Lecture (9)

blood borne hepatitis

Objectives:

No objectives !

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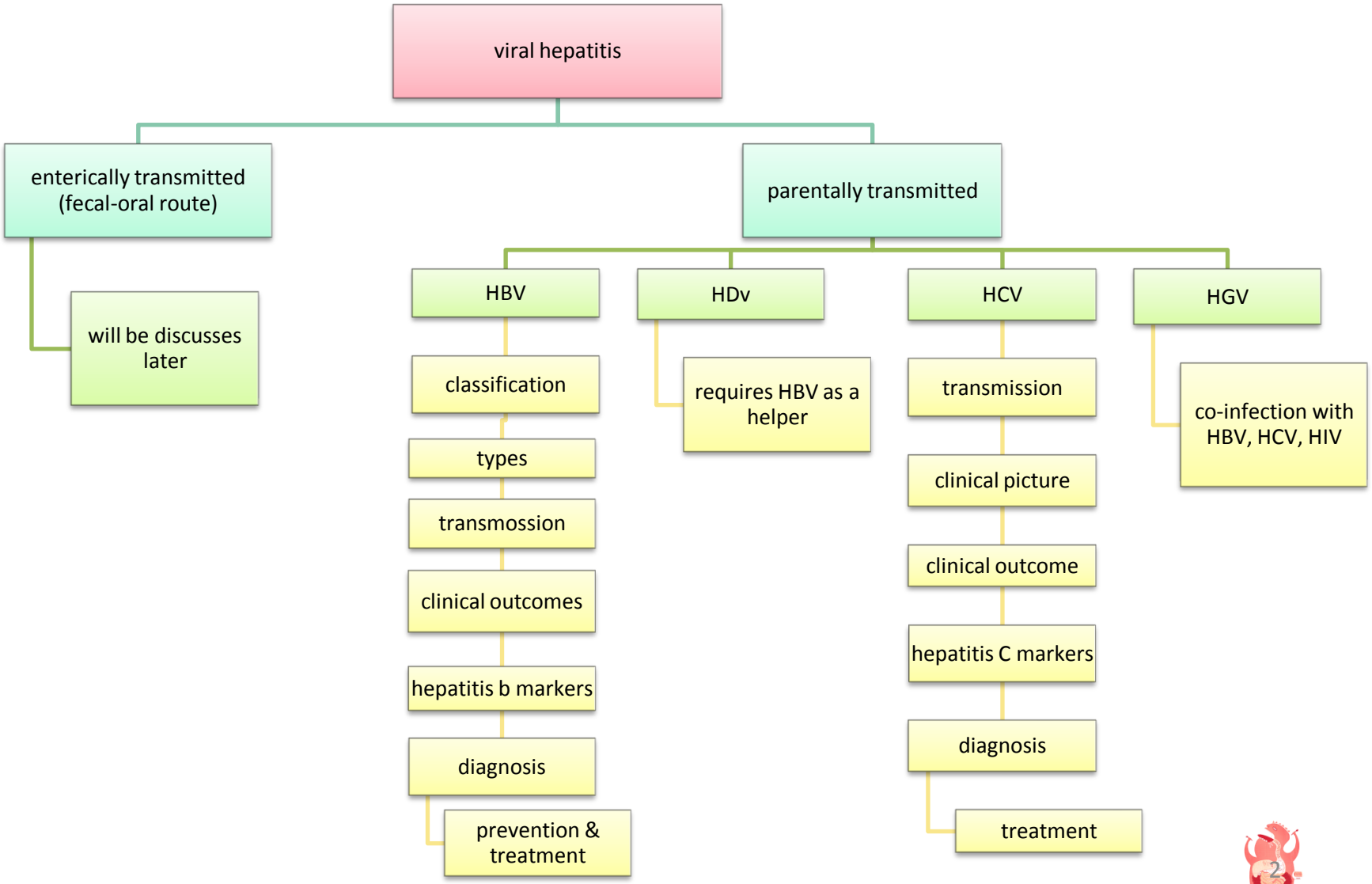
MIND MAP


viral hepatitis
enterically transmitted (fecal-oral route)
will be discusses later
parentally transmitted
HBV
classification
types
transmossion
clinical outcomes
hepatitis b markers
diagnosis
prevention & treatment
HDv
requires HBV as a helper
HCV
transmission
clinical picture
clinical outcome
hepatitis C markers
diagnosis
treatment
HGV
co-infection with HBV, HCV, HIV

