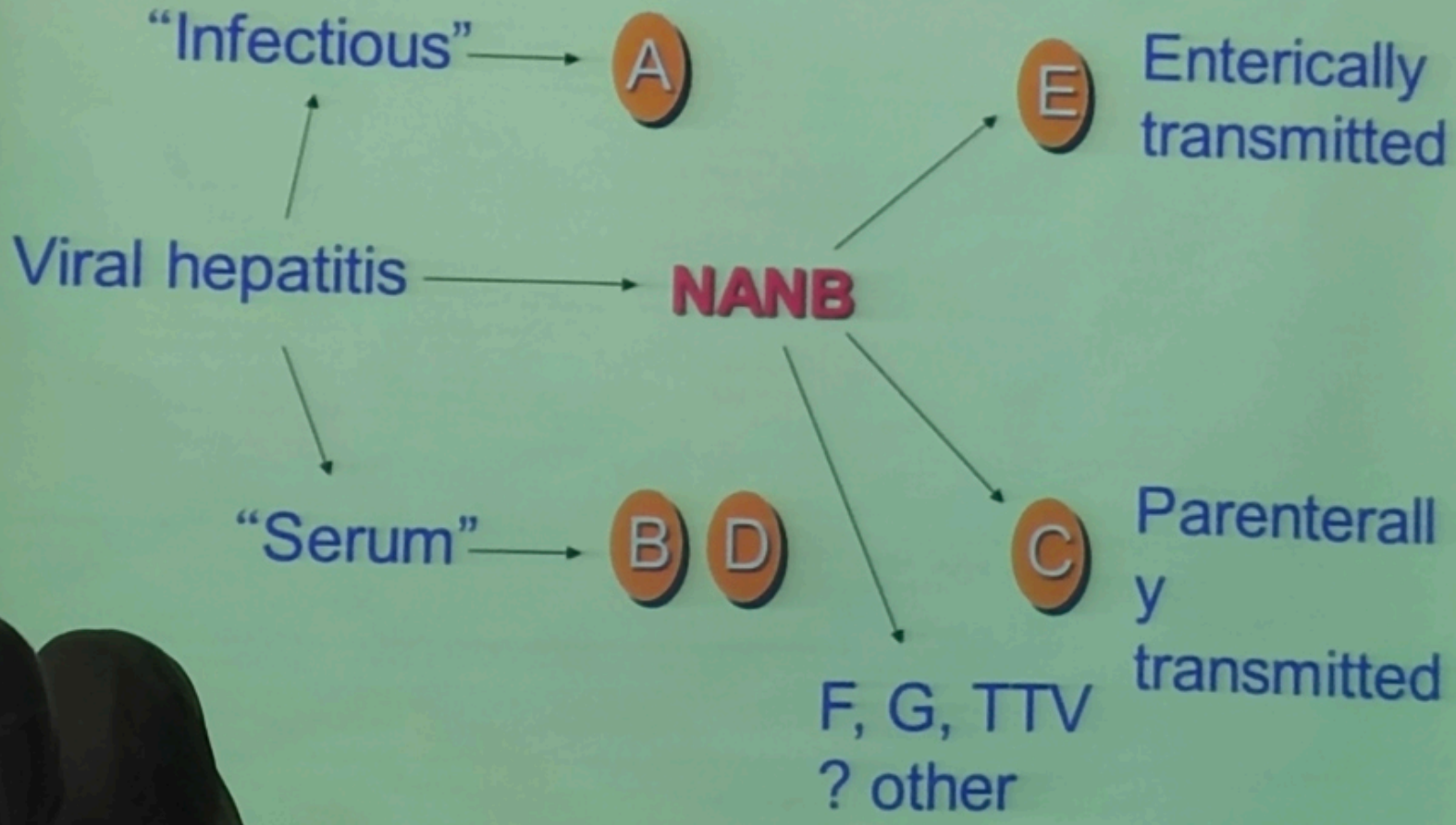
Acute Hepatitis A-E Viruses

Dr Shabir Ahmed
Professor of Paediatrcs

Viral Hepatitis - Historical Perspectives

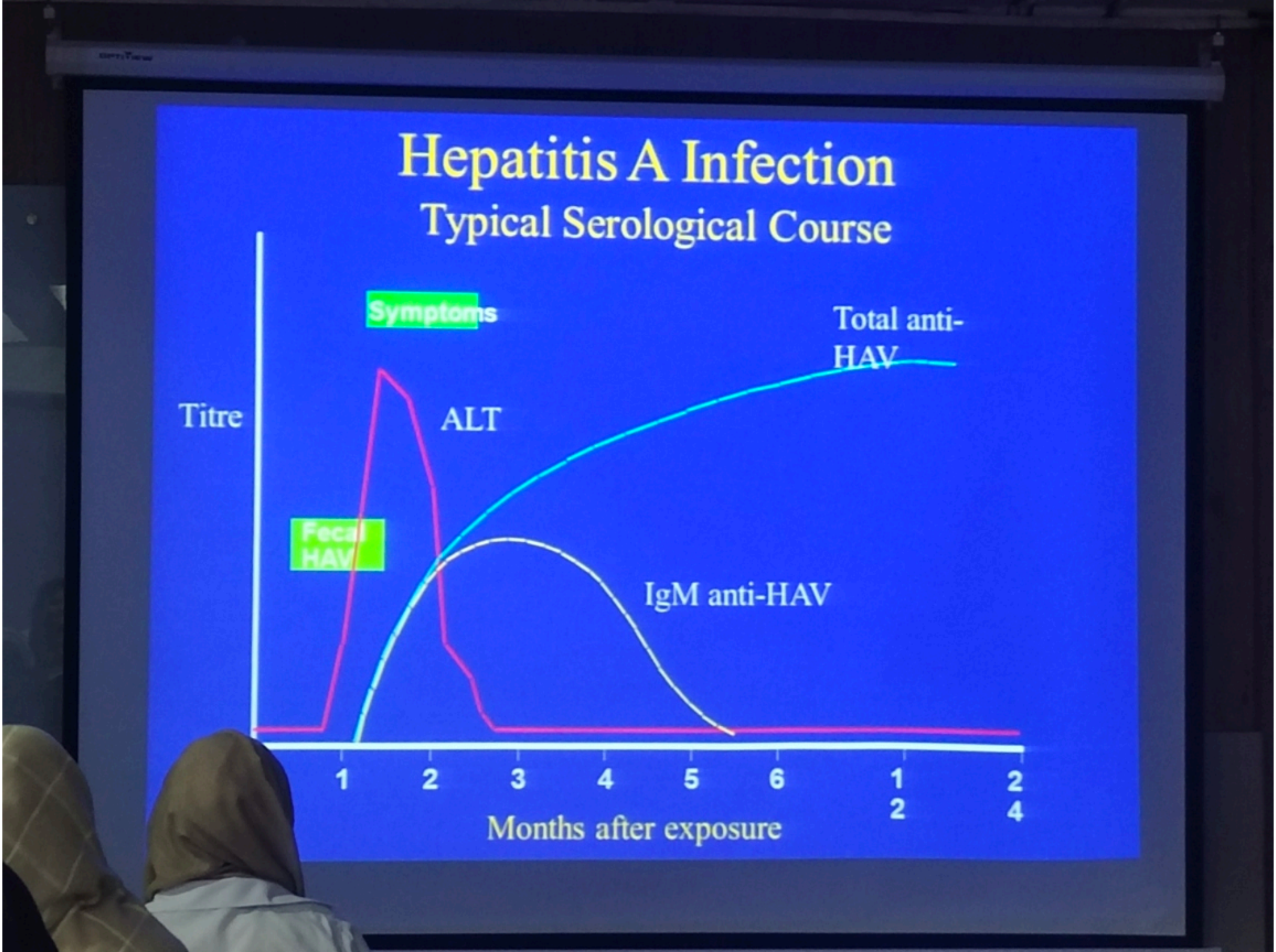


Type of Hepatitis

	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 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	pre/post-exposure immunization; risk behavior modification	ensure safe drinking water

Hepatitis A - Clinical Features

- Incubation period: Average 30 days
  Range 15-50 days
- 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
Symptoms
Total anti-HAV
Titre
ALT
Fecal HAV
IgM anti-HAV
1
2
3
4
5
6
12
24
Months after exposure

Hepatitis A Virus Transmission

- Close personal contact
- Contaminated food, water

  (e.g., infected food handlers, raw shellfish)
- Blood exposure (rare)

  (e.g., injecting drug use, transfusion)

Laboratory Diagnosis

- Acute infection is diagnosed by the detection of HAV-IgM in serum
- Past Infection i.e. immunity is determined by the detection of HAV-IgG

