Viral Hepatitis

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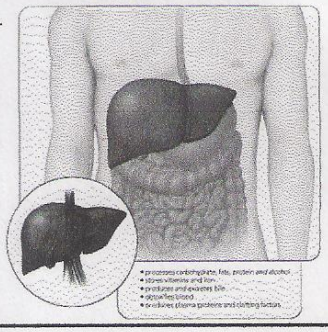
Human Liver Function . . .

Functions of the Liver



Viral Hepatitis - Types

"Primery" → A B C D E

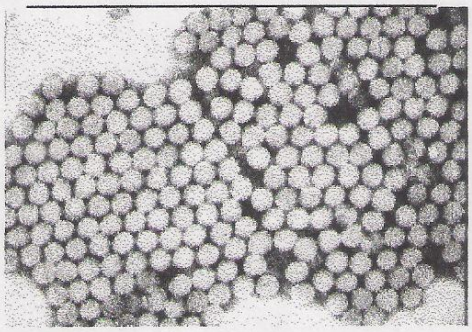
Viral hepatitis

"Systemic" → EBV, CMV, HSV, Yellow Fever

Type of Hepatitis

virus	A	B	C	D	E
Source of	feces	blood/ blood-derived body fluids	blood/ blood-derived body fluids	blood/ blood-derived body fluids	feces
Route of transmission	fecal-oral	percutaneous permucosal	percutaneous permucosal	percutaneous permucosal	fecal-oral
Chronic infection	no	yes	yes	yes	no
Prevention	pre/post-exposure immunization	pre/post-exposure immunization	blood donor screening; risk behavior modification	risk behavior modification	ensure safe drinking water

Hepatitis A Virus



Hepatitis A Virus

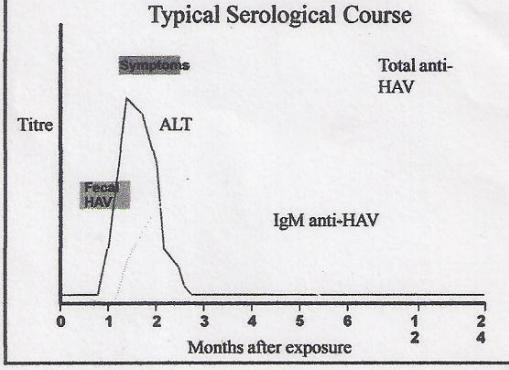
- Non enveloped icosahedral nucleocapsid
- Genome SS RNA virus
- Related to enteroviruses, formerly known as enterovirus 72, a picornavirus
- One stable serotype only
- Difficult to grow in cell culture: primary marmoset cell culture and also in vivo in chimpanzees and marmosets

Hepatitis A - Clinical Features

- Incubation period: Average 30 days
  Range 3-4 weeks
- mostly asymptomatic
- Symptom : fever, anorexia, nausea, vomiting, jaundice
- Jaundice by age group: <6 yrs : <10%
  6-14 yrs : 40%-50%
  >14 yrs : 70%-80%
- *Complications:* *Fulminant hepatitis*
  Cholestatic hepatitis
  Relapsing hepatitis
- Chronic sequelae: None

Hepatitis A Infection

Typical Serological Course

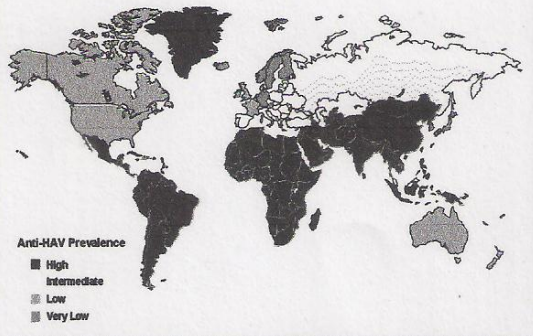


Jaundice

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, raw shellfish)
- Blood exposure (rare)
  (e.g., injecting drug use, transfusion)

Geographic Distribution of HAV Infection



Laboratory Diagnosis

- HAV-IgM : acute infection
- HAV-IgG : Past infection
- Cell culture – difficult and take up to 4 weeks, not routinely performed
- Direct Detection – EM, RT-PCR of faeces. Can detect illness earlier than serology but rarely performed.