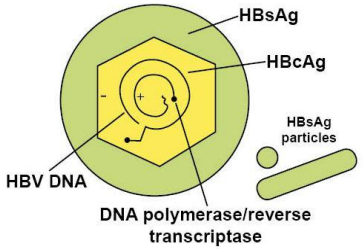
Viral hepatitis

- Hepatitis feature of many diseases usually as a part of a generalized infection e.g. cytomegalovirus, yellow fever, Epstein-Barr virus. For example, cytomegalovirus affects almost every organ in the body, resulting in hepatitis (the virus is not targeting the liver directly)
- However, some viruses primarily target the liver to cause viral hepatitis. our lecture is about such viruses
- Viral Hepatitis presents more or less similar clinical picture whatever the causative viruses.
- Laboratory tests can differentiate between different viruses. Differentiation is important because the prognosis, treatment, and caution will be different
- We have to determine the causative virus to know how to treat and what the prognosis.
- The enterically transmitted viruses will not cause any chronic disease, while the parentally transmitted viruses will cause chronic disease

Hepatitis B virus

Classification:

1- Family : hepadnaviridae
2- The complete virus particle is 42-nm in diameter .
3- It consists of an **outer envelope containing hepatitis B surface antigen (HBsAg)**. Marker of infection
4- And internal core (nucleocapsid) composed of hepatitis B core antigen (HBcAg).
5- The viral genome is small partially circular ds-DNA (the only DNA virus causing hepatitis)
6- There are eight known genotypes (A – H).
7- Genotype D is the dominant in Saudi patients
8- The virus contains the polymerase enzymes



Doctor said it is important for the practical ;)

Types:

The serum of infected individual contains three types of hepatitis B particles:
1- Large number of small spherical free HBsAg particles .
2- Some of these HBsAg particles are linked together to take the form of filaments .
3- In addition to the complete HBV-particles (Dane particles)

Transmission

1- Infected blood (parenterally): Direct exposure to infected blood. Using contaminated needles (specially in drug addict they use the same needle), syringes, dental and surgical instruments. Using contaminated instruments in the practice of tattooing, body piercing, cupping. Sharing contaminated tooth brushes, razors, cuticle scissors and nail clippers.

2- sexually: By having sexual contacts with infected person ,virus is present in semen and vaginal secretion. Specially homosexual and individuals with multiple sexual partners

3- from mother to child: Mostly(perinatally) during delivery ,nursing ,breast feeding and less likely through placenta (during pregnancy) (vertical transmission)

