

Hepatitis Viruses

By Nader Alaridah MD, PhD

Introduction

- Hepatitis: inflammation of liver; presence of inflammatory cells in organ tissue
- The causes of hepatitis are varied and include viruses, bacteria, and protozoa, as well as drugs and toxins (eg, isoniazid, carbon tetrachloride, and ethanol).
- Acute hepatitis: symptoms last less than 6 months
- Viral Hepatitis: is inflammation of the liver induced by viral infections
- The clinical symptoms and course of acute viral hepatitis can be similar, regardless of etiology, and determination of a specific cause depends on laboratory tests.

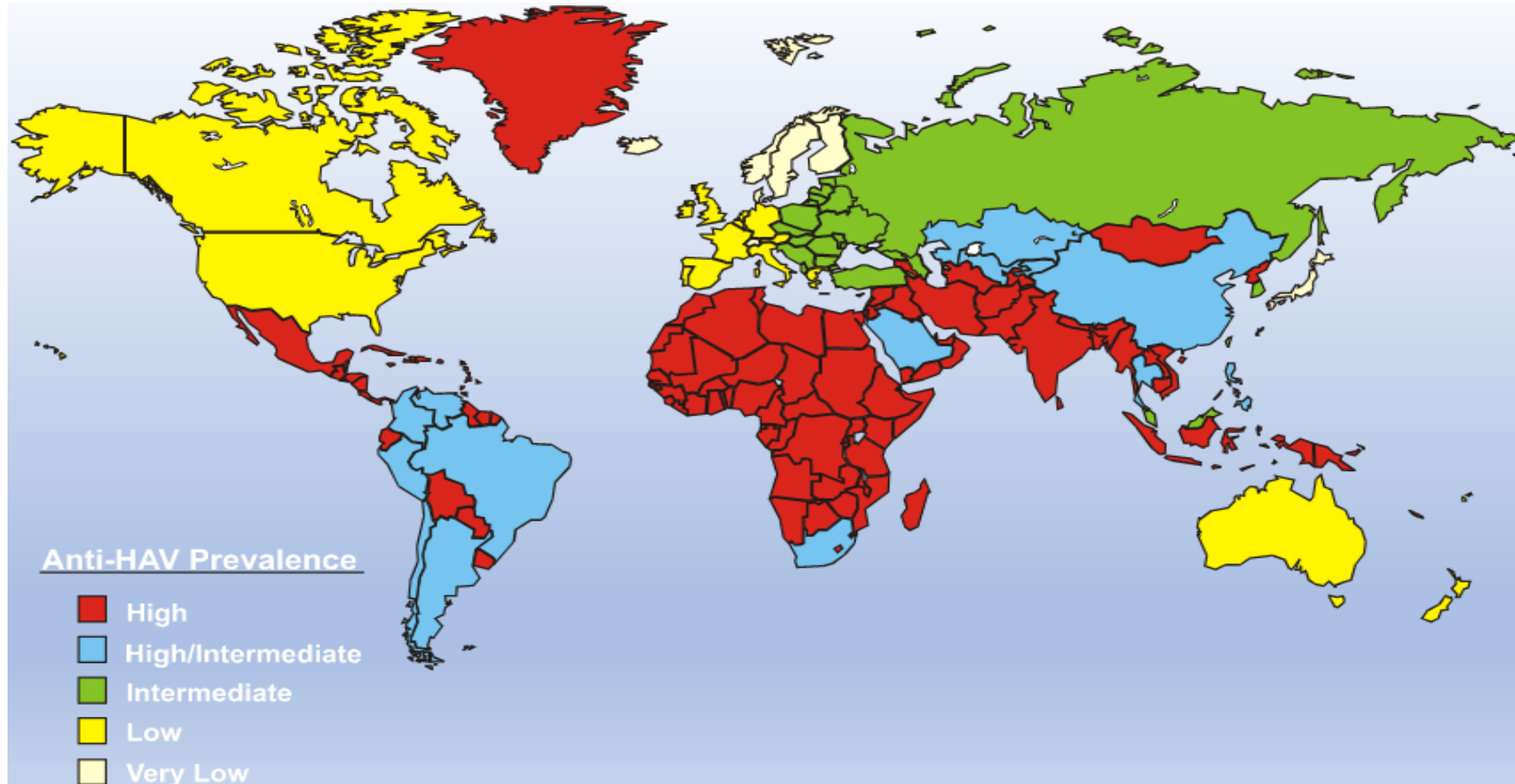
Viral hepatitis *types*:

- A: Picornavirus: +ssRNA, Non enveloped
- B: Hepadnavirus Ds DNA, Partial, has enzyme, enveloped
- C: Flavivirus, +ssRNA genome, enveloped
- *D: Deltaviruses, Defective –ssRNA virus*
- E: Hepevirus, +ssRNA non enveloped

Hepatitis A

- A typical Enterovirus , also known as enterovirus 72
- Naked Icosahedral nucleocapsid virus with a single stranded positive polarity RNA. No virion polymerase. One serotype
- Enterically transmitted (fecal/oral route)
- *Ingestion* > Multiplies in oropharynx and intestinal epithelial cells > blood > Liver > Periportal necrosis + mononuclear infiltrates
- Virus is not cytopathic but the CMI causes cell necrosis

Epidemiology of *Hepatitis A*



Clinical Manifestations

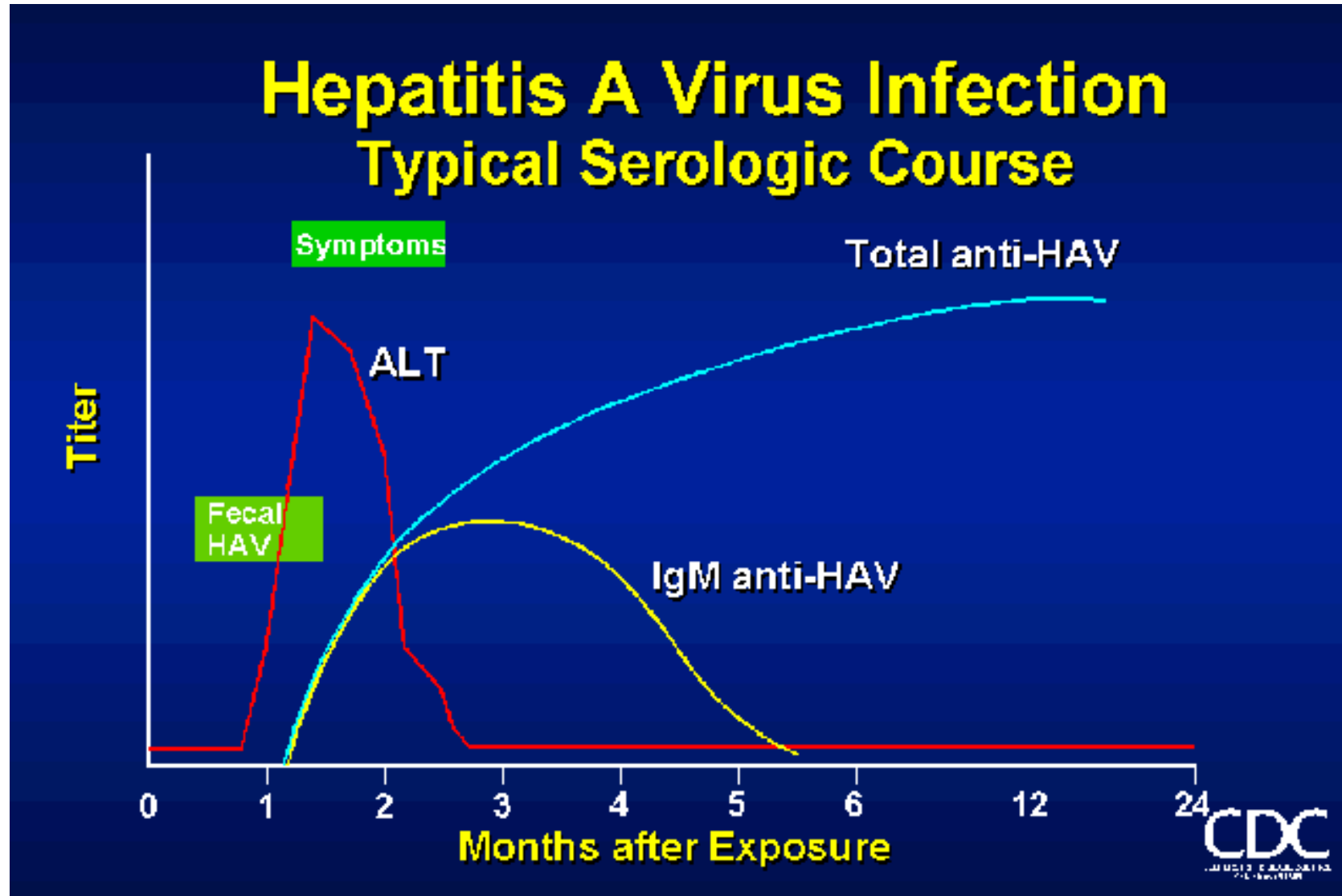
- Incubation period: 2-6 WEEKS
- Most HAV infections are asymptomatic.
- fever; anorexia; nausea, vomiting and jaundice .
- Abdominal pain, hepatomegally, splenomegally, Dark urine and clay-colored stools and elevated transaminase levels.
- Resolve spontaneously in 2-4 weeks.

