vaccine	B. immune from vaccine	C. immune from disease	D.Acute hepatitis
Q8 - An employee was required to screen for HBV infection, a serological profile was done and the following results were obtained **HBe: -ve HBs: -ve Anti HBs: +ve Anti HBc: +ve**			
A. Needs vaccine	B. immune from vaccine	C. immune from disease	D. Acute hepatitis
Q9 - A patient was suspected to have HBV infection, a serological profile was done and showed the following results: **HBe: -ve HBs: -ve Anti HBs: -ve Anti HBc: +ve**			
A. chronic hepatitis	B. Recovery period	C. Window period	D. Acute hepatitis

Answer Key: A1. C A2. A A3. D A4. B A5. C A6. A A7. B A8. C A9. C

TEAM 443
MICR▸ BI▸ L▸ GY

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