



GIT Module 2021-2022

Viral Hepatitis

Dr. Mohammad Odaibat
Department of Microbiology and Pathology
Faculty of Medicine, Mutah University

Types of viral hepatitis

HAV:

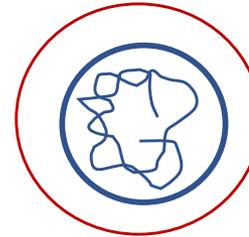
- Acute (<6months)
- Fecal Oral



ssRNA
Nonenveloped

HBV:

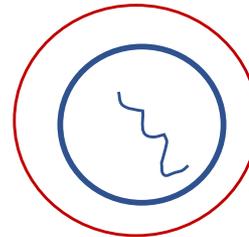
- Acute and chronic
- Sex, blood, perinatal



dsDNA
Enveloped

HCV:

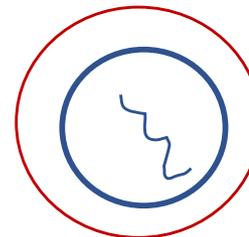
- Acute and chronic
- Sex, blood, perinatal



ssRNA
Enveloped

HDV:

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



ssRNA
Enveloped

HEV:

- Acute (<6months)
- 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
- *Contaminated 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

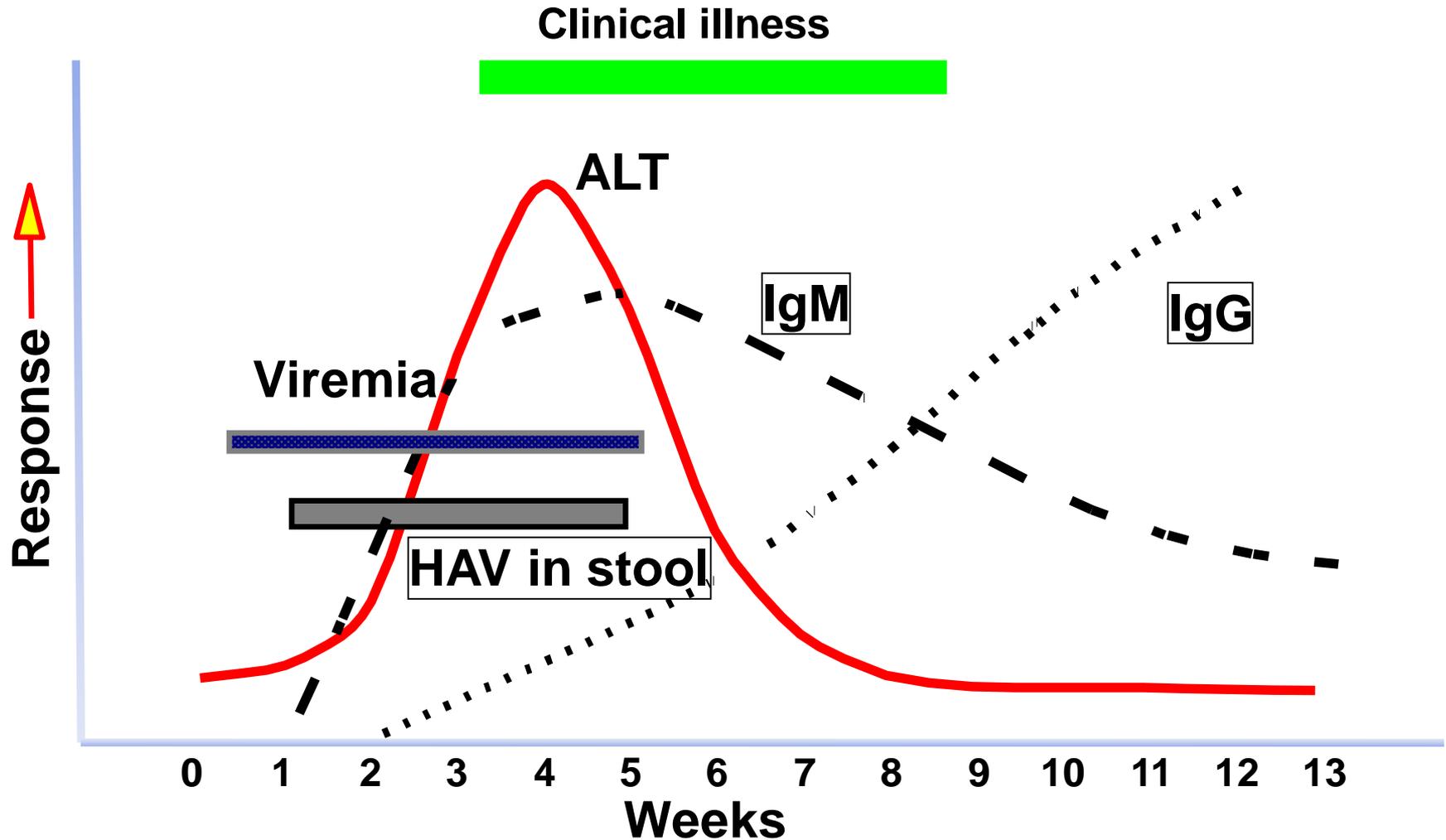
Clinically:

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

Diagnosis:

- Clinically
- Liver enzyme (reflect hepatocellular injury and aminotransferase levels may be elevated between 500 and 5000).
- Serology: diagnosis requires presence of 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.
- ✓ Sometimes Hepatitis A can cause 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)
 - Available since 1940
 - Immunoglobins administered low dose provides protection for 1-2 months
- Inactivated HAV vaccine
 - Available since 1992

Hepatitis A

Diagnosis

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

Prognosis

- HAV is usually a benign course in young, healthy people and is associated with a low mortality.
- Older adults, immunosuppressed patients and those with chronic liver disease have greater morbidity and mortality
- Mortality 0.1-2%

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)

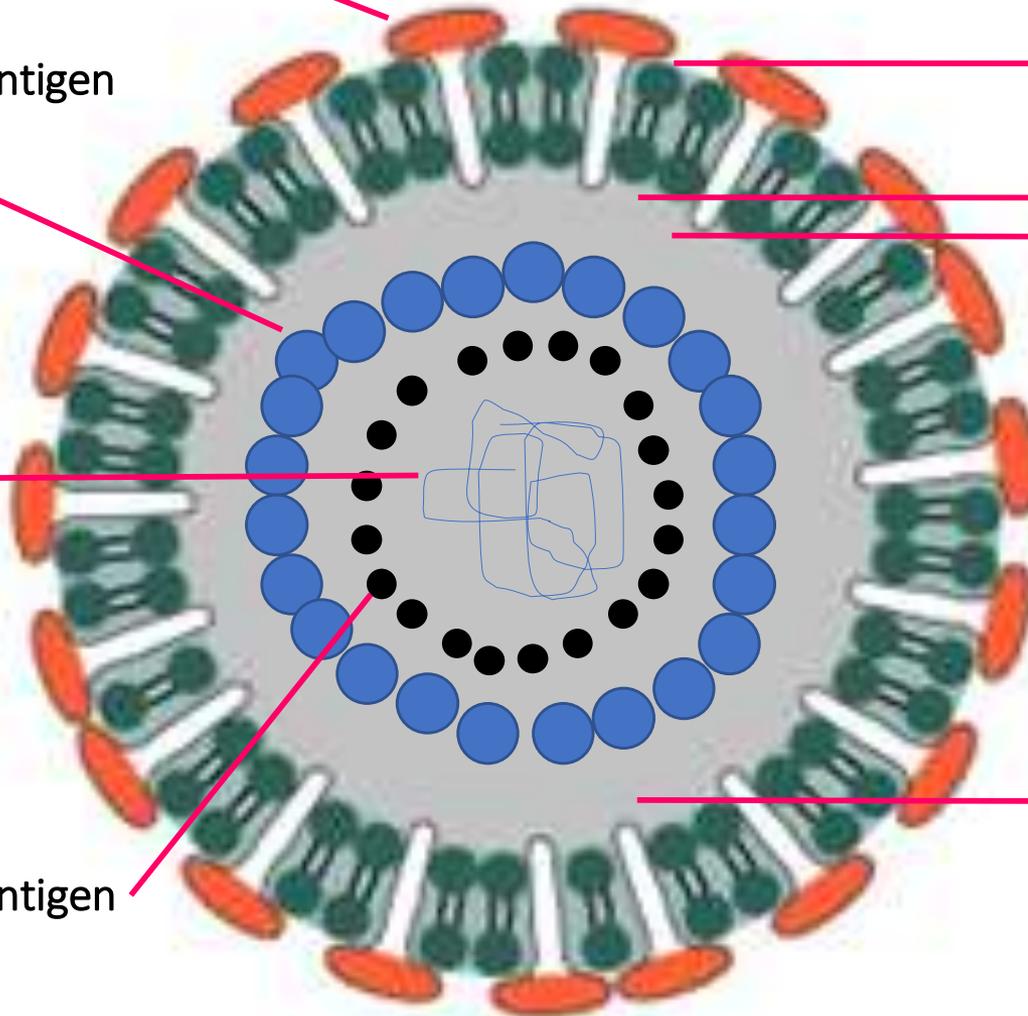
Hepatitis B core antigen
(HBcAg)

