Viral Hepatitis

Harsha Perera

Liver

- The liver is a vital organ
- Diverse but closely connected functions
  - carbohydrates
  - proteins
  - lipids

  } Metabolism

  - clearance of toxins
  - pathogens
  - regulation of immune responses

Terminology

- Hepatitis: inflammation of liver
- Acute Viral Hepatitis:
  - symptoms last less than 6 months
- Chronic Hepatitis:
  - Inflammation of liver for at least 6 months

Overview
Aetiological of Liver Infections

- Viral infections
- Pyogenic Liver Abscess
- Fungal and mycobacterial infections
- Parasitic infections

Viral Hepatitis

Primary Hepatitis Virus

- Primarily involving the liver

Five unrelated hepatotropic viruses

- Hepatitis A, B, C, D, E, G, “X”

Viruses cause hepatitis

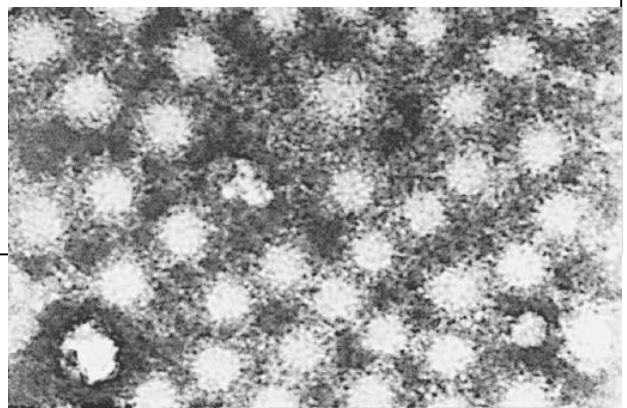
- CMV
- EBV
- HSV
- VZV
- HIV
- Yellow Fever
- Dengue

	Viral Hepatitis A	Viral Hepatitis B	Viral Hepatitis C	Viral Hepatitis D	Viral Hepatitis E
Agent	(HAV) ssRNA no envelope	(HBV); dsDNA envelope	(HCV) ssRNA envelope	(HDV) ssRNA envelope from HBV	(HEV) ssRNA no envelope
Route of Transmission	Fecal-oral	Parenteral, Vertical, Sexual.	Parenteral	Parenteral	Fecal-oral
Age affected	Children	Any	Adults	Any	Young adults
Carrier state	Nil	Common	Present	Nil (only with HBV)	Nil
Incubation period	10-50 days (avg. 25-30)	50-180 days (avg. 60-90)	40-120 days	2-12 weeks	2-9 weeks
Chronic infection	No	Yes	Yes	Yes	No
Specific Prophylaxis	Ig and Vaccine	Ig and Vaccine	Nil	HBV vaccine	Nil

TRANSMITTED PARENTERALLY	TRANSMITTED ENTERICLLY
• HEPATITIS B, C, D and G	• HEPATITIS A and E

Hepatitis A
Infectious Hepatitis

- Enterovirus of the Picornaviridae family
- It multiplies only in hepatocytes
- Resistant to heat and chemicals
- -Withstands heating to 60^0 C for 1 hr.
  - Inactivated by Chlorine, UV and by boiling for 5 minutes or autoclaving
  - Formalin is effective



