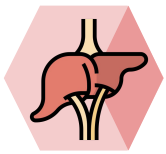
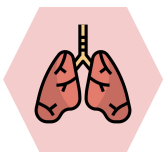
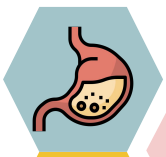
Medicine
TEAM 437

MED437
KING SAUD UNIVERSITY

Acute Viral Hepatitis

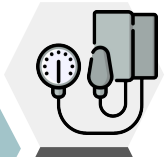




Objectives :

- Clinical Presentation
- Diagnosis
- Epidemiology of viral hepatitis infection A,B,C in KSA.
- Management

Done by :

Leader: Hadeel Awartani
Members: Khalid Aldossari, Shahad Alzahrani, Ghaida Alsanad, Anas Alsaif



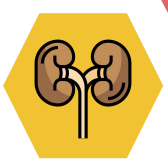

Revised by :

Aseel Badukhon

Lecturer: Dr. Faleh Alfaleh
Same 436 lecture slides: Few differences

Resources :

Doctors Slides-Team 436




Acute Viral Hepatitis definition:

An infection or inflammation of the liver. most cases of acute hepatitis are from viral hepatitis A or B. Hepatitis C for unknown reasons rarely presents with an acute infection, and is found as a silent infection on blood tests.

Types of Hepatitis (extra)	
Infectious	**Noninfectious**
-Hepatitis A -Hepatitis B -Hepatitis C -Hepatitis D -Hepatitis E *note that hep E is MOST dangerous in PREGNANT WOMEN!!!! -Others include :EBV (infectious mononucleosis), CMV and HSV seen in immunocompromised patients.	- The most common cause of non-infectious hepatitis in KSA is obesity causing NASH (Non-Alcoholic SteatoHepatitis) -Alcoholic hepatitis - Drug induced hepatitis - Autoimmune hepatitis - Numerous hereditary diseases that can cause hepatitis (such as haemochromatosis and wilson's)

Viral Hepatitis is Classified into:

1. Acute viral hepatitis: lasts less than 6 Months
2. Chronic viral hepatitis: lasts More than 6 Months

Type of Hepatitis					
	A	E	B	C	D
Source of virus	feces		blood/blood derived body fluids		
Route of transmission	feces-oral		Percutaneous permucosal		
Chronic infection	no		yes		
Prevention	per/post-exposure immunization	Ensure safe drinking water	per/post-exposure immunization	Blood donor screening; risk behavior modification	per/post-exposure immunization; risk behavior modification

-Hepatitis A & B are more prevalent in developing countries.
-Hepatitis E is particularly prevalent in india, pakistan, southeast Asia, and parts of Africa.
-Hepatitis D requires the outer envelope of the Hepatitis B surface antigen for replication and therefore can be transmitted only as a coinfection with HBV, or as a superinfection in a chronic HBV carrier.
-HAV & HEV : fEcAl

Symptoms and Signs

Pre-icteric phase:

1-Anorexia
2-Fatigue
3-Nausea
4-Vomiting
5-Arthralgia
6-Myalgia
7-Headache
8-Photophobia
9-Pharyngitis

Icteric phase:

1-Enlarged liver
2-Tender upper quadrant
3-Discomfort
4-Splenomegaly (10-20%)
5-General adenopathy

Post-icteric phase

- Cessation of symptoms, liver enlargement and continuous fatigue

-Acute hepatitis has a wide spectrum of clinical presentations, ranging from virtually asymptomatic to fulminant liver failure.
- Sometimes acute hepatitis may only present with transient flu-like symptoms such as fever, myalgias, and malaise. “note that icteric means jaundice” icteric=jaundice

Diagnosis of Hepatitis

Patient History | **Physical Exam** | **Serology**

Liver Function Test (LFT)

- 5 categories of markers may be found :HAV, HBV, HCV, HEV, or autoimmune markers.
- Most important factor for diagnosing viral hepatitis. (will be discussed).

- Elevation of serum transaminases is not diagnostic, but they are helpful.
- ALT is typically elevated more than AST for all forms of viral hepatitis (Opposite of alcoholic hepatitis).
- In acute hepatitis, ALT is >1,000. It is generally not as high as in drug-induced hepatitis.
- The plasma bilirubin reflects the degree of liver damage.
- The alkaline phosphatase (ALP) rarely exceeds twice the upper normal limit.
- Prolongation of prothrombin time (PT) indicates the severity of the hepatitis.

Lab Findings

1- LFT increase >5-10 times of normal.
2- Markers of hepatitis B or C or A might be positive.

differential diagnosis of Viral Hepatitis

1-Infectious Mononucleosis
2-Drug Induced Hepatitis
3-Chronic Hepatitis.
4-Alcohol Hepatitis
5-Cholecystitis,can come with high LFT, confirm with US, Cholelithiasis.
6-Autoimmune hepatitis

Complications of Acute Hepatitis

1-Chronic Hepatitis → Cirrhosis, HCC
2-Fulminant Hepatitis

FULMINANT HEPATITIS

- Definition: Hepatic Failure Within 8 Weeks Of Onset Of Illness.
- In severe cases, acute hepatitis may result in liver failure and its complications. This is known as fulminant hepatitis-happens within 8 weeks! (Uncommon) and may be life-threatening It occurs commonly in Hepatitis B, D, and E than in other types.
- Manifestation:

-Encephalopathy and Prolonged PT

-Hepatorenal syndrome: A life-threatening medical condition that consists of rapid deterioration in kidney function in individuals with cirrhosis or fulminant liver failure.

