Acute Viral Hepatitis

Objectives:

- Recognise the different type of acute viral hepatitis
- Know the possible complications and outcome of acute viral hepatitis
- Aware of the other cause of acute hepatitis in KSA
- To have fair knowledge about the latest results of epidemiological aspect of viral hepatitis A,B,C IN KSA

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Resources: 436 slides, 435 team, Davidson,

- Editing file
- Feedback

Acute 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	
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.	- 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

Viral Hepatitis Overview:

	A	E	B	C	D
Source	Feces		Blood/blood-derived body fluids		
Route of transmission	Fecal-oral		Percutaneous – permucosal		
Chronic infection	No		yes		
prevention	pre/post-exposure immunization	Ensure safe drinking water	Pre/post-exposure immunization	-Blood donor screening -Risk behavior modification	-Pre/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.
- H**A**V & H**E**V : f**E**c**A**l

Signs and Symptoms of the 3 phases of acute Hepatitis:

- 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

Pre-icteric phase	Icteric phase	Post-icteric phase
- Anorexia - Fatigue - Nausea - Vomiting - Arthralgia - Myalgia - Headache - Photophobia - Pharyngitis	- Enlarged liver - Tender upper quadrant - Discomfort - Splenomegaly (10-20%) - General adenopathy	- Cessation of symptoms, liver enlargement and continuous fatigue.

Basic 4 steps for the Diagnosis of hepatitis:

1-Take the patient's history.

2-Physical examination.

3-Liver function tests: (ALT ,AST are elevated >5-10 times of normal)

- 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.

4-Serological tests:

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

Lab findings:

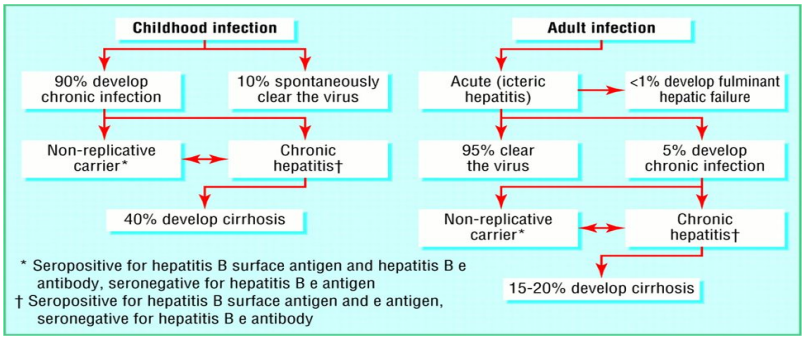
- LFT increase >5-10 times of normal.
- Markers of hepatitis B or C or A might be positive.

What is the differential diagnosis of Viral Hepatitis ?

1. Infectious Mononucleosis. usually seen in children, lymphadenopathy with normal LFT
2. Drug Induced Hepatitis. Due to antibiotics and other drugs
3. Chronic Hepatitis.
4. Alcohol Hepatitis.
5. Cholecystitis can come with high LFT, confirm with US, Cholelithiasis.
6. Autoimmune hepatitis.

Hepatitis A (for Acute) prevalent in south SA (jazan)	
Geographical distribution	• Southern part of the globe is more affected by HAV .
Transmission	• Fecal-oral route (95%): - person to person contact. - contaminated food or water. - Salads and fruits washed in contaminated water. - Contaminated shellfish. (Infection is also more common in areas of overcrowding and poor sanitation. In occasional outbreaks, water and shellfish have been the vehicles of transmission). • Infected plasma (< 5%). • Sexual route (< 5%).
Markers (Diagnosis)	Anti-HAV: 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
Prevention	• Hygiene (eg: hand washing) • Sanitation (eg: clean water sources) • Hepatitis A vaccine (pre-exposure) "Active vaccine" • Immunoglobulin (pre- and post-exposure) "passive" 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.

