GIS
PBL

Problem-based learning

Edited slides lec. 2

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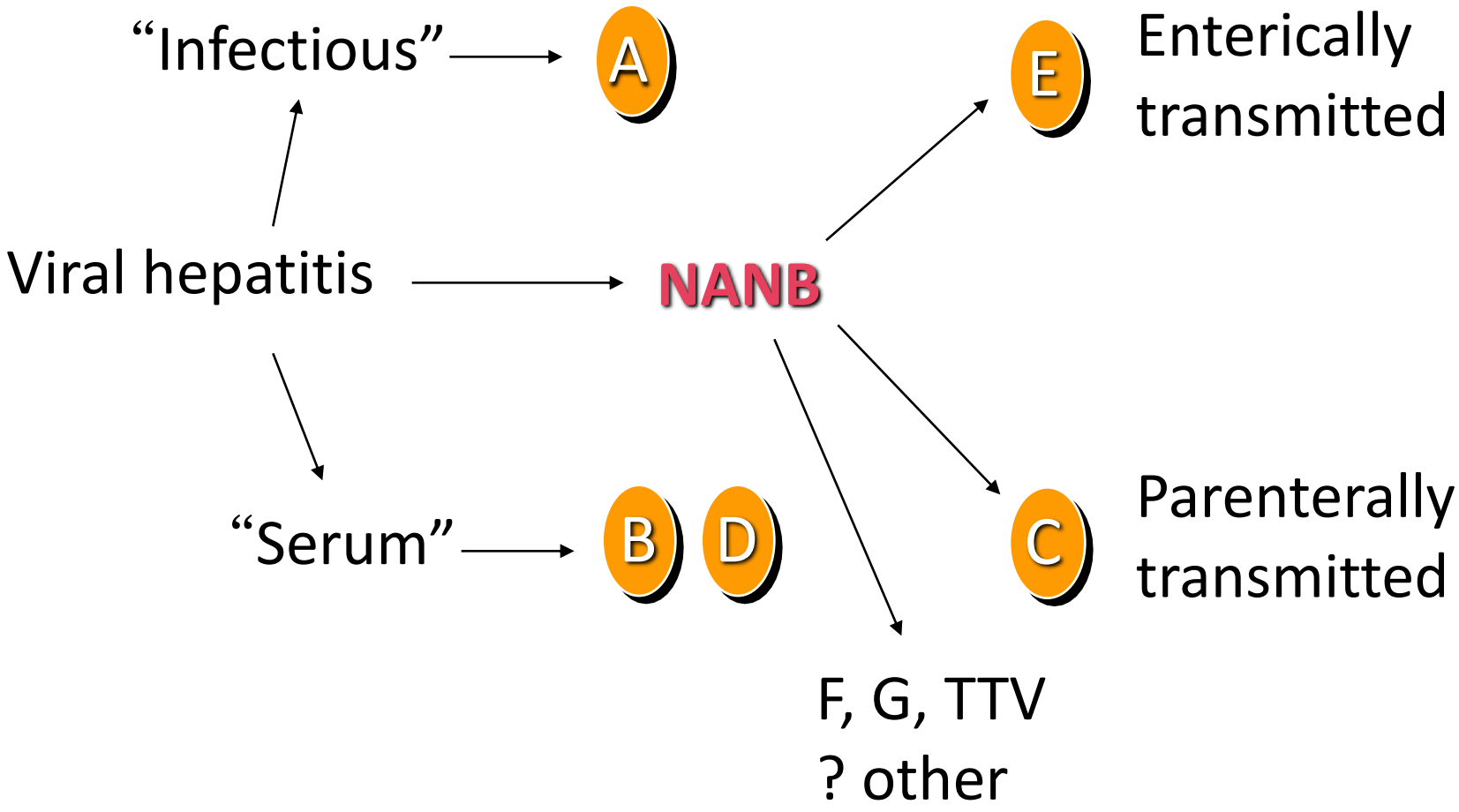
Hepatitis A-E Viruses

An Overview

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

Pay attention to the highlighted pieces of information.