- Histopathology: Massive Hepatic Necrosis.

Treatment and management

The goal of chronic hepatitis therapy is:
1) Reduce DNA polymerase to undetectable level
2) Convert those patients with e-antigen to having anti-hepatitis e-antibody
Most individuals do not need hospital care. Acute hepatitis is usually self-limiting that return to normal structure and function.
What should be avoided?
- Drugs such as sedatives and narcotics, which are metabolised in the liver.
- Alcohol should be avoided during the acute illness.
- Elective surgery (a risk of postoperative liver failure.).

Hepatitis A and E	Supportive therapy.
Hepatitis B	**Acute:** supportive. **chronic:** with interferon or lamivudine
Hepatitis C	Dual therapy with pegylated interferon-alpha given as weekly subcutaneous injection, together with oral ribavirin, a synthetic nucleotide analogue.

Only acute hepatitis C gets medical therapy (Interferon+Ribavirin) and in acute hepatitis A (accompanied with HepB) if the patient presents with detectable HBsAg and clinical and epidemiological factors suggestive of chronic infection can be considered for hytreatment without waiting 6-month period (Interferon or lamivudine or tenofovir or adefovir or entecavir)

AUTOIMMUNE HEPATITIS MARKERS

- ANF (ANA) (ANF= Antinuclear factor, ANA= Antinuclear antibody)
- ANTI MITOCHONDRIAL AB
- ANTI SMOOTH MUSCLES ABS.
- A Hallmark of Autoimmune hepatitis is rich plasma interface

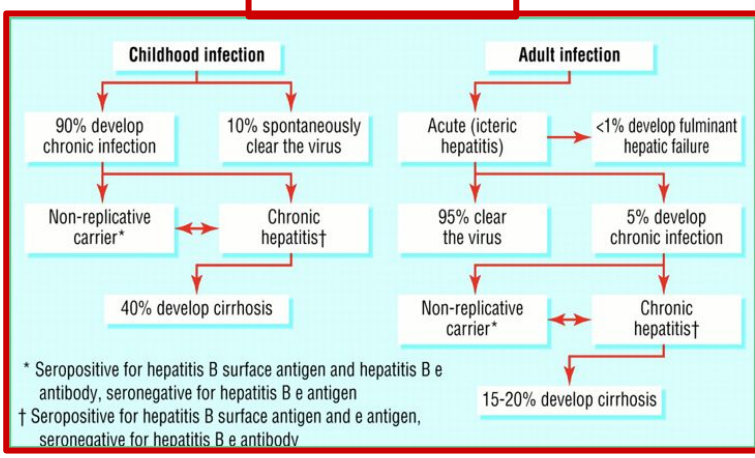
Hepatitis B virus mode of transmission

- Sexual
- Paranteral
- perinatal

IMPORTANT!

Natural History of Hepatitis B

Children gets HBV more, but nowadays they get vaccinated.
Understand the diagram.



Concentration of Hepatitis B virus in various Body Fluids

Low/not Detectable	Moderate	High
-urine -feces -sweat -tears -breastmilk	-semen -vaginal fluid -saliva	-blood -serum -wound exudates

Possible transmission route of HBV in KSA

1-Horizontal transmission (person to person) is the main transmission route

2-Perinatal transmission (positive HBSAG mothers) especially if they are HBEAG positive (nowadays it is very easy to prevent it by giving a mother a treatment in the last 3 months of gestation so the virus load decrease to a very minimum rate and we prevent the infection)

3- Heterosexual transmission

4-Illegal injection drug use still there, you need to ask about it in the history

5- Contaminated equipment used for therapeutic injections and other health care related procedures it is very important to look around and make sure everything is sterile

6- Folk medicine practice Don't forget to ask about it!!

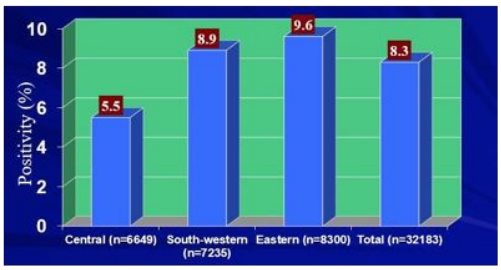
7-Blood and blood products transfusion without prior screening