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:

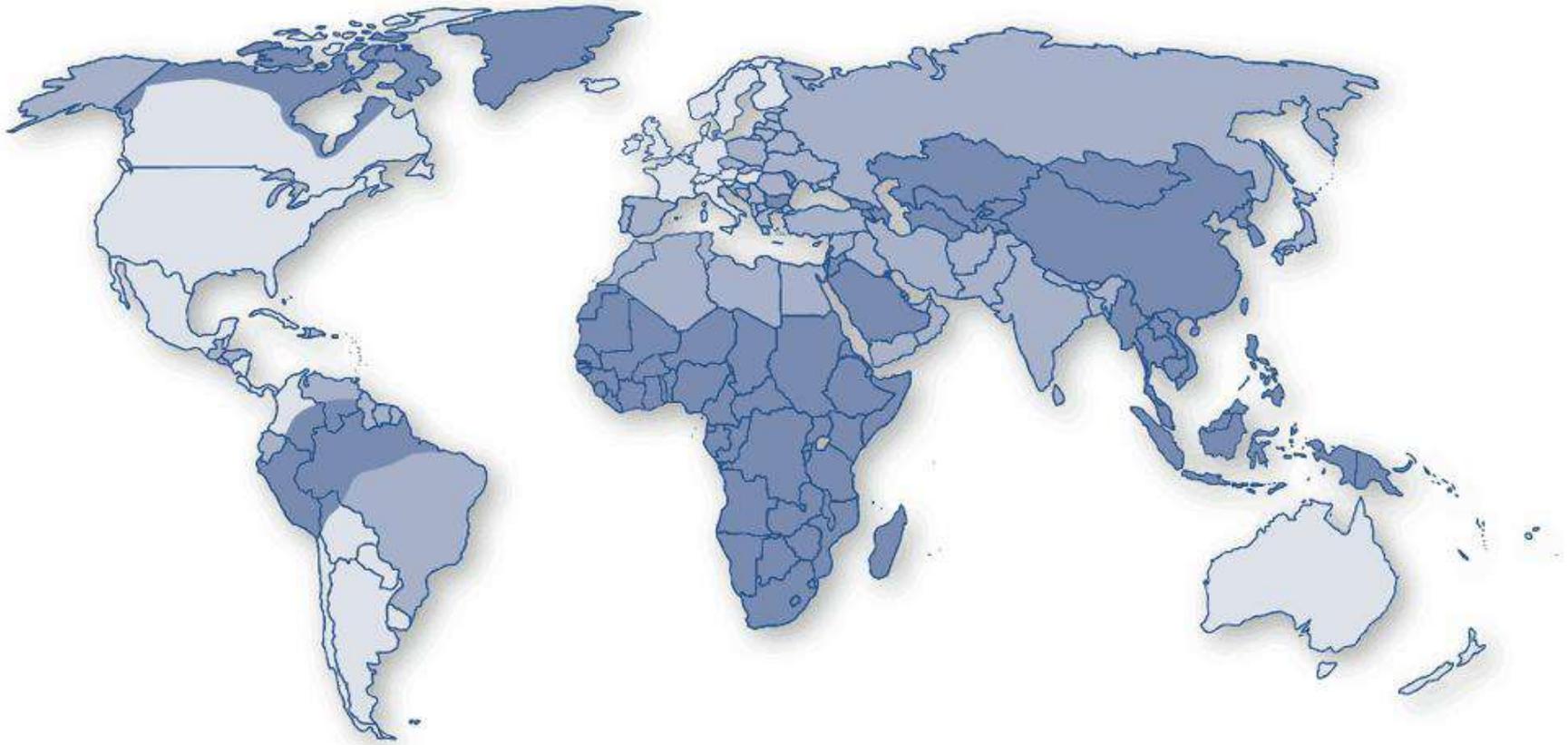
- Blood borne > liver cells > hepatocytes injury and necrosis.
- Largely cell mediated

Epidemiology:

- 350 million carriers worldwide
- 10-30 million infected each year.
- 1 million people die each year.
- Approximately 2 people die each minute.