Hepatitis A Vaccination Strategies
Epidemiologic Considerations

- Persons at increased risk of infection
  - Travelers

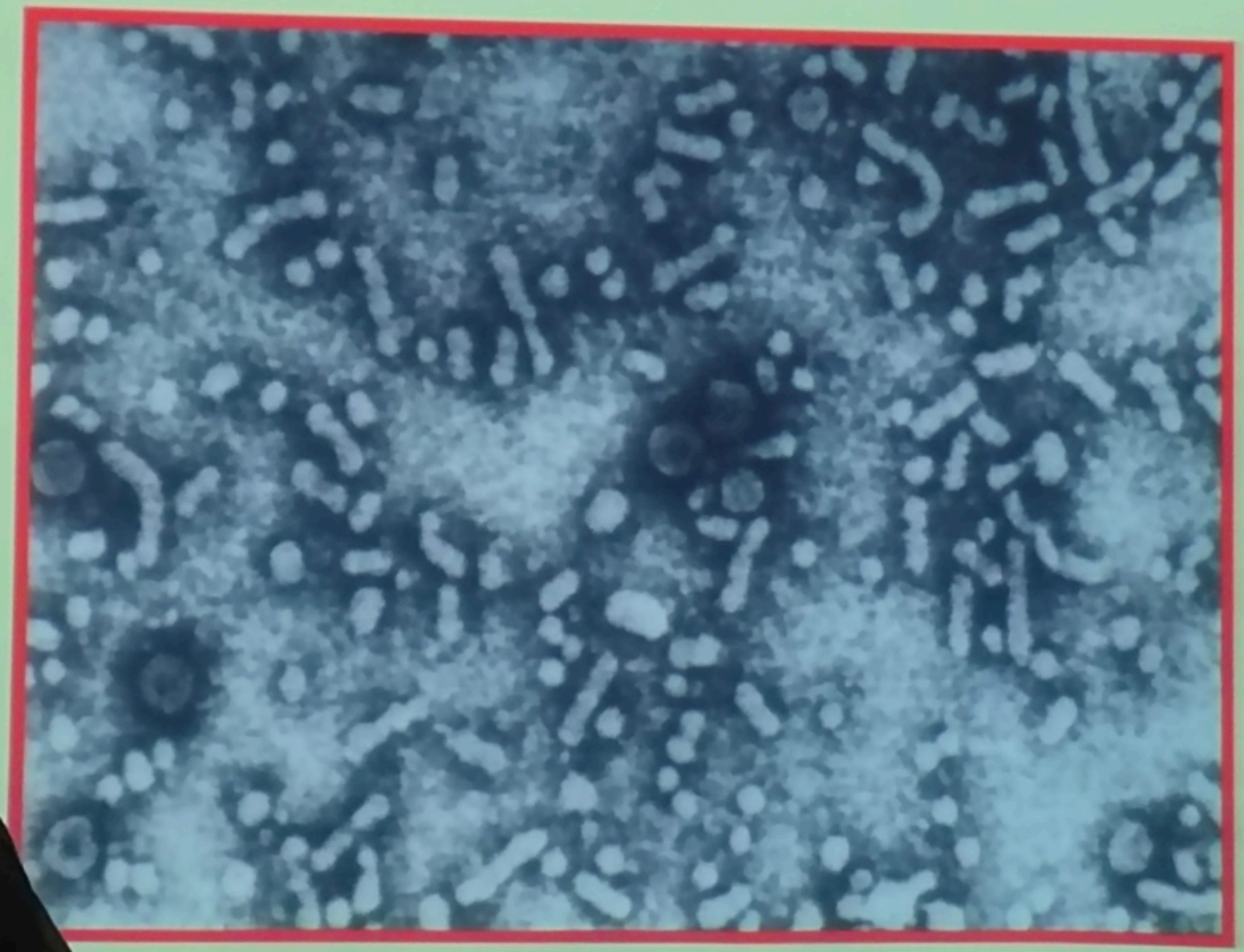
Hepatitis A Prevention - Immune Globulin

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

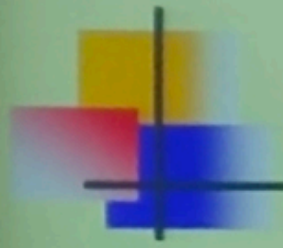
  Routine
  - household and other intimate contacts

