Team Medicine

Acute Viral Hepatitis

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■ Important notes

Types of viral hepatitis					
	A	***B***	***C***	***D***	***E***
Source of virus	Feces	Blood/ blood-derived body fluids	Blood/ blood-derived body fluids	Blood/ blood-derived body fluids	Feces
Route of transmission	Fecal-Oral	Percutaneous Permucousal	Percutaneous Permucousal	Percutaneous Permucousal	Fecal-Oral
Chronic infection	No	Yes	Yes	Yes	No
Prevention	Pre/post exposure immunization	Pre/post exposure immunization	Blood donor screening; risk behavior modification	Pre/post exposure immunization; risk behavior modification	Ensure safe water drinking

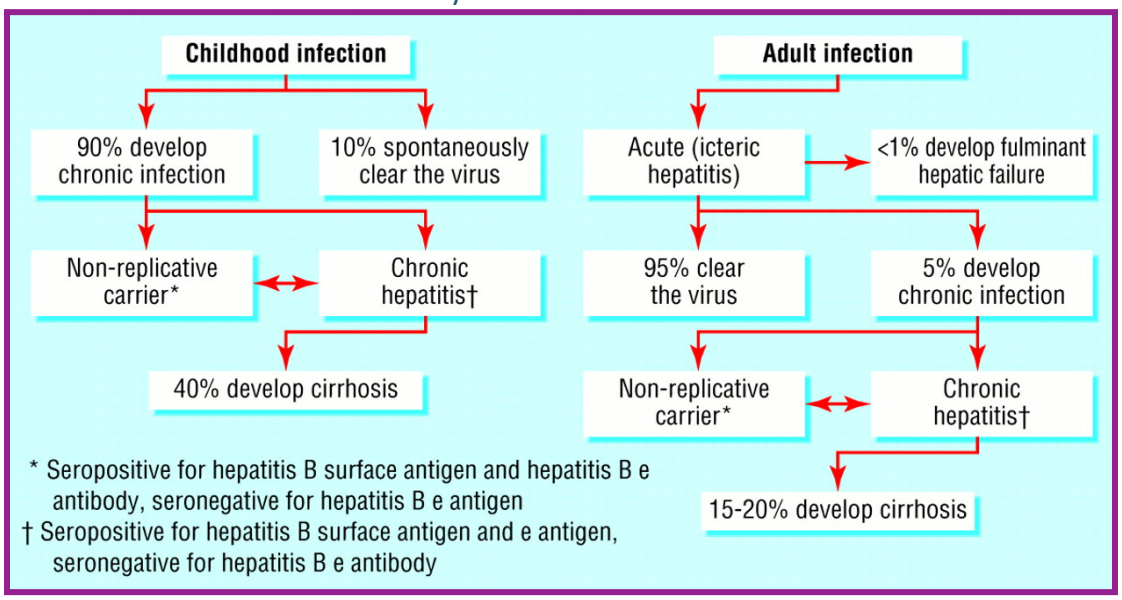
- **Acute Viral Hepatitis(recent infection, relatively rapid onset)**
- Chronic hepatitis is defined as inflammatory disease of the liver lasting for more than six months
- Three phases: 2-6 weeks from pre to post icteric phase
    - Pre-icteric(jaundice):
        - (Anorexia, Fatigue, Vomiting, **Arthralgia,** Nausea, Myalgia, Headache, Photophobia, Pharyngitis) **(similar to flu symptoms but dark urine and pale stool may precede jaundice and help with diagnosis)**
    - Icteric:
        - **(Enlarged liver ,Tender upper quadrant,Splenomegaly (10-20%),genraladenopathy, discomfort)**
    - Post icteric phase: (no jaundice)
- **Self limiting disease if there is no complication**
- Complications of hepatitis:
    1. Chronic hepatitis → cirrhosis- HCC
    2. **Fulminant hepatitis**
- **Fulminant hepatitis:**
    - **Definition: Hepatic Failure within 8 Weeks of Onset of Illness.**
    - **Manifestation: Hepatic encephalopathy: Arising from advanced cirrhosis of the liver and Prolonged PT .30% will die if not treat him.**
    - **Histopathology: Massive Hepatic Necrosis.**
- Lab Findings:
    - **LFT (liver function test) increase >5-10 times of normal**
    - Markers of hepatitis B or C or A might be positive

Markers of viral hepatitis:

- **HBV MARKERS:**
  - anti-HBc → exposure (IgM = acute)
  - HBsAg → infection (carrier) **(HBsAg is the surface antigen of the hepatitis B virus and there is antibody for this antigen(anti-HBs))**
  - anti-HBs → immunity
  - HBeAg → viral replication
    - **HBeAg and HBcAg are same but HBeAg is secreted and found in the serum of patients.**
    - **HBeAg is the (core antigen of the hepatitis B virus and there is antibody for this antigen (anti-HBe)**
  - anti-HBe → seroconversion
  - HBV-DNA → viral replication
- **HCV MARKERS (There's no surface antigen, only Antibodies)**
  - ANTI –HCV **(If this is positive we cannot say for sure that the patient has HCV, therefore we always have to check for the next marker if the first one's positive)**
  - PCR-RNA HCV **(This marker confirms presence of HCV)**
- **HAV MARKERS**
  - HAV igM **(Acute exposure) – (Current infection)**
  - HAV igG **(Indicates previous exposure to HAV) – (Previous infection)**
- **HEV Markers:**
  - HEV igM **(Acute exposure) – (Current infection)(Indicates previous**
  - HEV igG **(Indicates previous exposure to HAV) – (Previous infection)**
  - HEV RNA PCR
- **AUTOIMMUN HEPATITIS MARKERS**
  - ANA antinuclear antibody (1:1280)
  - ANTI MITOCHONDRIAL antibody (1:400)
  - ANTI SMOOTH MUSCLES antibody (1:400)