Hepatitis A Prevention - Immune Globulin

- Pre-exposure
  - travelers to intermediate and high HAV - endemic regions
- Post-exposure (within 14 days)

  Routine
  - household and other intimate contacts

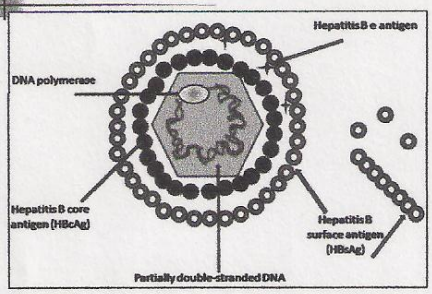
  Selected situations
  - institutions (e.g., day care centers)
  - common source exposure (e.g., food prepared by infected food handler)

Hepatitis B Virus

- Hepadnavirus with Double stranded circular DNA virus
- Particle size 42 nm, containing :

  core antigen (HBcAg) and e antigen (HBeAg), surface antigen particles HBsAg
- Hepatitis B virus (HBV) : 8 genotypes (A-H).
  - Genotypes A and C predominate in the US. However, genotypes B and D are also present in the US.
  - Genotype F predominates in South America and in Alaska, while A, D and E predominate in Africa.
  - In Asia, genotypes B and C predominate.
- It has not yet been possible to propagate the virus in cell culture.

Hepatitis B virus



Hepatitis B - Clinical Features

- Incubation period: Average 60-90 days
  Range 45-180 days

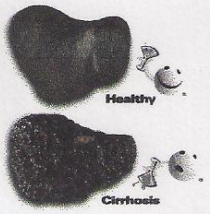
Symptom : fever, anorexia, nausea, vomiting, jaundice

- 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%

Spectrum of Chronic Hepatitis B Diseases

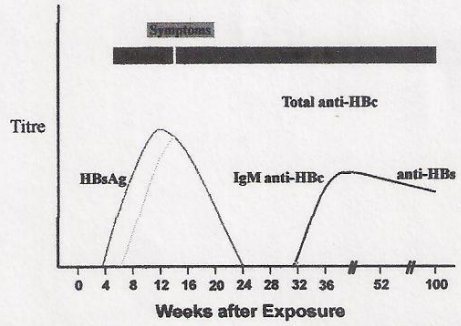
1. Chronic Persistent Hepatitis - asymptomatic
2. Chronic Active Hepatitis - symptomatic exacerbations of hepatitis
3. Cirrhosis Hepatis
4. Hepatocellular Carcinoma (HCC)

Cirrhosis Hepatis



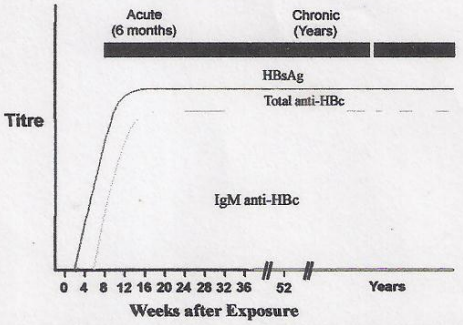
Acute Hepatitis B Virus Infection with Recovery