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

Hepatitis B Virus



Hepatitis B - Clinical Features



▪ Incubation period:	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%

Spectrum of Chronic Hepatitis B Diseases

1.Chronic Persistent Hepatitis - asymptomatic

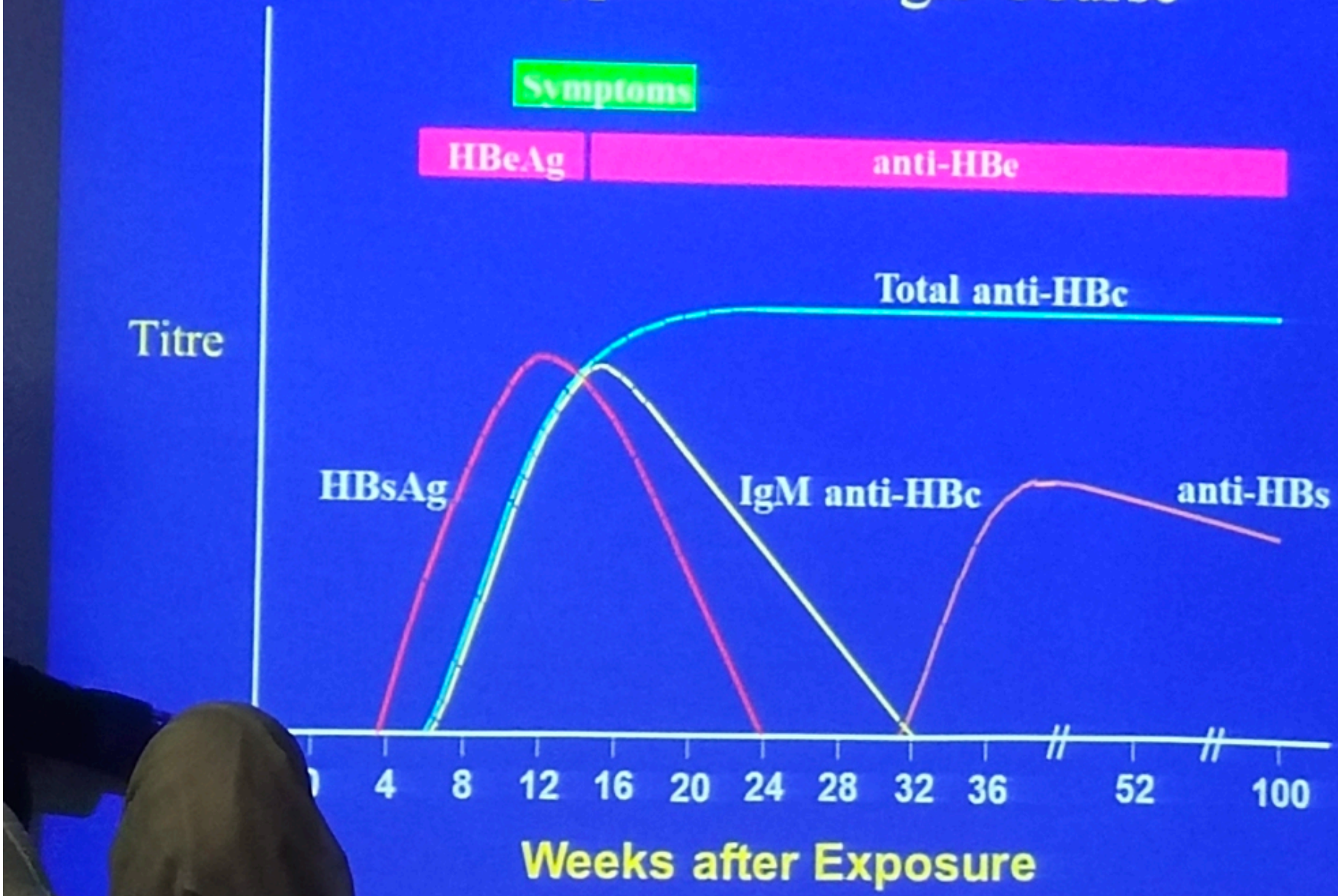
2.Chronic Active Hepatitis - symptomatic exacerbations of hepatitis

