GIT Module
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Viral Hepatitis

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Types of viral hepatitis

HAV:

- ❑ Acute (<6momnths)
- ❑ Fecal Oral

ssRNA
Nonenveloped

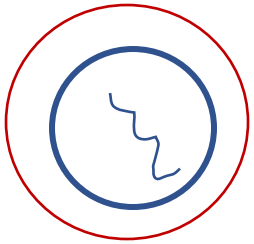
HBV:

- ❑ Acute and chronic
- ❑ Sex, blood, perinatal

dsDNA
Enveloped

HCV:

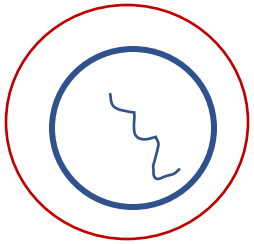
- ❑ Acute and chronic
- ❑ Sex, blood, perinatal



ssRNA
Enveloped

HDV:

- ❑ **Acute and** Chronic
- ❑ Sex, blood, perinatal
- ❑ Needs B to infect



ssRNA
Enveloped

HEV:

- ❑ Acute (<6momnths)
- ❑ Fecal Oral

ssRNA
Nonenveloped

Hepatitis A

Characteristic:

- Picornavirus (+ssRNA, Non enveloped)
- Enterically transmitted (fecal/oral route)
- Only a single serotype exists
- Estimated to be the cause of 40% of acute hepatitis cases
- *Contamonated food, hands* > *ingestion* > Multiplies in oropharynx and intestinal epithelial cells > blood > Liver > Periportal necrosis + mononuclear infiltrates

Hepatitis A

- IP: 2-6 WEEKS
- Infectious dose 100 particles.
- Communicability: 2w before and after jaundice.
- Mortality rate: 0.1 – 0.2%.
- (1/1000 will get fulminant liver disease (80% of these cases will be fatal)

Hepatitis A

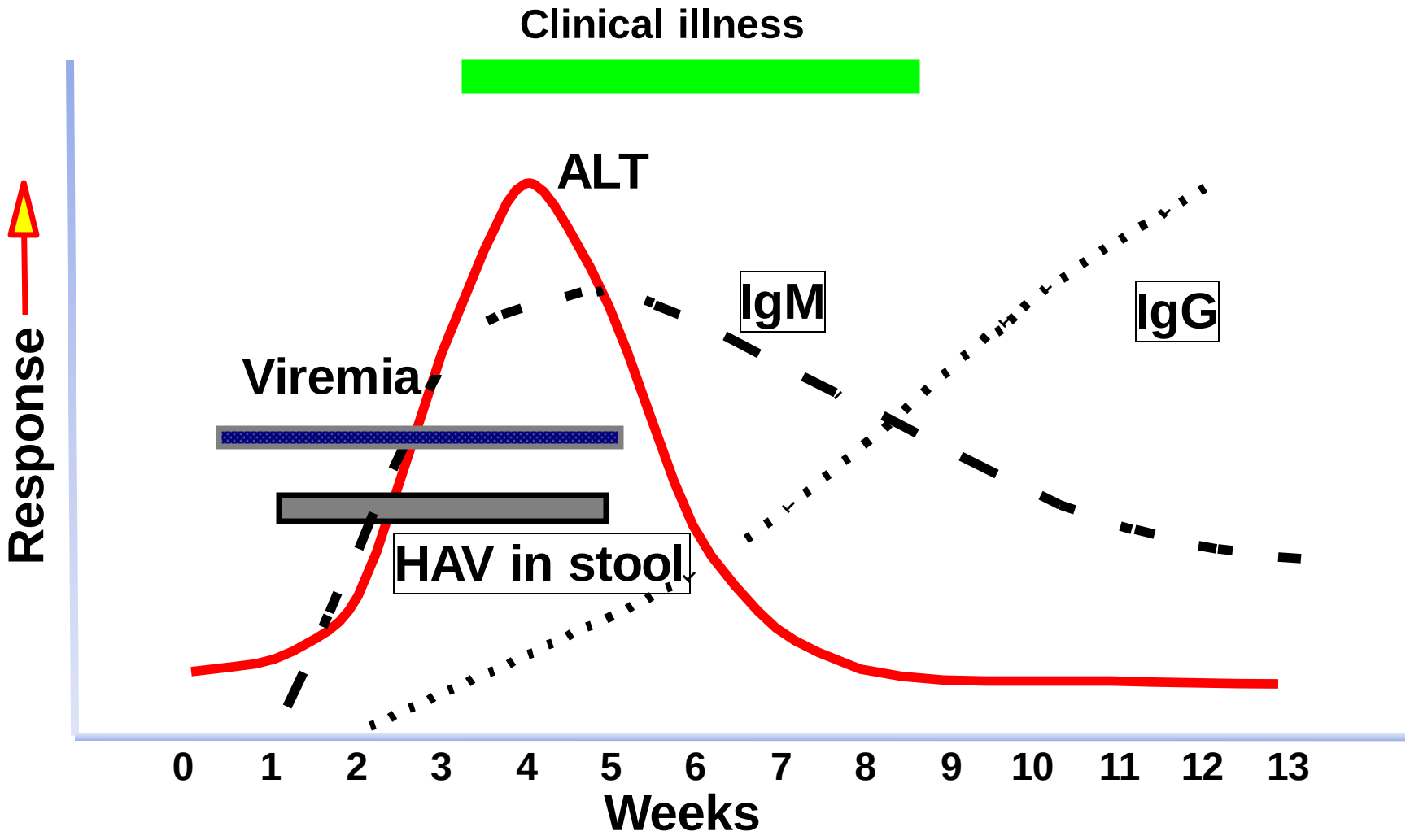
Clinically:

- Asymptomatic: most children
- Symptomatic: most adults
- Preicteric phase: flu like + nausea, vomiting, anoprexia
- Icteric phase: jaundice, abdominal pain, hepatomegaly, increased liver enzymes and bilirubin
- No chronic status

Diagnosis:

- Clinically
- Liver enzyme (may be elevated between 500 and 5000).
- Serology: serum HAV IgM; IgM antibody persists for 3-6 months after onset of symptom.
- IgG (life long immunity)

Events in hepatitis A virus infection



Hepatitis A

How serious is Hepatitis A?

✓ Most people who get Hepatitis A feel sick for several months, but they usually recover completely and do not have lasting liver damage.

✓ Liver failure and death, although this is rare and occurs more commonly in people older than 50 and people with other liver diseases

Hepatitis A

Treatment

- There is no specific treatment for hepatitis A. Recovery from symptoms following infection may be slow and can take several weeks or months.

Prevention*:*

- Hygiene
- Supportive
- Immune globulin (IG)
  - Immunoglobins administered low dose provides protection for 1-2 months
- Inactivated HAV vaccine

Diagnosis

- Tests for fecal or serum HAV are not routinely available
- Diagnosis of hepatitis A is based on detection of IgM anti-HAV during acute illness

Hepatitis E

- Belongs to Hepevirus:
  - +ssRNA non enveloped
- Faecal-oral transmission (mainly water-borne)
- Mostly sub-clinical in children
- Acute hepatitis E is clinically similar to HAV except:
- Bilirubin levels higher
- Jaundice is deeper and more prolonged

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

Hepatitis E

Clinical Presentation

- Similar to HAV

Diagnosis

- Diagnosis requires presence of serum HEV IgM
- *Seroconversion + Molecular RT-PCR*