Hepatitis A Diagnosis:

- Clinically
- *Liver enzyme: High AST and ALT, mild elevation of bilirubin.*

- *Serology: IgM, IgG (life long immunity)*
 - *IgM: Acute infection remains high for 3-6 months*
 - *IgG: Past infection or vaccine*

Hepatitis A



- *Rx: Usually full recovery in 90% of patients in 3-6m*

➤ *Acute:*

- *Supportive: Do not give Paracetamol and Alcohol*
- *Immunoglobulins*

➤ *Fulminant hepatitis:*

- *Supportive, but may need liver transplantation*

• *Prevention:*

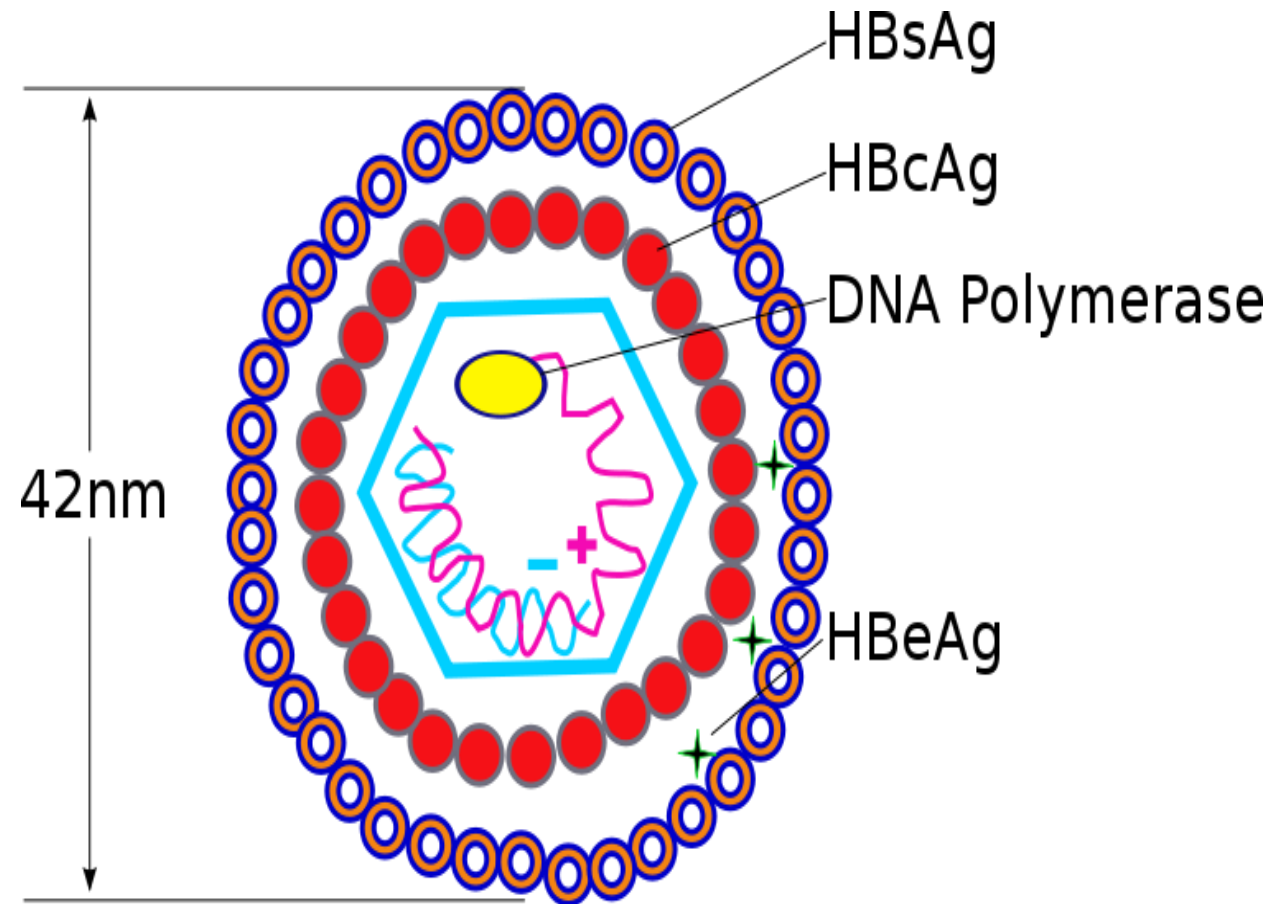
- *Hygiene, Vaccine: killed, IM 2 doses separated by 3- 6 months*

Hepatitis E Virus

- Hepatitis E virus is a none enveloped, single stranded RNA virus.
- The viral particles in stool are spherical, 27 to 34 nm in size, and unenveloped and exhibit spikes on their surface.
- Feco-oral transmission
- Waterborne epidemics of hepatitis
- High mortality rate in pregnant women.
- No chronicity , No carrier state.

Hepatitis B virus

- Hepadnavirus , Partially –Double stranded circular DNA genome.
- Enveloped
- Icosahedral nucleocapsid
- Antigens:
- The main components of the virus include the core - hepatitis B core antigen (HBcAg) and the pre-core hepatitis B e antigen (HBeAg), and the envelope of the virus contains the hepatitis B surface antigen (HBsAg)



Hepatitis B virus

➤ Transmission:

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

➤ Risk groups:

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

Hepatitis B virus

- Pathogenesis:
- Blood borne > liver cells > hepatocytes injury and necrosis (piecemeal necrosis) --
-Largely cell mediated.
- Clinically :
- Incubation period: 1-4 months (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



Hepatitis B virus

➤ 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 of HBV :

1. Clinical picture

2. Liver, kidney function tests, other tests to rule out other causes e.g: CMV, EBV infection

3. Serology:

- We rely on:

- S, e antigens and antibodies

- Anti core antibodies

- DNA detection

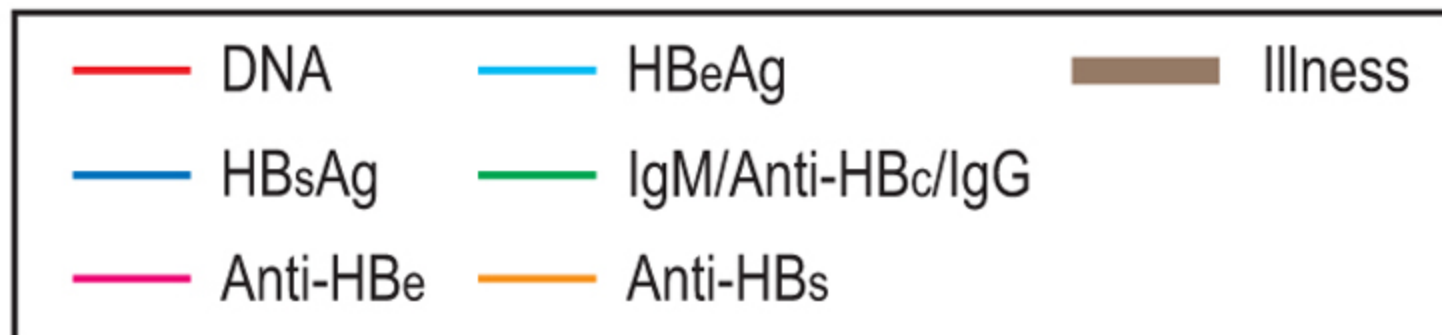
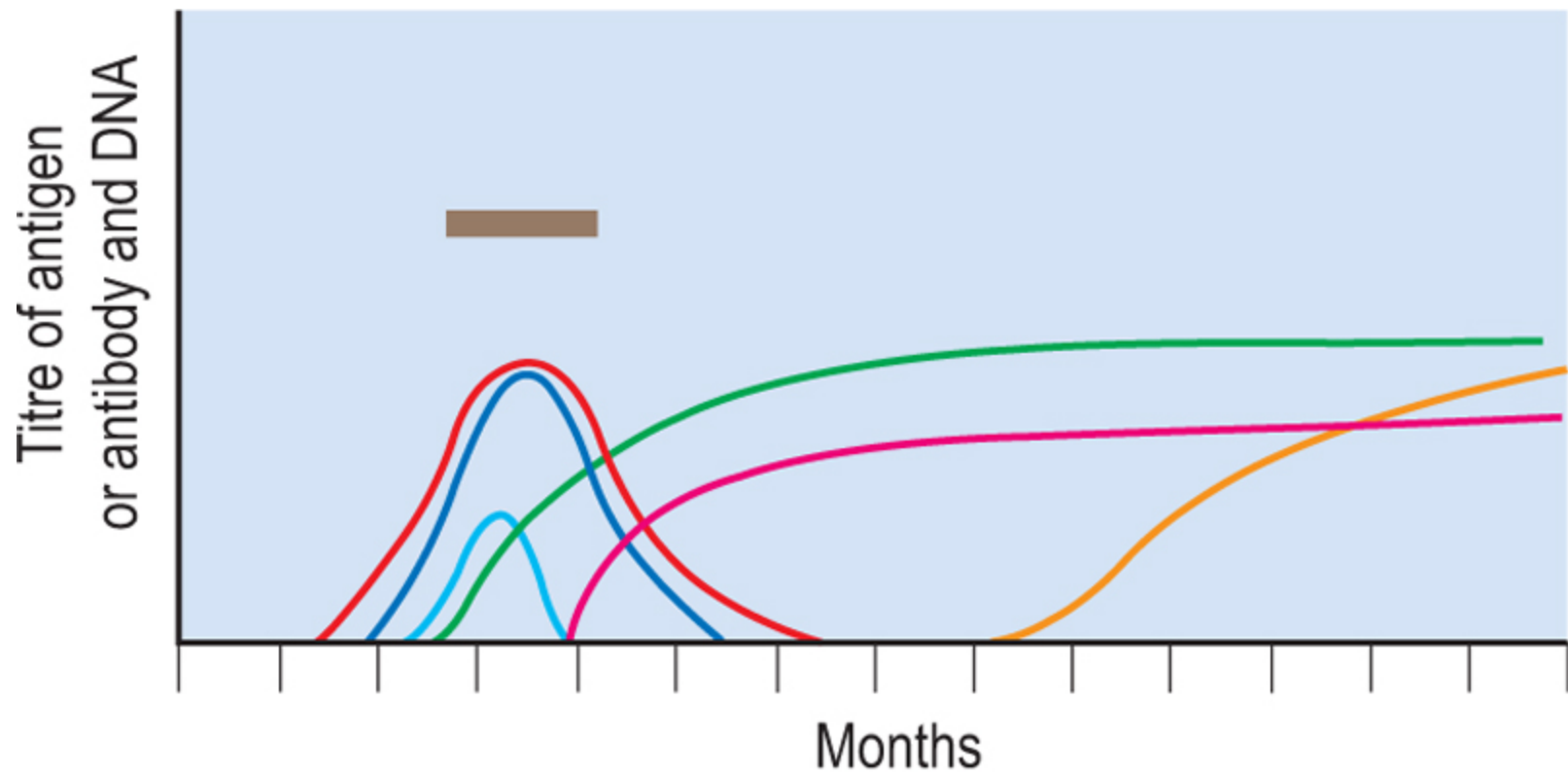