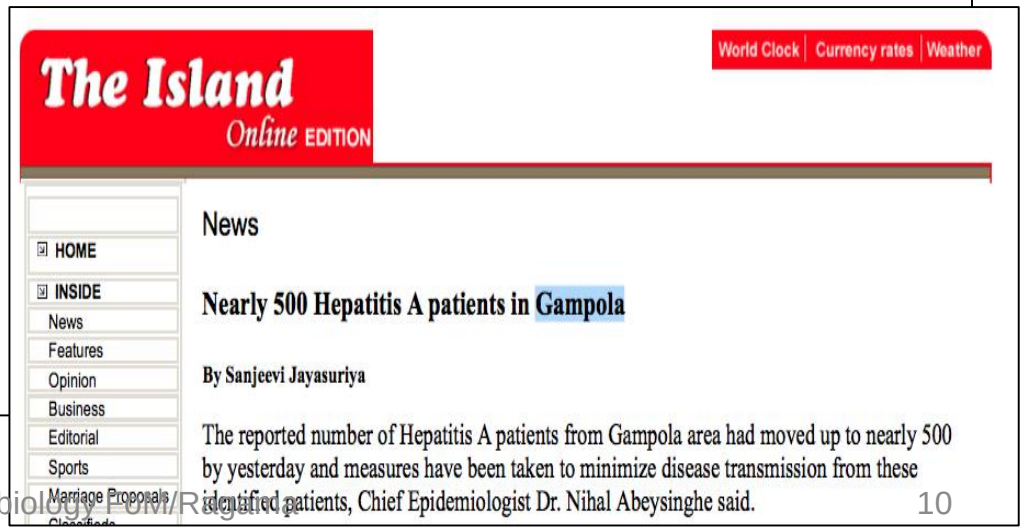
Hepatitis A

Epidemiology

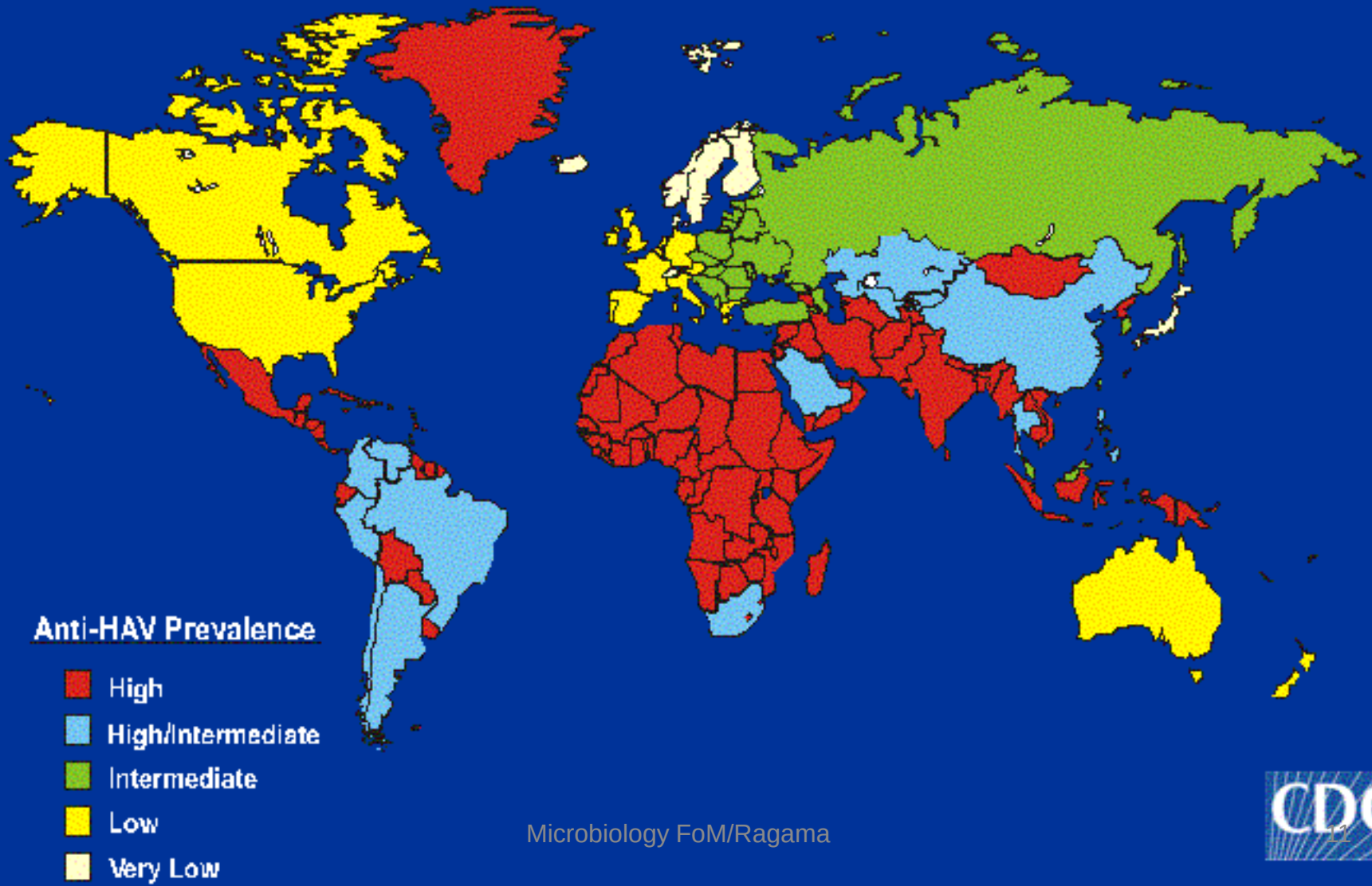
- Globally, 1.4 million/annually
- 100 deaths/yr from fulminant hepatitis A
- Human; only reservoir of infection
- Associated with a lack of safe water/poor sanitation
- Transmitted through ingestion of contaminated
  - food and water
  - direct contact with an infectious person