Prevention

- The same as HAV

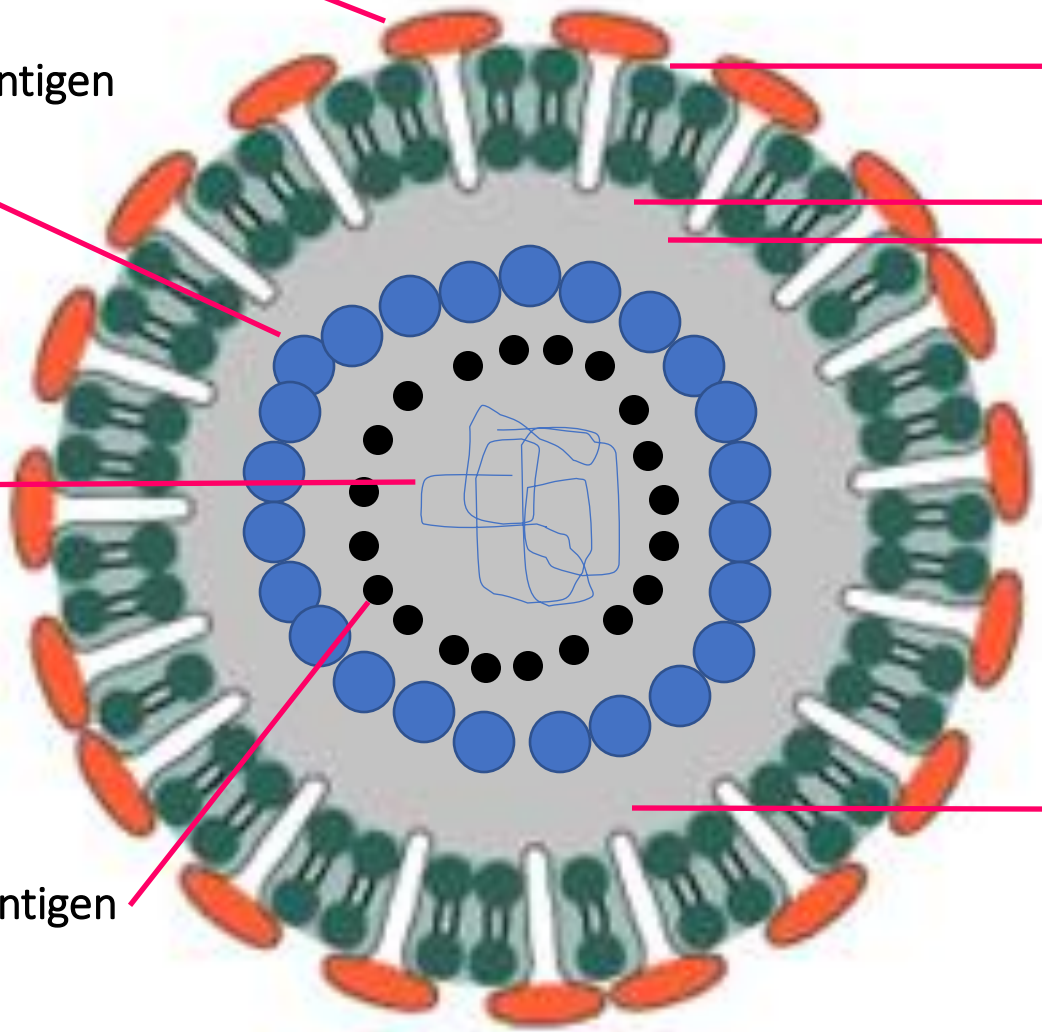
Hepatitis B

- Hepadnavirus:

Ds DNA, Partial, has enzyme

- For vaccine purposes: HBV has one serotype
- For epidemiology and medicolegal purposes there are 4 strains of HBV (ayw, adw, ayr, adr).

Hepatitis B


Hepatitis B surface antigen
(HBsAg)
Hepatitis B core antigen
(HBcAg)
Viral DNA
Hepatitis B e antigen
(HBeAg)
Envelope
Nucleocapsid

Hepatitis B

Transmission (blood borne):

- Parenteral via blood or plasma, needle stick injury
- Body fluids
- Vertically: mother to baby

Risk groups:

- Health care workers
- Drug abusers
- Recipients of blood or its products (blood should be ideally screened)
- Dialysis patients
- Homosexual men

Hepatitis B

Pathogenesis:

- Blood borne > liver cells > hepatocytes injury and necrosis.
- Largely cell mediated