TABLE 41-4 Serologic Test Results in Four Stages of HBV Infection

Test	Acute Disease	Window Phase	Complete Recovery	Chronic Carrier State
HBsAg	Positive	Negative	Negative	Positive
HBsAb	Negative	Negative	Positive	Negative ¹
HBcAb	Positive ²	Positive	Positive	Positive

	HBsAg HBeAg* HBV-DNA	HBcAb IgM	HBcAb IgG	HBeAb	HBsAb
Acute infection	+	+	-	-	-
Window period	-	+/-	+	+	-
Prior infection	-	-	+	+	+
Immunization	-	-	-	-	+
Chronic infection	+	-	+	+/-	-

Hepatitis B virus

Treatment:

- 1. Peg Interferon alpha*
- 2. Lamivudine, Tenofovir, entecavir*

Prevention:

- 1. Immunoglobulin / passive*

Accidental exposure in non vaccinated

Newborns of infected mothers

- 2. Vaccine (Recombinant HBsAg) 3 I.M doses at 0, 1, 2 OR 6 months*

- Fridge storage*
- Check response by measuring anti HBsAg antibodies 2 months after last dose (>10mIU/ml is protective)*
- Part of ministry of health vaccination program (2, 3, 4 months)*

Hepatitis D virus

- *It needs HBV to replicate (provide the envelop)*
- *Route of transmission:*
- ✓ *As HBV*
- *conditions:*
- ✓ *Co- infection with HBv*
- ✓ *Super infection of HBV chronically infected patients
(High risk of liver failure)*
- *Diagnosis: serology*
- *Rx: as HBV*