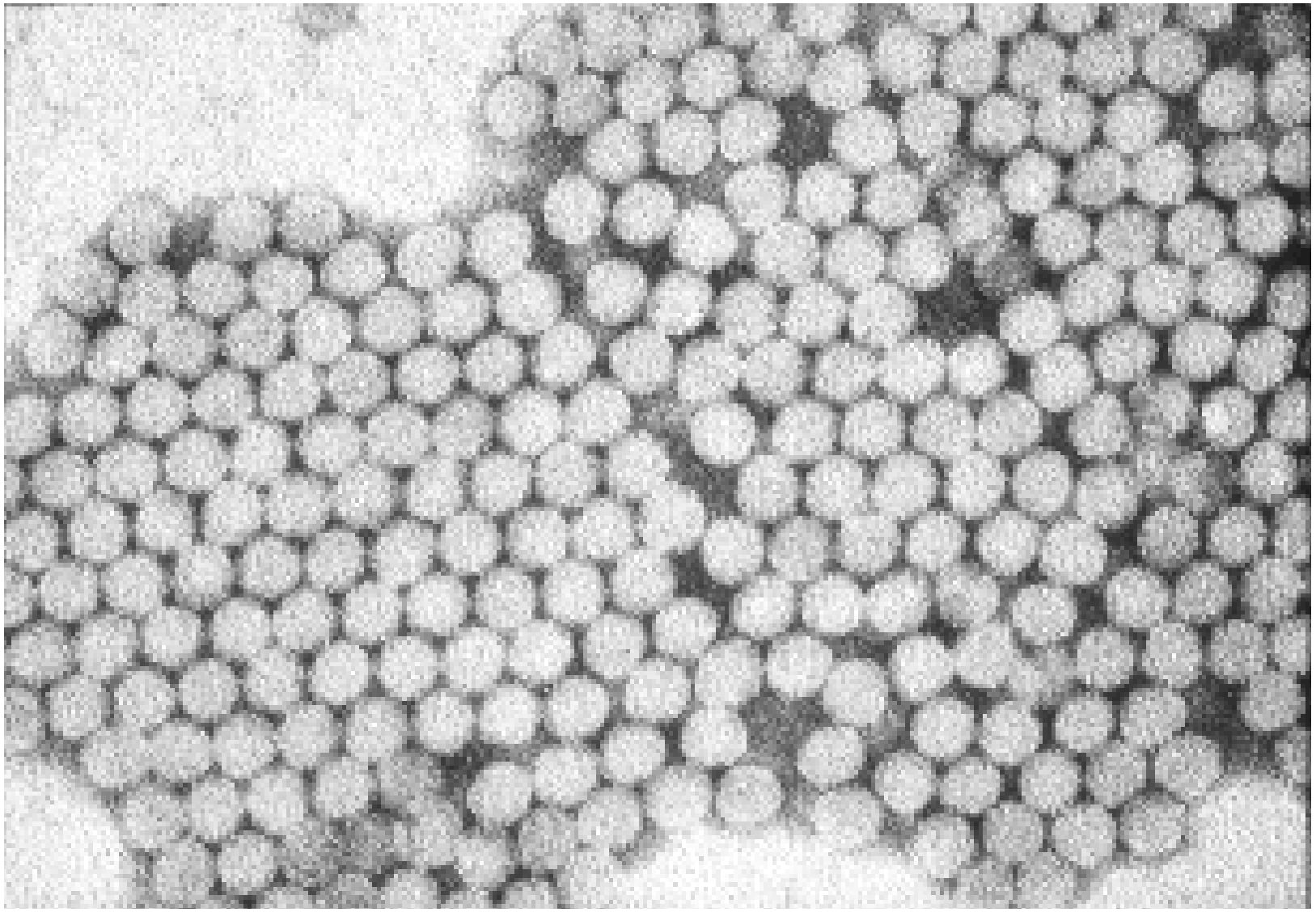
Notes regarding the previous slide

- HEV usually silent except in pregnant women.

- HDV can not cause an infection by its own, it presents with HBV as a super-infection (someone who suffers from HBV from a long time and acquire HDV later on) or co-infection (someone gets infected with HBV & HDV at the same time from the same source).

- HBV has a vaccine and all healthcare workers should be vaccinated against HBV.
- There's no vaccine against HCV.
- There's a vaccine against HAV but it's given to patients with chronic liver disease like liver cirrhosis.

