

Hepatitis A, C, D & E viruses

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Hepatitis viruses

- Heterogenous group of different hepatotropic viruses
- Cause systemic disease primarily involving liver
- Caused by-
 - i. Hepatitis A virus
 - ii. Hepatitis B virus
 - iii. Hepatitis C virus
 - iv. Hepatitis D virus
 - v. Hepatitis E virus

Hepatitis A virus

- Belongs to Picornaviridae
- Previously classified as enterovirus 72
- Now assigned to new genus Hepatovirus
- 27-32nm, icosahedral, **nonenveloped**, linear, **single stranded RNA**, linear, positive polarity.
- Only **one serotype exists**
- Only human hepatitis viruses that can be **cultivated in vitro**

Hepatitis A virus- Pathogenesis

- Virus is shed in the stools of infected persons
- Infection is transmitted by feco-oral route
- First multiplies in the intestinal epithelial cells→ spreads to the liver via blood
- **Hepatitis A is most common cause of acute viral hepatitis in children**

Hepatitis A virus- Epidemiology

- **Humans are only host**
- **Children and adolescents most commonly affected (5-14 yrs)**
- Infections mostly subclinical (80-95%)
- Adults comparatively more icteric than children with a higher mortality rate
- >50% of the adults develop jaundice, 5% children < 3 years develop jaundice
- Important risk factors: Poor hygiene & overcrowding leading to outbreaks
- Virus excretion: in feces, 2 weeks before to 2 weeks after appearance of jaundice

Hepatitis A virus- Clinical features

- Acute self limiting disease, I.P.: 2-6 weeks
- Abrupt onset with fever, malaise, anorexia, nausea, lethargy followed by jaundice and hepatomegaly
- Complete recovery in 8-12 weeks in most cases (98%), severity of the disease varies with the age
- No extra hepatic manifestation, no chronic/carrier state
- Less than 0.5% cases develop fulminant hepatitis
- Not associated with cirrhosis/ hepatocellular carcinoma

Hepatitis A virus- Laboratory diagnosis

- Raised AST& ALT
- Demonstration of virus particles: immunoelectron microscopy
- Serology:
 - IgM/IgG antibodies, ELISA
 - Antigen detection: ELISA (-2 too +2 weeks of jaundice)
- Isolation: Tissue culture
- Nucleic acid detection: PCR
- Non specific test: raised liver enzymes & serum bilirubin

Treatment & prophylaxis

- **No specific treatment**
- **Prophylaxis:** Killed vaccine available
 - Also LA vaccine
 - HAV- Ig

Hepatitis c virus

- **Belongs to family Flaviviridae**
- **Genus: Hepacivirus**
- 50-60nm, spherical, **single stranded RNA**, positive sense, positive sense, **enveloped**
- Classified into 7 major genotypes based on heterogeneity of nucleotide sequence, further divided into many subtypes.
- Genotypes vary in distribution
- **Genotype 1 most prevalent worldwide & genotype 3 most prevalent in India, followed by genotype 1**
- Important cause of post transfusion hepatitis in developing countries

Hepatitis c virus

- Prim. Transmission: Blood route
- About **3% of world population estimated to be infected with HCV.**
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- HCV accounts for 27% & 25 % of **cirrhosis & HCC** respectively, worldwide.
- HCV hepatitis is **predominantly asymptomatic**, gradually evolves into **chronic hepatitis in 70- 85%**