Typical Serologic Course

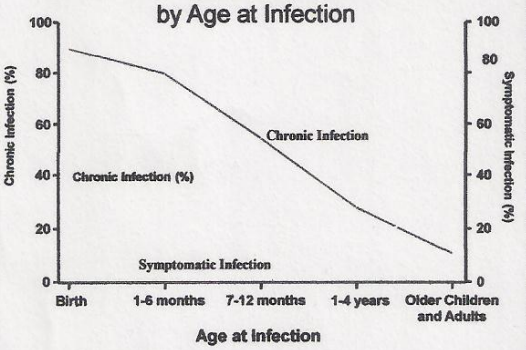


Progression to Chronic Hepatitis B Virus Infection

Typical Serologic Course



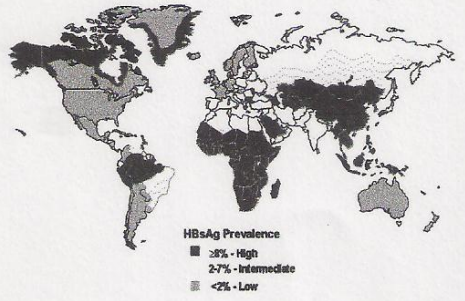
Outcome of Hepatitis B Virus Infection by Age at Infection



Global Patterns of Chronic HBV Infection

- High (>8%): 45% of global population
  - lifetime risk of infection >60%
  - early childhood infections common
- Intermediate (2%-7%): 43% of global population
  - lifetime risk of infection 20%-60%
  - infections occur in all age groups
- Low (<2%): 12% of global population
  - lifetime risk of infection <20%
  - most infections occur in adult risk groups

Geographic Distribution of Chronic HBV Infection



Concentration of Hepatitis B Virus in Various Body Fluids

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

Hepatitis B Virus
Modes of Transmission

- Sexual - sex workers and homosexuals are particular at risk.
- Parenteral - IVDA, Health Workers are at increased risk.
- Perinatal - Mothers who are HBeAg positive are much more likely to transmit to their offspring than those who are not.

Diagnosis

SEROLOGICAL TEST

- HBsAg - used as a general marker of infection.
- HBsAb - used to document recovery and/or immunity to HBV infection.
- anti-HBc IgM - marker of acute infection.
- anti-HBcIgG - past or chronic infection.
- HBeAg - indicates active replication of virus and infectiveness.
- Anti-Hbe - virus no longer replicating.

MOLECULAR TEST

- HBV-DNA - indicates active replication of virus, more accurate than HBeAg especially in cases of escape mutants.

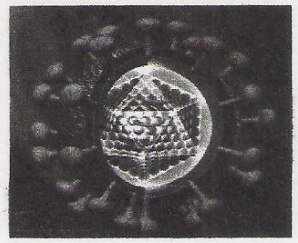
Treatment

- Interferon - for HBeAg +ve carriers with chronic active hepatitis. Response rate is 30 to 40%.
- Lamivudine - Well tolerated, most patients will respond favorably. Another problem is the rapid emergence of drug resistance.
- Adefovir – less likely to develop resistance than Lamivudine and may be used to treat Lamivudine resistance HBV. However more expensive and toxic
- Entecavir – most powerful antiviral known, similar to Adefovir

Prevention

- Vaccination - health care workers. Neonates as universal vaccination in many countries.
- Hepatitis B Immunoglobulin (HBIG) - It is particular efficacious within 48 hours of the incident. It may also be given to neonates who are at increased risk of contracting hepatitis B i.e. whose mothers are HBsAg and HBeAg positive.
- Other measures - screening of blood donors, blood and body fluid precautions.

Hepatitis C virus



Hepatitis C Virus

- An enveloped flavivirus
- positive stranded ss RNA genome
- morphological structure remains unknown
- HCV has been classified into a total of six genotypes (type 1 to 6) on the basis of phylogenetic analysis
- Genotype 1 and 4 has **a poorer prognosis** and response to interferon therapy

Hepatitis C - Clinical Features

Incubation period:	Average 6-7 wks Range 2-26 wks
Clinical illness (jaundice):	30-40% (20-30%)
Chronic hepatitis:	70%
Persistent infection:	85-100%
Immunity:	No protective antibody response identified

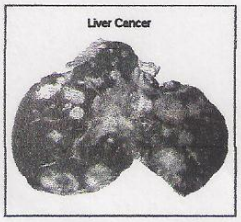
Chronic Hepatitis C Infection

- The spectrum of chronic hepatitis C infection is essentially the same as chronic hepatitis B infection.
- All the manifestations of chronic hepatitis B infection may be seen, i.e. chronic persistent hepatitis, chronic active hepatitis, cirrhosis, and hepatocellular carcinoma.