Hepatitis A Virus



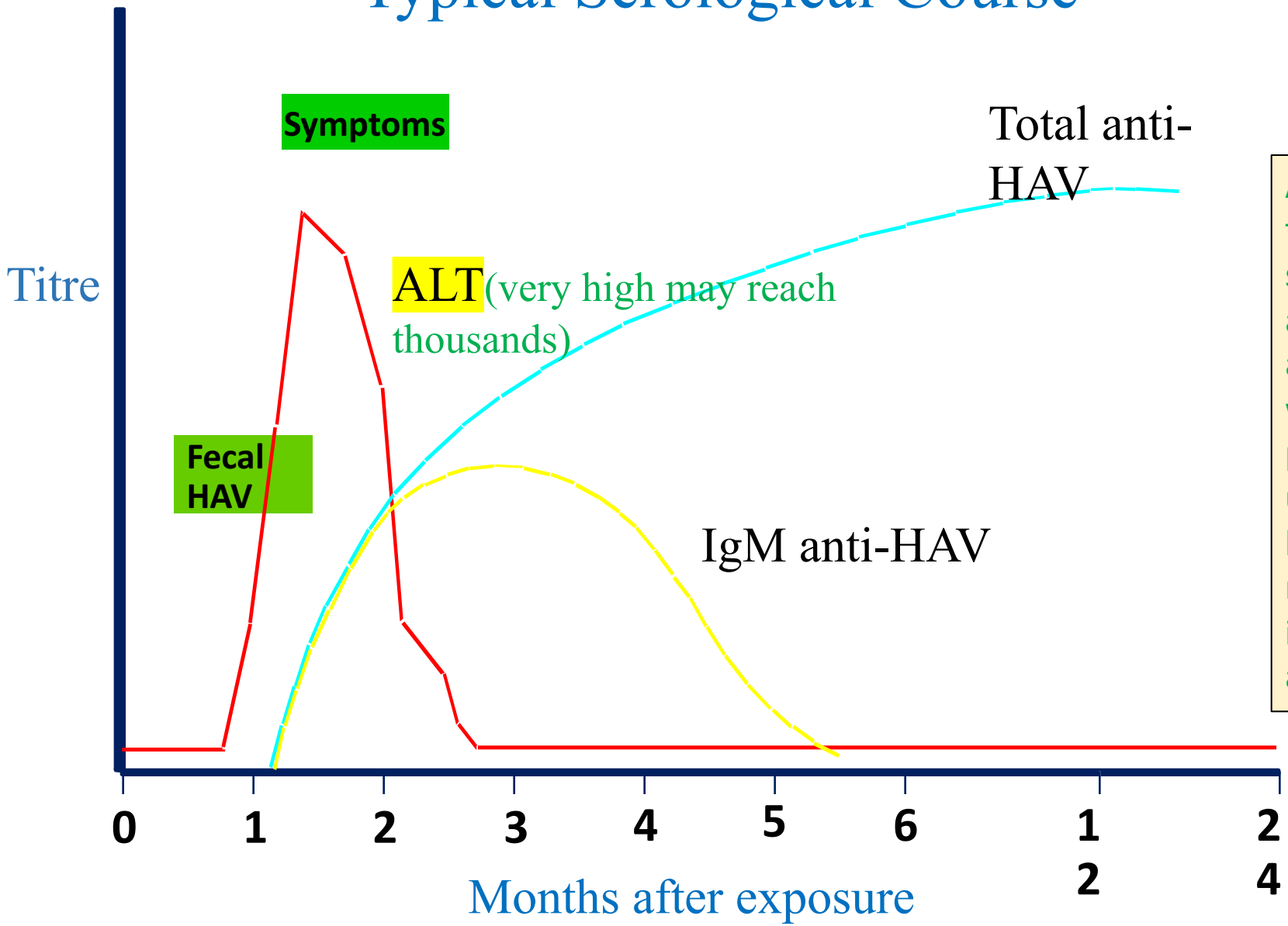
Hepatitis A - Clinical Features

- 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 (unlikely)
  Relapsing hepatitis
- Chronic sequelae: None

In cholestatic hepatitis there will be an increase in titers of alkaline phosphatase (ALP) and γ-glutamyl transferase (GGT), although it's unlikely to happen with infections of HAV but it's possible.

Hepatitis A Infection

Typical Serological Course



As we know HAV is transmitted fecal-orally so the patient may acquire it after ingesting a meal in a restaurant where sanitation practices are not good, usually they come with hepatocellular injury meaning there's an increase in titers of ALT and AST.

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)

Global Patterns of Hepatitis A Virus Transmission

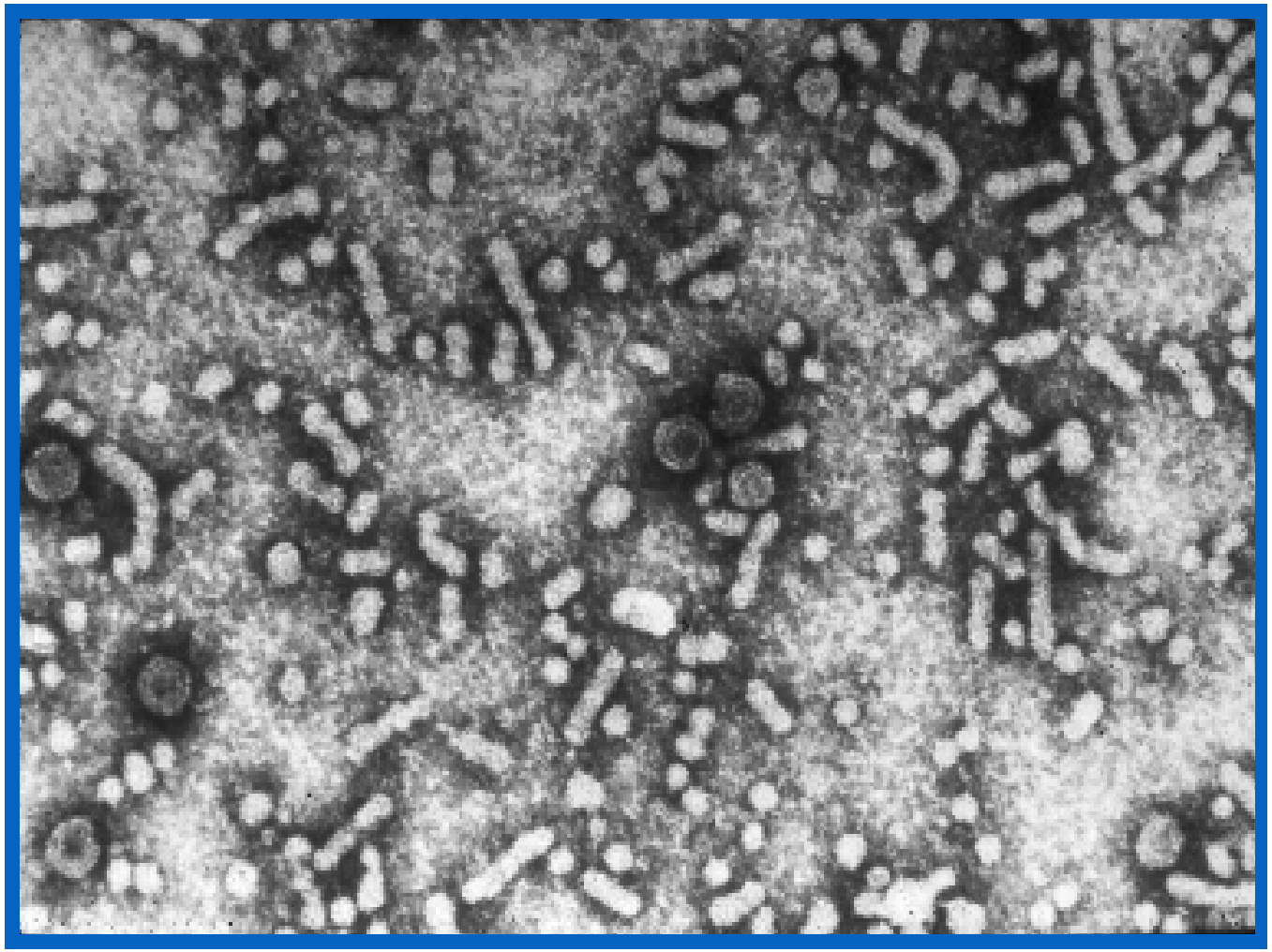
Endemicity	Disease Rate	Peak Age of Infection	Transmission Patterns
High	Low to High	Early childhood	Person to person; outbreaks uncommon
Moderate	High	Late childhood/ young adults	Person to person; food and waterborne outbreaks
Low	Low	Young adults	Person to person; food and waterborne outbreaks
Very low	Very low	Adults	Travelers; outbreaks uncommon