Hepatitis C virus

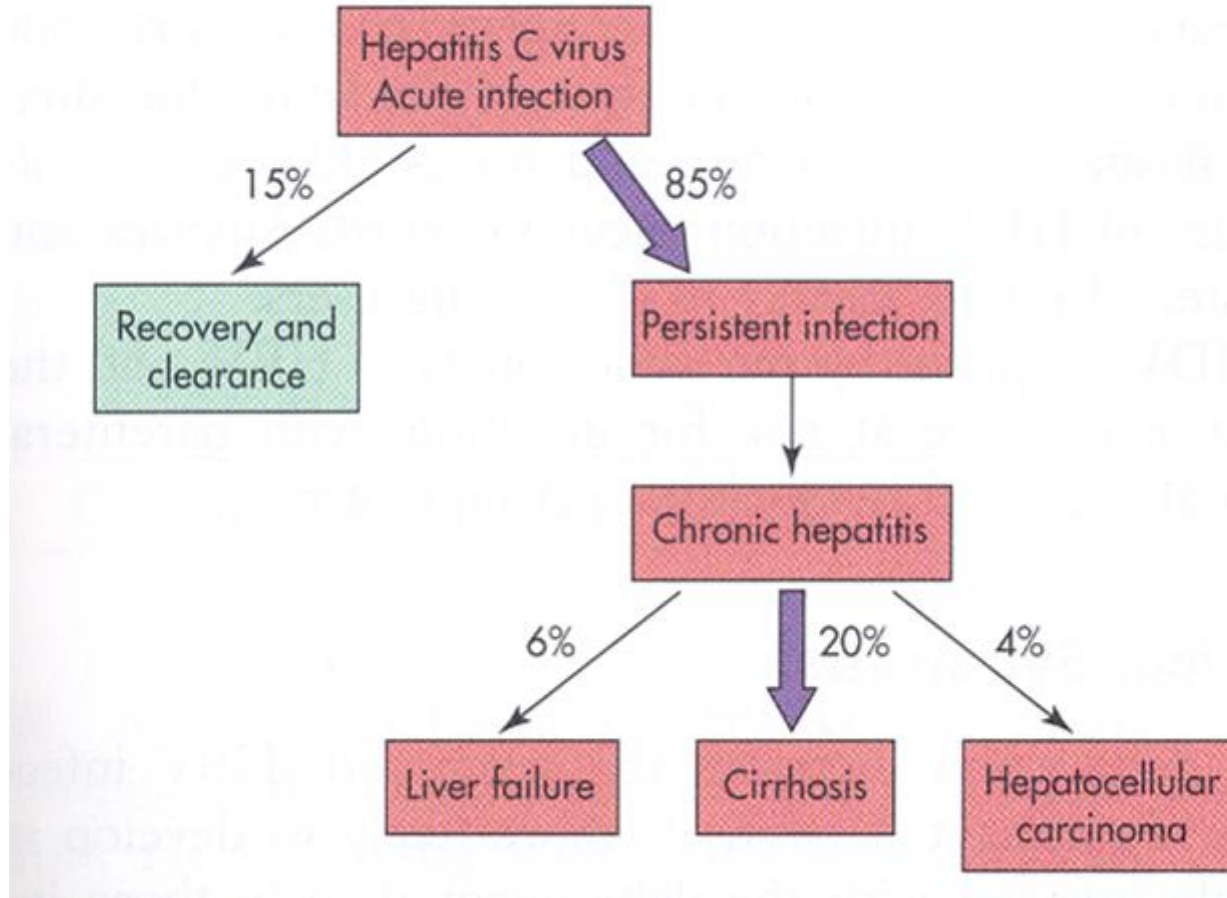
- Flavivirus, Enveloped , single stranded , positive sense RNA virus
- No polymerase in the virion
- 6 genotypes: needed for Rx and medicolegal
- Spread via infected blood and sexual contact
- 6 - 8 week incubation period / most infections are sub-clinical

- Clinical infections are generally less severe than HBV, damage due to cell mediated immune response

- *HVC 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 virus



Hepatitis C virus

Diagnosis:

- 1. Anti HCV IgM*
- 2. RNA detection*

Treatment:

antivirals

Hepatitis C virus / prevention

- No vaccine
- Blood screening

Public Health Service Guidelines for Counseling Anti-HCV-Positive Persons

Anti-HCV-positive persons should:

- Be considered potentially infectious
- Keep cuts and skin lesions covered
- Be informed of the potential for sexual transmission
- Be informed of the potential for perinatal transmission
 - no evidence to advise against pregnancy or breastfeeding

Anti-HCV-positive persons should not:

- Donate blood, organs, tissue, or semen
- Share household articles (e.g., toothbrushes, razors)