Hepatitis B

Transmission	1-Horizontal transmission (person to person) is the main transmission route e.g. sexual intercouse 2-Perinatal transmission (positive HBsAg mothers) especially if they are HBeAg positive. Vertical transmission from mother to child in the perinatal period is the most common cause of infection worldwide and carries the highest risk of ongoing chronic infection. 3-Illegal injection drug use (Paranteral). 4- Heterosexual transmission. 5- Contaminated equipment used for therapeutic injections and other healthcare related procedures (paranteral). 6- Folk medicine practice. 7-Blood and blood products transfusion without prior screening.
Concentration in fluid	• **High:** in blood ,serum,wound exudate**.** • **Moderate:** semen ,vaginal fluid,saliva. • **Low/not detectable:** urine, feces, sweat, tears, breastmilk**.**
Natural history	Chronic infection: **children 90%, Adults 5% , try to understand the diagram.**  - Children gets HBV more, but nowadays they gets vaccinated. - Don't panic when you accidentally inject yourself with the virus! There is a chance 95% that you won't develop the disease.
Markers Diagnosis (Important)	Serum serology: • Antigens: 1. HBsAg → infection (carrier): surface antigen - 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 2. HBeAg → viral replication: - Reflects active viral replication, and presence indicates infectivity. - Appear shortly after HBsAg.

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3. Viral load: HBV DNA → viral replication:
- measured by PCR; if it persists > 6 weeks, patient is likely to develop chronic disease.
● Antibodies:
1. 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.
2. Anti-HBe → seroconversion
3. Anti-HBc (Hepatitis B core antibody) → 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.

extra:
<table>
<tr><th colspan="5">Serologic Patterns</th></tr>
<tr><th></th><th>Surface antigen</th><th>e-antigen</th><th>Core antibody</th><th>Surface antibody</th></tr>
<tr><td>Acute or chronic infection</td><td>Positive</td><td>Positive</td><td>Positive IgM or IgG</td><td>Negative</td></tr>
<tr><td>Resolved, old, past infection</td><td>Negative</td><td>Negative</td><td>Positive IgG</td><td>Positive</td></tr>
<tr><td>Vaccination</td><td>Negative</td><td>Negative</td><td>Negative</td><td>Positive</td></tr>
<tr><td>"Window period"</td><td>Negative</td><td>Negative</td><td>Positive IgM, then IgG</td><td>Negative</td></tr>
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<tr>
<td>Prevention strategies in KSA</td>
<td>
● Introducing HBV vaccine in EPI[1] program; and
● Mandatory screening of blood donors and expatriates.
● Vaccination of risk groups.
● Health education especially among medical personnel.
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<tr><th colspan="3">Hepatitis C</th></tr>
<tr>
<td>Transmission</td>
<td>
Routes of Hep C transmission:
1. Percutaneous:
- Injecting drug use.
- Clotting factors before viral inactivation.
- Transfusion, transplant from infected donor.
- Occupational (needlestick).
2. Permucosal which includes (Not common):
- Perinatal
- Sexual
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<td>
Nosocomial transmission:
● Recognized primarily in context of outbreaks.
● Contaminated equipment
- hemodialysis.
- endoscopy.
● Unsafe injection practices
- plasmapheresis, phlebotomy.
- multiple dose medication vial.
- therapeutic injections.
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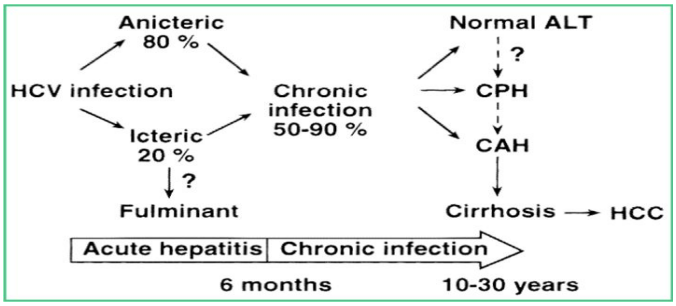
[1] Expanded Program on Immunization: was established in 1976 to ensure that infants/children and mothers have access to routinely recommended infant/childhood vaccines.

Natural history	• Chronic infection is common 90% 
Markers **(Diagnosis)**	**Serum serology:** • **Anti-HCV (Hepatitis C antibody):** Key marker of HCV infection. Sometimes not detectable until months after infection, so its absence does not rule out infection. • **Viral load:** HCV RNA measured by PCR . Detectable 1 to 2 weeks after infection- more sensitive than HCV antibody.
Prevention	• HCV has a very low prevalence, nowadays there is a drug taken for 3 months and cured 98% of patients. • 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.