Laboratory Diagnosis

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

- In low economic status communities, people acquire HAV from a very young age and since their immunity is not well-developed yet so it wouldn't affect the patient too much they may have simple viral infection symptoms but people in communities with good hygiene practices would have delayed exposure to HAV, they acquire it in an older age where their immunity would react strongly leading to jaundice and acute illness.
- So acquiring HAV in young age would lead to no or simple symptoms and the older the age the more symptoms will appear and even HBV share this aspect with HAV.

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%

Hepatitis B Virus
Modes of Transmission

- Sexual - sex workers and homosexuals are particular at risk.
- Parenteral or percutaneous - IVDA, Health Workers are at increased risk.
- Perinatal (vertical) - 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.

- Pregnant women should be subjected to do screening test for HBV, because if the mother had high titers that means that there's also a high chance of transmitting HBV to their child.
- HBV vaccine given to infants at the age of 1-2 months.

Immune tolerant phase

- An individual may acquire HBV by two ways either they get the infection at an older age through blood transfusion, percutaneously or during a surgery …etc. **or** they may acquire HBV vertically from their mothers, in this case the child's immunity won't be developed enough to recognize the virus as a foreign body so the virus replicates in the liver while the immune system isn't attacking, we call this phase IMMUNE TOLERANT PHASE, the virus in this phase is not causing harm to the body but it's replicating at a high rate **(high viral load may reach to millions)** later on at the age of 3 yrs mostly or a bit older the immune system will suddenly recognize the virus as a foreign body and start attcking it leading to **chronic active hepatitis** where AST and ALT would increase and the viral load would decrease a bit, no matter how strong the immune system is attacking the virus you can not defeat it, HBV has already established itself in the body.

- Repetitive states of chronic active hepatitis then chronic inactive hepatitis then chronic inactive again will finally lead to fibrosis and liver cirrhosis.

- While in the case of HBV in adults, the immune system will immediately recognize the virus as a foreign body and initiate an immune response, all the symptoms of the disease such as jaundice, ↑AST & ALT and hepatocytes' destruction are caused by the immune response against the virus but mostly the immune system will defeat the virus, that's why 95% of cases HBV in adults will end by recovery and positive HBsAb (Hepatitis B surface Antibody)

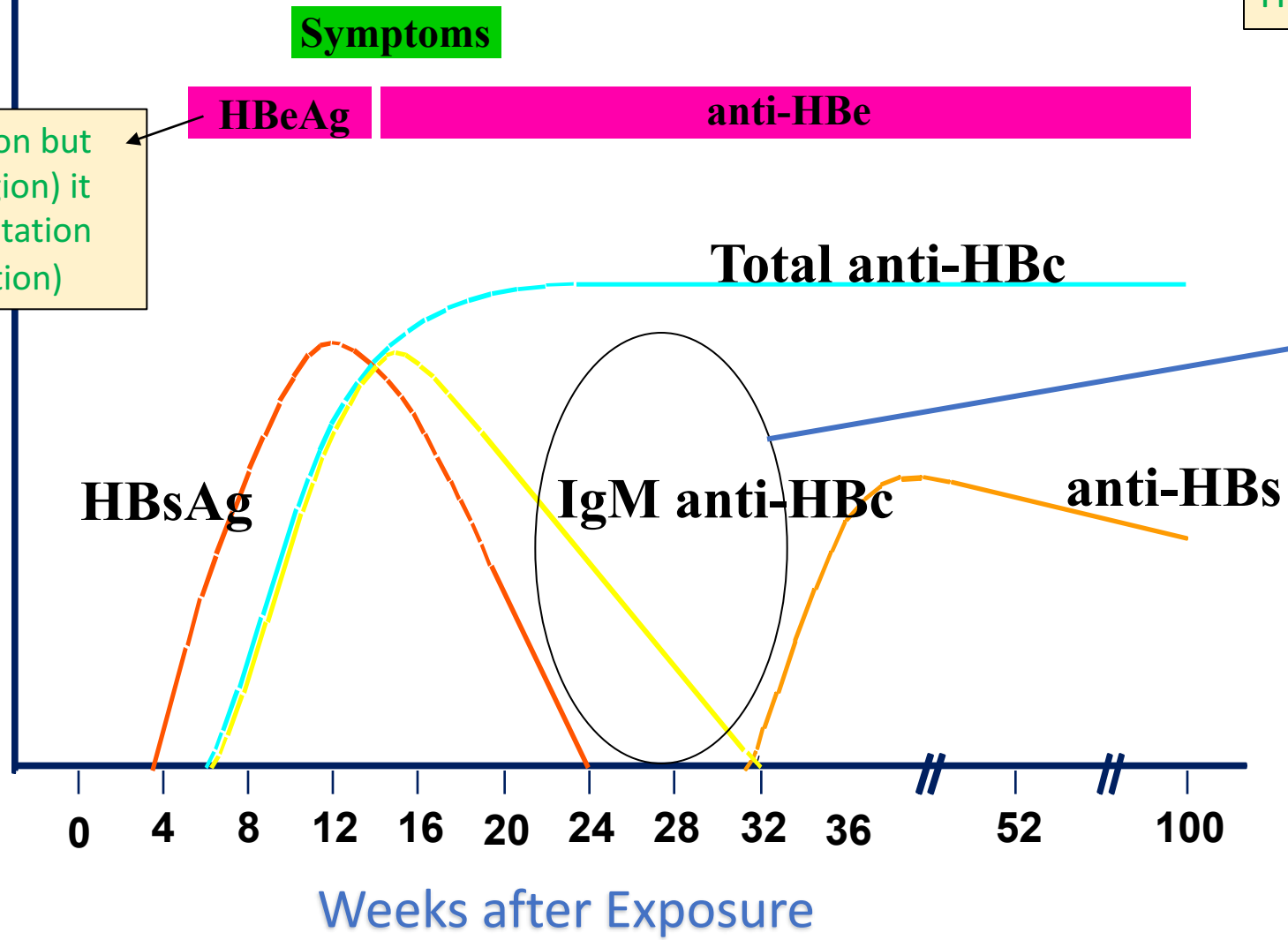
Spectrum of Chronic Hepatitis B Diseases