Hepatitis B:

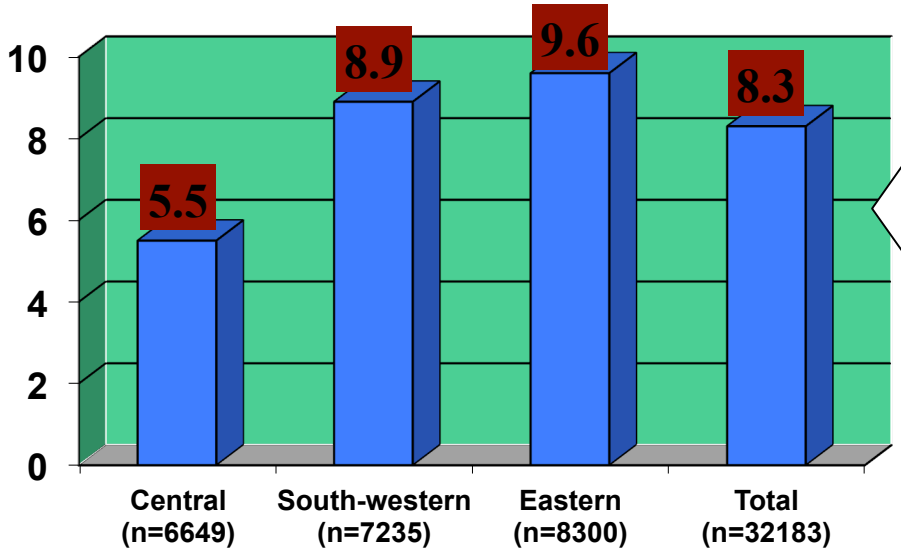
- **Clinical features:**
  - Incubation period: **(period from exposure to signs and symptoms)**
    - Average 60-90 days
    - Range 45-180 days
  - Clinical illness (jaundice):
    - <5 yrs, <10%
    - >= 5 yrs, 30%-50%
  - Acute case-fatality rate: 0.5%-1%
  - Chronic infection:
    - <5 yrs, 30%-90%
    - >= 5 yrs, 2%-10%
  - Premature mortality from chronic liver disease: 15%-25%



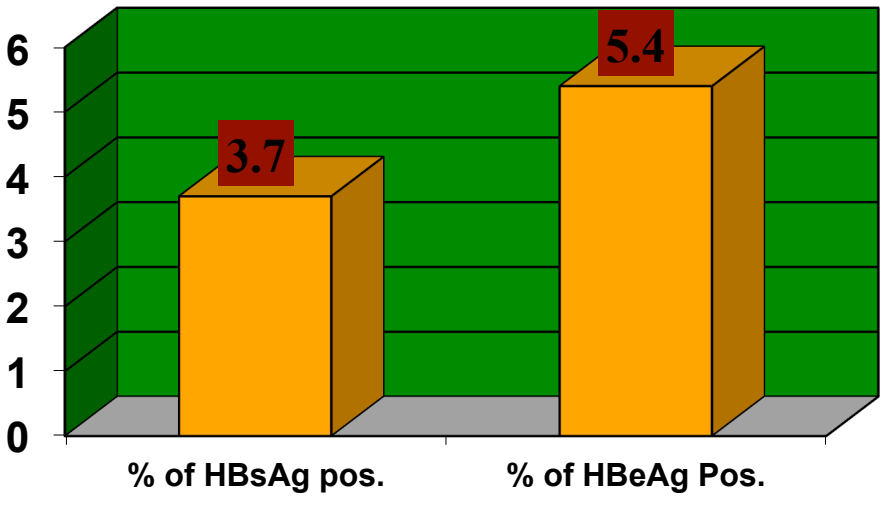
90 % of childhood infection will lead to chronic hepatitis if not vaccinated
5% of adult infection will lead to chronic hepatitis if not vaccinated

- **Modes of transmission:**
  - Sexual
  - Parenteral
  - Perinatal
- **Concentration of Hepatitis B Virus in Various Body Fluids:**
  - High in: Blood, Serum and wound exudates
  - Moderate in: Semen, Vaginal fluids and saliva
  - Low/not detectable in: Urine, feces, sweat, tears and breast milk.