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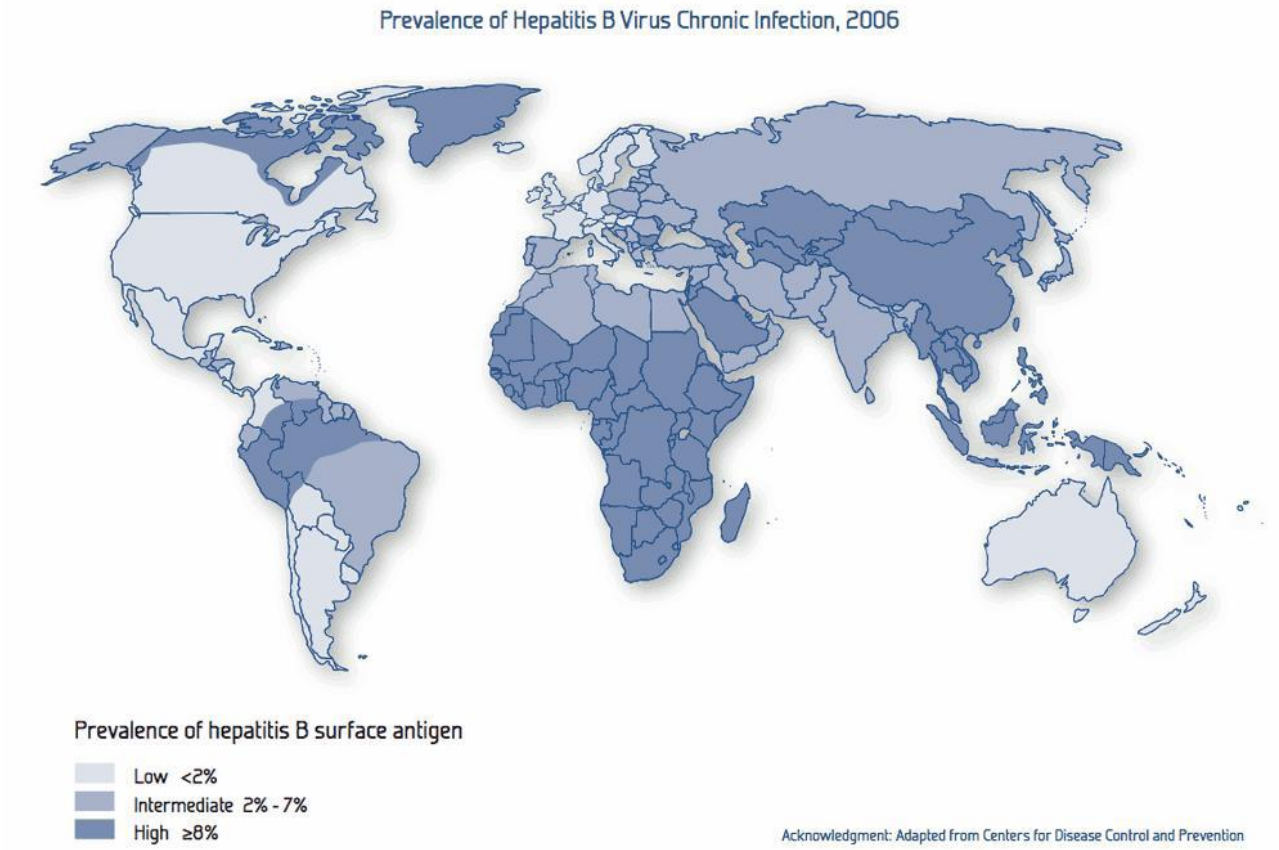


Hepatitis B

Clinically:

- **Incubation period:** 1-6 months (depends on the infectious dose)
- **Asymptomatic:** 90% of children and 50% of adults (increased liver enzymes)

- **Symptomatic:**
- Preicteric phase: flu like symptoms nausea, anorexia, malaise
- Icteric phase: Jaundice, pale stool, dark-coloured urine, increased liver enzymes and billirubin

Hepatitis B

Outcome:

- 90-95% recovery
- 5-10% chronic carriers (sAg > 6 months):
- chronic active hepatitis (more fatal)
- 1% fatality
- 1% of HBV chronic carriers develop hepatocellualr carcinoma

Diagnosis:

1. Clinical picture
2. Liver, kidney function tests, other tests to role out other causes e.g: CMV, EBV infection
3. Serology: very important in diagnosis.

- DNA detection

Hepatitis B Serology

	HBsAg	Anti-HBs	Anti-HBc
Susceptible	Negative	Negative	Negative
Vaccinated	Negative	Positive	Negative
Past Infection	Negative	Positive	Positive
Acute Infection	Positive	Negative	IgM Positive
Chronic Infection	Positive	Negative	IgG Positive

Hepatitis B

Prevention:

1. Immunoglobulin / passive for:

- Accidental exposure in non vaccinated
- Newborns of infected mothers

2. Vaccine (Recombinant HBsAg):

- Check response by measuring anti HBsAg antibodies (>10mIU/ml is protective)
- Part of ministry of health vaccination program (three IM doses at 2, 3, 4 months)

Hepatitis B

Hepatitis B Vaccine

Infants: several options that depend on status of the mother

- If mother HBsAg negative: normal HBV vaccination schedule (2, 3, 4 months)
- If mother HBsAg positive:
  - vaccine and Hep B immune globulin within 12 hours of birth
  - The vaccine should be given at zero time, 1st month, 2nd month, 3rd month, and at 4th month.