1. Chronic hepatitis B
2. Cirrhosis of Liver
3. Hepatocellular Carcinoma ; HBV increases the risk of hepatocellular carcinoma without causing cirrhosis unlike HCV, in HCV to have an increase risk of hepatocellular carcinoma the patient should be already cirrhotic but in the case of HBV since it's a DNA virus it can interfere with hepatocyte thus increasing the risk of HCC without causing cirrhosis especially in Afro-Americans and individuals with a family history of HCC

Acute Hepatitis B Virus Infection with Recovery Typical Serologic Course

*HBsAg= Hepatitis B surface antigen
* anti-HBc= Hepatitis B core antibody

pay attention that it's with **recovery** most likely this is a case of HBV in an adult

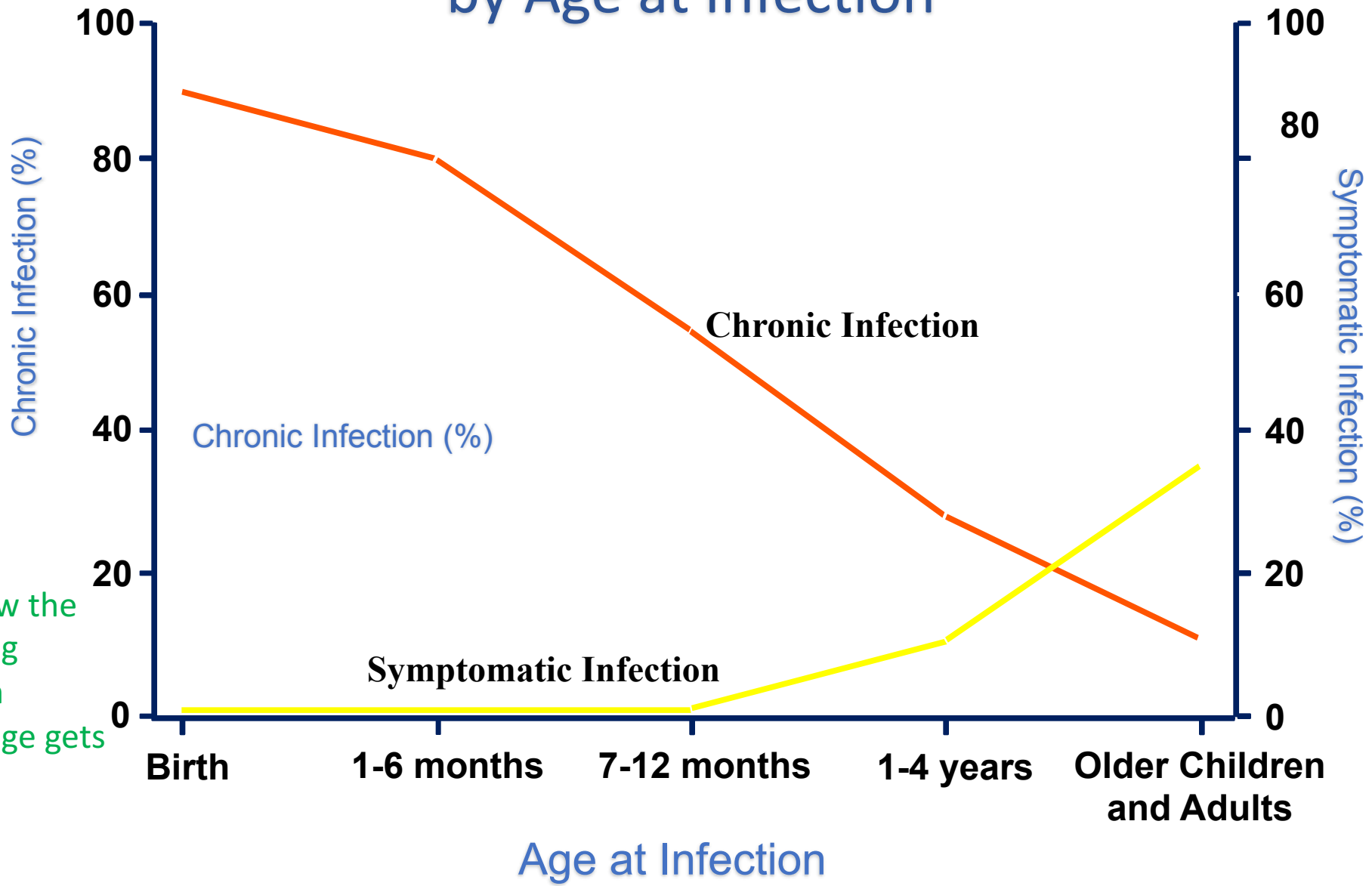


3- Indicates active replication but some times (esp. in our region) it may be absent due to a mutation in the virus (pre core mutation)

2- this is the window period where only **IgM anti-HBc** is positive, so when doing serology to rule out acute HBV you should check for HBsAG and IgM anti-HBc just in case the patient was in the window period

1- Firstly there will be an increase in HBsAg and then it will decline, at this phase anti-HBc will start to increase