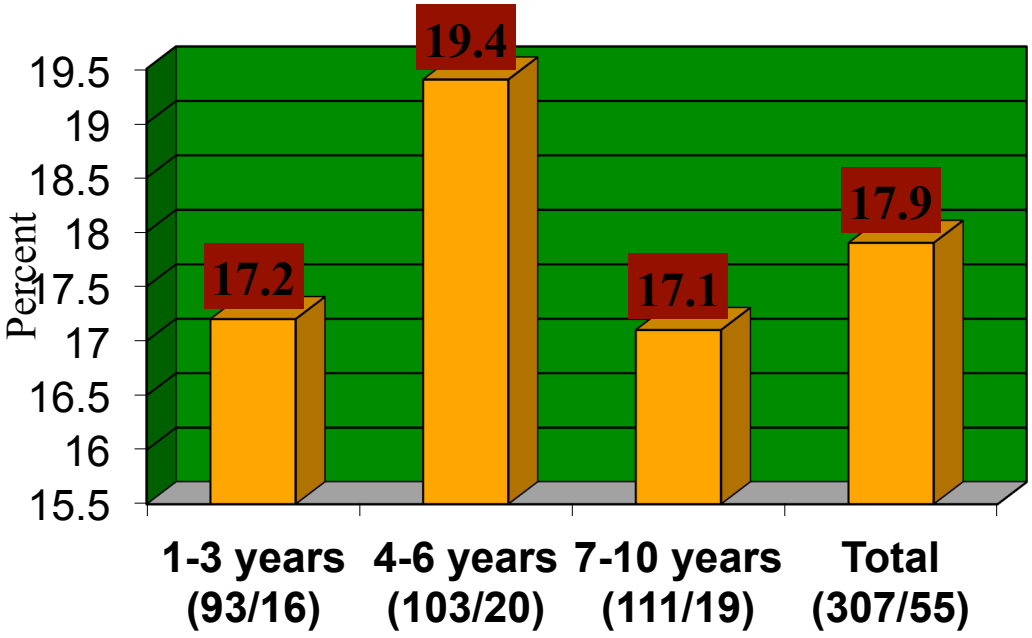
- **Possible transmission route of HBV in KSA:**
  - **Horizontal transmission (person to person) is the main transmission route. (Main mode of transmission in KSA)**
  - **Perinatal transmission (positive HBsAG mothers) especially if they are HBeAG positive.**
  - Heterosexual transmission.
  - Illegal injection drug use.
  - Contaminated equipment used for therapeutic injections and other health care related procedure
  - Folk medicine practice
  - Blood and blood products transfusion without prior screening
- **PREVENTION STRATEGIES OF MINISTRY OF HEALTH IN KSA:**
  - Mandatory screening of blood donors and expatriates.
  - Vaccination of risk groups.
  - Health education especially among medical personnel.
- **HBV INFECTION before and after vaccination program:**



OVERALL PREVALENCE OF HBsAg AMONG SAUDIS IN THE 80'S ACCORDING TO REGIONS: **HIGH PRAVALENCE OF HEPATITIS B AMONG SAUDI (AVERAGE 10 %) BEFORE VACCINATION**



PREVALENCE OF HBeAg AMONG HBsAg POSITIVE SAUDIS PREGNANT WOMEN (n = 20920):
HBeAG is more easily transmitted in pregnant woman in china (40%) than in Saudi (5%) because there are 6 genotypes which is more than in Saudi.



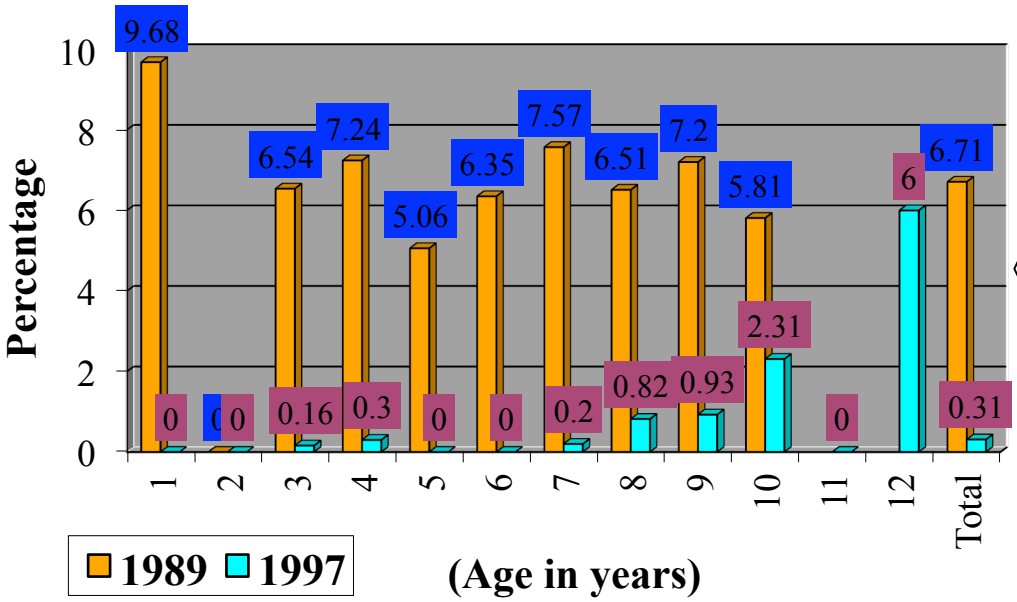
FREQUENCY OF HBeAg AMONG HBsAg POSITIVE SAUDI CHILDREN (n=307)

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.