Hepatitis B

Prevalence of Hepatitis B Virus Chronic Infection, 2006



Prevalence of hepatitis B surface antigen

- Low <2%
- Intermediate 2% - 7%
- High $\geq 8\%$

Acknowledgment: Adapted from Centers for Disease Control and Prevention

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 hepatocellular carcinoma

Diagnosis:

1. Clinical picture
 2. Liver, kidney function tests, other tests to rule out other causes
e.g: CMV, EBV infection
 3. Serology: very important in diagnosis.
 - s, e antigens and antibodies
 - Anti core antibodies
- DNA detection

Screening tests for virologic markers of HBV infection include HBsAg, anti-HBs, and anti-HBc^{1,2}

Screening Tests ^{1,2}			Interpretation	Recommended Follow-up
HBsAg	Anti-HBs	Anti-HBc ^a		
+	-	+	Acute or chronic infection ^b	Contact patient for evaluation and further testing
-	+	+	Patient has immunity from previous infection	Follow up as appropriate ^{c,d}
-	+	-	Patient has immunity from vaccination	No further action required
-	-	-	Patient is at-risk for HBV infection	Vaccinate

^aAnti-HBc refers to total anti-HBc.¹

^bPatient is chronically infected if HBsAg+ for ≥6 months.³

^cPatients who are anti-HBc positive should be monitored closely during and after the administration of cytotoxic chemotherapy for signs of HBV reactivation.³

^dPatients with cirrhosis may need to be monitored for hepatocellular carcinoma per the AASLD guidelines.⁴

1. Keeffe EB, et al. *Gastroenterol Hepatol*. 2008;8(3):335-343; 2. CDC. Interpretation of Hepatitis B Serologic Test Results. <http://www.cdc.gov/hepatitis/HBV/testingchronic.htm>. Updated December 11, 2013. Accessed March 25, 2015; 3. CDC. *Morbidity and Mortality Weekly Rep*. 2008;57(1-20); 4. Brails J, Sherman M. *Hepatology*. 2011;53. http://www.aasld.org/sites/default/files/guideline_documents/HCCupdate2010.pdf. Accessed March 25, 2015.