Check response by measuring anti HBsAg antibodies (>10mIU/ml is protective).

Treatment:

1. Interferon alpha
2. Lamivudine, Tenofovir

Hepatitis B Virus

Why does HBV cause chronic infection?

- Chronic hepatitis B infection lasts six months or longer.
- It lingers because your immune system can't fight off the infection.
- Differences in the strength and broad polyclonality of CD8+ cytolytic-T cell responsiveness and in the elaboration of antiviral cytokines by T cells explained the differences in outcomes between those who recover after acute hepatitis, and those who progress to chronic hepatitis, or between those with mild and those with severe (fulminant) acute HBV infection.
- Chronic hepatitis B infection may last a lifetime, possibly leading to serious illnesses such as cirrhosis and liver cancer.

Hepatitis D

- Defective –ssRNA virus
- It needs HBV to replicate (provide the envelop)

- Route of transmission:

As HBV

Conditions:

1. Co- infection with HBV
2. Super infection of HBV chronically infected patients (High risk of liver failure).

Diagnosis: serology

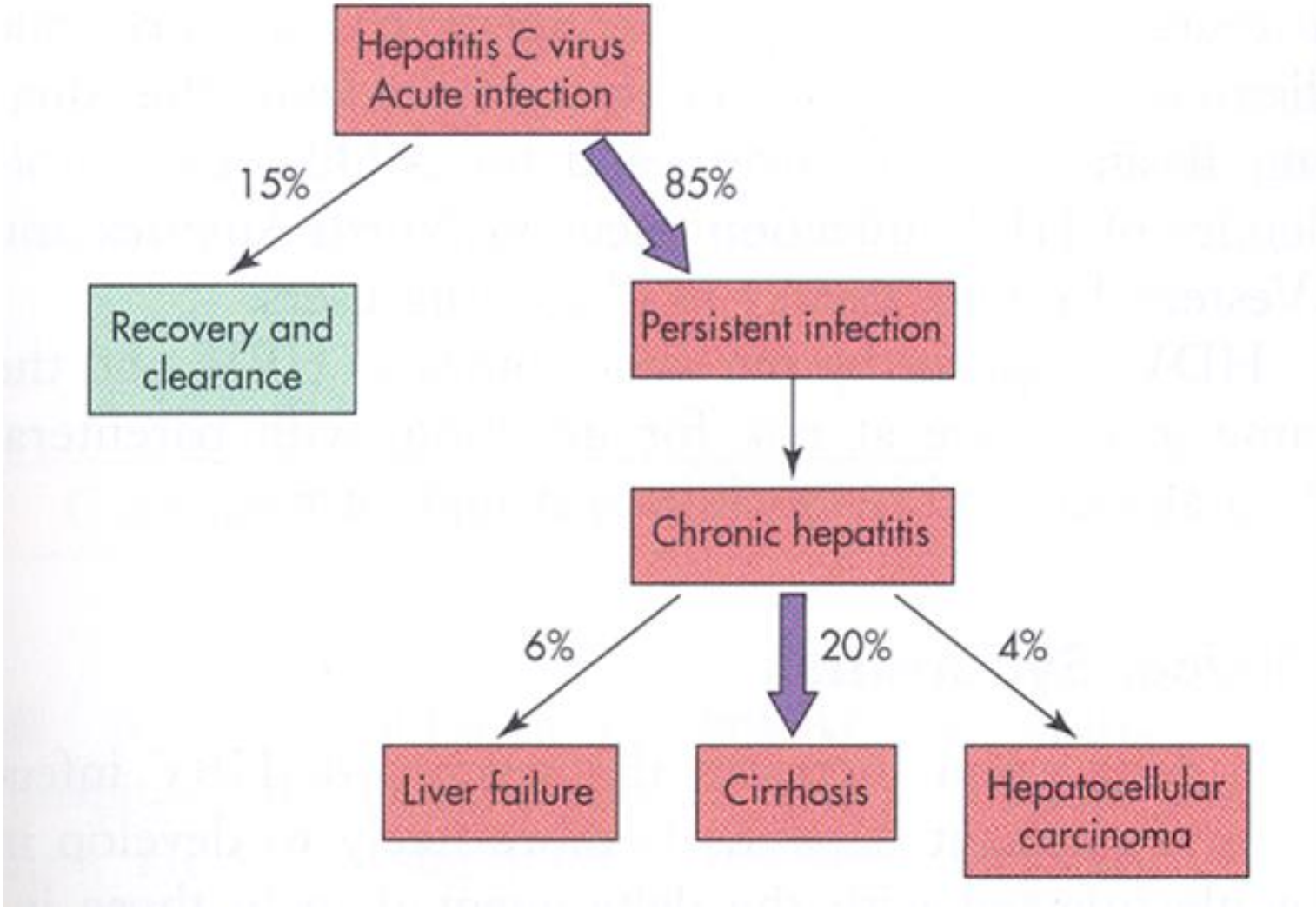
Rx: as HBV

Hepatitis C

- Flavivirus, (+) ssRNA genome, enveloped icosahedral capsid
- 6 genotypes
- Spread via infected blood and sexual contact
- 6-8 week incubation period / most infections are sub-clinical
- Clinical infections are generally less severe than HBV, damage due to cell mediated immune response
- HCV has a higher incidence of chronic liver disease than HBV (70-80% of patients remain viremic for more than 1 year)
- 170 million cases globally