3. Cirrhosis of Liver

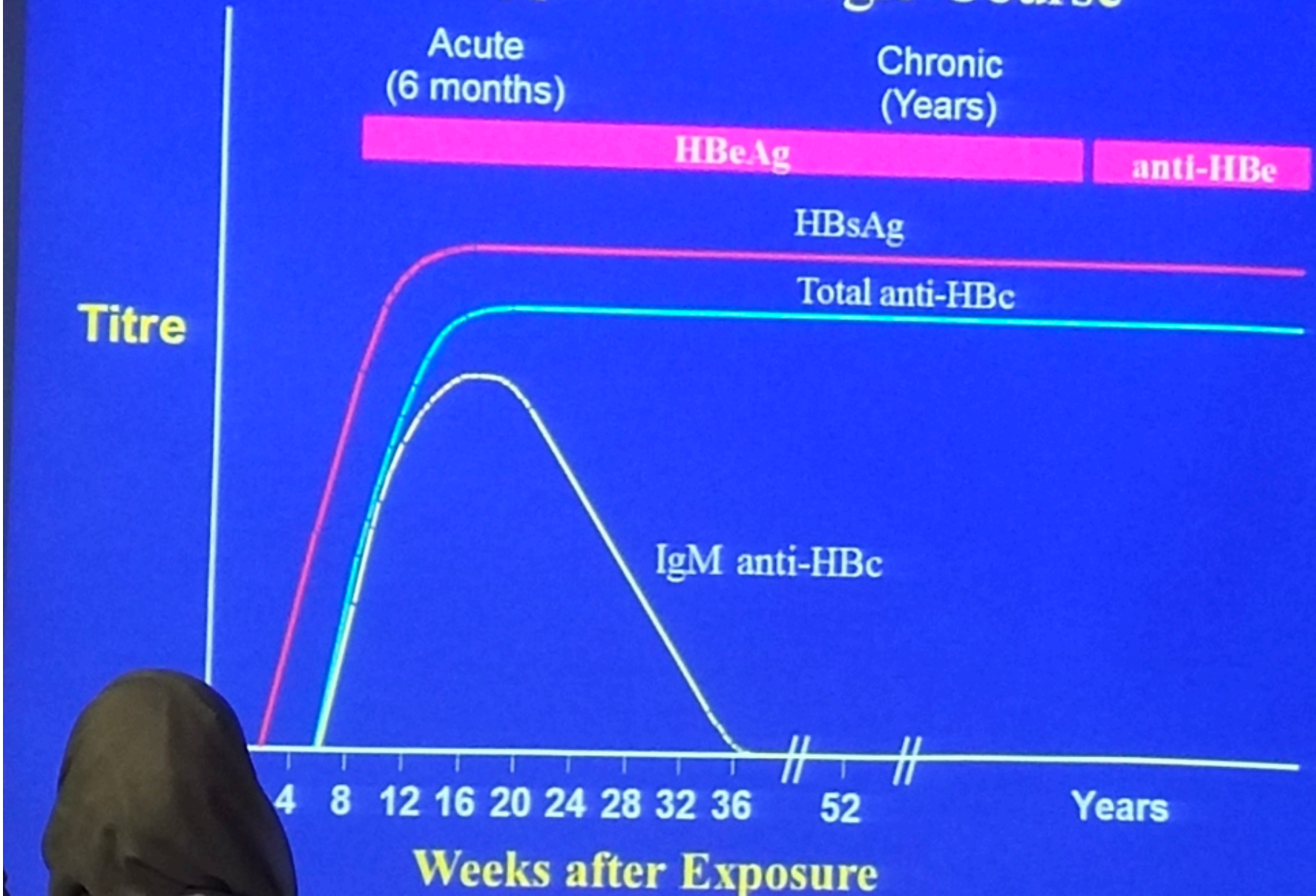
4. Hepatocellular Carcinoma

Acute Hepatitis B Virus Infection with Recovery

Typical Serologic Course



Progression to Chronic Hepatitis B Virus Infection
Typical Serologic Course

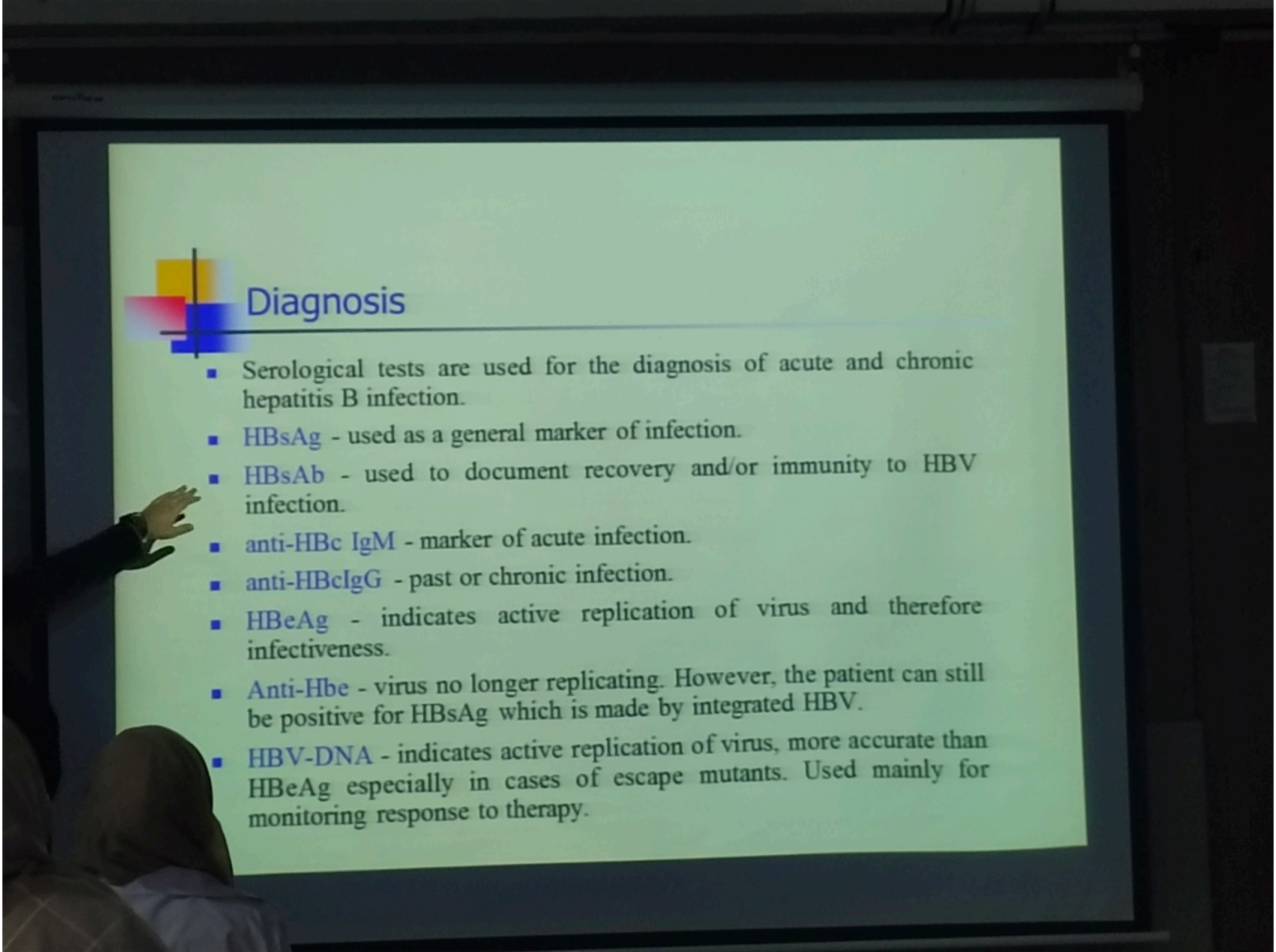


Concentration of Hepatitis B Virus in Various Body Fluids

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

Hepatitis B Virus
Modes of Transmission

- 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. Perinatal transmission is the main means of transmission in high prevalence populations.
- Sexual - Homosexuals are particular at risk.


Diagnosis
Serological tests are used for the diagnosis of acute and chronic hepatitis B infection.
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 therefore infectiveness.
Anti-Hbe - virus no longer replicating. However, the patient can still be positive for HBsAg which is made by integrated HBV.
HBV-DNA - indicates active replication of virus, more accurate than HBeAg especially in cases of escape mutants. Used mainly for monitoring response to therapy.

Treatment

- Interferon - for HBeAg +ve carriers with chronic active hepatitis. Response rate is 30 to 40%.
  - alpha-interferon 2b (original)
  - alpha-interferon 2a (newer, claims to be more efficacious and efficient)
- Lamivudine - a nucleoside analogue reverse transcriptase inhibitor. Well tolerated, most patients will respond favorably. However, tendency to relapse on cessation of treatment. 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