Hepatitis c virus-Pathogenesis

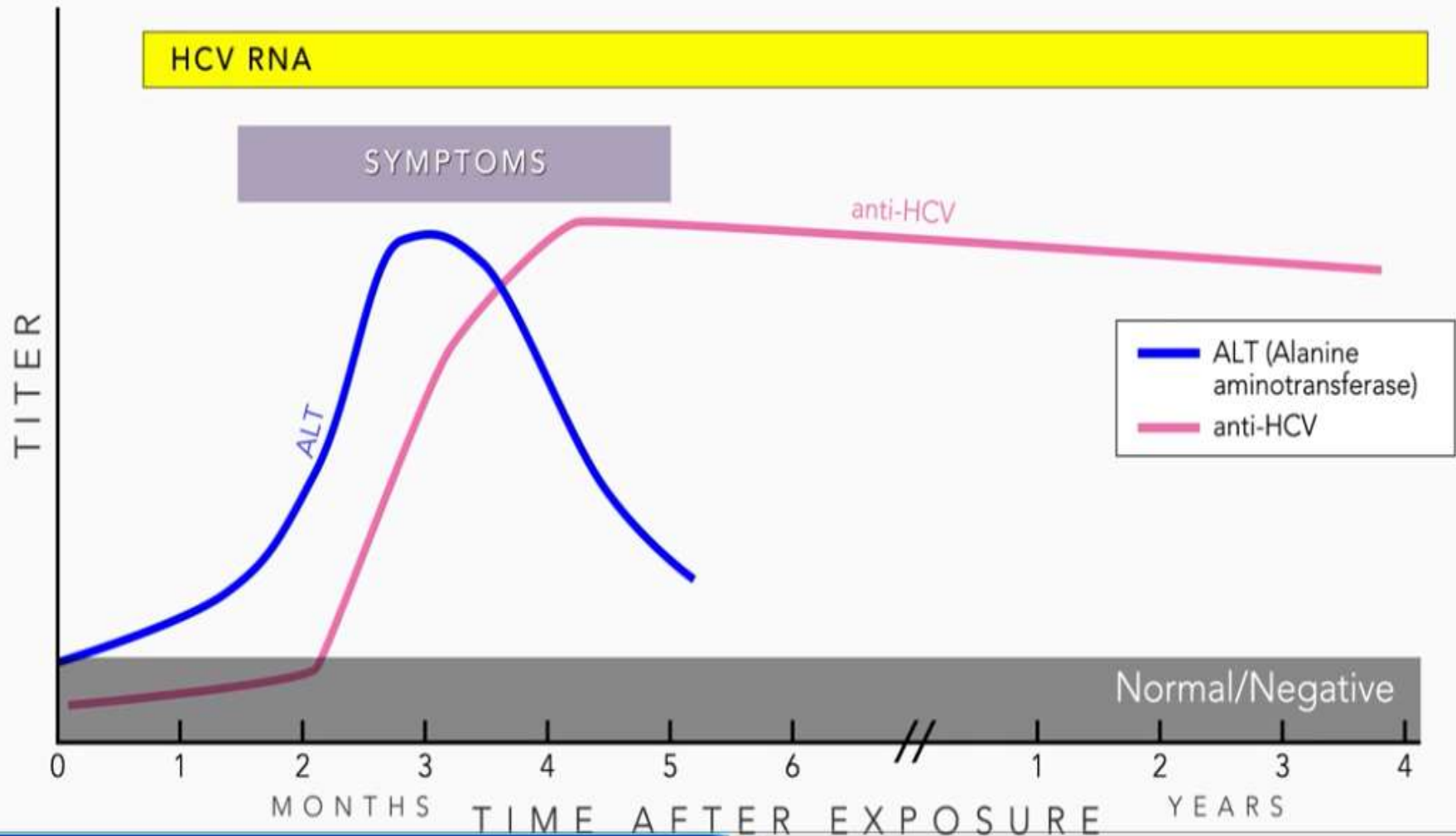
Three main modes of transmission

- 1. Parenteral-** Accidental inoculation of body fluids during medical, surgical, dental procedures, intravenous drug abusers, blood transfusion
- 2. Perinatal**
 - Prenatal: transplacental
 - Perinatal: contamination of mucous membranes of the baby with maternal blood
 - Post natal: breast feeding
- 3. Sexual**