Hepatitis A

- Epidemics-explosive
- Cause significant economic losses.
- Accounts for 20-25% of clinical hepatitis
- Most often affects persons 5-14 years-old
- **no chronic state**


The Island
Online EDITION
World Clock | Currency rates | Weather
HOME
INSIDE
News
Features
Opinion
Business
Editorial
Sports
Marriage Proposals
News
Nearly 500 Hepatitis A patients in Gampola
By Sanjeevi Jayasuriya
The reported number of Hepatitis A patients from Gampola area had moved up to nearly 500 by yesterday and measures have been taken to minimize disease transmission from these identified patients, Chief Epidemiologist Dr. Nihal Abeysinghe said.

GEOGRAPHIC DISTRIBUTION OF HEPATITIS A VIRUS INFECTION



Infectivity

VIRUS EXCRETION:

faeces for about 2 weeks before onset of jaundice and for up to 2 weeks thereafter

PERIOD OF INFECTIVITY

greatest from 2 weeks before to 1 week after the onset of jaundice

INFECTIVE MATERIAL

Mainly faeces

.

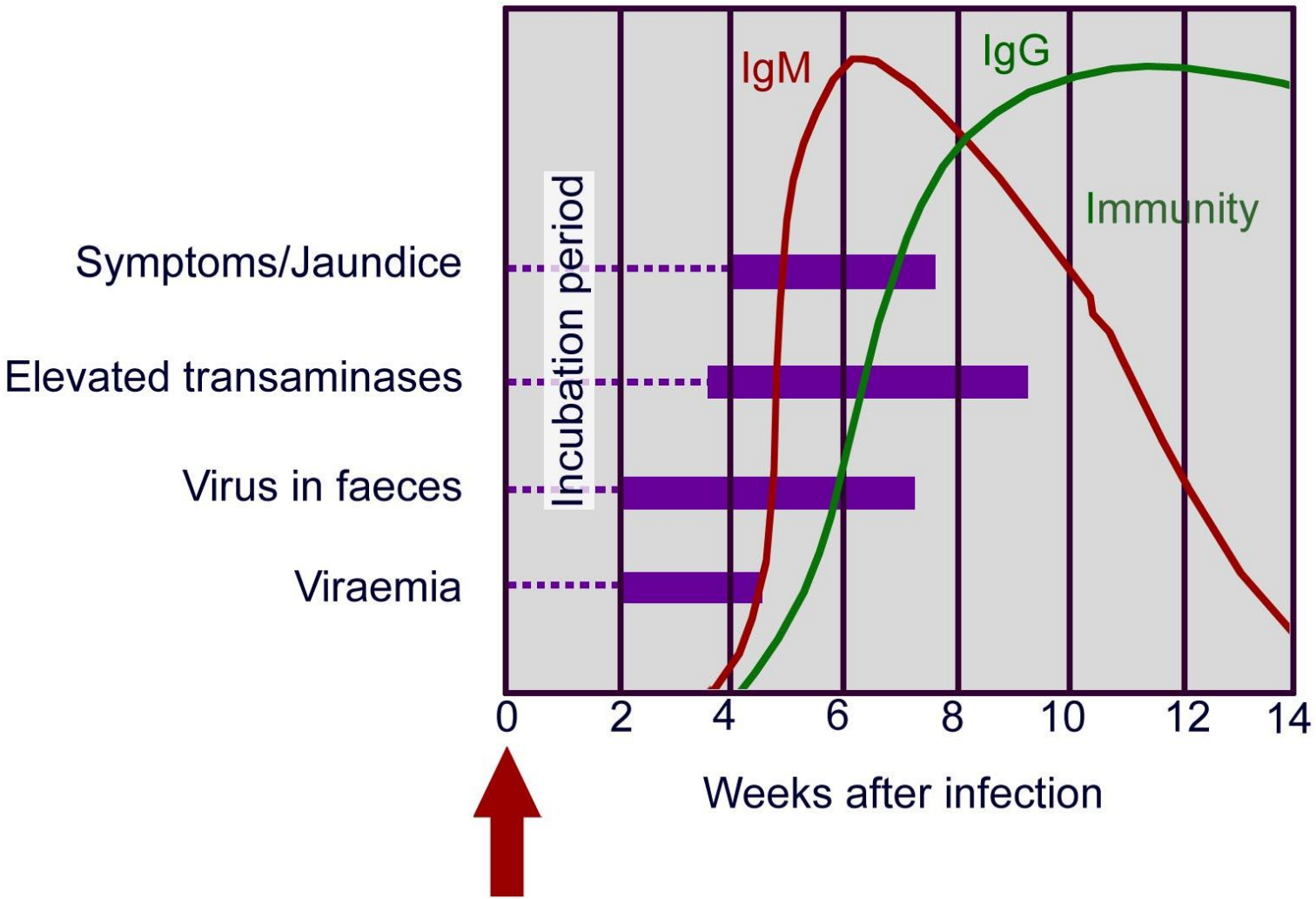
Pathogenesis
Hepatitis A

- Incubation 15-50 days
- Viral particles are orally ingested
- Enter bloodstream via the lining of the GIT
- Migrates to the liver parenchymal cells
- Infected via immunoglobulin-like HAV cellular receptor on liver parenchymal cells

Diagnosis

- Detection of anti-HAV IgM is diagnostic
- Demonstration of virus in feces, blood, bile
- Molecular Diagnosis : RT-PCR of feces
- The presence of IgG within the first few weeks of infection
  - prior infection
  - Vaccination

Hepatitis A time course of infection



Control

- Improved hygiene
- Passive immunization
- (Human Immunoglobulin Gamma globulin)
- Active immunization
  inactivated / live attenuated vaccines

Hepatitis B

Formerly known as “serum” hepatitis

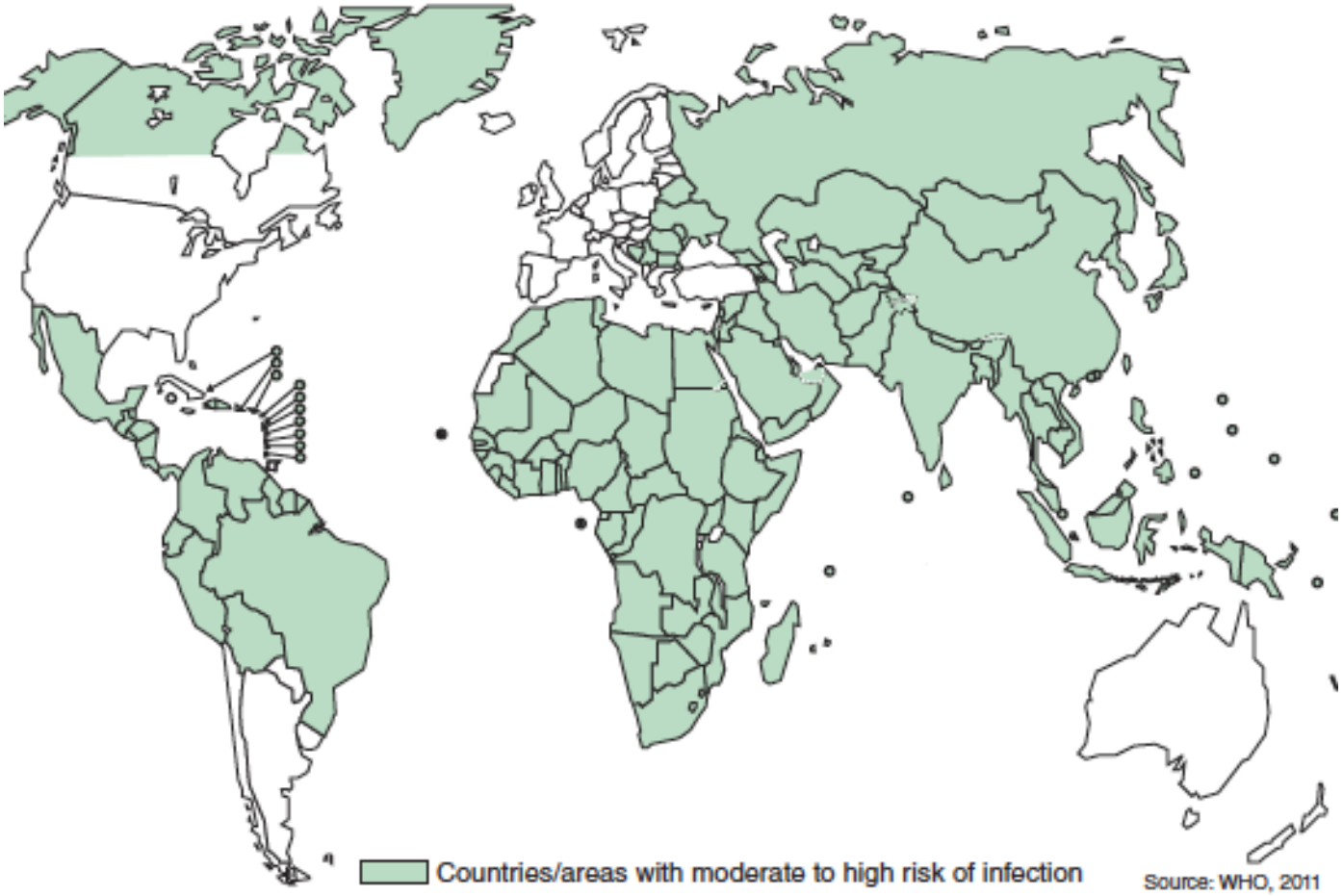
An acute systemic infection with major pathology