- Successful response to treatment will result in the disappearance of HBsAg, HBV-DNA, and seroconversion to HBeAg.

Prevention

- Vaccination - highly effective recombinant vaccines are now available. Vaccine can be given to those who are at increased risk of HBV infection such as health care workers. It is also given routinely to neonates as universal vaccination in many countries.
- Hepatitis B Immunoglobulin - HBIG may be used to protect persons who are exposed to hepatitis B. 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.

Type of 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 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	pre/post-exposure immunization; risk behavior modification	ensure safe drinking water

Hepatitis C Virus

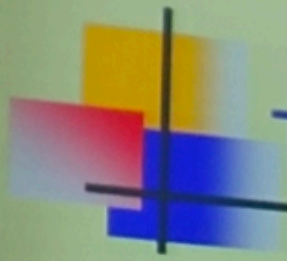
- Genome resembled that of a flavivirus
  positive stranded RNA genome of around 10,000 bases
- HCV has been classified into a total of six genotypes (type 1 to 6) on the basis of phylogenetic analysis
- Genotype 1 and 4 has a poorer prognosis and response to interferon therapy,

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

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
- Birth to HCV-infected mother



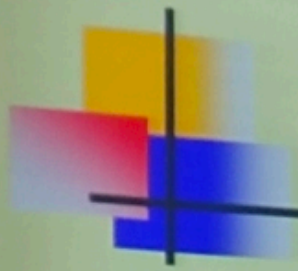
Treatment

- 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 - there is less experience with ribavirin than interferon. However, recent studies suggest that a combination of interferon and ribavirin is more effective than interferon alone.