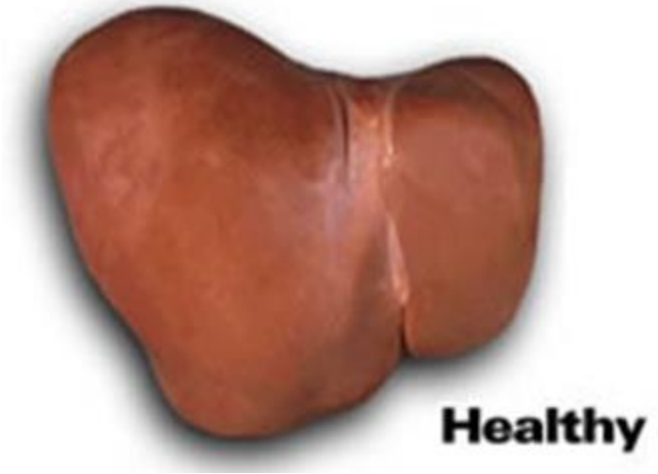
Hepatitis C

Outcomes of HCV infection



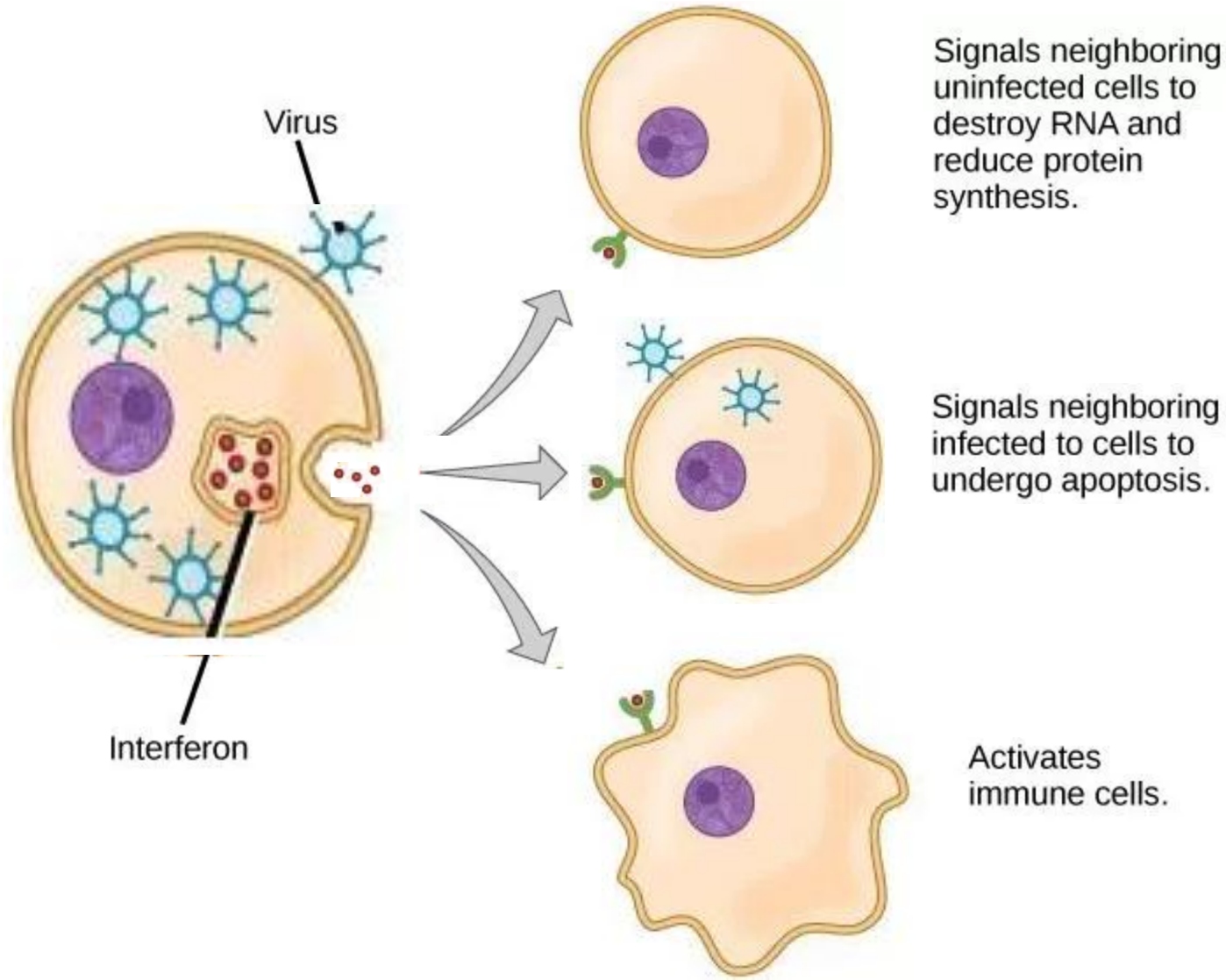
Hepatitis C

Why dose HCV infection progress from acute into chronic infection?