Transmitted by the parenteral route

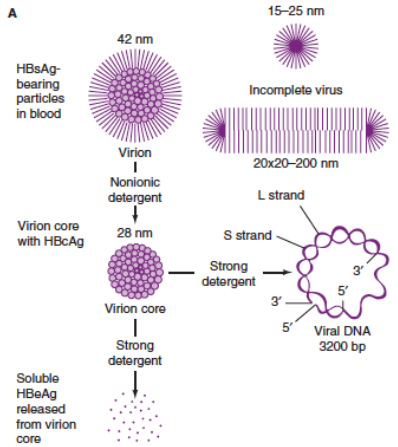
Endemic throughout the world

especially in tropical & developing countries

Global distribution of B: Hepatitis B virus.



Agent



Hepatitis B Virus (HBV)

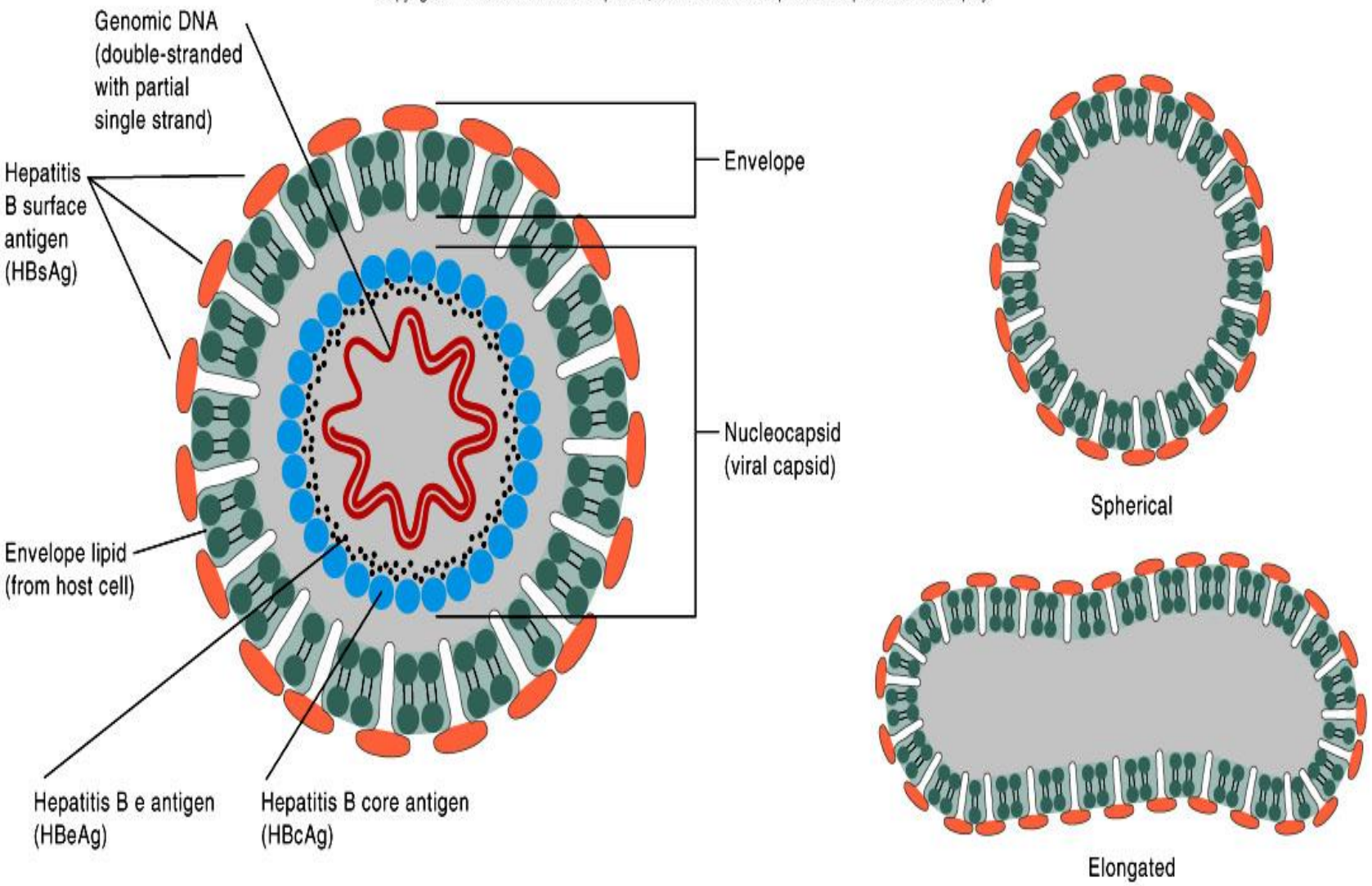
-42 nm double-shelled DNA virus-“Dane Particle”.
-It replicates in liver cell