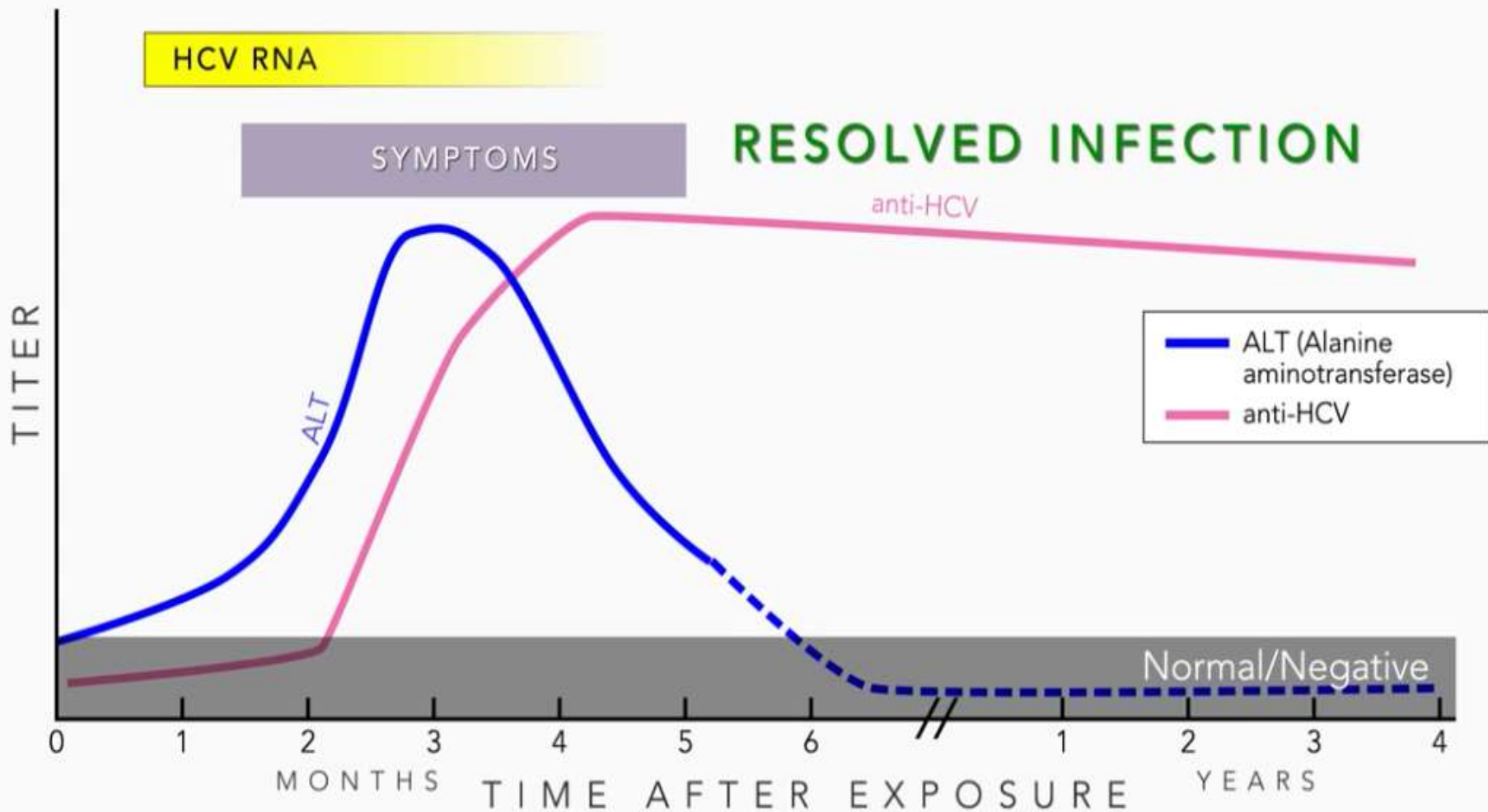
Hepatitis c virus-Clinical features

- Incubation period: 15-160 days
- About 75% infections sub-clinical
- **80-85% patients develop chronic infection**
- Acute infection as compared to HBV infection is less severe, shorter duration of prodromal phase, milder symptoms.
- Fulminant infection: 0.1%
- Patients with chronic disease may later on develop cirrhosis & hepatocellular carcinoma
- **Prophylaxis:** no vaccine available currently