Other markers	
HEV	• HEV IgM • HEV IgG • HEV RNA (by PCR)
Autoimmune Hepatitis A Hallmark of Autoimmune hepatitis is rich plasma interface	• ANA (ANF)[2] • Anti-mitochondrial antibody • Anti-smooth Muscle antibody

Complications:

1. Chronic Hepatitis → cirrhosis - HCC[3] (with chronic hepatitis = C + B + D)
2. Fulminant hepatitis:

- Definition: Hepatic Failure Within 8 Weeks Of Onset Of Illness.

[2] Antinuclear antibody (Antinuclear factor) both are the same.
[3] Hepatocellular carcinoma.

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 (Complications of fulminant hepatitis include): Encephalopathy and Prolonged PT.
    a. Hepatic encephalopathy: look for asterixis and palmar erythema.
    b. Prolonged prothrombin time (bleeding diathesis).
    c. 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.

Management and Treatment:

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.

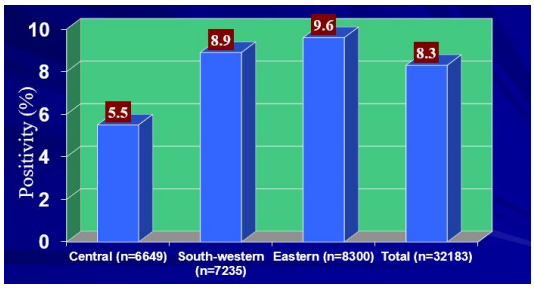
What should be avoided?

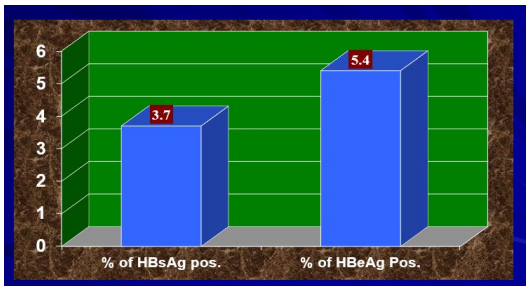
- Drugs such as sedatives and narcotics, which are metabolised in the liver.
- Alcohol should be avoided during the acute illness.
- Elective surgery (a risk of postoperative liver failure.).

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.

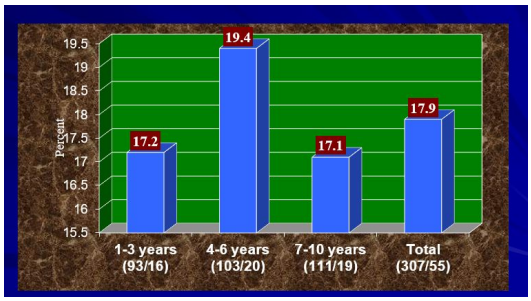
Only acute hepatitis C gets medical therapy (Interferon+Ribavirin) and in acute hepatitis A (accompanied with HepB) if the patient presents with detectable HBsAg and clinical and epidemiological factors suggestive of chronic infection can be considered for treatment without waiting 6-month period (Interferon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

Studies on HBV infection	
Overall Prevalence Of HBsAg Among Saudis In The 80's According To Regions:	Prevalence Of Hbeag Among Hbsag Positive Saudi Pregnant Women (N = 20920):

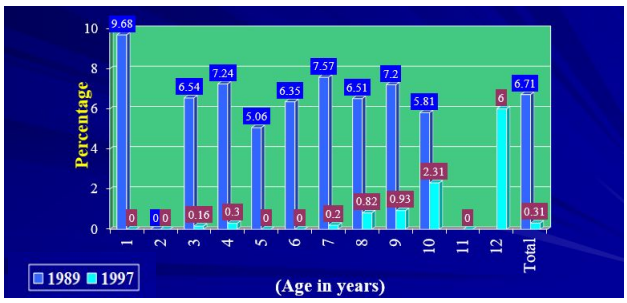




Frequency Of HBeAg Among HBsAg Positive Saudi Children (N=307):



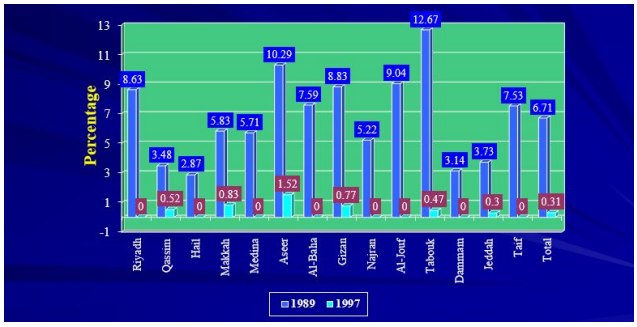
Comparison Of Prevalence Of HBsAg Among Saudi Children In 1989 (N=4575) And 1997 (N=5355) – According To Age:



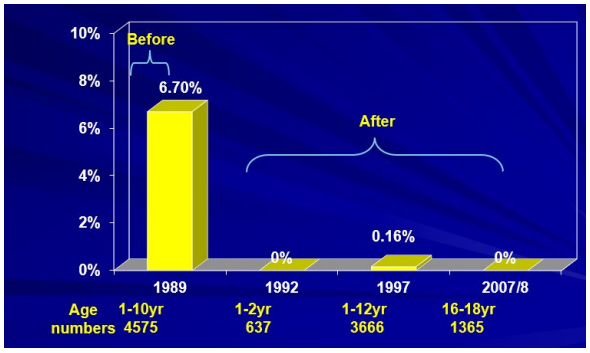
They went to 12 regions and screened too many patients!!

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)

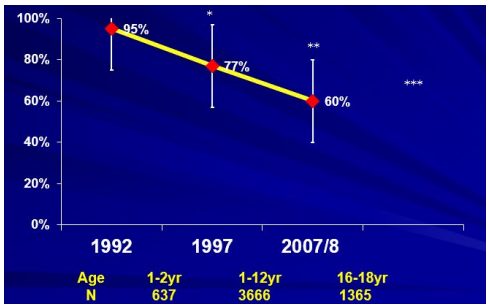


Prevalence Of HBsAg Among Saudi Population Before & After Vaccination over 18y:

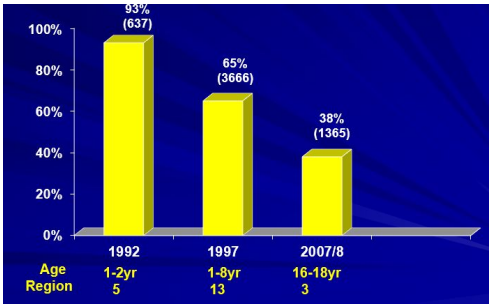


Long Term Seroconversion Rate Over 18 Years (Anti-HBS):

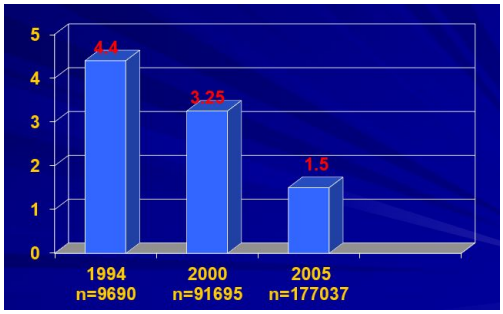
Long-Term protection of HB- vaccine over 18 years (anti-HBS >10 IU/L)(n=1355):



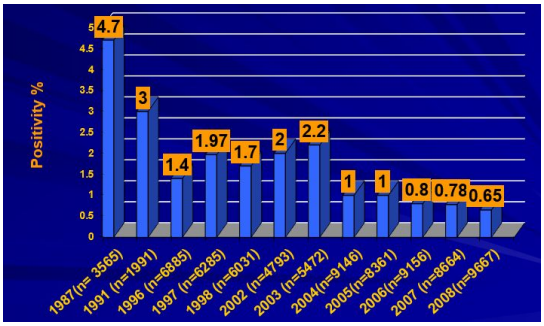
You only may need booster dose from time to time



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:

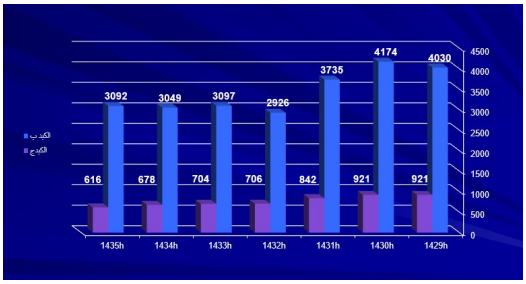


Pre-marital Screening:

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	Hb2
At 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