HBV occurs in 3 morphology form in serum:

i. Small spherical particles with an average Diameter of 22nm.
ii. Filamentous or Tubules of varying length & of 22 nm diameter.
iii. Dane particle.

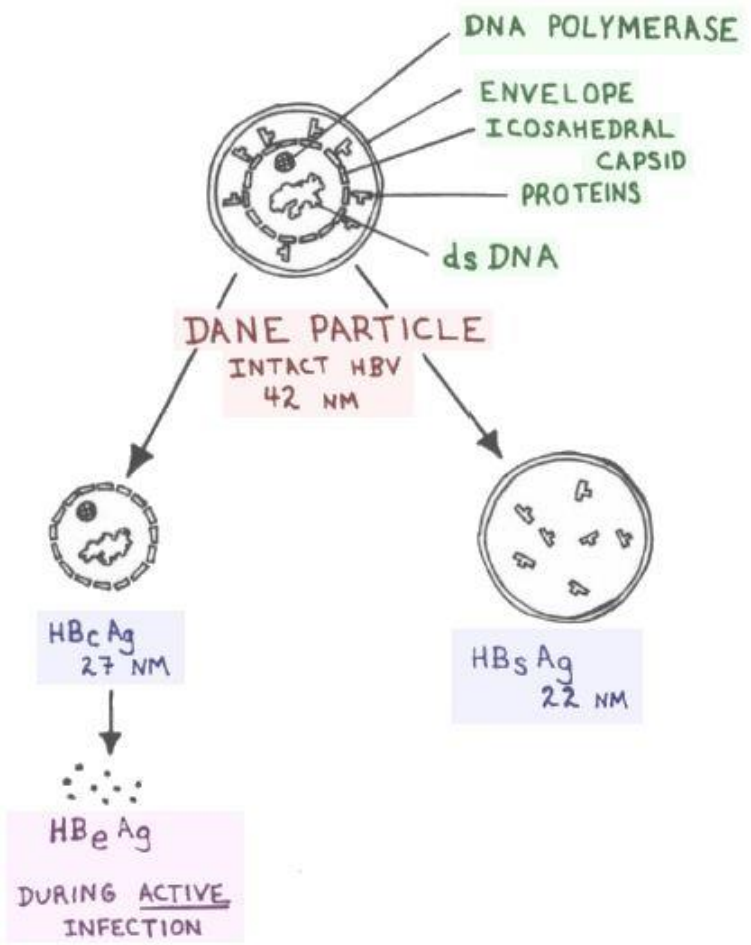
– only the Dane particle is considered infectious
– Other forms are not infectious.