Outcome of Hepatitis B Virus Infection by Age at Infection



*Here notice how the risk of developing chronic infection declines as the age gets older

Measures taken to decrease the risk of developing chronic infection in children:

If we found out that the pregnant woman is a carrier for HBV, 1- **we check the viral load in the third trimester** if it's high the patient should be given **2- treatment to decrease the viral load** and once the pregnant woman has delivered the baby **, 3- the baby should take IV IgG in a hand and HBV vaccine in the other hand as soon as possible**. That's why screening for HBV is so important during pregnancy

The doctor said memorize these 3 points they're very important

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

Diagnosis

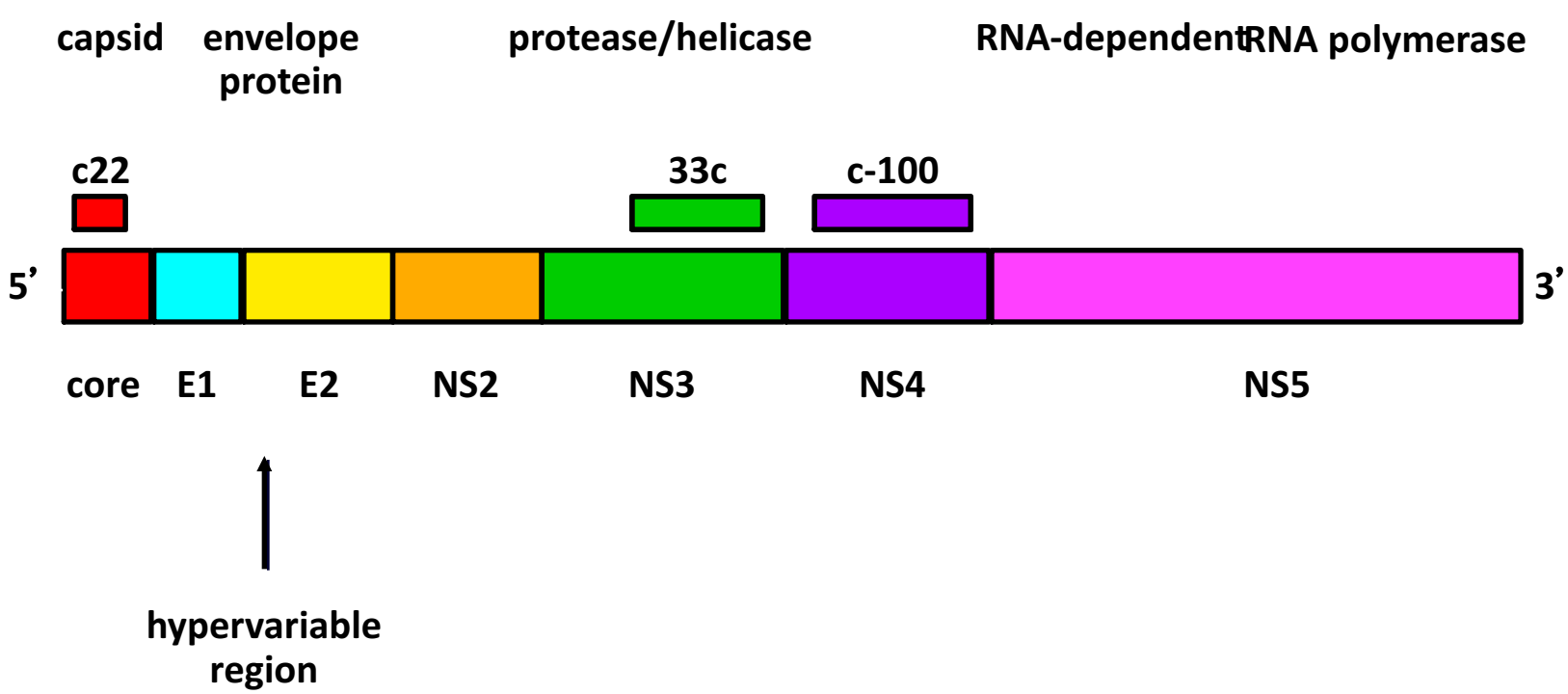
- A battery of serological tests are used for the diagnosis of acute and chronic hepatitis B infection.
- HBsAg - used as a general marker of infection.
- HBsAb - used to document recovery and/or immunity to HBV infection.
- anti-HBc IgM - marker of acute infection.
- anti-HBcIgG - past or chronic infection.
- 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.