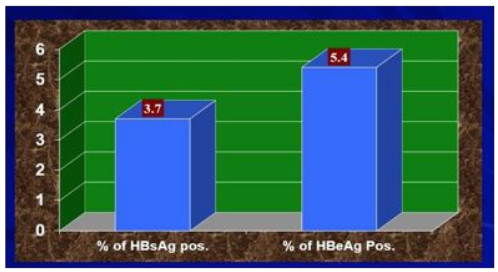
HEPATITIS MARKERS

Hepatitis B Markers (Diagnosis)	**Antigens:** - HBsAg → infection (carrier) -Present in acute or chronic infection -Detectable as early as 1-2 weeks after infection -It persists in chronic hepatitis regardless of whether symptoms are present or not. If virus is cleared, then HBsAg is undetectable. In acute liver failure from hepatitis B, the liver damage is mediated by viral clearance and so HBsAg is negative, with evidence of recent infection shown by the presence of hepatitis B core IgM - HBeAg → viral replication -Reflects active viral replication, and presence indicates infectivity. -Appear shortly after HBsAg - HBV-DNA → viral replication **Antibodies:** - anti-HBc→ exposure (IgM = acute) -Assay of IgM & IgG combined. -Useful because it may be the only serologic marker of HBV infection during the "window peek" in which HBsAg is disappearing, but anti-HBsAg is not yet detectable - anti-HBs → immunity - Present after vaccination or after clearance of HBsAg, usually detectable 1 to 3 months after infection. - In most cases, it indicates immunity - anti-HBe → seroconversion
Hepatitis C Markers (Diagnosis)	- ANTI -HCV - PCR-RNA HCV HCV RNA measured by PCR
Hepatitis A Markers (Diagnosis)	- HAV igM diagnostic of acute infection. fall to low levels within about 3 months of recovery - HAV igG previous infection or immunity. persists for years
Hepatitis E Markers (Diagnosis)	- HEV igM - HEV igG - HEV RNA PCR

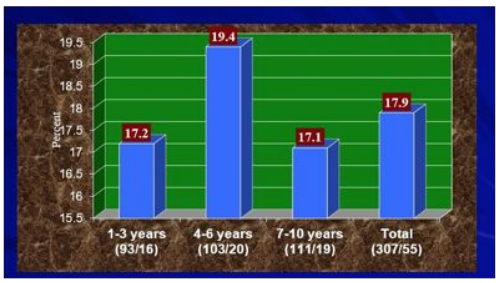
PREVENTION STRATEGIES OF MINISTRY OF HEALTH IN KSA

- Introducing **HBV vaccine (it is the most important method to get rid of the virus)** in EPI program; and Mandatory screening of blood donors and expatriates.
- Vaccination of risk groups.
- Health education especially among medical personnel.

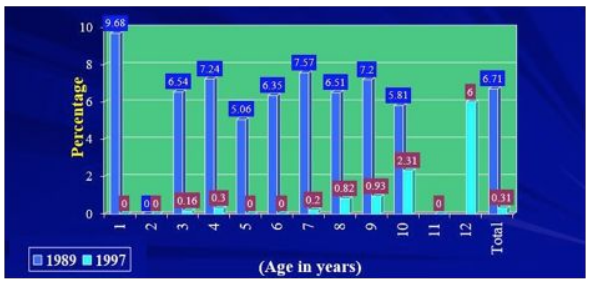




Frequency Of HBeAg Among HBsAg Positive Saudi Children (N=307):



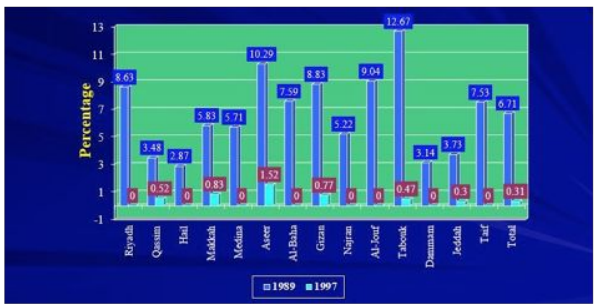
Comparison Of Prevalence Of HBsAg Among Saudi Children In 1989 (N=4575) And 1997 (N=5355) – According To Age:



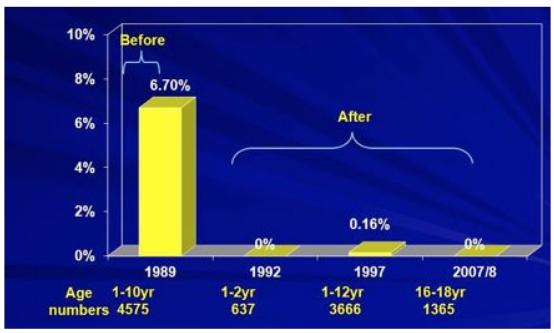
They went to 12 regions and screened too many patients!!