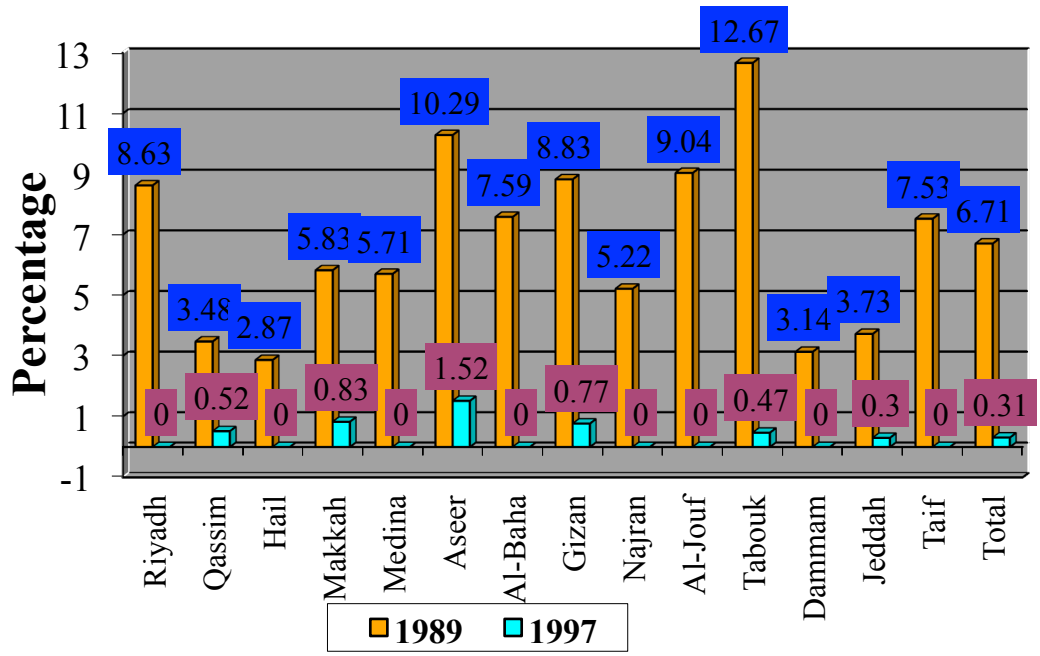
THE CURRENT EPI (Expanded Program on Immunization) IN THE KINGDOM OF SAUDI ARABIA:

1.	**At birth**	BCG + **HB1**	
2.	**At 6 weeks**	DPT1 + OPV1 **HB2**	
3.	At 3 months	DPT2 + OPV2	
4.	At 5 months	DPT3 + OPV3	
5.	**At 5months**	Measles+ **HB3**	
6.	At 12 months	MMR	
7.	At 18 months	(DPT + OPV)	Booster 1
8.	At 4-6 years	(DPT + OPV)	Booster 2



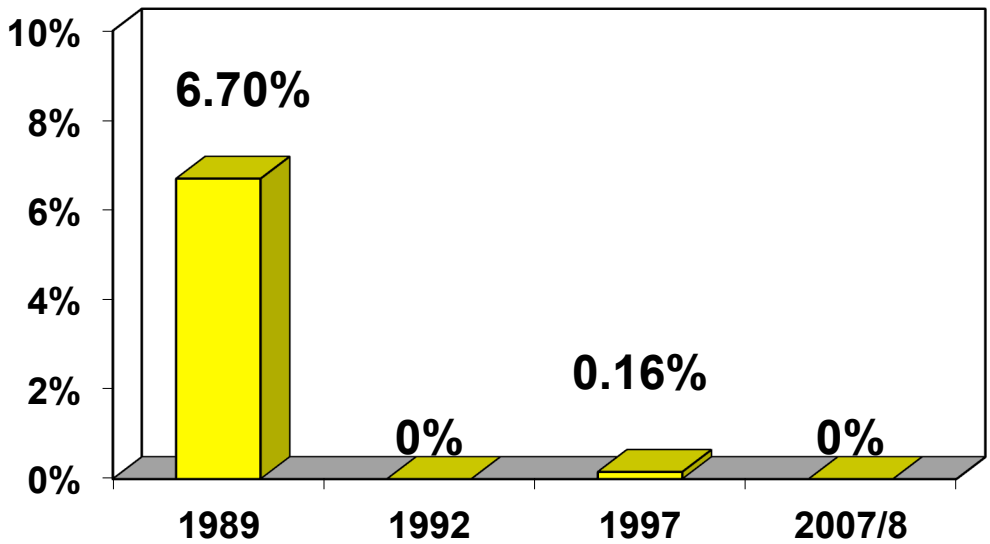
COMPARISON OF PREVALENCE OF HBsAg AMONG SAUDI CHILDREN IN 1989 (n=4575) AND 1997 (n=5355) – ACCORDING TO AGE

The data from Riyadh in the 80s lead to the ministry of health's decision to permit vaccine introduction 1989 which lead to a decrease in the prevalence in 1997