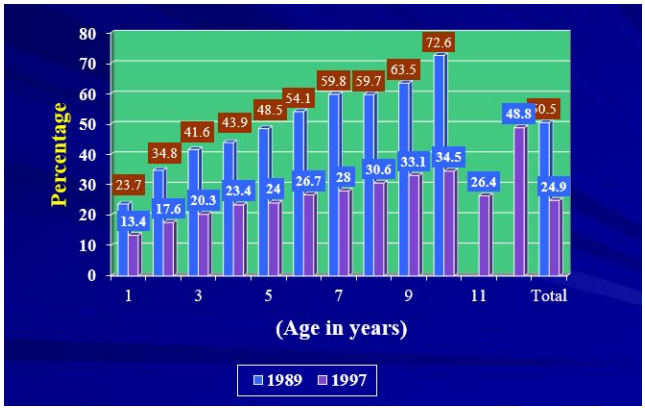
Studies on HCV infection:

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

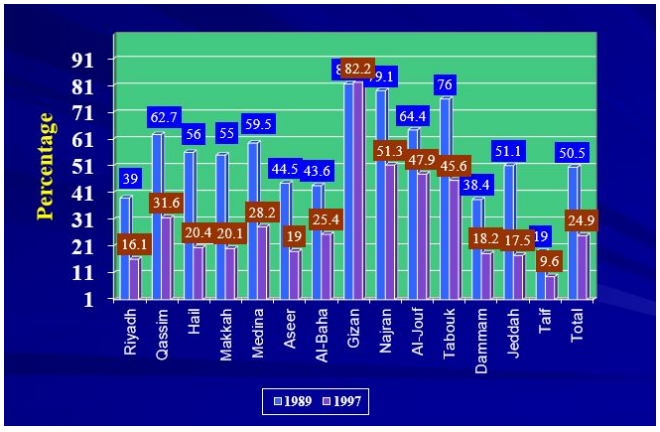
1989		1997		2008	
No. of children	Positive (%)	No. of children	Positive (%)	No. of students	Positive (%)
4496	39* (0.87%)	5350	2 (0,04%)	1357	(5)3 0.22%
Diagnostic test only by 1st-generation EIA kit		Diagnostic test by 3rd-generation EIA kit and confirmatory test by RIBA kit.		Diagnostic test by PCR for anti- HCV Positive cases	

Studies on HAV infection:

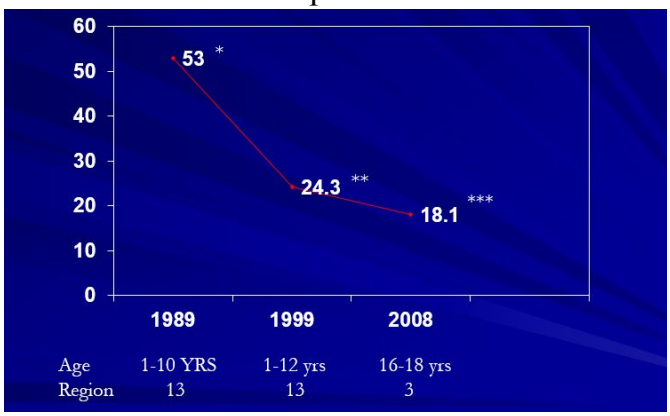
Comparison Of Prevalence Of Anti-HAV Among Saudi Children In 1989 (N=4375) And 1997 (N=5255) – According To Age:



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



Why is it high on Gizan, Najran & Tabouk?! The infrastructure (good housing, clean water & food, it is near to Yemen) increases the chance of disease transmission.

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

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

Case report:

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

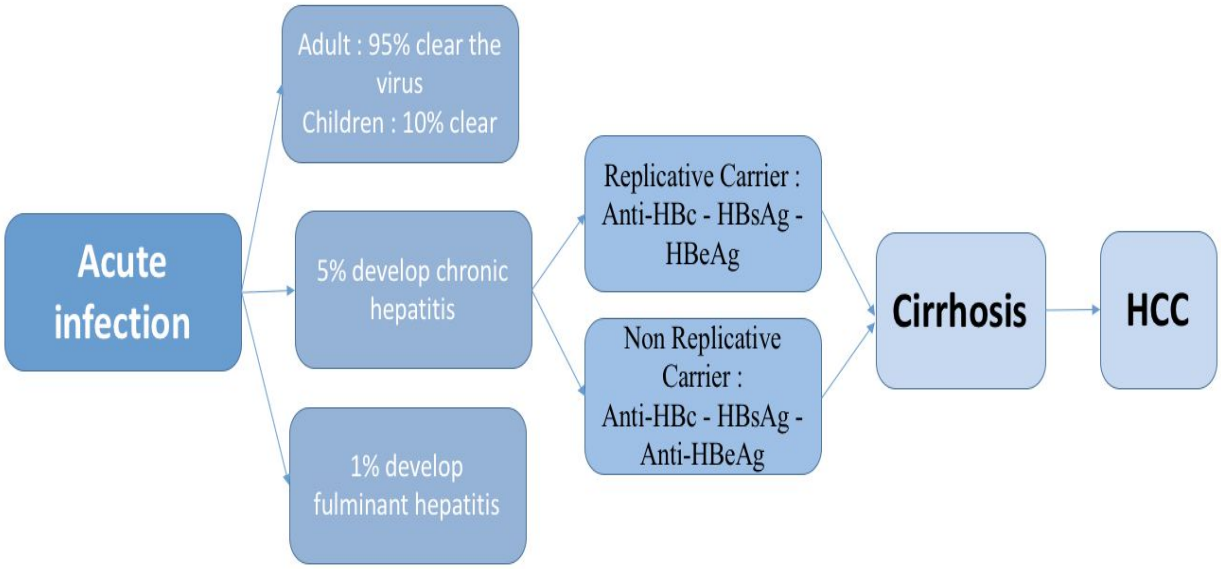
Lab results:

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

SUMMARY

Type	A	B	C	D	E	Autoimmune
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 Marker	IgM → active IgG → Recovery or Vaccination	**Acute :** 1- HBsAg 2-IgM 3-Anti-HBc **Chronic :** 1-Anti-HBc 2-HBsAg **Recover:** 1-Anti-HBc 2-Anti-HBsAg **Immunity :** 1-Anti-HBsAg **High active :** HBeAg **Low active :** Anti-HBeAg	Anti-HCV		IgM → active IgG → Recovery or Vaccination	• ANA (ANF) • Anti-mitochondrial antibody • Anti-smooth Muscle antibody
Prevention	Pre and Post Exposure Immunization	- Pre Post Exposure Immunization - Blood donor screening	Blood donor screening	Pre Post Exposure Immunization	Ensure Safe Drinking water	
Complication		1- Chronic hepatitis --> Cirrhosis 2- Hepatocellular carcinoma (HCC) 3- Fulminant hepatitis				



Questions

1-Which form of hepatitis can be passed on through contaminated food or water?

A. B

B. C

C. A and E

D. All of the above

2-An indicator of good response to interferon for a patient with chronic hepatitis C infection is?

A. low pretreatment HCV RNA.

B. genotype 1.

C. high pretreatment aminotransferases.

D. hepatic fibrosis.

3-a 35-year-old man, was diagnosed with chronic hepatitis B infection 5 years ago. His primary risk factor is intravenous drug use. His liver disease is progressing, as measured by persistently elevated alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels. He had a liver biopsy 6 months ago that showed chronic active hepatitis. He has never been treated for his chronic hepatitis.

Which of the following is the most important goal of treating chronic viral hepatitis B infection?

A. Normalize ALT and AST.

B. Improve symptoms.

C. Lose HBsAg from serum.

D. Decrease symptoms.

4-Hepatitis D is commonly associated with what other type of viral hepatitis?

A. Hepatitis E

B. Hepatitis C

C. Hepatitis B

D. Hepatitis G

5-When a patient is HBsAg-negative and anti-HBs-positive, what is the status of his or her hepatitis B infection?

A. Resolved

B. Chronic carrier

C. Early acute

D. Chronic hepatitis

6-What can be passed from a pregnant women to her child?

A. HCV

B. HBV

C. Both HBV and HCV

D. HAV

E. All if these can

7-In which substance is hepatitis A not present?

A. Blood

B. Faces

C. Urine

8-Which of the following forms of hepatitis are spread via the faecal/oral route?

A. Hepatitis A

B. Hepatitis B

C. Hepatitis C

D. Hepatitis D

Answers:

1-C

2-A

3-C

4-C

5-A

6-C

7-C

8-A