Prognostic Tests

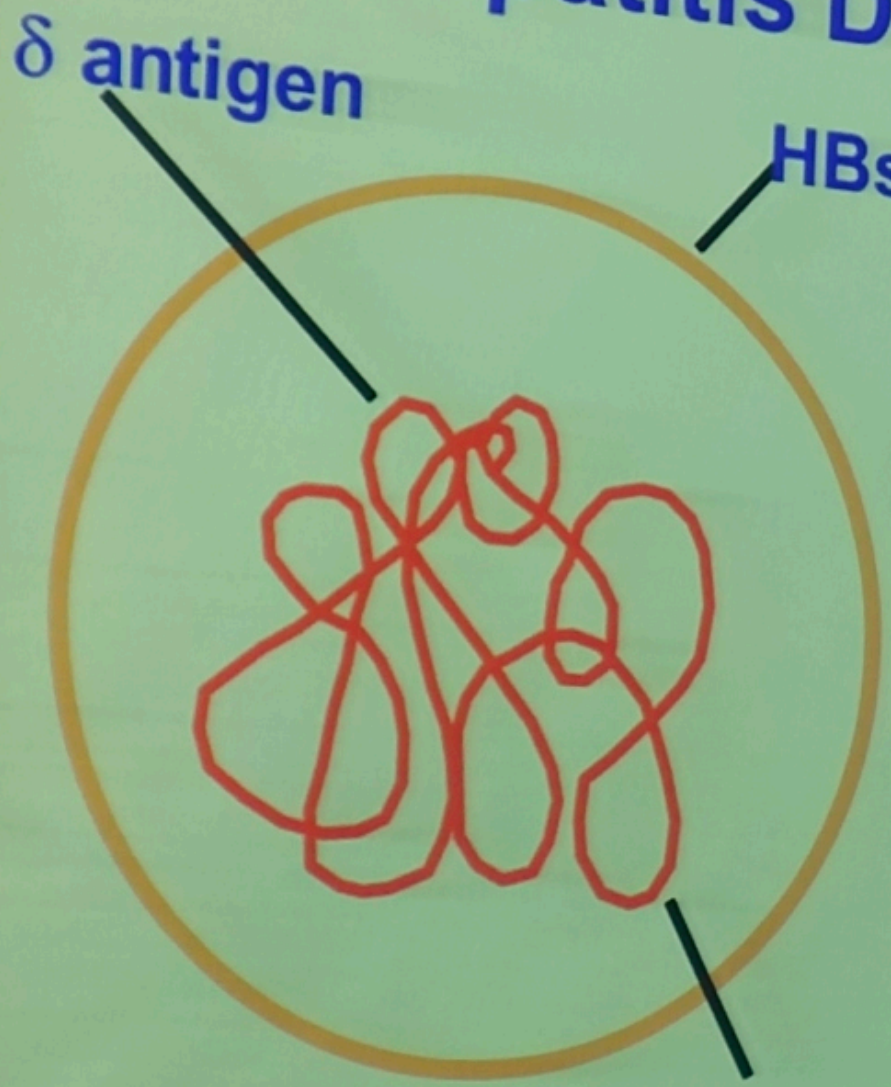
- Genotyping – genotype 1 and 4 have a worse prognosis overall and respond poorly to interferon therapy. A number of commercial and in-house assays are available.
- Viral Load – patients with high viral load are thought to have a poorer prognosis. Viral load is also used for monitoring response to IFN therapy. A number of commercial and in-house tests are available.

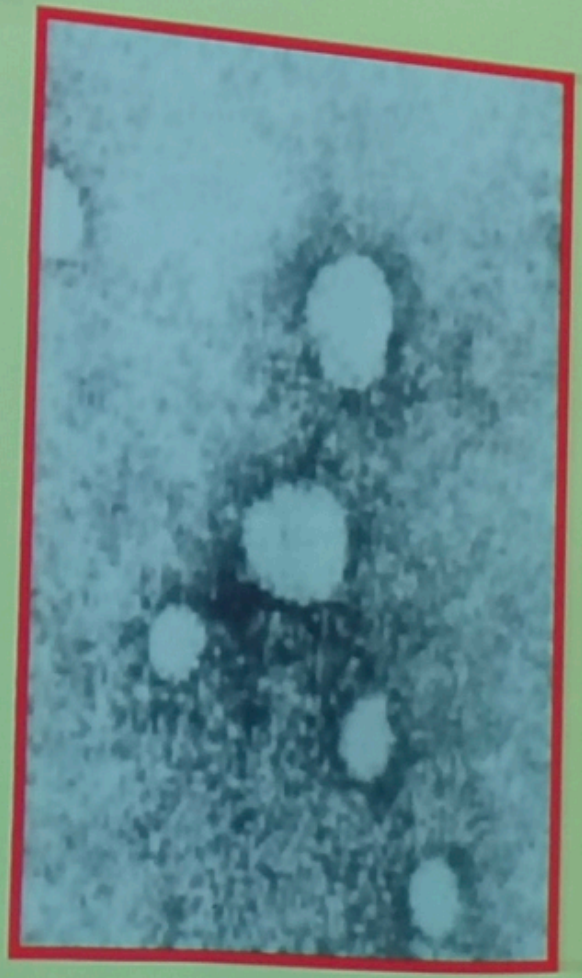
Prevention of Hepatitis C



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

Hepatitis D (Delta) Virus

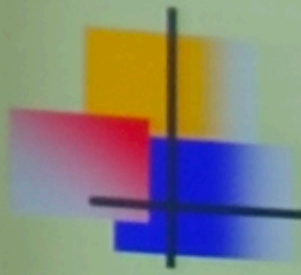




Hepatitis D - Clinical Features

- Coinfection
  - severe acute disease.
  - low risk of chronic infection.
- Superinfection
  - 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