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

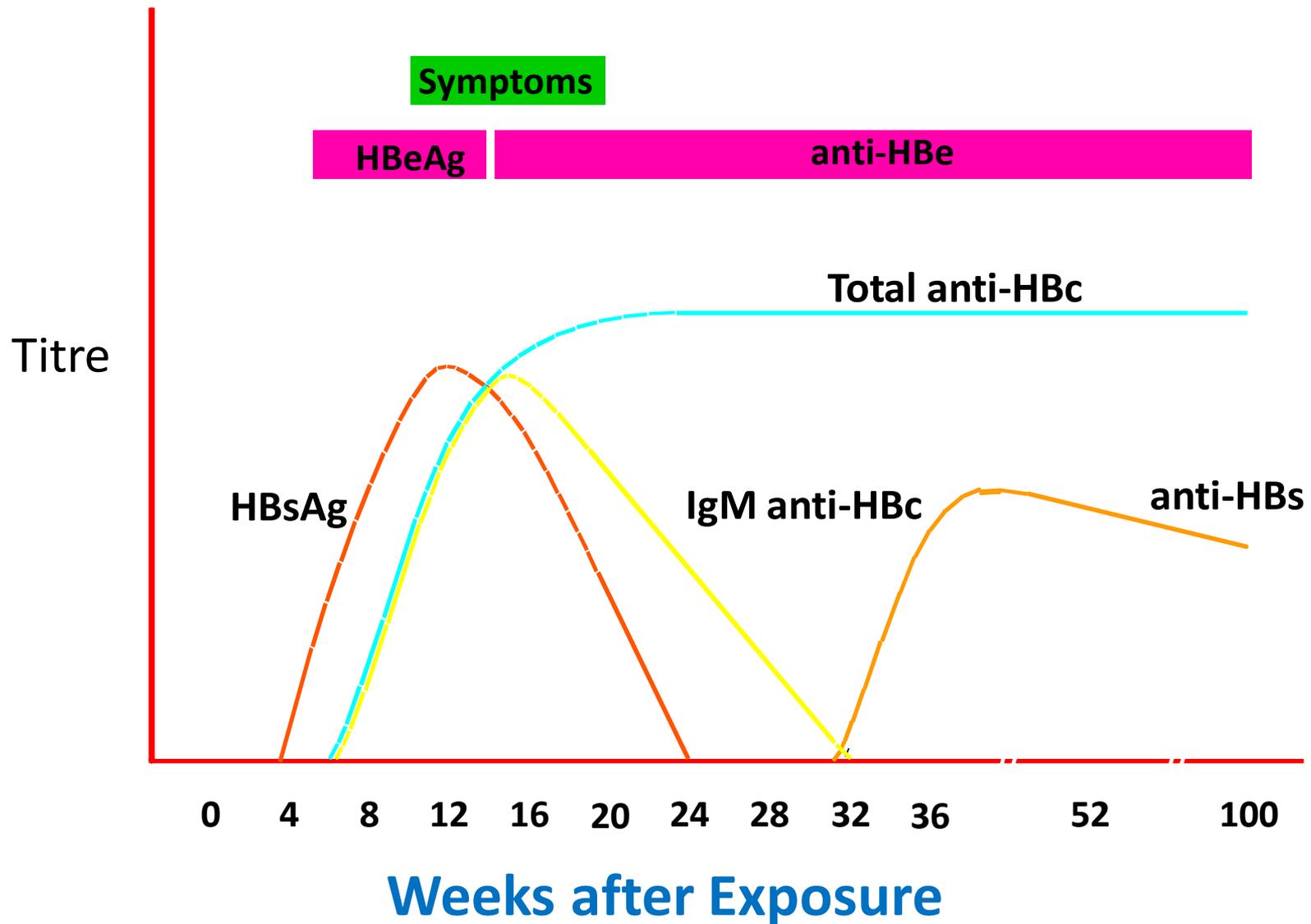
Hepatitis B Virus

Why does HBV cause chronic infection?

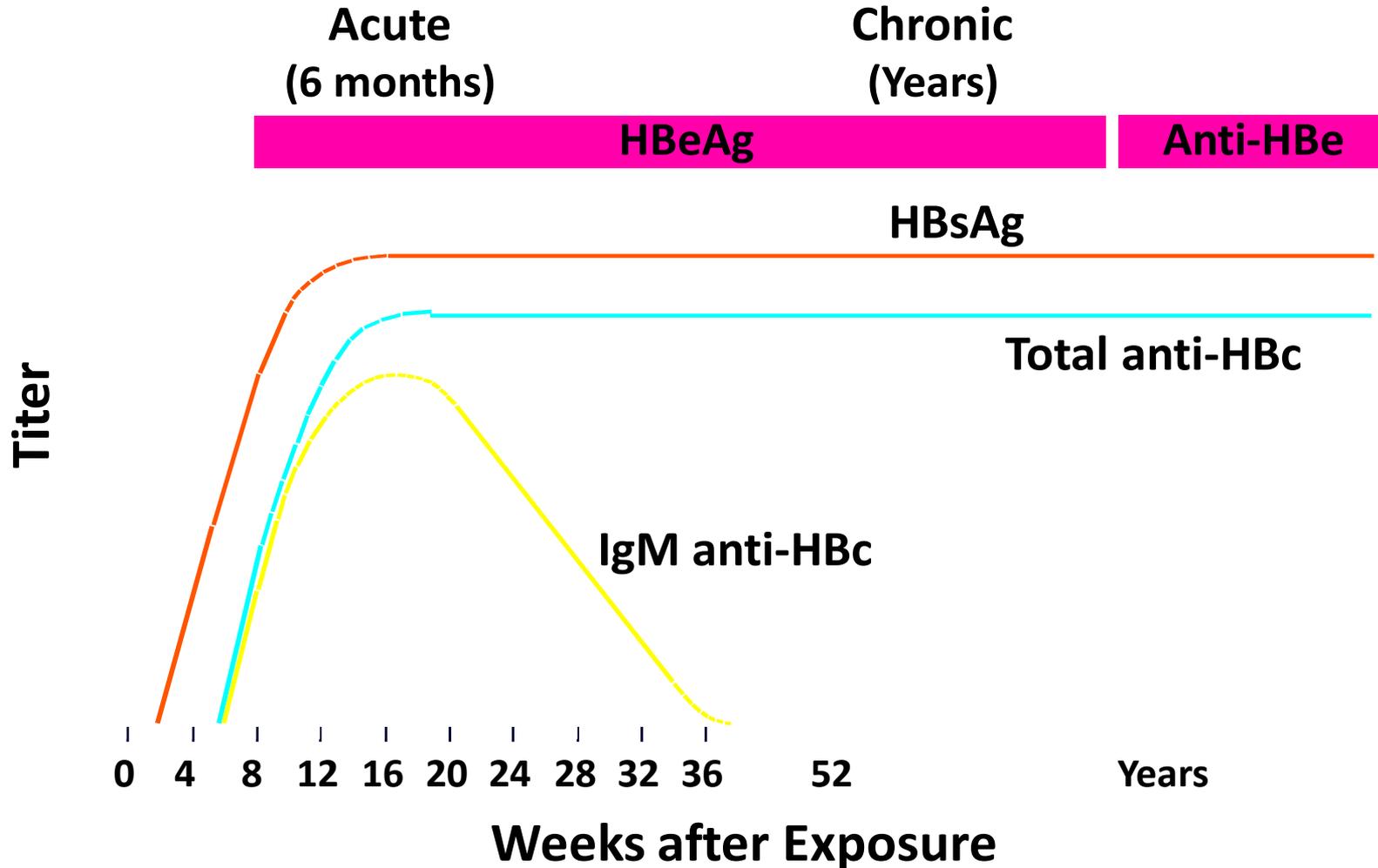
- Chronic hepatitis B infection lasts six months or longer.
- It lingers because your immune system can't fight off the infection.
- Differences in the robustness and broad polyclonality of CD8+ cytolytic T cell responsiveness and in the elaboration of antiviral cytokines by T cells explained the differences 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.