Hepatitis B virus

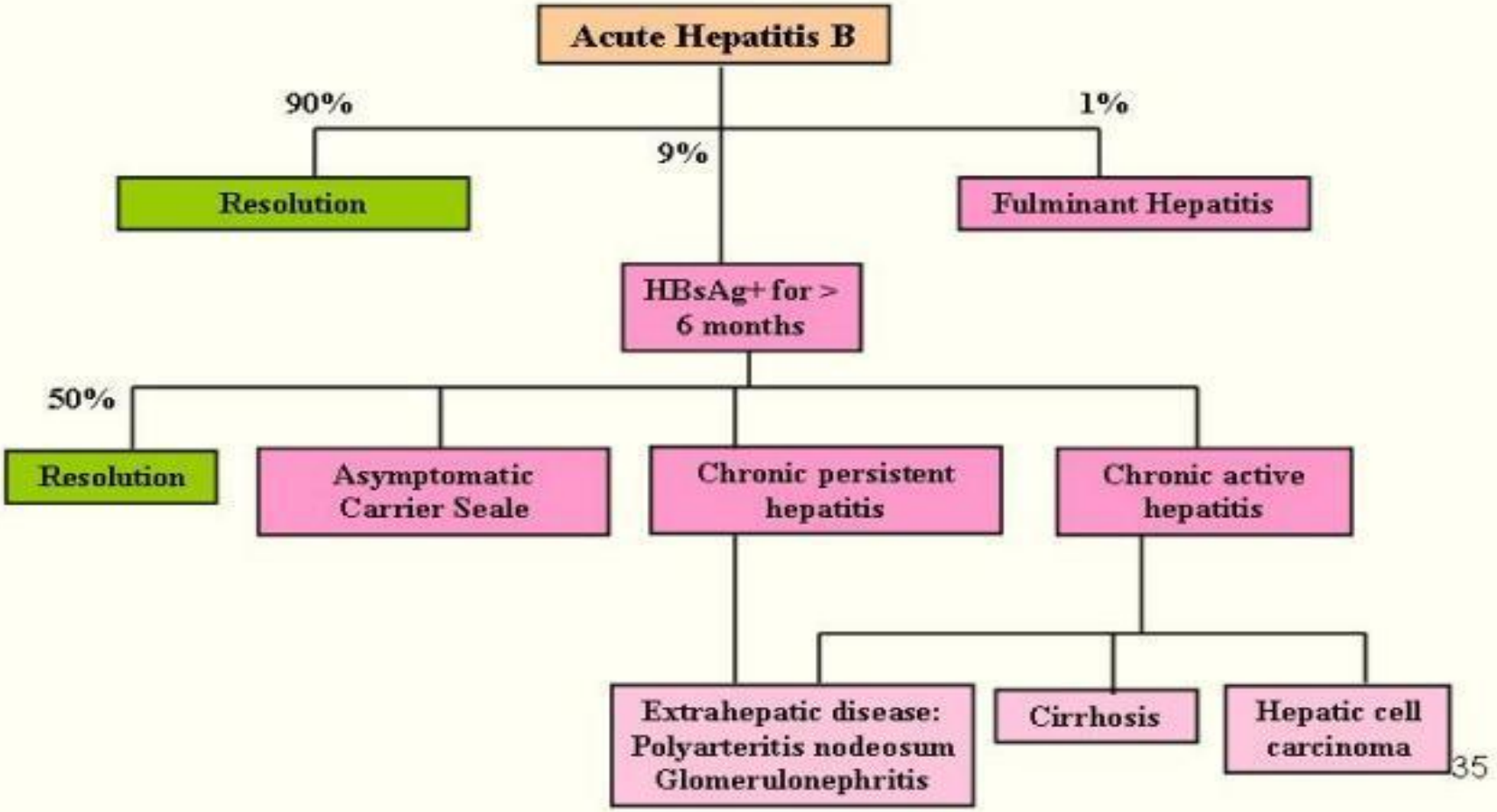
Groups at higher risk of devolving hepatitis B	•Intravenously drug users. •Hemodialysis patients. •Patients receiving clotting factors. •Individuals with multiple sexual partners. •Recipient of blood transfusion , before 1992. •Health care workers with frequent blood contact. •Individuals exposed to risk factors such as tattooing, body piercing and cupping.

•Infection with hepatitis B virus (HBV) Can result in; acute hepatitis and then resolve, fulminant hepatitis, chronic asymptomatic carrier, chronic active hepatitis that will lead to cirrhosis or hepatocellular carcinoma.

• HBV replicates in HEPATOCYTES and possibly the entire genome can be integrated into the host genome. That's why it causes cancer

The clinical outcome of HBV infection	About 90 % of infected adult individuals will develop acute hepatitis B infection and recover completely and become immune.
	Less than 9 % of the infected adult will develop chronic hepatitis. (HBsAg is present more than 6 months) 50% will resolve completely. Go through the next slide
	Less than 1 % will develop fulminant hepatitis, characterized by massive liver necrosis, liver failure and death.
	90% of infected infants and 20% of infected children will progress to chronic hepatitis.