Comparison Of Prevalence Of Hbsag Among Saudi Children In 1989 (N=4575) And 1997 (N=5355) – According To Region:

Year 1989 (before vaccination), Year 1997 (after)

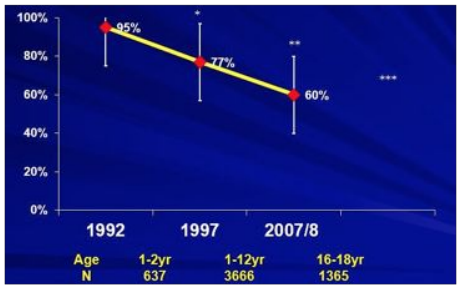


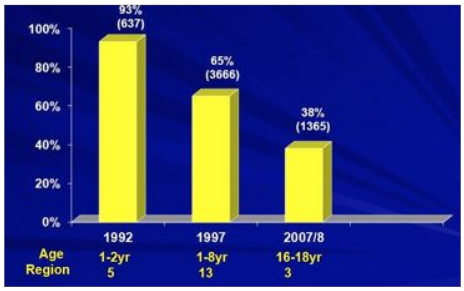
Prevalence Of HBsAg Among Saudi Population Before & After Vaccination over 18y:



Long Term Seroconversion Rate Over 18 Years (Anti-HBS):

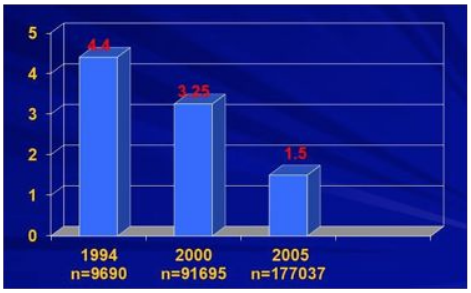
Long-Term protection of HB- vaccine over 18 years (anti-HBS >10 IU/L)(n=1355):



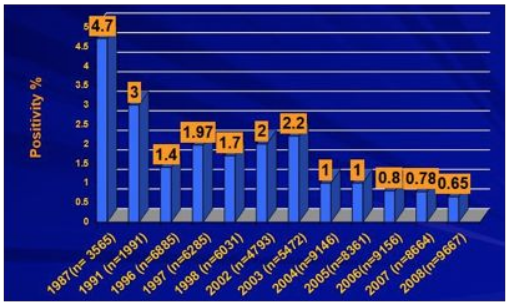


* You only may need booster dose from time to time

Changing Patterns Of HBsAg Positivity Among Blood Donors In Moh,Central Blood Bank 1994-2005:



Prevalence Of HBsAg Positivity Among Blood Donors In KKUH From 1987 To 2008:

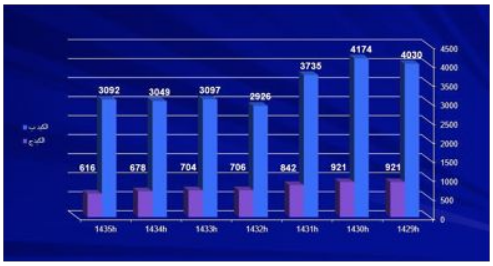


Pre-marital Screening:

التهاب الكبد ب و ج 1429-1435هـ HBV,HCV INFECTION FROM2009-2014			
الكبد ب HBV	الكبد ج HCV	HIV	عدد المتقدمين NR.OF SCREENDS
24103	5388	512	2.131.018
1%	0.3%	%0.02	

Number Of Positive HBV & HCV Cases (2009-2014)

HCV=Red



History of HBV infection control in KSA:

1989: vaccination of all infants at birth.
1990: vaccination of all children at school entry.
1990-until now:
- vaccination of all risk groups is mandatory.
- screening of all expatriates coming to work in KSA.

The current EPI in KSA:

At birth BCG +	HB1
At 6 weeks DPT1 + OPV1 At	Hb2
3 months DPT2 + OPV2 At 5	
months DPT3 + OPV3 At 5	
months Measles	HB3
At 12 months MMR	
At 18 months (DPT + OPV)	Booster 1
At 4-6 years (DPT + OPV)	Booster 2

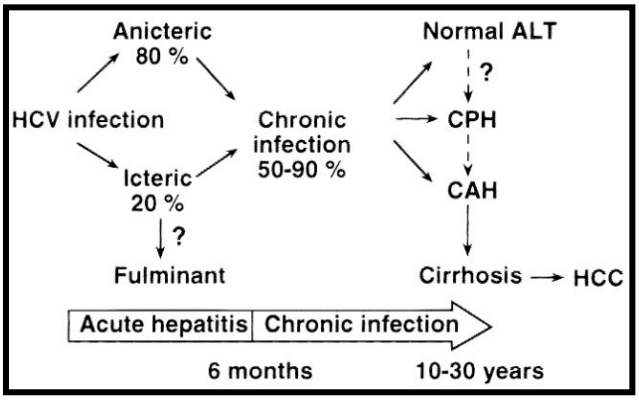
*Because the antibodies will go down

HCV infection

Transmission

Routes of Hep C transmission	Nosocomial transmission
●**Percutaneous**: - Injecting drug use. - Clotting factors before viral inactivation. - Transfusion, transplant from infected donor - therapeutic (contaminated equipment, unsafe injection practices) - Occupational (needlestick). ●**Permucosal** : - Perinatal - Sexual	● **Recognized primarily in context of outbreaks.** ● **Contaminated equipment** **- hemodialysis.** - endoscopy. ● **Unsafe injection practices** - plasmapheresis, phlebotomy. - multiple dose medication vial. - therapeutic injections.