Hepatitis C

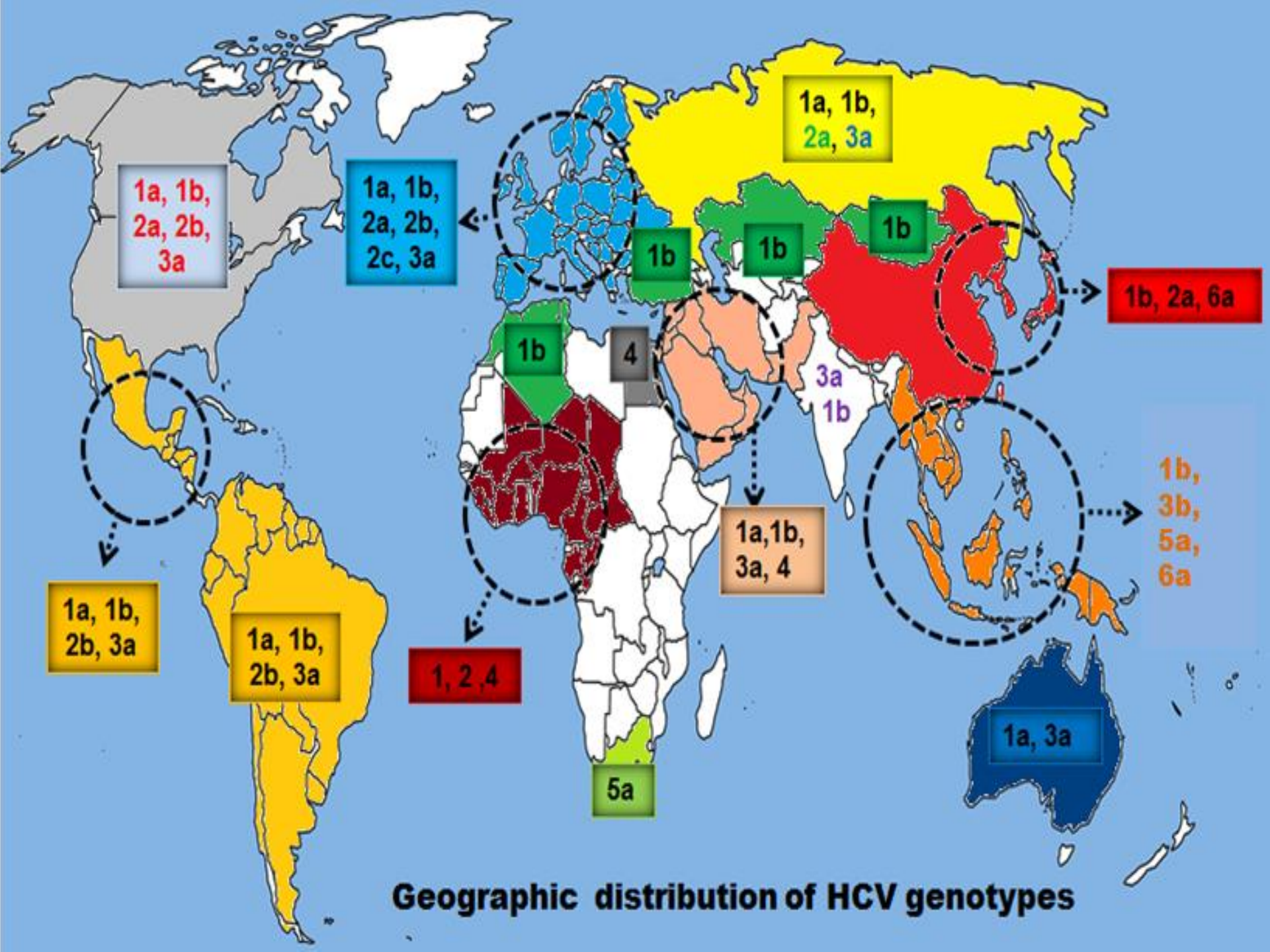
The functions of interferons



Hepatitis C

Why dose HCV progress into chronic infection?

- HCV inhibits the effect of interferon responses .
- HCV downregulates the expression of HLA class 1.
- Some viral antigens resemble the host cell antigens which causes autoimmune response against self antigens which explains the association between hepatitis C and a subset of patients with autoimmune hepatitis.
- High mutation rates: **At least six** distinct major genotypes and **>50 subtypes within genotypes this will be associated with a** lack of a robust T-lymphocyte response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1b, 3b, 5a, 6a
1a, 1b, 2b, 3a
1a, 1b, 2b, 3a
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5a
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Geographic distribution of HCV genotypes

Hepatitis C

Symptoms of Hepatitis C

- Majority of people (70-80%) do not experience symptoms
- If symptoms do arise, they are generally mild/flu-like:
  - Fatigue
  - Muscle pain
  - Poor appetite
  - Nausea/vomiting
  - Fever
  - Itchy skin
  - Dark urine