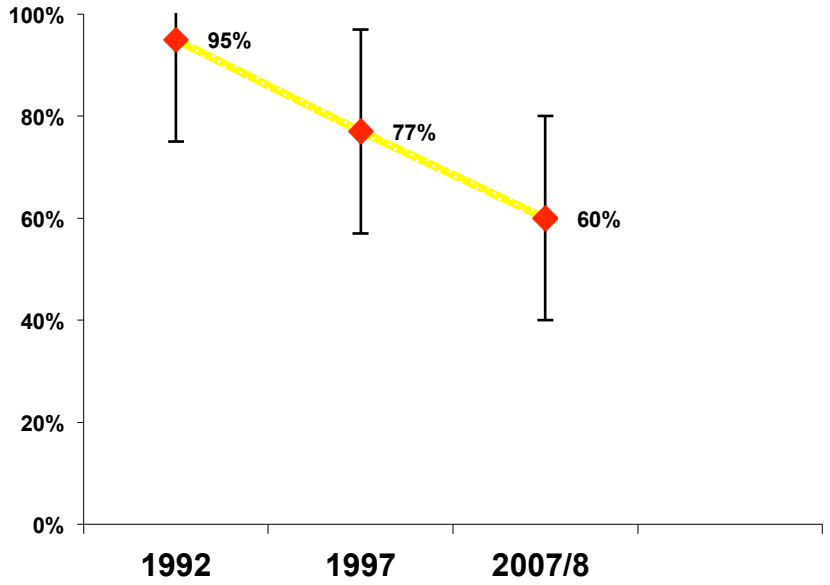


COMPARISON OF PREVALENCE OF HBsAg AMONG SAUDI CHILDREN IN 1989 (n=4575) AND 1997 (n=5355) – ACCORDING TO REGION

Tabuk have the highest prevalence of HBsAG

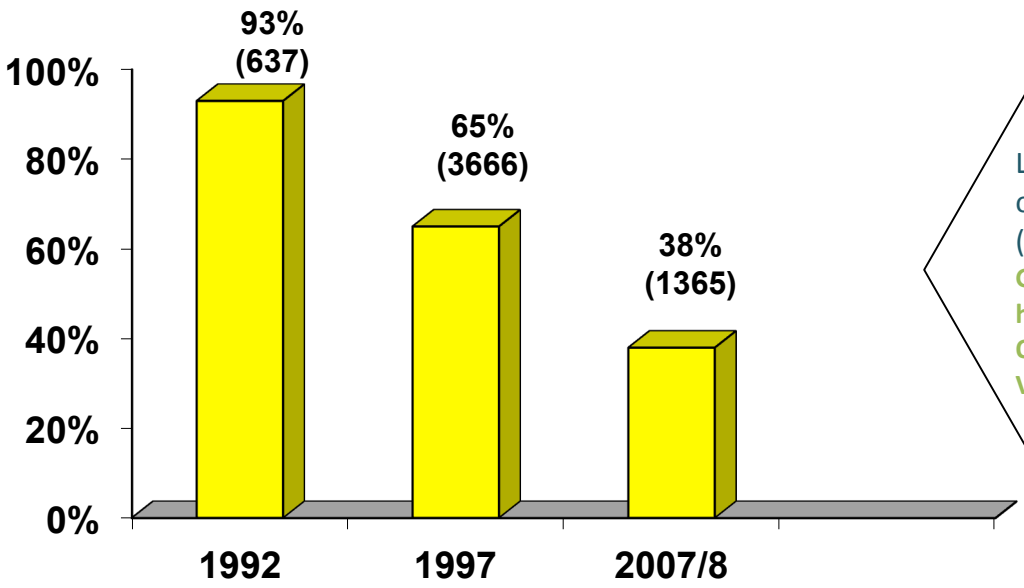


Prevalence of HBsAg Among Saudi Population Before & After Vaccination over 18 years



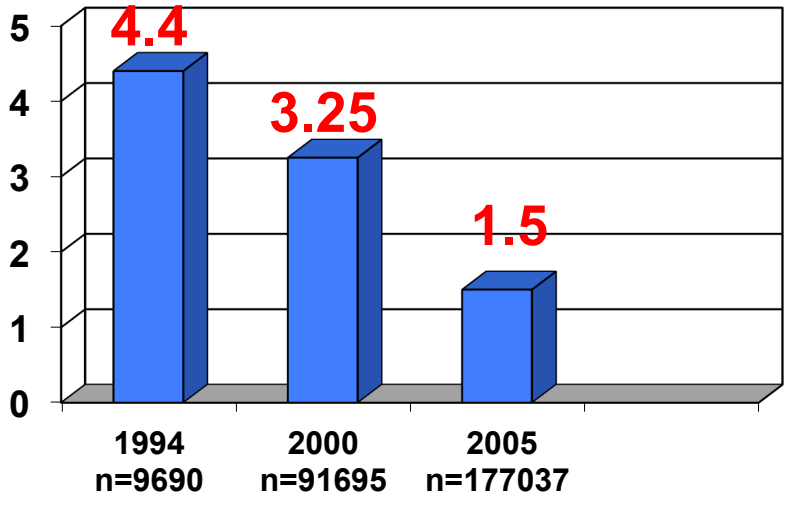
Long Term Seroconversion Rate Over 18 Years (Anti-HBS):

- What test do you do to check your immunity against Hepatitis B? Anti-HBS
- -1992 (3 years after the introduction of the vaccine) → 95% are positive for HBV
- -1997 → 77%
- -2007/8 → 60%
- -Being positive does not insure protection
- -You need to reach a "Protective Level "of **10IU**
- -Only 38% of people "our age = 20s"have that protection level
- -You don't need to get revaccinated your immunity's "memory" will act against any newfound infection. (If you've been previously vaccinated)



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

Gradual increase of IMMUNITY OF hepatitis B and decrease of prevalence OF hepatitis B WITHIN 18YEARS DUE TO VACCINATION