Hepatitis C co-infection

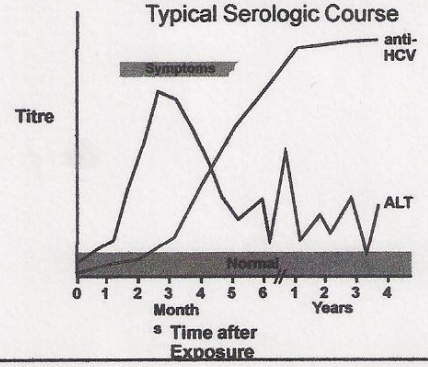
- w/ hepatitis A :
  increase risk of fulminant hepatitis
- w/ hepatitis B :
  increase risk of cirrosis and liver cancer
- w/ HIV :
  clinical complication and troubles in therapy

Hepatocellular Carcinoma (HCC)/ Liver Cancer



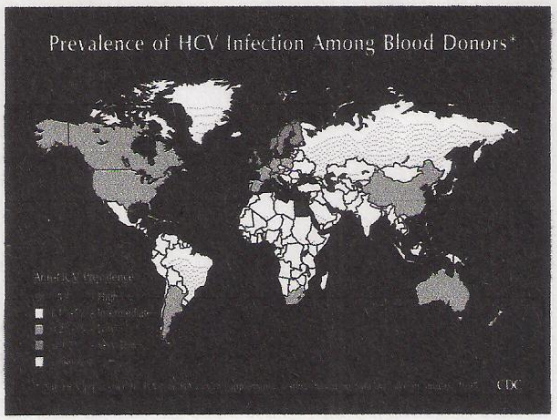
Hepatitis C Virus Infection

Typical Serologic Course



Risk Factors Associated with Transmission of HCV

- Transfusion or transplant from infected donor
- Injecting drug use
- Hemodialysis (yrs on treatment)
- Accidental injuries with needles/sharps
- Sexual/household exposure to anti-HCV-positive contact
- Multiple sex partners
- Birth to HCV-infected mother



Laboratory Diagnosis

- HCV antibody - generally used to diagnose hepatitis C infection.
- HCV-RNA - PCR and branched DNA. May be used to diagnose HCV infection in the acute phase. However, its main use is in monitoring the response to antiviral therapy.
- HCV-antigen - an EIA for HCV antigen is available. It is used in the same capacity as HCV-RNA tests but is much easier to carry out.

Treatment

- Interferon - may be considered for patients with chronic active hepatitis. The response rate is around 50% but 50% of responders will relapse upon withdrawal of treatment.
- Ribavirin - Recent studies suggest that a combination of interferon and ribavirin is more effective than interferon alone.

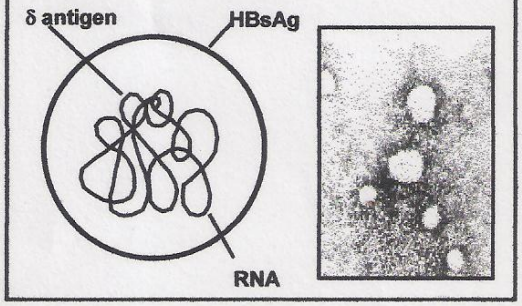
Prevention of Hepatitis C

- Screening of blood, organ, tissue donors
- High-risk behavior modification
- Blood and body fluid precautions