  - Jaundice

Hepatitis C Virus

Types of Tests Used to Diagnose Hepatitis C

- Screening tests for antibody to HCV (anti-HCV)
- HCV RNA polymerase chain reaction [PCR])
- Quantitative tests to detect amount (titer) of virus
- Genotyping
- Liver biopsy

Treatment:

Interferon alpha

Ribavirin

Characteristics	Hepatitis A	Hepatitis B	Hepatitis C
Virus type	RNA	DNA	RNA
Virus size	27 nm	42 nm	30-60 nm
Incubation period	15 – 50 days	30 – 180 days	30 – 160 days
Transmission	Fecal – oral	Parentral or body fluid	Parentral sporadic
Vertical transmission to fetus	In rare circumstances	Common	Uncommon
Serologic diagnosis	Hepatitis A antibody IgM and IgG types	HBs Ag, HBs Ab, IgM, and IgG types HBe Ag, Ab, Hepatitis B virus DNA	Hepatitis C antibody RNA by PCR
Maximum infectivity	Prodrome	Prodrome or HBe Ag Positive	HIV co- infected
Carrier state	None	5 – 10%	50 – 85%
Acute clinical forms	Asymptomatic to fulminant	Asymptomatic to fulminant	Asymptomatic to sev relapsing
Chronic clinical forms	None	Chronic persistent hepatitis Chronic active hepatitis Cirrhosis	Chronic persistent hepatitis Chronic active hepatitis Cirrhosis