Acute Hepatitis B Virus Infection with Recovery

Typical Serologic Course



Acute HBV Infection with Progression to Chronic Infection: Typical Serologic Course



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

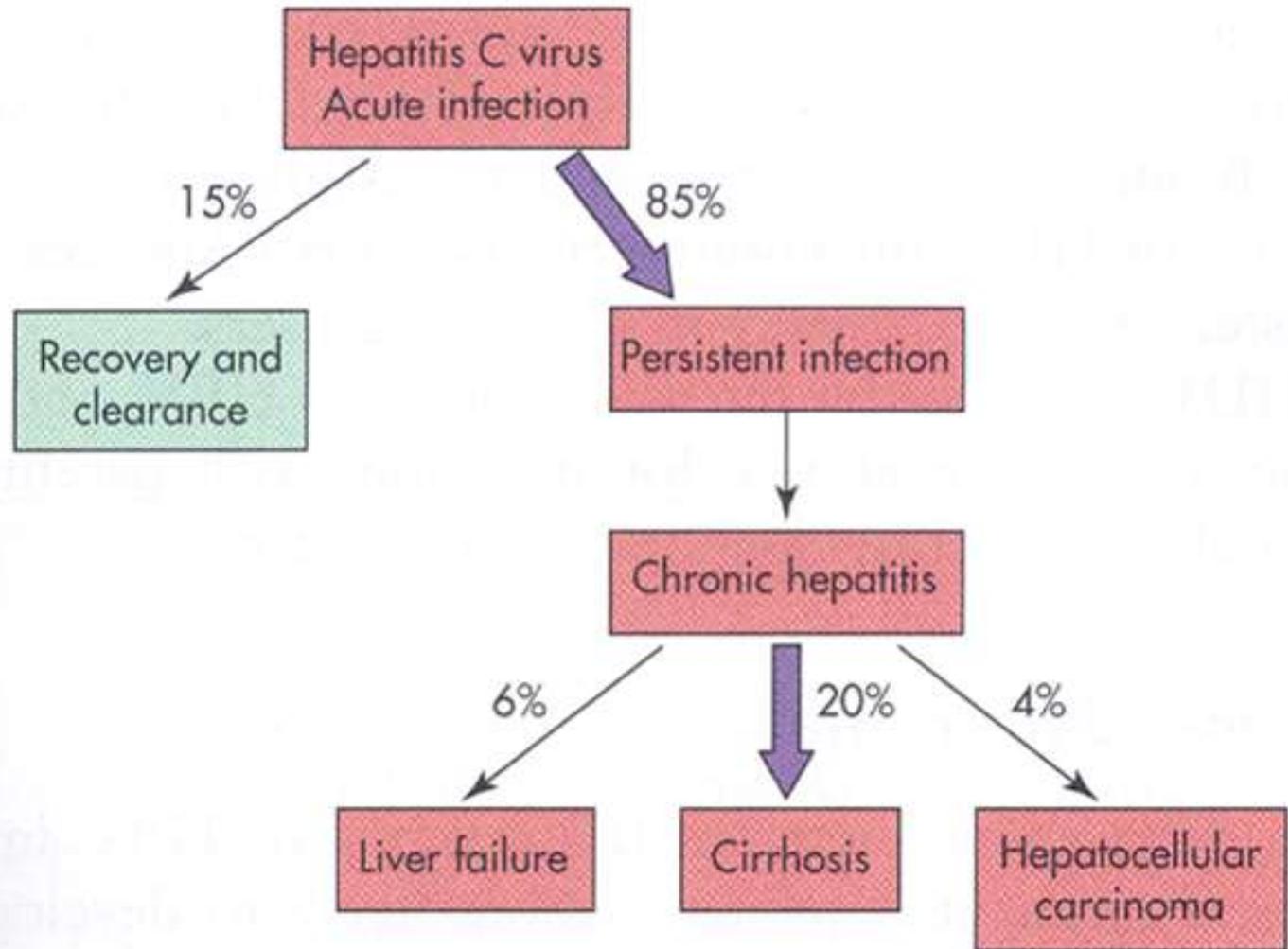
Rx: as HBV

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

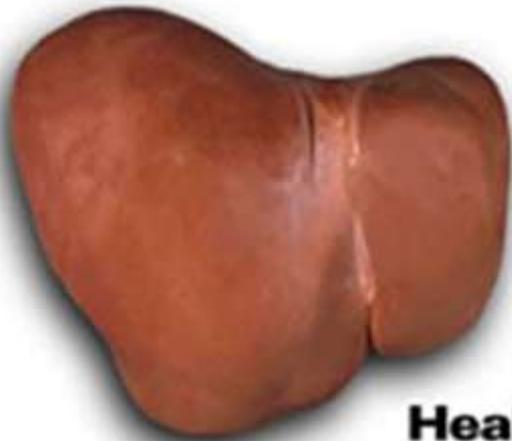
Hepatitis C

Outcomes of HCV infection



Hepatitis C

Why does HBV infection progress from acute into chronic infection?