Natural history



Prevention Of HCV Transmission

- ●Avoiding shared use of razors or brushes and any item that pierces the skin.
- ● Strict adherence of the universal precautions in health facilities.
- ● Educating and training of health care workers to the proper use of standard precautions.

HCV infection

Overall prevalence rate of HCV infection in KSA among children and adolescent during the last 18 years:

1989		1997		2008	
No. Of children	Positive (%)	No. of children	Positive (%)	No. of students	Positive (%)
4496	39 (0.87%)	5350	2 (0.04%)	1357	(5)3 0.22%
Diagnostic test only by 1st-generation EIA kit		Diagnostic test by 3rd-generation EIA kit and confirmatory test by RIBA kit.		Diagnostic test by PCR for anti-HCV Positive cases	

(A for Acute) prevalent in south SA (jazan)

HAV infection very rare due to vaccination

Transmission

- **Fecal-oral route (95%):**
  - person to person contact.
  - contaminated food or water.
  - Salads and fruits washed in contaminated water.
  - Contaminated shellfish.
- **Infected plasma (< 5%).**
- **Sexual route (< 5%).**
- **Close personal contact** (e.g: household contact, Sex contact, child day care center)
- **contaminated food and water** (e.g: infected food handlers)
- **blood exposure (rare)**
  (e.g: injection drug use, rarely by transfusion)

Prevention

- Hygiene (eg: hand washing)
- Sanitation (eg: clean water sources)
- Hepatitis A vaccine (pre-exposure)
- Immunoglobulin (pre- and post-exposure)

Recommended Dosages of Hepatitis A Vaccines

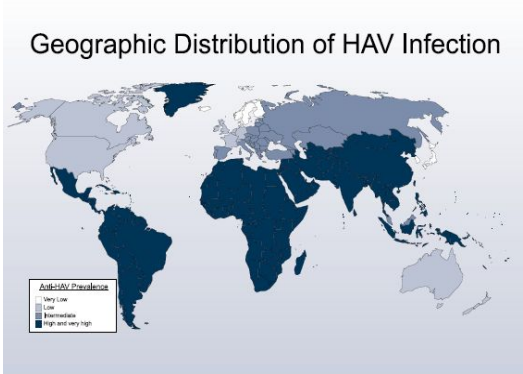
Schedule Vaccine	Age (yrs)	Dose	Volume (mL)	2-Dose (mos)
HAVRIX ®,	1-18	720 (EL.U.*)	0.5	0, 6-12
	>18	1,440	1.0	0, 6-12
VAQTA ®#	1-18	25 (U**)	0.5	0, 6-18
	>18	50	1.0	0, 6-18

Immunization should be considered for those at particular risk, such as:
- close contacts of HAV-infected patients, elderly, those with other major disease, perhaps pregnant women, and for individuals with chronic hepatitis B or C infections.

HAV infection in patients with chronic liver disease may cause serious or life-threatening disease.

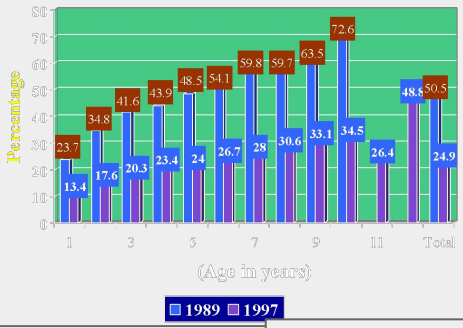
HAV infection

Geographical distribution

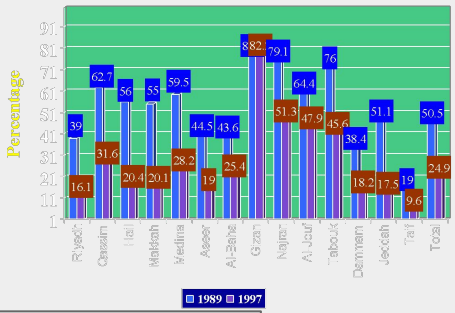


Studies on HAV infection:

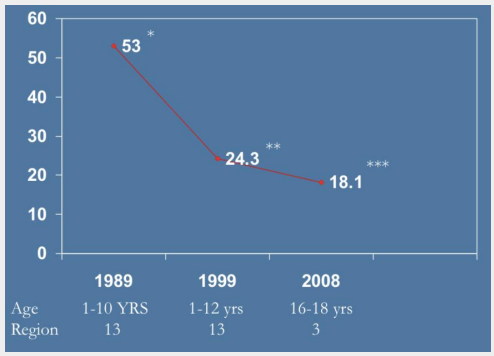
Comparison Of Prevalence Of Anti-HAV Among Saudi Children In 1989 (N=4375) And 1997 (N=5255) – According To Age:



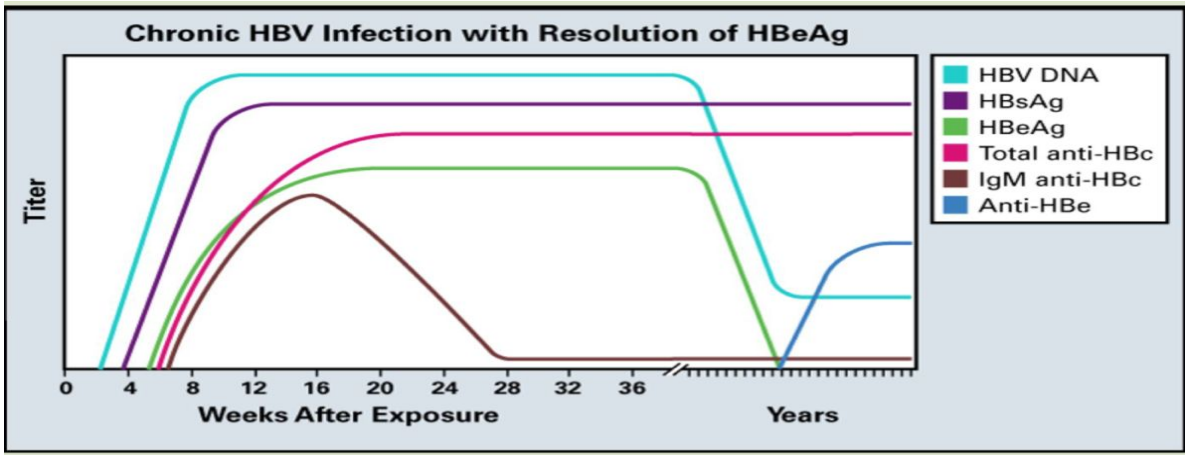
Comparison Of Prevalence Of Anti-HAV Among Saudi Children In 1989 (N=4375) And 1997 (N=5255) – According To Region:

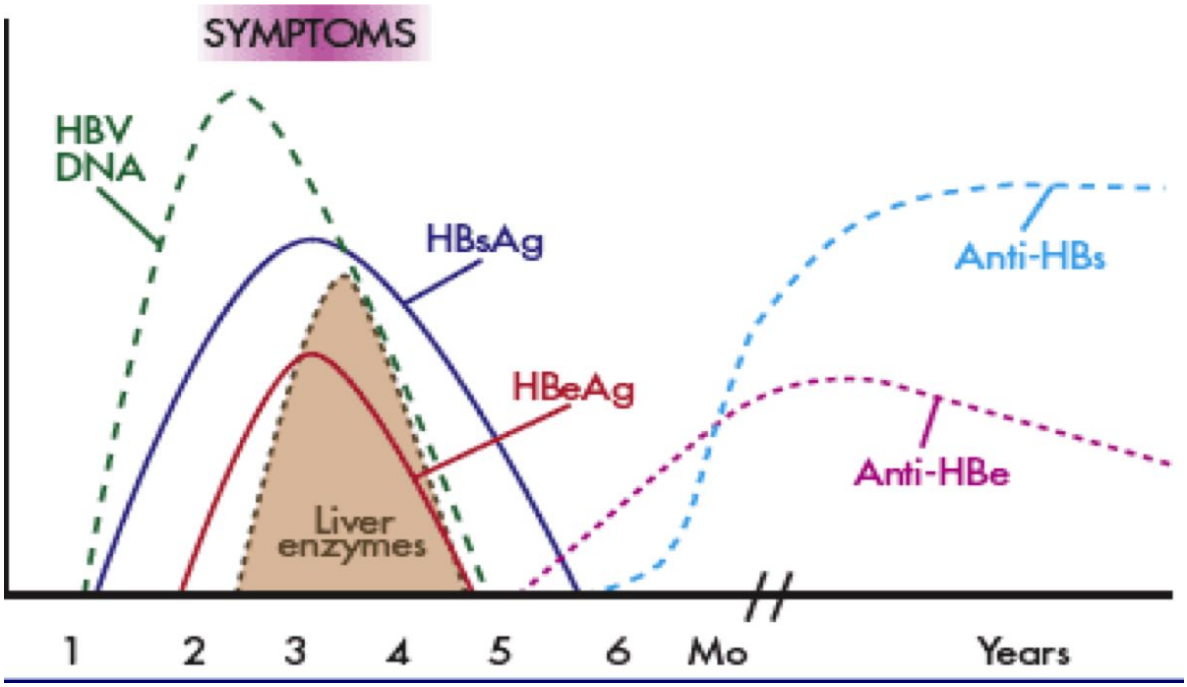


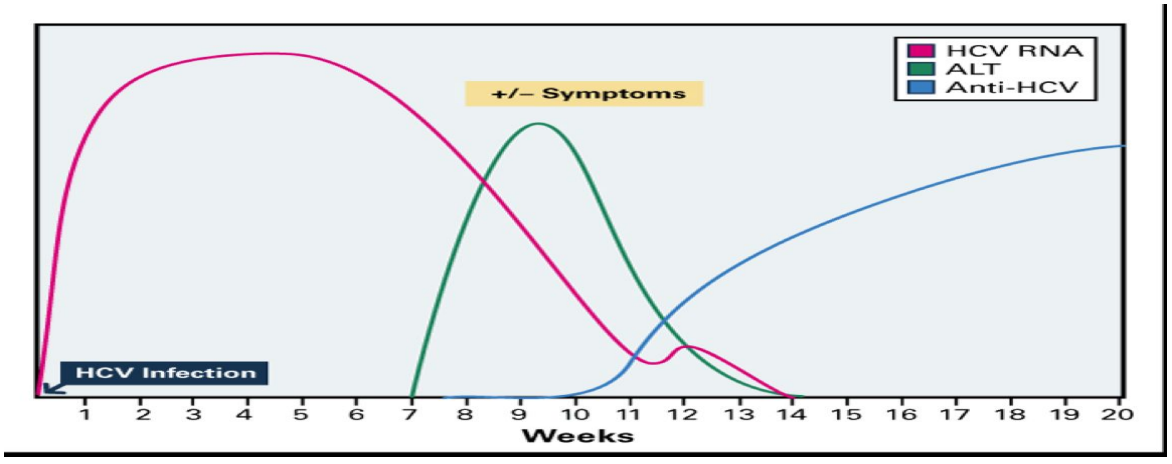
Changing Pattern Of Hepatitis A Prevalence Within The Saudi Population Over 18 Years:



Extra


Chronic HBV Infection with Resolution of HBeAg
Titer
HBV DNA
HBsAg
HBeAg
Total anti-HBc
IgM anti-HBc
Anti-HBe
0 4 8 12 16 20 24 28 32 36
Weeks After Exposure
Years


SYMPTOMS
HBV DNA
HBsAg
HBeAg
Anti-HBs
Anti-HBe
Liver enzymes
1 2 3 4 5 6 Mo
Years


HCV RNA
ALT
Anti-HCV
+/– Symptoms
HCV Infection
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20
Weeks

Case report

5/11/18 Sara is 35 Y/O Teacher ,living in TABUK. She came for marriage consultation.

Lab results:

12/11/18 :

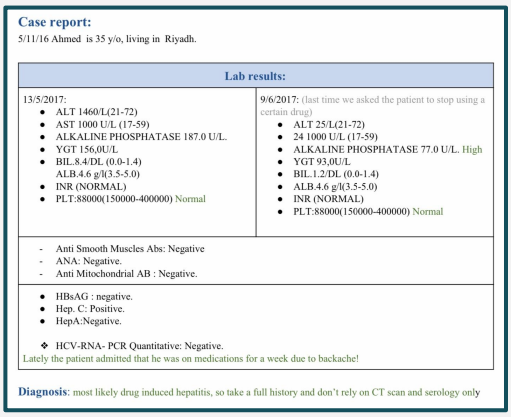
ALT 40/L(21-72)
AST 30 U/L (17-59)
ALKALINE PHOSPHATASE 80.0 U/L.
YGT 40,0U/L
BIL.1MG/DL (0.0-1.4)
ALB.4.6 g/l(3.5-5.0)
INR (NORMAL)
HBsAG : POSITIVE PCR QUANTITATIVE :200IU/ML
If PCR less than/equal to 200= inactive carrier

Diagnosis

Inactive CARRIER OF VIRAL HEPATITIS B

Her main problem whenever she got engaged and do the marriage screening, nobody accept to proceed with the marriage. How can we solve the problem ?

explain that she can be treated, he can be protected from infection, and there are measures to prevent their children from being infected



Case report:

5/11/16 Ahmed is 35 y/o, living in Riyadh.

Lab results:

13/5/2017:
- ALT 1460/L(21-72)
- AST 1000 U/L (17-59)
- ALKALINE PHOSPHATASE 187.0 U/L.
- YGT 156,0U/L
- BIL.8.4/DL (0.0-1.4)
  ALB.4.6 g/l(3.5-5.0)
- INR (NORMAL)
- PLT:88000(150000-400000) Normal

9/6/2017: (last time we asked the patient to stop using a certain drug)
- ALT 25/L(21-72)
- 24 1000 U/L (17-59)
- ALKALINE PHOSPHATASE 77.0 U/L. High
- YGT 93,0U/L
- BIL.1.2/DL (0.0-1.4)
- ALB.4.6 g/l(3.5-5.0)
- INR (NORMAL)
- PLT:88000(150000-400000) Normal

- Anti Smooth Muscles Abs: Negative
- ANA: Negative.
- Anti Mitochondrial AB : Negative.

- HBsAG : negative.
- Hep. C: Positive.
- HepA:Negative.

❖ HCV-RNA- PCR Quantitative: Negative.

Lately the patient admitted that he was on medications for a week due to backache!