Post exposure prophylaxis

جدول رقم (9) الاجراءات الفورية بعد اصابة عمل

المريض مصدر الاصابة	الاجراء	الوضع التطعيمي للموظف
التهاب الكبد (B) موجب HBsAg (positive)	- اعطاء التطعيم فوراً + جرعة جليوبوليون مناعي* - إكمال كل الجرعات و اعطاء جليوبوليون مناعي* - فحص الاجسام المناعية (اذا كان أكثر أو يساوي 10 وحدة دولية لا شيء) **	- لم يتم تطعيمه - غير مكتمل الجرعات - ثلاث جرعات من التطعيم
التهاب الكبد (B) سالب HBsAg (negative)	- يتم تطعيمه - لا شيء	- لم يتم تطعيمه - تم تطعيمه
غير معروف اصابته بالتهاب الكبد ب	- يعامل كما لو كان مصدر الاصابة ايجابيا - يعامل كما لو كان مصدر الاصابة ايجابيا - يعامل كما لو كان مصدر الاصابة ايجابيا	- لم يتم تطعيمه - غير مكتمل الجرعات - ثلاث جرعات من التطعيم
حامل لمضاد فيروس التهاب الكبد (C)	فحص الموظف بعد الاصابة مباشرة ثم بعد اسبوعين و بعد شهر ثم بعد 3 اشهر بطريقة HCV-Ab و PCR و اذا ظهرت بوادر اصابته يحول الى أخصائي جهاز هضمي	لا يوجد لقاح للالتهاب الكبد (C)
غير معروف اصابته بالتهاب الكبد (C)	فحص الموظف بعد الاصابة مباشرة ثم بعد اسبوعين و بعد شهر ثم بعد 3 اشهر بطريقة HCV-Ab و PCR و اذا ظهرت بوادر اصابته يحول الى أخصائي جهاز هضمي	لا يوجد لقاح للالتهاب الكبد (C)
حامل لفيروس العوز المناعي البشري HIV	- مدة اربعة اسابيع يتم فيه تناول ثلاثة ادوية مضادة للفيروسات (مثل زيدوفودين ولاميفودين) ويجب الرجوع الى البرنامج الوطني لمكافحة الايدز*** - يبدأ العلاج فوراً (خلال ساعات)	لا يوجد لقاح لفيروس العوز المناعي البشري HIV

* يتم ذلك خلال 24 ساعة من التعرض للعدوى

** تقاس الاستجابة المناعية لمطعم الكبد (B) بفحص الاجسام المضادة (Hbs Ab) وتعتبر ايجابية اذا كانت أكبر أو يساوي 10

وحدة دولية

Table 1 summary

Comparison of A, B, D (Delta), C, and E Hepatitis

FEATURE	A	B	D	C ^a	E
Virus type	Single-stranded RNA	Double-stranded DNA	Single-stranded RNA	RNA	RNA
Percent of viral hepatitis	50	41	<1	5	<1
Incubation period (days)	15–45 (mean, 25)	7–160 (mean, 60–90)	28–45	15–160 (mean, 50)	?
Onset	Usually sudden	Usually slow	Variable	Insidious	?
Age preference	Children, young adults	All ages	All ages	All ages	Young adult
Transmission					
Fecal–oral	+++	±	±	–	+++
Sexual	+	++	++	+	+?
Transfusion	–	++	+++	+++	–
Severity	Usually mild	Moderate	Often severe	Mild	Variable
Chronicity (%)	None	10	50–70	>50%	None
Carrier state	None	Yes	Yes	Yes	?
Immune serum globulin protective	Yes	Yes ^b	Yes ^c	Uncertain	?

Abbreviation: Plus and minus signs indicate relative frequencies.

^a Many individuals with hepatitis C virus are also infected with the hepatitis G virus, which is similar to hepatitis C.

^b Hyperimmune globulin more protective.

^c Prevention of hepatitis B prevents hepatitis D.

The End