Hepatitis D - Prevention

- HBV-HDV Coinfection

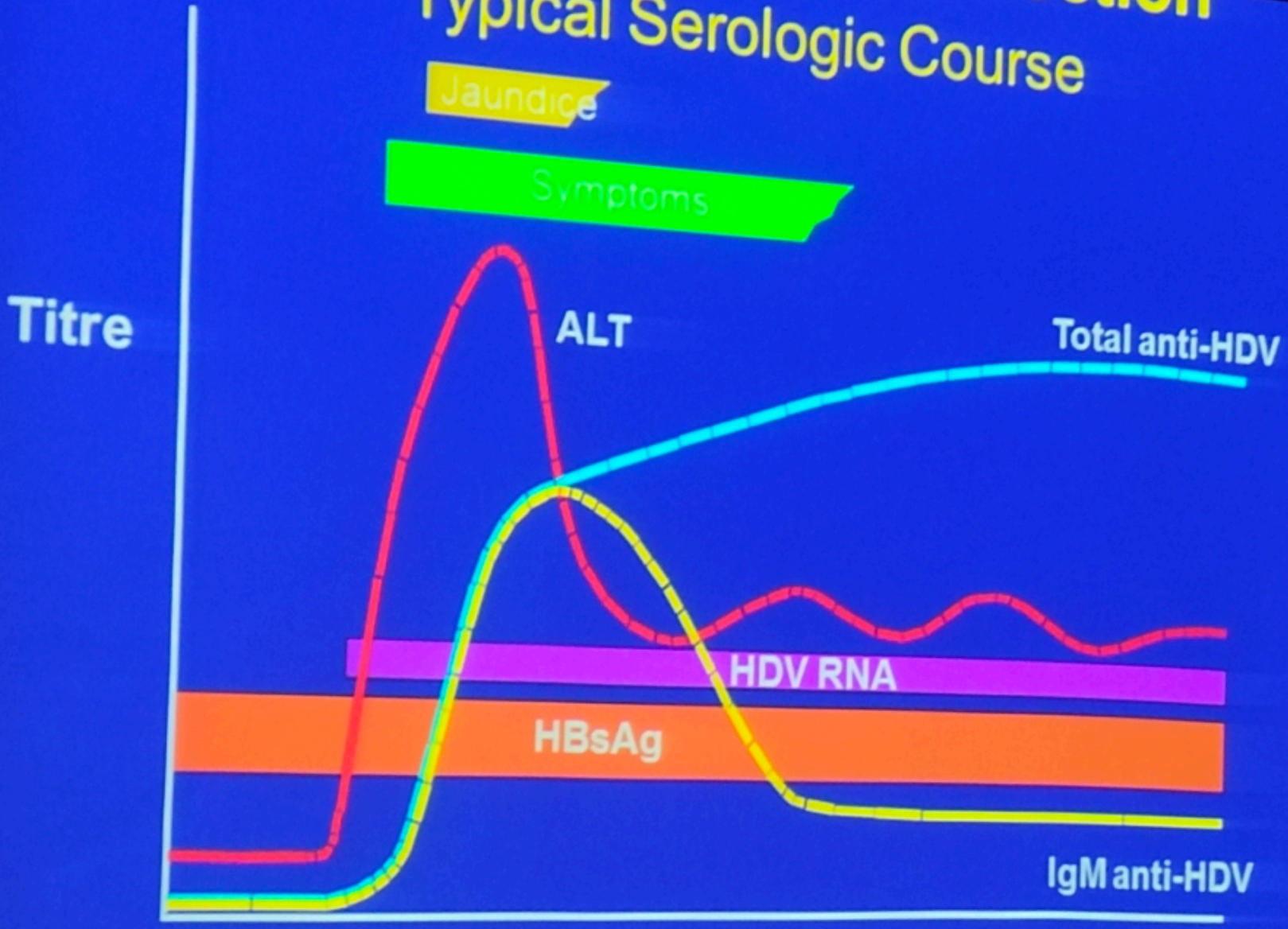
  Pre or postexposure prophylaxis to prevent HBV infection.

- HBV-HDV Superinfection

  Education to reduce risk behaviors among persons with chronic HBV infection.

HBV - HDV Superinfection

Typical Serologic Course



Hepatitis D - Prevention

- HBV-HDV Coinfection

  Pre or postexposure prophylaxis to prevent HBV infection.

- HBV-HDV Superinfection

  Education to reduce risk behaviors among persons with chronic HBV infection.

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: Increased with age
- Chronic sequelae: None identified

Prevention

- Avoid drinking water (and beverages with ice) of unknown purity, uncooked shellfish, and uncooked fruit/vegetables not peeled or prepared by traveler.