Diagnosis: most likely drug induced hepatitis, so take a full history and don't rely on CT scan and serology only

Case from 436

Summary

Type	A	B	C	D	E	Auto-immune
Source of virus	Feces	-Blood Blood derived. -Body fluids.			Feces	
Route of Transmission	Feco-Oral	Percutaneous Permucosal			Feco-Oral	-
Chronic Infection	No	Yes			No	
Serology Markers	-IgM→ active -IgG→ recovery or vaccination	See it below		-	-IgM→ active -IgG→ recovery or vaccination	-ANA (ANF). -Anti-mitochondrial antibody. -Anti-smooth muscle antibody.
Prevention	Pre and Post Exposure Immunization	-Pre and Post Exposure Immunization. -Blood donor screening.	Blood donor screening	Pre and Post Exposure Immunization	Ensure Safe Drinking Water	-
Complication	-	1.Chronic Hepatitis→ Cirrhosis. 2.Hepatocellular Carcinoma (HCC). 3.Fulminant Hepatitis.		-		

Serology Markers of HBV:

-HBV DNA and HBsAg→ marker of infectious contagious.
-HBeAg→ marker of **active virus** replication, the patient is **highly infectious**.
-Anti-HBc→ marker of **exposure** to HB infection, contiguous.
-Anti-HBs→marker of immunity not contiguous.
-Note:

- Anti-HBcAg **IgM** is found before any antibodies.
- Anti-HBcAg indicate viral infection in the past.
- Immune patient: Anti-HBsAg+ Anti-HBcAg.
- Vaccinated patients: only Anti-HBsAg.

Serology Markers of HCV:

-HCV RNA→ 1st marker that appears (it's a marker of infection).
-Anti-HC→ second marker (it is not marker of immunity, can be detected in completely recovered patient, acute and chronic.

HEPATITIS MARKERS

Hepatitis B Markers (Diagnosis)	**Antigens:** - HBsAg → infection (carrier) -Present in acute or chronic infection -Detectable as early as 1-2 weeks after infection -It persists in chronic hepatitis regardless of whether symptoms are present or not. If virus is cleared, then HBsAg is undetectable. In acute liver failure from hepatitis B, the liver damage is mediated by viral clearance and so HBsAg is negative, with evidence of recent infection shown by the presence of hepatitis B core IgM - HBeAg → viral replication -Reflects active viral replication, and presence indicates infectivity. -Appear shortly after HBsAg - HBV-DNA → viral replication **Antibodies:** - anti-HBc→ exposure (IgM = acute) -Assay of IgM & IgG combined. -Useful because it may be the only serologic marker of HBV infection during the "window peek" in which HBsAg is disappearing, but anti-HBsAg is not yet detectable - anti-HBs → immunity - Present after vaccination or after clearance of HBsAg, usually detectable 1 to 3 months after infection. - In most cases, it indicates immunity - anti-HBe → seroconversion
Hepatitis C Markers (Diagnosis)	- ANTI -HCV - PCR-RNA HCV HCV RNA measured by PCR
Hepatitis A Markers (Diagnosis)	- HAV igM diagnostic of acute infection. fall to low levels within about 3 months of recovery - HAV igG previous infection or immunity. persists for years
Hepatitis E Markers (Diagnosis)	- HEV igM - HEV igG - HEV RNA PCR

Questions

Q1: A 31-year-old Latino woman presents with complaints of fatigue. She returned from a business trip to Mexico 10 days ago. She visits her primary care physician who orders laboratory tests. The results indicate the ALT level is mildly elevated and hepatitis serologies are anti-HAV IgM(+), anti-HAV IgG (-), HBsAg(-), anti-HBc IgG(-), anti-HBc IgM (-) and anti-HCV (-). Which vaccine should be recommended?

A) Immune globulin (IG).
B) Hepatitis A vaccine only.
C) Hepatitis B vaccine only.
D) Hepatitis A and Immune globulin.

Q2: A 27-year-old Asian woman is due to give birth to a baby boy in 1 month. Prior to becoming pregnant, she drank alcohol occasionally and did not smoke. She never used IV drugs or had a blood transfusion. The HBsAg test is negative. Which vaccination regimen should be recommended for her newborn baby?

A) Hepatitis A vaccine at birth.
B) Hepatitis A and B vaccine at 6 months.
C) Immune globulin within 24 hours of birth.
D) Hepatitis B vaccine only at discharge.

Q3: A 50 years old gentleman who is suffering from chronic active hepatitis. What do you expect to see in his serum?

A) HBsAg and HBeAg.
B) Anti-HBsAb.
C) HB-DNA only.
D) HBsAg only.

Q4: What is the marker of immunity in HBV ?

A) HCV RNA.
B) Anti-HBe.
C) Anti-HBsAg.
D) HAV-IgM.

Answers:

1. **B**
2. **D**
3. **A**
4. **C**

Questions

Q5: A 35 years old women with a history of alcohol consumption and I.V drug use, she was diagnosed with hepatitis C before one year. What is the first marker that appears in her serum ?

A) HCV RNA.
B) Anti-HBsAg..
C) HAV-IgM
D) Anti-HCV.

Q6: Which of the following types of viral hepatitis could cause hepatocellular carcinoma(HCC) and fulminant hepatitis ?

A) Hepatitis A.
B) Hepatitis B.
C) Hepatitis C.
D) Hepatitis D.

Answers:

5. A
6. B & C