Hepatitis B: Clinical Outcomes of Acute HBV Infections



Hepatitis B markers VERY VERY IMPORTANT!

1- Hepatitis B surface antigen (HBsAg): Marker of infection.
2- Hepatitis B e antigen (HBeAg) : Marker of active virus replication, the patient is highly infectious, high viral load, the virus is present in all body fluids.
3- Antibody to hepatitis B e antigen (Anti-HBe): Marker of low infectivity, the patient is less infectious. Not a marker of immunity
4- Antibody to hepatitis B surface antigen (Anti-HBs): the only Marker of immunity (natural or vaccination).
5- Antibody to hepatitis B core IgG (Anti-HBc IgG) : It indicates exposure to hepatitis B infection.(only natural infection)

Acute hepatitis B infection

Icteric means jaundice

- Incubation period varies from 2 to 4 months.
- Most of HBV infection are asymptomatic.
- An-icteric hepatitis: fever, malaise , anorexia, rash, nausea, vomiting and high upper quadrant abdominal pain with raised liver enzyme.
- Icteric hepatitis: about 25% of the patient become icteric Jaundice with raised bilirubin, dark bile containing urine and pale stools.
- Acute hepatitis B infection usually last for several weeks to maximally 6 months.

Serological profile: see the chart in the next slide

- Hepatitis B DNA is the first marker that appears in circulation, 3-4 weeks after infection(PCR) .
- Hepatitis B surface antigen (HBsAg) is the second marker that appears in the blood and persists for less than 6-months, then disappears.
- Hepatitis B e-antigen (HBeAg) is the third maker that appears in circulation
- Antibody to the core (IgM anti-HBcore Ag) is the first antibody that appears in the blood and followed by IgG anti HBcore Ag, usually persists for several years .
- with the disappearance of HBeAg, anti- HBe appears and usually persists for several weeks to several months .
- Antibodies to hepatitis B surface antigen (anti-HBsAg) is the last marker that appears in the blood.