Hepatitis C risk factor

- Donor
- Needle stick injury
- IVDA
- Hemodialisis
- Sexual contact

Hepatitis D (Delta) Virus



Hepatitis D Virus

- The delta agent is a defective virus
- The agent consists of a particle 35 nm in diameter consisting of the delta antigen surrounded by an outer coat of HBsAg.
- The genome of the virus is very small and consists of a single-stranded RNA

Hepatitis D - Clinical Features

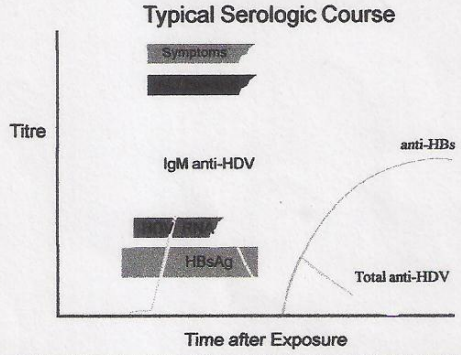
- Coinfection with HBV
  - severe acute disease.
  - low risk of chronic infection.
- Superinfection (HBV carrier → HDV)
  - usually develop chronic HDV infection.
  - high risk of severe chronic liver disease.
  - may present as an acute hepatitis.

Hepatitis D Virus Modes of Transmission

- Percutanous exposures
  - injecting drug use
- Permucosal exposures
  - sex contact

HBV - HDV Coinfection

Typical Serologic Course



Geographic Distribution of HDV Infection

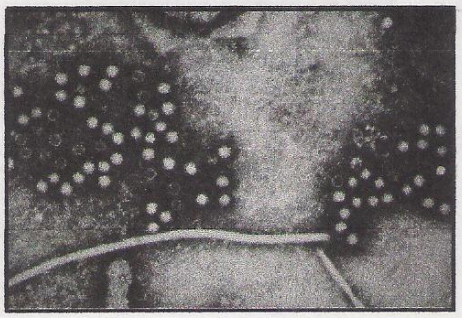
Hepatitis D - Prevention

- HBV-HDV Coinfection

  Pre or postexposure prophylaxis to prevent HBV infection (HBV vaccine).
- HBV-HDV Superinfection

  Education to reduce risk behaviors among persons with chronic HBV infection.
- Screen blood donor, never share needle

Hepatitis E Virus



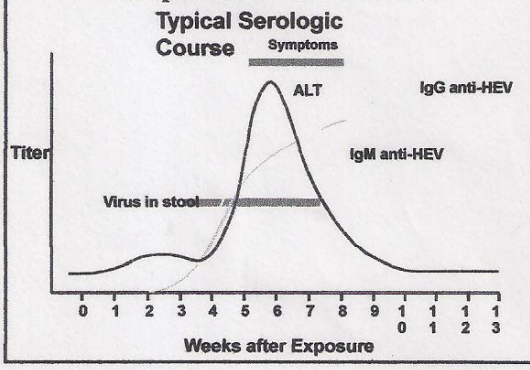
Hepatitis E Virus

- Non enveloped virus, 32-34nm diameter
- +ve stranded RNA genome
- very labile and sensitive
- Spread fecal orally
- Commonly by water : India, Africa, Central America
- Can only be cultured recently

Hepatitis E - Clinical Features

▪ Incubation period:	Average 40 days Range 15-60 days
▪ Case-fatality rate:	Overall, 1%-3% Pregnant women, 15%-25%
▪ Illness severity:	like hepatitis A
▪ Chronic sequelae:	None identified

Hepatitis E Virus Infection



Geographic Distribution of Hepatitis E

Outbreaks or Confirmed Infection in >25% of Sporadic Non-ABC Hepatitis

Prevention and Control Measures for Travelers to HEV-Endemic Regions

- Avoid drinking water (and beverages with ice) of unknown purity,
- uncooked shellfish,
- and uncooked fruit/vegetables not peeled or prepared by traveler.
- Unknown efficacy of IG prepared from donors in endemic areas.
- Vaccine ?