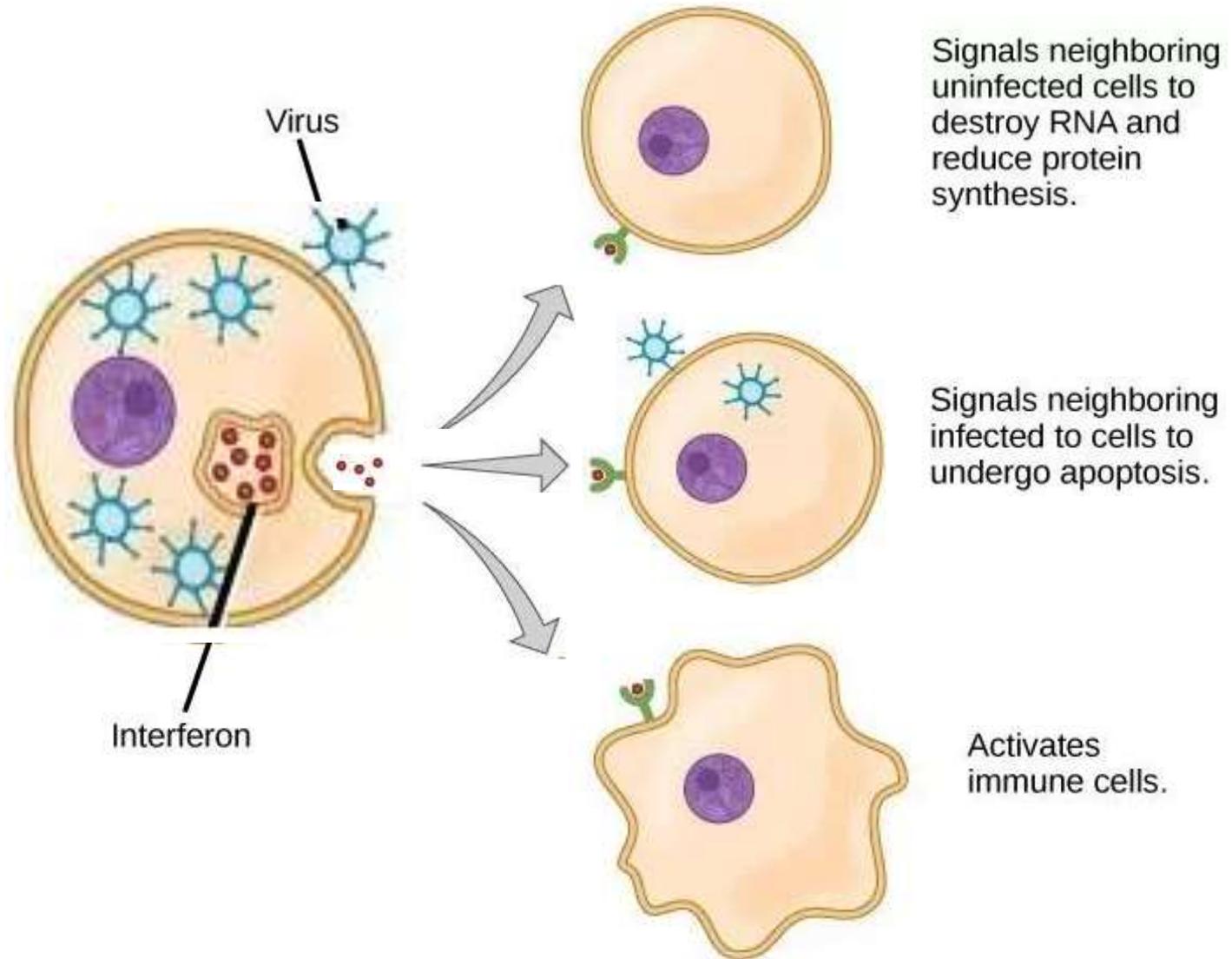
Healthy



Cirrhosis

Hepatitis C

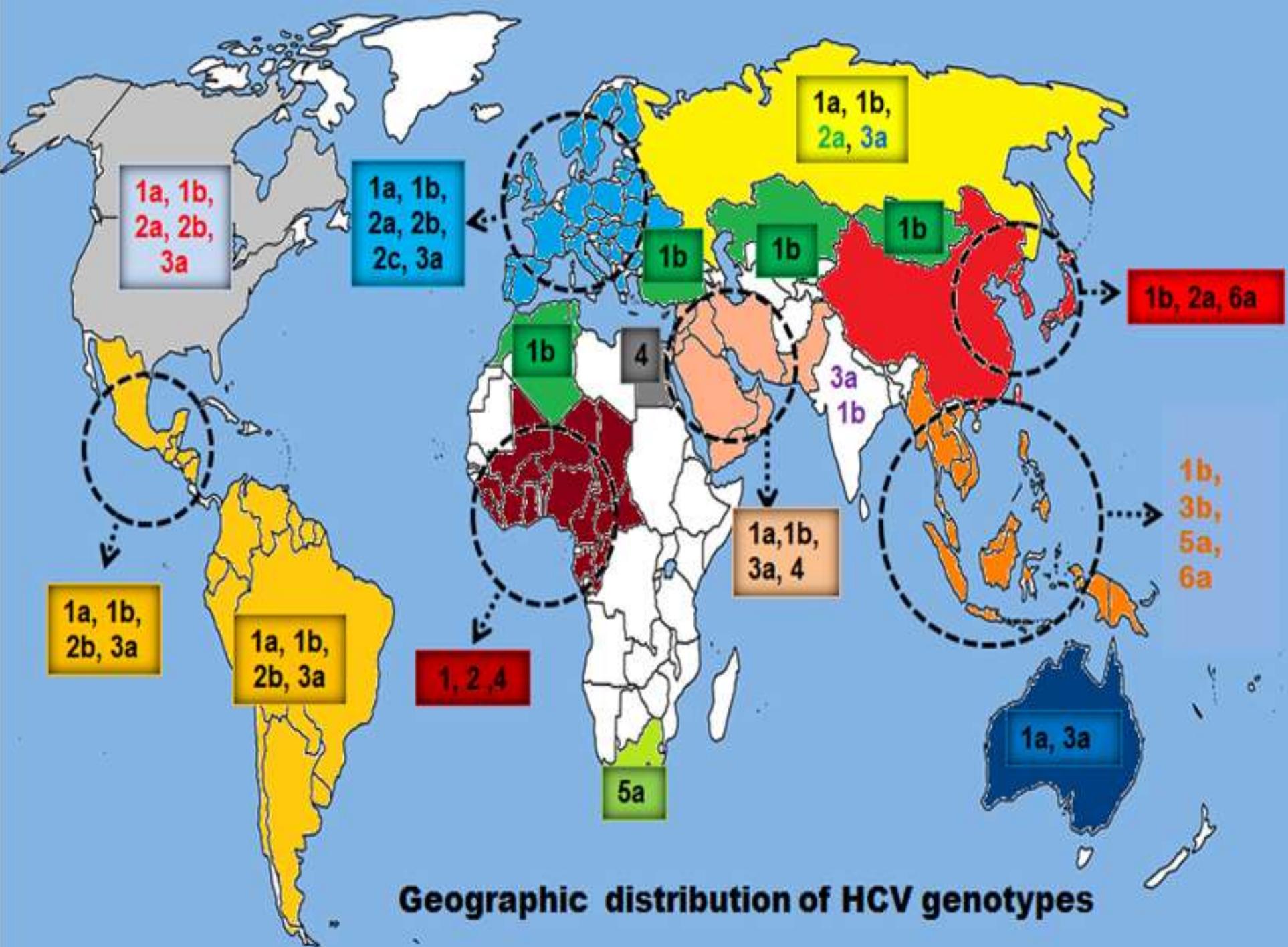
The functions of interferons



Hepatitis C

Why dose HCV progress into chronic infection?

- HCV proteins have been shown to inhibit 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



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	Parental or body fluid	Parental 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