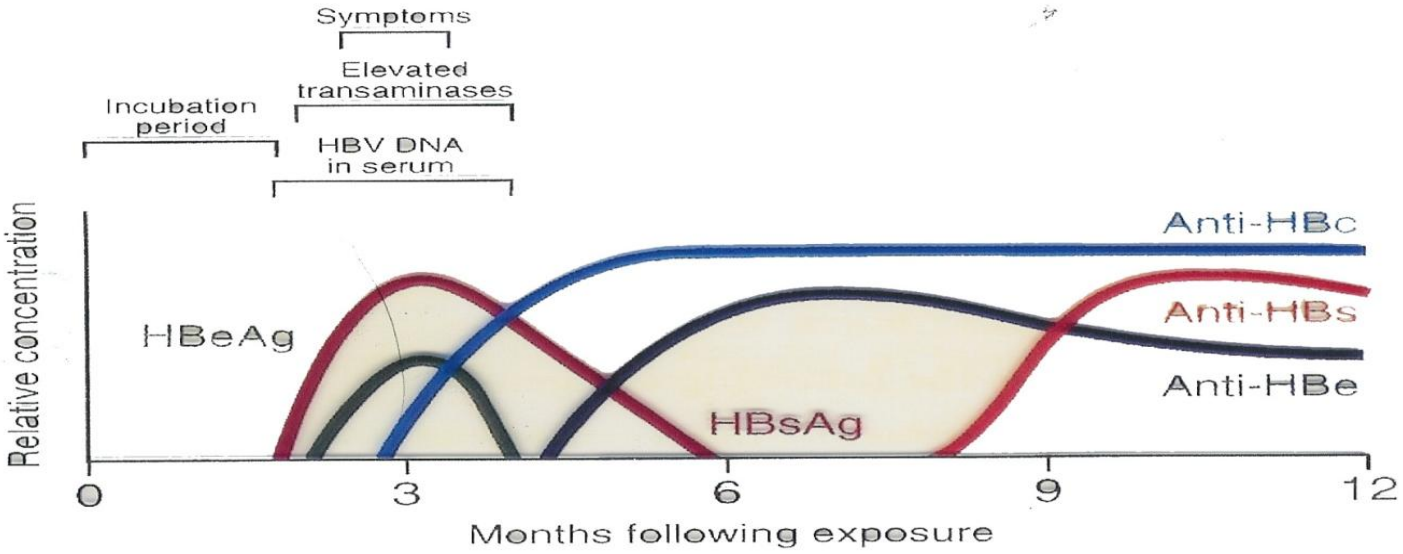
Chronic hepatitis B infection

- Chronic hepatitis B is defined 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 may only be detected by elevated liver enzyme on a routine blood chemistry profile , some have mild fatigue, Right upper quadrant abdominal pain or enlarged liver &spleen
- The major long term risk of chronic HBV infection are cirrhosis with hepatic failure and hepatocellular carcinoma ,when HBV genome integrates into hepatocytes DNA.

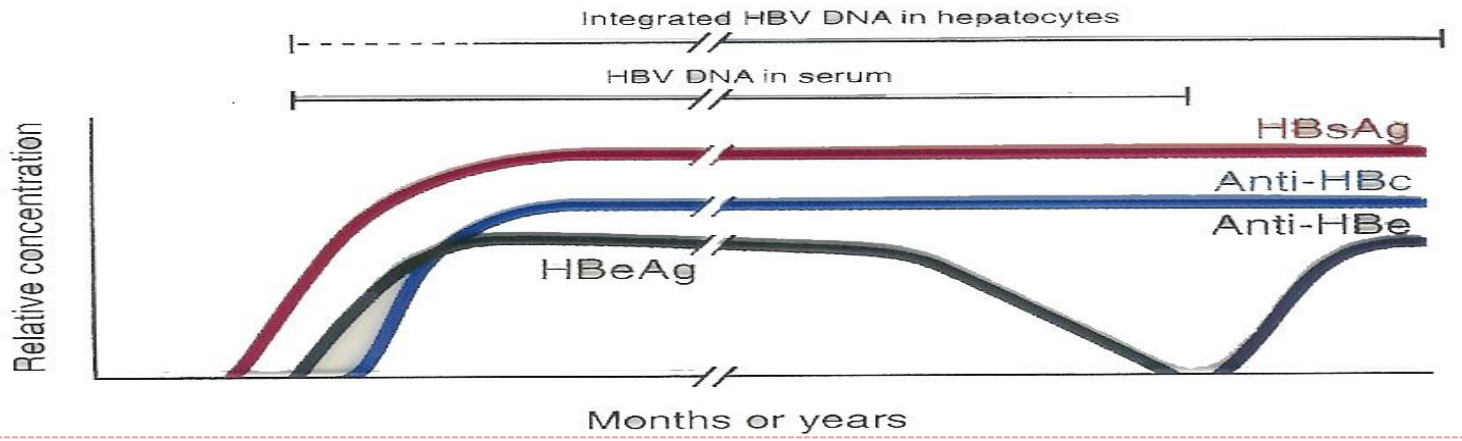
Serological profile: see the chart in the next slide

- Chronic hepatitis B infection is defined by the presence of HBsAg in the blood for more than 6-momths .
- HBsAg may persists in the blood for life
- Some patients may clear HBsAg and develop anti surface (Anti-HBs),they become immune.

a) **Serological profile of acute, resolving hepatitis B**



b) **Serological profile of chronic hepatitis B with seroconversion**



Hepatitis B markers

Types	Description
Hepatitis B DNA	is the first marker that appears in circulation, 3-4 weeks after infection(PCR) .
Hepatitis B surface antigen(HBsAg):	Marker of infection (ELISA)
Hepatitis B e antigen (HBeAg)	Marker of active virus replication, the patient is highly infectious, virus is present in all body fluids.
Antibody to hepatitis B e antigen (Anti-HBe):	Marker of low infectivity, the patient is less infectious. Not a marker of immunity "patient recovering "
Antibody to hepatitis B surface antigen (Anti-HBs):	Marker of immunity (natural or vaccination).
Antibody to hepatitis B core IgG (Anti-HBc IgG)	It indicates exposure to hepatitis B infection.(only natural infection)