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.

There's no treatment to eradicate HBV, all treatments are used only to suppress the viral load and not all patients are subjected to the treatment there are certain indications should be taken in the consideration to decide whether to give the treatment or not, unlike HCV where all patients should be treated

Hepatitis C Virus



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, albeit with a lower frequency i.e. chronic persistent hepatitis, chronic active hepatitis, cirrhosis, and hepatocellular carcinoma.

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**

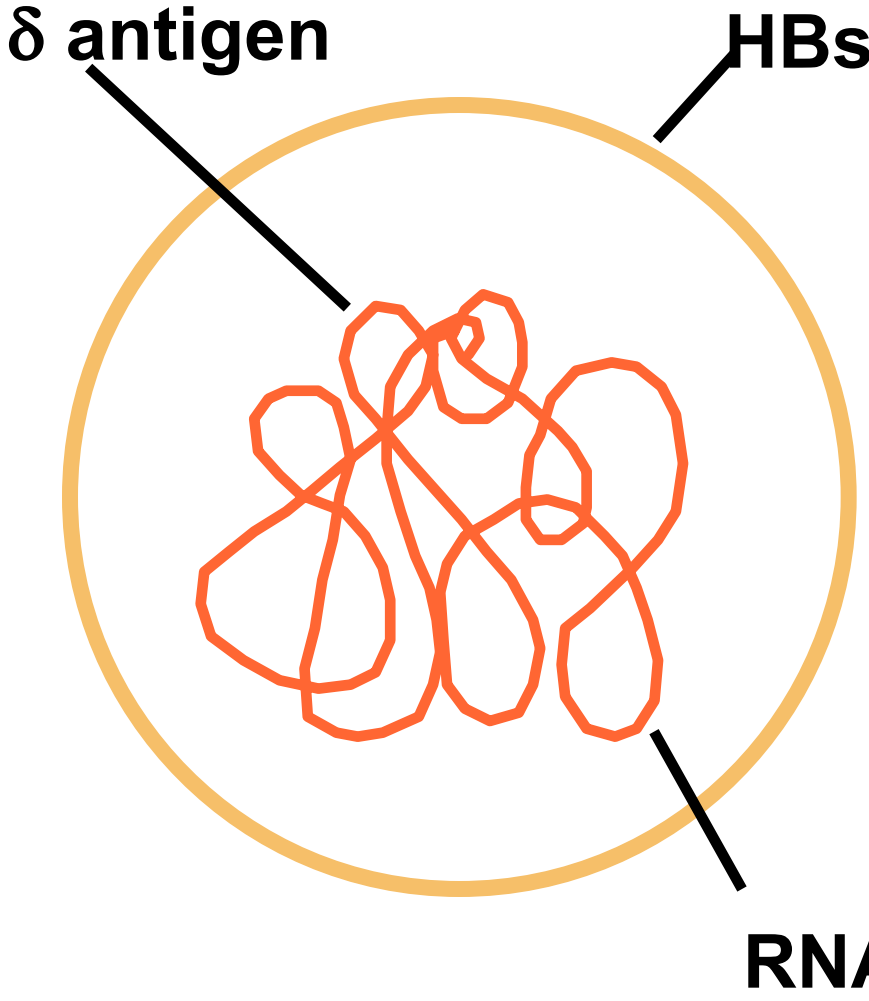
Laboratory Diagnosis

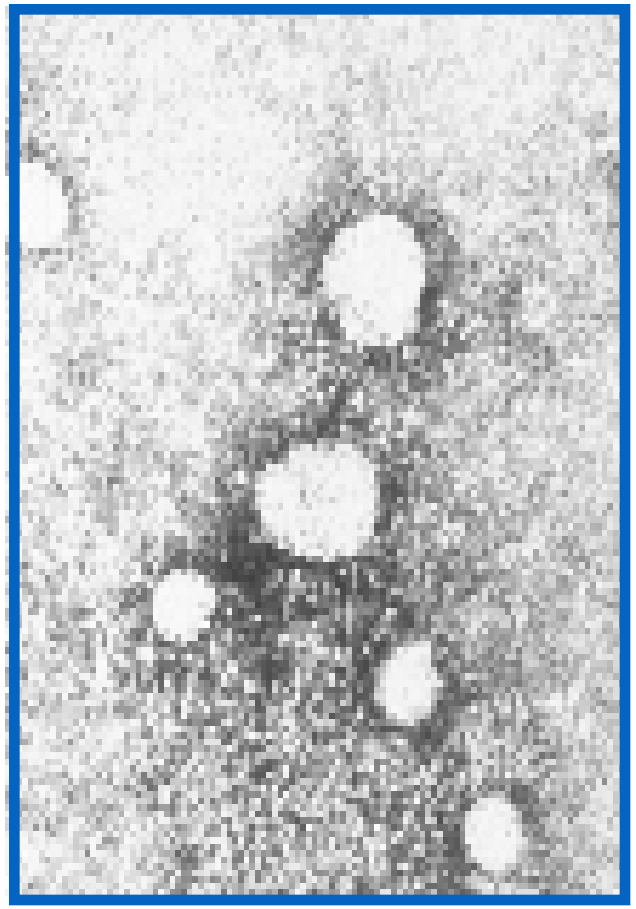
- HCV antibody - generally used to diagnose hepatitis C infection. Not useful in the acute phase as it takes at least 4 weeks after infection before antibody appears. (positive HCV Ab means either the patient has been infected with HCV and now is a **carrier** or he had the infection in the past and now he has **recovered.**)
- HCV-RNA (to measure viral load) - various techniques are available e.g. 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. (negative HCV RNA indicates that the patient has been infected previously and he's recovered while positive indicates that the patient is a carriers and should be treated.)
- 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.