CHANGING PATTERNS OF HBsAg POSITIVITY AMONG BLOOD DONORS IN MOH, CENTRAL BLOOD BANK 1994-2005:

Gradual decrease of hepatitis A PREVALENC WITHIN 10 YEARS IN BLOOD DONOR DUE TO VACCINATION

Table 1 Positive results by sex from premarital screening of infectious diseases in the regions of Saudi Arabia, January–May, 2008

Region	No of tests	Positive results		HIV						HBV						HCV					
				Total		Men		Women		Total		Men		Women		Total		Men		Women	
		No.	%	No	%	No	%	No	%	No	%	No	%	No	%	No	%	No	%	No	%
Riyadh	11771	213	1.81	8	0.07	6	25.0	2	8.3	164	1.39	99	10.1	65	6.7	41	0.35	34	13.6	7	2.8
Makkah	1577	59	3.74	0	0.00	0	0.0	0	0.0	44	2.79	32	3.3	12	1.2	15	0.95	12	4.8	3	1.2
Jeddah	3434	69	2.01	4	0.12	2	8.3	2	8.3	42	1.22	29	3.0	13	1.3	23	0.67	15	6.0	8	3.2
Madinah	8200	147	1.79	0	0.00	0	0.0	0	0.0	131	1.60	91	9.3	40	4.1	16	0.20	11	4.4	5	2.0
Qasseem	2687	23	0.85	0	0.00	0	0.0	0	0.0	20	0.74	16	1.6	4	0.4	3	0.11	3	1.2	0	0.0
Taif	4217	96	2.28	1	0.02	1	4.2	0	0.0	84	1.99	60	6.1	24	2.5	11	0.26	10	4.0	1	0.4
Hail	2893	24	0.83	2	0.07	2	8.3	0	0.0	15	0.52	13	1.3	2	0.2	7	0.24	6	2.4	1	0.4
Baha	2131	45	2.11	2	0.09	2	8.3	0	0.0	27	1.27	21	2.1	6	0.6	16	0.75	13	5.2	3	1.2
Assir	6779	143	2.11	4	0.06	3	12.5	1	4.2	109	1.61	83	8.5	26	2.7	30	0.44	19	7.6	11	4.4
Sharqyah	10585	163	1.54	1	0.01	1	4.2	0	0.0	123	1.16	88	9.0	35	3.6	39	0.37	29	11.6	10	4.0
Ahsa	4079	48	1.18	0	0.00	0	0.0	0	0.0	31	0.76	26	2.7	5	0.5	17	0.42	11	4.4	6	2.4
Qunfudah	560	24	4.29	0	0.00	0	0.0	0	0.0	20	3.57	14	1.4	6	0.6	4	0.71	3	1.2	1	0.4
Hafr Batin	1617	22	1.36	0	0.00	0	0.0	0	0.0	19	1.18	16	1.6	3	0.3	3	0.19	3	1.2	0	0.0
Jazan	4090	8	0.20	0	0.00	0	0.0	0	0.0	8	0.20	8	0.8	0	0.0	0	0.00	0	0.0	0	0.0
Najran	2331	51	2.19	0	0.00	0	0.0	0	0.0	47	2.02	40	4.1	7	0.7	4	0.17	4	1.6	0	0.0
Bisha	1592	20	1.26	1	0.06	1	4.2	0	0.0	14	0.88	10	1.0	4	0.4	5	0.31	4	1.6	1	0.4
Tabuk	2506	58	2.31	0	0.00	0	0.0	0	0.0	47	1.88	43	4.4	4	0.4	11	0.44	8	3.2	3	1.2
Jouf	976	5	0.51	0	0.00	0	0.0	0	0.0	2	0.20	2	0.2	0	0.0	3	0.31	3	1.2	0	0.0
Arar	1739	28	1.61	1	0.06	1	4.2	0	0.0	26	1.50	21	2.1	5	0.5	1	0.06	1	0.4	0	0.0
Qurayat	898	5	0.56	0	0.00	0	0.0	0	0.0	4	0.45	3	0.3	1	0.1	1	0.11	1	0.4	0	0.0
Total	74662	1251	1.67	24	0.03	19	79.2	5	20.8	977	1.31	715	73.2	262	26.8	250	0.33	190	76.0	60	24.0

Age range 15–63, mean 30 (10.2).

J Epidemiol Community Health 2010;64:989–997. doi:10.1136/jech.2009.093302

In this study over 7500 male and female
Hepatitis B PREVALENCE IS 1.3%
Hepatitis C PREVALENCE IS 0.3%

Hepatitis C:

Transmission of HCV:

- Percutaneous
  - Injecting drug use
  - Clotting factors before viral inactivation
  - Transfusion, transplant from infected donor
  - Therapeutic (contaminated equipment, unsafe injection practices)
  - Occupational (needle stick)
- Permucosal
  - Perinatal
  - Sexual

Features of Hepatitis C Virus Infection:

- Incubation period
  - Average 6-7 weeks
  - Range 2-26 weeks
- Acute illness (jaundice)→Mild (<20%)
- Case fatality rate→ Low
- Chronic infection→ 75%-85%
- Chronic hepatitis→ 70% (most asx) **(HCV is more prone to turn chronic than HBV)**
- Cirrhosis→ 10%-20%