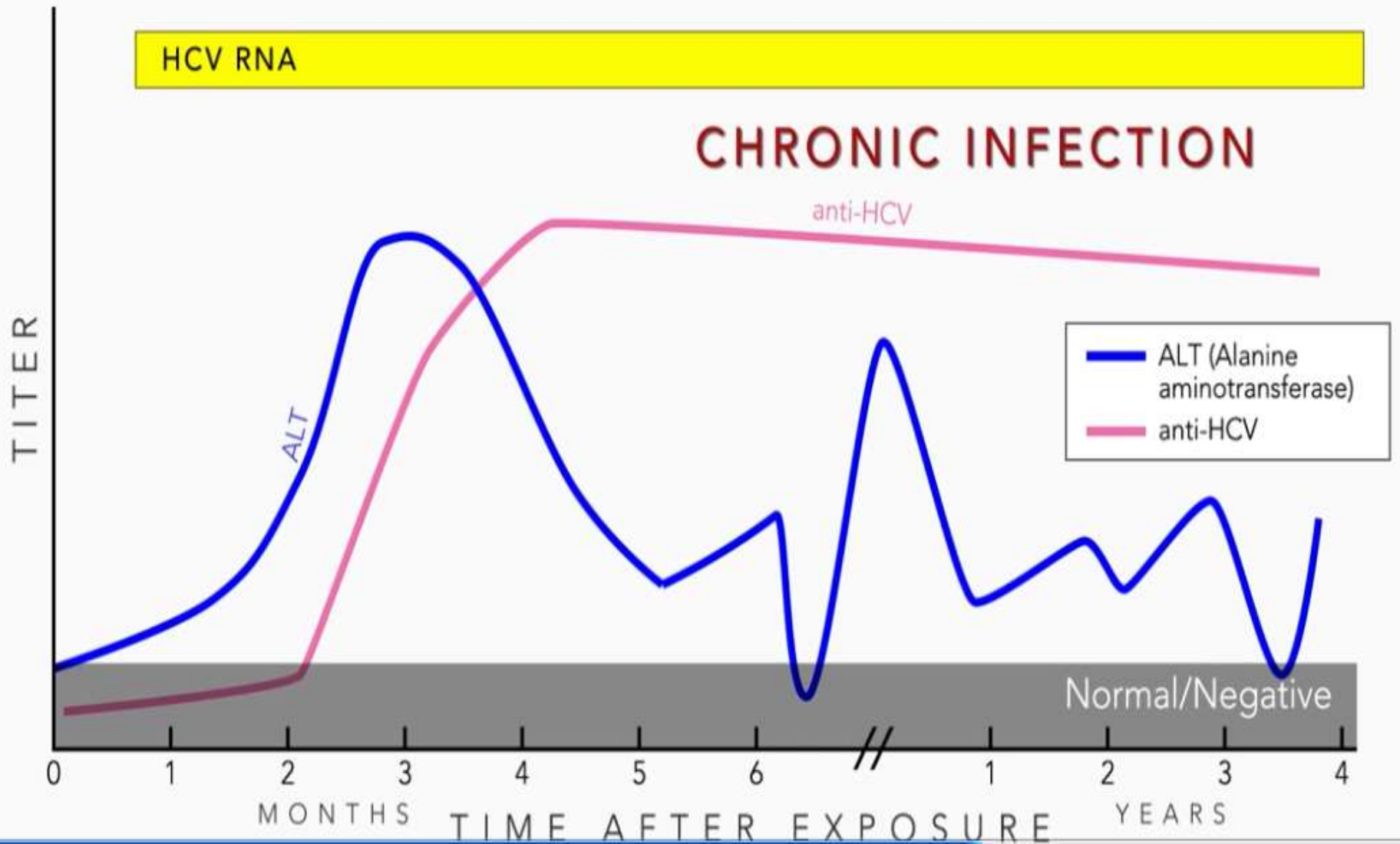
Acute/recently acquired HCV infection



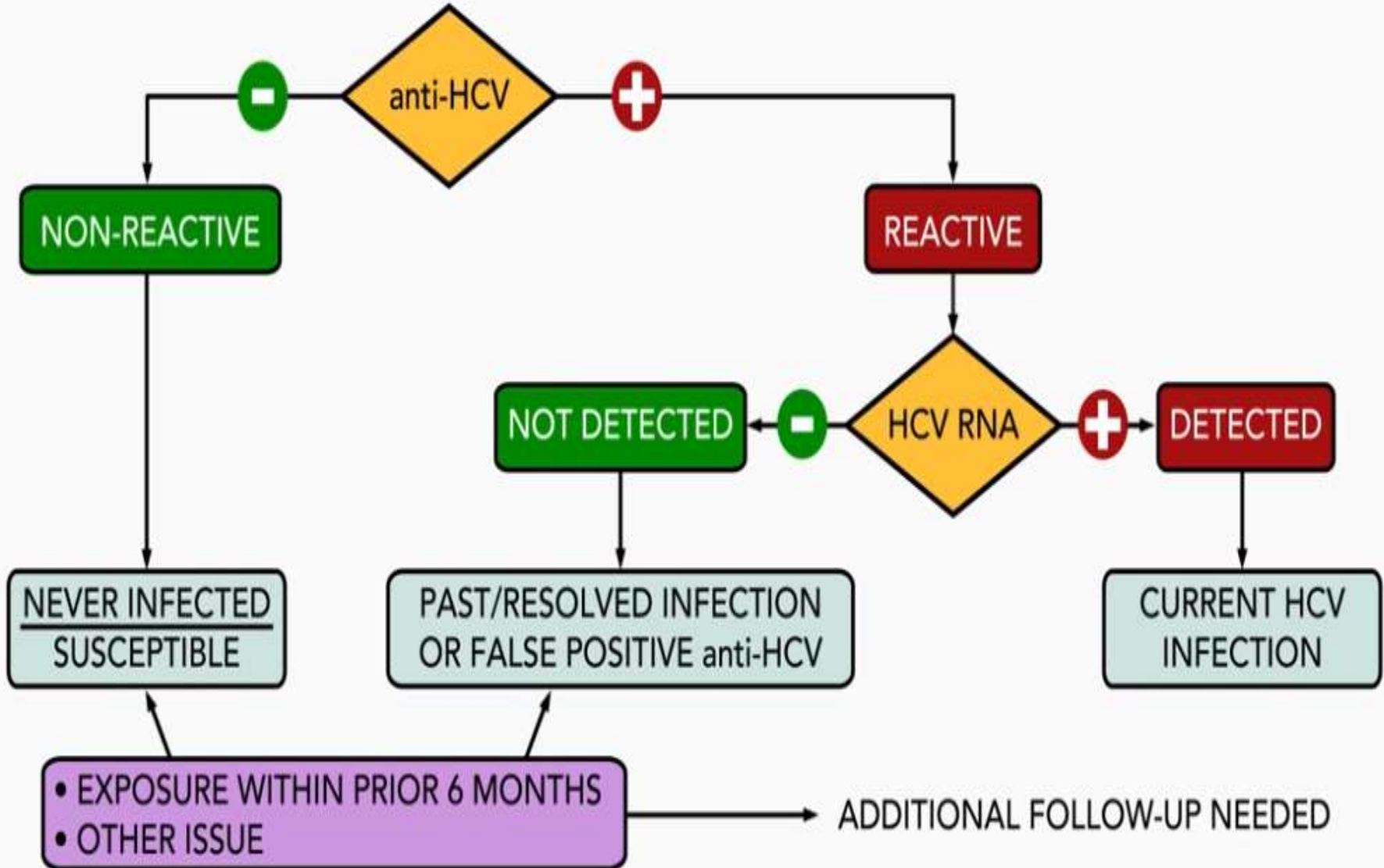
Resolved HCV infection



Chronic HCV infection



HCV Testing sequence



Hepatitis C-Lab Diagnosis

- Virological tests play key role in the diagnosis of infection, therapeutic decision making & assesment of virological response to therapy.
- Mainstay of diagnosing infection:

1. Serological test: Based on anti-HCV, (for screening)

- ELISA
- ELFA
- Rapid tests

2. Nucleic acid tests (NAT): (Confirmatory)

- PCR
- Sequencing for GT & subtypes

Hepatitis C-Treatment

- Conventional: PEG-IFN plus RBV combination
- Directly Acting antivirals (DAAs): **'Game changers'** in HCV management.
- DAAs example: Sofosbuvir, daclatasvir, ledipasvir.....
- Remarkable improvement in cure rates, shorter duration of treatment, better tolerability in comparison to PEG-IFN- and RBV-based therapies

Hepatitis D virus

- Defective virus, requiring help from HBV for survival (HBV necessary for the production of HDV virions)
- Genus: Delta virus
- Spherical, 36-38nm, HBsAg coat, HDAg nucleocapsid, single, **circular RNA, minus strand**
- Transmission: Similar to HBV & HCV, Parenteral/
Perinatal/ Sexual

Hepatitis D virus

Two types of infection:

- **Coinfection:**

- Simultaneous infection with HBV, HDV.
- Most commonly results from parenteral transmission.
- Infection more severe than HBV alone.
- Chronicity 1- 10%

- **Super infection:**

- Infection of HBV carrier with HDV.
- Commoner and more serious than coinfection (as liver function already compromised by HBV infection).
- Develops into fulminant infection.
- Chronicity 100%

Hepatitis D virus-

Laboratory diagnosis

- HDV Ag detection: ELISA
- HDV RNA detection: PCR
- IgM/IgG Anti-HDV detection: ELISA
- Co-infection: IgM Anti-HDV & IgM Anti-HBc, HBsAg, HDV RNA
- Super-infection: IgM/IgG Anti-HDV & IgG Anti-HBc, HBeAg, HBsAg, HDV RNA

Prophylaxis

- Prevention of infection with HBV

Hepatitis E virus

- Belongs to family Caliciviridae
- Genus; Hepevirus
- Spherical, 27-35nm, **single stranded, positive sense RNA**
- **Non enveloped**
- Virus first identified in New Delhi, India in 1955

Pathogenesis- Ingestion of contaminated drinking water

Hepatitis E virus

- Single serotype
- 4 genotypes in humans (GT 1-4)
- GT 1& 2 more virulent

Hepatitis E virus- Epidemiology

- Transmission: Feco-oral
- Zoonotic pathogen
- Common cause of acute hepatitis

Hepatitis E virus- Clinical features

- I.P.: 2-8 weeks
- Disease resembles that produced by Hepatitis A virus, mainly involve young adults
- **Fulminant infection: 1-2% in general population; 10-20% in pregnant women**
- Does not progress to carrier/chronic infection, cirrhosis or hepatocellular carcinoma

Hepatitis E virus-Laboratory diagnosis

- Demonstration of virus particles: immunoelectron microscopy
- Antigen detection: ELISA
- Serology: IgM/IgG antibodies, ELISA
- Nucleic acid detection: PCR

HEV prevention

- General sanitation & infection control measures
- Recombinant vaccine developed by China: HEV 239 (not available globally)

Characteristics/Hepatitis virus	A	B	C	D	E
IP	15-45 days	30-180 days	15-160 days	30-180 days	14-60 days
Route	FO	Sx, PE, PN	Sx, PE, PN	Sx, PE, PN	FO
Family	Enterovirus-72	HepadnaVirus	Hepacivirus	Delta virus	Calicivirus
Genome	Ss-RNA	ds-DNA	Ss-RNA	Ss-RNA	Ss-RNA
E/NE	NE	E	E	E	NE
Cultivable in tissue culture	√				
Vaccine	√	√		√ (Hep B)	√
Ch. Hepatitis		√10%	√ 70-80%	√ 10% CI 100% SI	
Cirrhosis/HCC		√	√	√	
Fulminant hepatitis	0.1%	0.1-1%	0.1%	5% CI 20% SI	1-2% Gen Pop 10-20% Preg

Questions

- Classification of hepatitis viruses
- Hepatitis A virus
- Lab diagnosis of hepatitis C virus
- Hepatitis E virus
- Hepatitis D virus