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

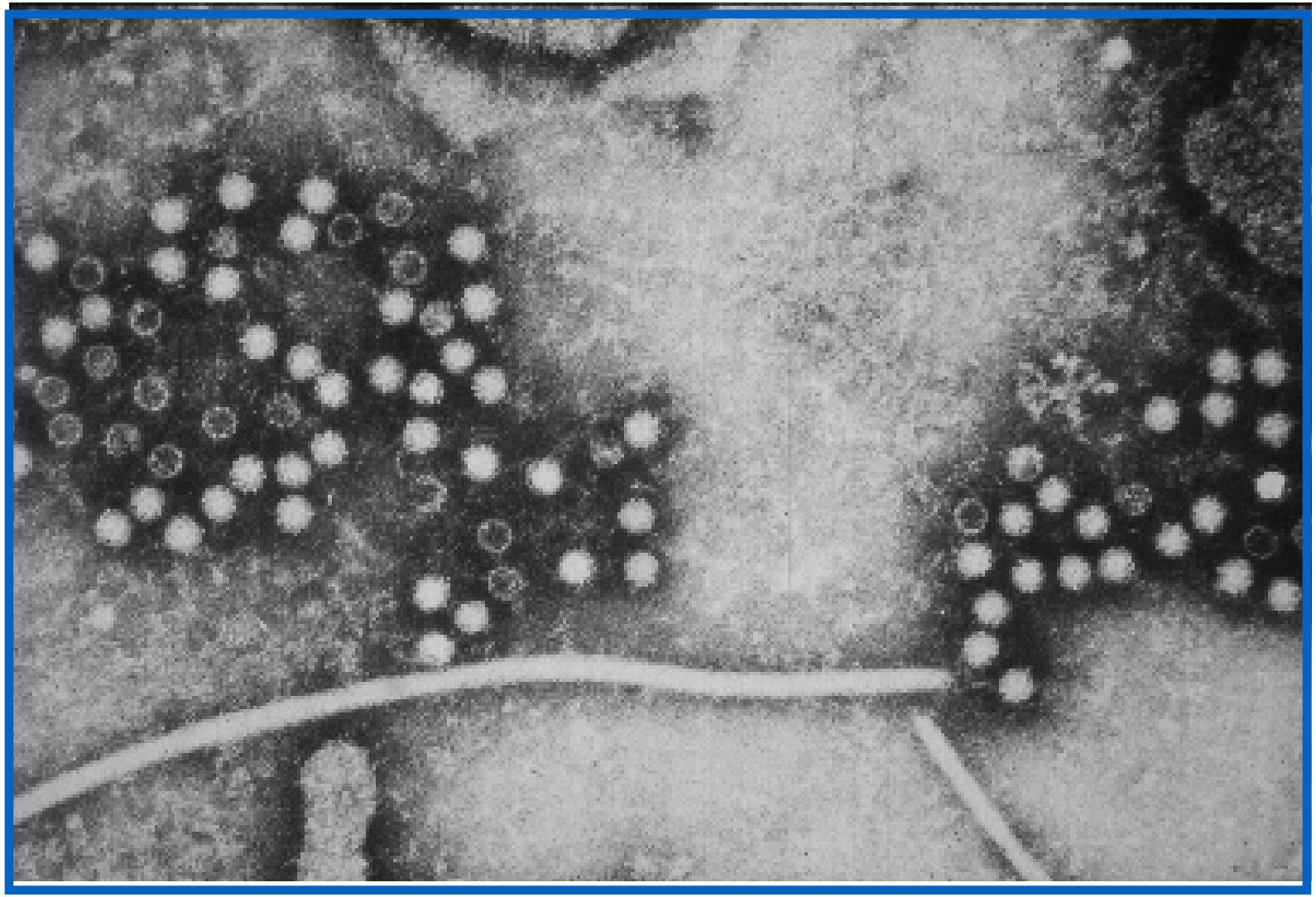
- Coinfection
  - severe acute disease.
  - low risk of chronic infection.
- Superinfection
  - usually develop chronic HDV infection.
  - high risk of severe chronic liver disease.
  - may present as an acute hepatitis. (lower risk of developing acute illness but higher to develop chronic infection in contrast to Coinfection)

In coinfection there will be a strong immune reaction so recovery will be better and risk of developing chronic infection will be lower

Hepatitis D Virus Modes of Transmission

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

Hepatitis E Virus



Hepatitis E - Clinical Features

- Incubation period: Average 40 days
  Range 15-60 days
- Case-fatality rate: Overall, 1%-3%
  Pregnant women, 15%-25%

  Higher in pregnant women
- Illness severity: Increased with age
- Chronic sequelae: None identified