- Mortality from CLD **(cold liver disease)**→ 1%-5%

Household Transmission of HCV:

- Rare but not absent
- Could occur through percutaneous/mucosal exposures to blood
  - Theoretically through sharing of contaminated personal articles (razors, toothbrushes)
  - Contaminated equipment used for home therapies
    - Injections
    - Folk remedies

Sexual Transmission of HCV:

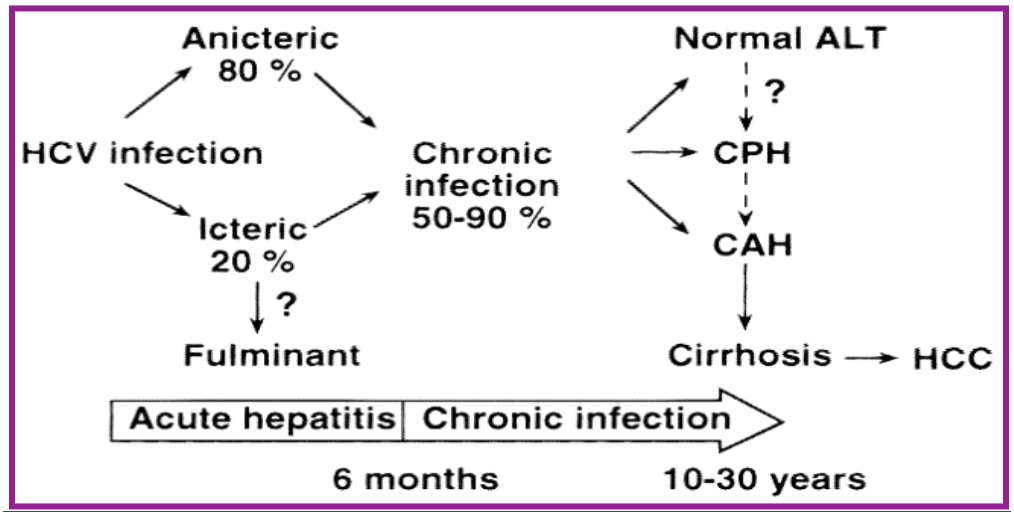
- Occurs, but efficiency is low
  - Rare between long-term steady partners
  - Factors that facilitate transmission between partners unknown (e.g., viral titer)
- Accounts for 15-20% of acute and chronic infections in the United States
  - Sex is a common behavior
  - Large chronic reservoir provides multiple opportunities for exposure to potentially infectious partners

Nosocomial Transmission of HCV:

- Recognized primarily in context of outbreaks
- Contaminated equipment
  - hemodialysis
  - endoscopy
- Unsafe injection practices
  - plasmapheresis, phlebotomy
  - multiple dose medication vials
  - therapeutic injections

Natural history: (The natural history of HCV takes a long time)

- **ANICTERIC (NO JAUNDICE), ICTERIRIC (JAUNDICE)**
- **It takes years for it to develop into a chronic disease**



Prevention of HCV Transmission:

- **No vaccine for HCV because it is able to mutate.**
- 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 HCW's to the proper use of standard precautions

Prevalence:

- **Overall, prevalence of HCV in KSA is rare**
- Prevalence rate of HCV infection in KSA among children and adolescent during the last 18 yrs.:
  - **Prevalence decresed from 1989 to 2008**
  - **Diagnostic tests to determine the pravlence changed in the years:**
    - **1989: Diagnostic test only by 1st-generation EIA kit.**
    - **1997: Diagnostic test by 3rd-generation EIA kit and confirmatory test by RIBA kit.**
    - **2000: Diagnostic test by PCR for anti- HCV Positive cases.**
- Prevalence of HCV Positivity Among Different Saudi population: (children, pregnant women, hemodialysis patients, drug addicts)
  - **Prevalence is highest in hemodialysis patients**

Hepatitis A:

Hepatitis A virus transmission:

- Close personal contact: (e.g. household contact, sex contact, child day care centers)
- Contaminated food, water (e.g. infected food handlers)
- Blood exposure (rare) (e.g. injection drug use, rare by transfusion)

Modes of HAV transmission:

- Feco- oral route (95%)
  - Person to person

- Contaminated food or water
- Salads and fruits washed in contaminated water
- Contaminated shell fish

- Infected plasma (<5%)
- Sexual route (<5%)

Preventing hepatitis A:

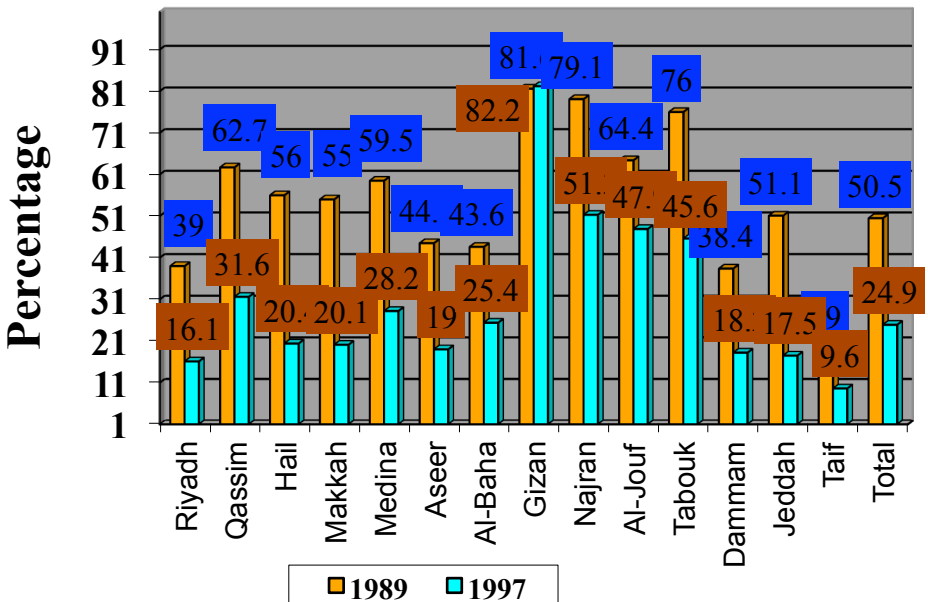
- **Hepatitis A vaccine(pre exposure)** **(vaccines: VAQTA, HAVRIX)**
- Hygiene (hand washing)
- Sanitation (clean water source)
- immune globulin(pre and post exposure)

Hepatitis A clinical features:

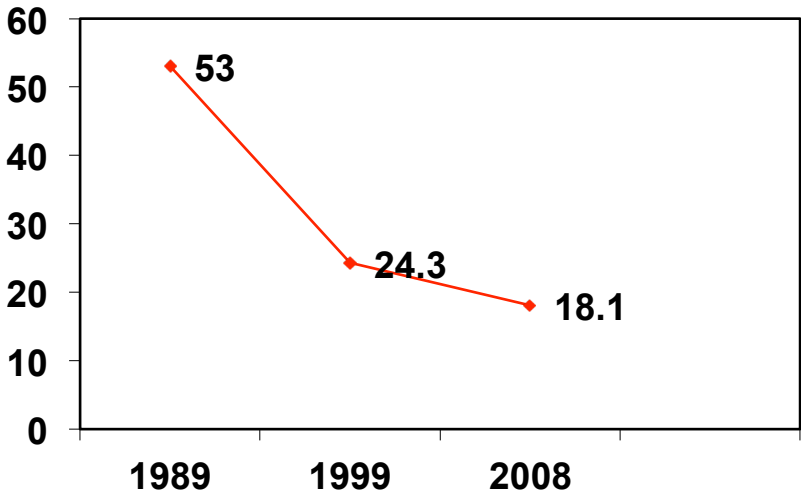
- Jaundice by age group:
  - < 6 yrs → <10%
  - 6-14 → 40%-50%
  - > 14 yrs →70%-80%
- Rare complications:
  - Fulminant hepatitis
  - Cholestatic hepatitis
  - Relapsing hepatitis
- Incubation period:
  - Average 30 days
  - Range 15-50 days

Prevalence:

- **higher in the southern region**
- **higher in rural than urban**
- **higher in male than female**
- **higher in age group 20-30**



COMPARISON OF PREVALENCE OF ANTI-HAV AMONG SAUDI CHILDREN IN 1989 (n=4375) AND 1997 (n=5255) – ACCORDING TO REGION:
Gradual decrease of hepatitis A PREVALENC WITHIN 18 YEARS ECXEPT IN Gizan BEACUASE IT IS NEAR Yemen



Changing pattern of Hepatitis A prevalence within the Saudi population over 18 yrs:

Gradual decrease of hepatitis A
PREVALENC WITHIN 18 YEARS
1989 53%
1999 24%
2008 18%

Case Report:

- Ahmed a 50 years old teacher living in jazan. Abdominal discomfort, nausea, loss of appetite, coloration of urine.
- **Exam:** Marked jaundice.
- **Lab results: date: (30/9/13)**
  - ALT:1745 U/L(40) (very high)
  - AST 990 U/L (17-59)very high)
  - BIL.9.5MG/DL (0.0-1.4)very high)
  - PLT:267000(150000-400000)normal
- **Lab results: date: (28/10/13)**
  - ALT 185U/L(21-72)
  - AST 41 U/L (17-59)
  - ALKALINE PHOSPHATASE 247.0 U/L.
  - YGT 97,0U/L
  - BIL.1.4MG/DL (0.0-1.4)
  - ALB.3.6 g/l(3.5-5.0)
  - PT 14,8.6 (10-14)

(There is improving because it Self-limited disease if there is no complication)

- **Lab results: date: (22/2/12)**
  - ALT 176 U/L(21-72)
  - AST 61 U/L (17-59)
  - ALKALINE PHOSPHATASE 47 U/L.
  - YGT 64U/L(15.0-73)
  - BIL.2.4MG/DL (0.0-1.4)
  - ALB.3.7 g/l(3.5-5.0)

(There is improving because it Self-limited disease if there is no complication)

- **Differential diagnosis:**
  - Infectious Mononucleosis
  - **Drug Induced Hepatitis (Ask about herbs as they are widely used in our country)**
  - Chronic Hepatitis. **(You can check for it via a liver biopsy)**
  - **Alcohol Hepatitis (you should ask for alcohol consumption)**
  - Cholecystitis, Cholelithiasis
  - Auto-immune hepatitis **(Has specific markers)**
- **Final diagnosis:** Acute autoimmune hepatitis
- **Management**