Lab diagnosis of hepatitis B infection		*imp* diagnosed detection of HBsAg in the blood (by screening test by ELISA) if it's positive -> results must be repeated in duplicate (do the test again two times) if it's positive -> 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 and Control	Pre-exposure prophylaxis	Active vaccination given to all newborn, children or adult. It contains highly purified preparation of HBsAg particles produced by genetic engineering in yeast. It is not live attenuated nor killed vaccine The vaccine is administered in three doses IM injection at 0.1 & 6 months. Booster doses may be reacquired after 3-5 years.
	Postexposure prophylaxis	HBsAg mother Persons exposed to needle prick or infant born to +ve should immediately receive both: Active Vaccine & Hepatitis B specific immunoglobulin (passive vaccine)
treatment		Treatment is limited to patients having chronic hepatitis B to reduce the risk of cirrhosiss and liver cancer. Criteria for treatment : liver biopsy - Positive for HBsAg & HBV-DNA high - ALT(Alanine aminotransferase) (liver enzymes) twice the upper normal limit - Moderate liver damage - Age > 18 years. *anti-viral drugs:1- pegylated alpha interferon . 2- Lamivudine . 3- Adefovir,

Hepatitis C

	Heterogenous: has a high mutation rate. This why no vaccine.		
Type	Flaviviridia virus. (RNA) enveloped		
Cycle	replicate in hepatocyte of the liver same as HBV		
Transmission	Same as HBV		
ClinicalPicture	IP 2-7 weeks –short-,The acute infection is milder than HBV. jaundice are common		
Clinical outcome	20% self-limiting acute and recover completely	80% chronic hepatitis C	<1% fulminant hepatitis C , liver failure and death
Marker	Hepatitis C virus – RNA	first marker that appears in the serum, it appears as early as 2-3 weeks after exposure , It is a marker of infection	
	IgG Antibody to hepatitis C	long window period. present in both Acute or chronic patient and resolved. There is no marker for immunity	
	Hepatitis C core antigen	2nd marker that appears in blood. Usally 3-4 weeks after exposer. Marker of infection	
Laboratory Diagnosis	which dose not distinguish between an acute , chronic, or resolved infection *imp*Detection of Anti HCV in the serum by ELISA > repeated it in duplicate > confirmatory test with RIBA , PCR for detection of viral RNA to detect viral replication, replication >acute, but if there is no replication that don't mean the patient is immuned, liver enzymes if high >acute, stabile >chronic		
Treatment	Criteria for treatment : + for HCV –RNA - + for anti-HCV - Known HCV genotype - ALT >twice the upper normal limit - Moderate liver damage ,based on liver biopsy . treatment :pegylated alpha interferon and ribavirin		

Hepatitis D Delta hepatitis

Imp	Defective virus: cause infection only in people with acute or chronic hepatitis B virus infection. It cannot produce infection in absence of HBV. Transmission of HDV can occur either via simultaneous infection with HBV (coinfection) or superimposed on chronic hepatitis B or hepatitis B carrier state (superinfection).
Type	RNA virus
Transmission	similar to HBV
Diagnosis	Anti-HDV antibodies.
Complication	results in more severe complications compared to infection with HBV alone.

The doctor said that she will not ask us about it

Hepatitis G

Type	Family: Flaviviridae. Enveloped, ss-RNA with positive polarity
Transmission	Similar to HBV
	Cause mild acute and chronic hepatitis G cases . Usually occurs as co-infection with HCV , HBV and HIV.

Summary

Virus	HBV	HCV Heterogenous	HDV Defective virus	HGV
Type	- hepadnaviridae Ds DNA	-Flaviviridia Enveloped RNA	RNA	Flaviviridia- Envelped ss RNA + -
Transmission	1)Infected blood 2) sexual 3) mother to infant			
Outcome	Adult: 90% resolved,9% chronic active or asymptomatic, 1% fulminant Hepatitis Infant: 90% chronic Children: 20% chronic	20% resolved 80% chronic 1%fulminant Hepatitis	HDV results is more severe complications compared to infection with HBV alone.	
Ip	Acute: 2-4 months Chronic: > 6 m	2-7 weeks	-	-
Vaccine	Pre-exposure: HBsAg Post-exposure: active & passive	NO vaccine	-	-
Treatment	pegylated alpha interferon & Lamivudine	pegylated alpha IF & ribavirin	-	-

Summary

•The clinical picture of different causative agents are almost similar, however laboratory tests can differentiate between different viruses that it helps to know the treatment & prognosis.
•Fecal-oral infection are not causing chronic disease while parentally transmitted infection causes a chronic disease
•Hepatitis B virus is the only DNA virus causing hepatitis. HDV, HCV and HGV are RNAs.
•Infants are more likely to develop chronic hepatitis.
•Hepatitis B virus is transmitted parentally, sexually and prenatally.
•90% of individuals infected by HBV will resolve completely only 9% will develop chronic hepatitis and less than 1% will develop fulminant hepatitis and eventually die.
•Hepatitis B markers are very important. It helps in prognosis.
•HBsAg is the mark of infection. Anti-HBs is a marker of immunity.
•Hepatitis B infection is diagnosed by detection of HBsAg in the blood. Possitive results must be repeated in duplicate and confirmed by neutralization tests.
•Hepatitis B virus is the only virus that has a vaccine.
•Antiviral drugs as Lamivudine or Adefovir and pegylated alpha interferon are used in treatment of HBV.
•Hepatitis D virus is a defective virus. it can not produce an infection in absence of HBV. It's an RNA virus.
•Hepatitic C virus has no vaccine due to its high mutation rate.
•HCV transmitted exactly the same as HBV.
•Fever, anorexia, nausea, vomiting and jaundice are commonly seen in hepatitis C infection.
•Majority of HCV infected patients will progress to chronic hepatitis C infection.
•Diagnosis of HCV is by detection of anti HCV in serum

QUESTIONS

Q1: A 28-year-old male ER resident was accidentally stuck with a needle from a hepatitis B virus-positive patient. Two months later, he began to feel fatigued and lost his appetite. When he ordered a hepatitis B serologic panel, he received the results as follows: HBsAg; positive HbsAb; negative HBcAb; positive HBeAg; positive HBeAb; negative. What is the status of the resident?

A.Acute infection

B.chronic infection

C.immune

Q2: a patient was diagnosed with hepatitis B 6 months ago is tested for his progress with the following results; HBsAg; negative HBsAb; positive HBcAb; positive HBeAg; negative HBeAb; positive. What is the status of the patient?

A.Acute infection

B.chronic infection

C.immune

Q3: We found in the serum of a patient Anti-hepatitis B surface antigen + Anti-hepatitis core antigen this mean:

A- The patient received the vaccine lately.

B. The patient was infected by hepatitis B.

C. The patient is infectious.

QUESTIONS

Q4: We confirm the positive result of the screening test of hepatitis B virus by:

A: neutralization test .

B. Liver enzymes test.

C. RIBA

Q5. A Nurse exposed to needle prick while she is taking a blood sample of a patient with hepatitis-B what she supposed to do:

A. Clean it with a swap.

B. Start the treatment with Lamivudine

C. Take Hepatitis B specific immunoglobulin

Q6. A patient with hepatitis C we want to detect his immunity:

A. Check his IgG antibody to hepatitis C.

B. Do PCR.

C. There is no available test.

1	A
2	C
3	B
4	A
5	C
6	C

FOR ANY SUGGESTIONS AND PROBLEMS PLEASE CONTACT:
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