HBV : Structure



(a) Complete infectious virion

(b) Viral envelope particles containing HBsAg


DNA POLYMERASE
ENVELOPE
ICOSAHEDRAL CAPSID PROTEINS
ds DNA
DANE PARTICLE
INTACT HBV
42 NM
HBc Ag
27 NM
HBs Ag
22 NM
HBe Ag
DURING ACTIVE INFECTION

Hepatitis B

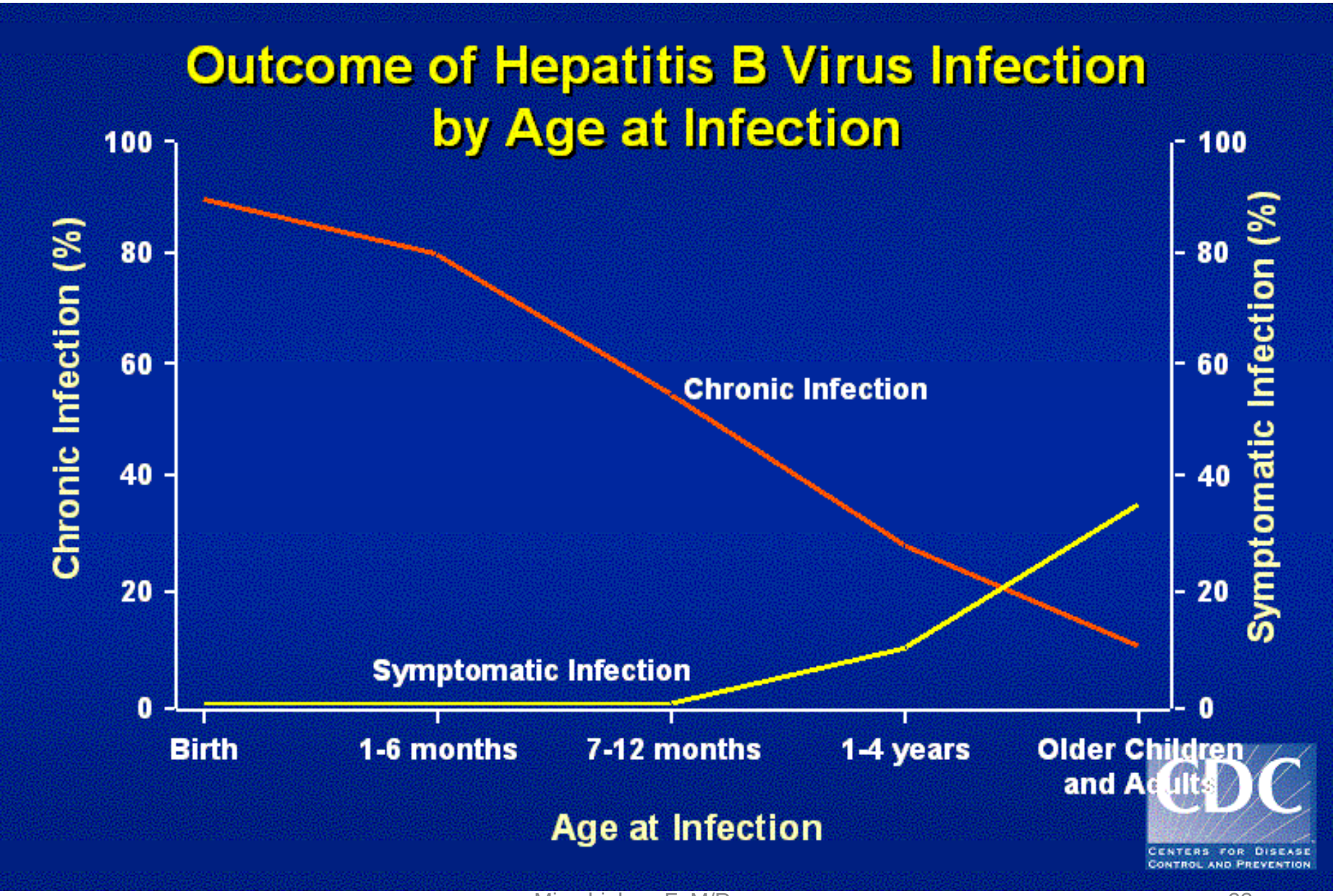
Epidemiology

- 350 million carriers worldwide
- More than 1 million HBV related deaths annually
- 10% of adults and 90% of children become carriers
- Transmission:

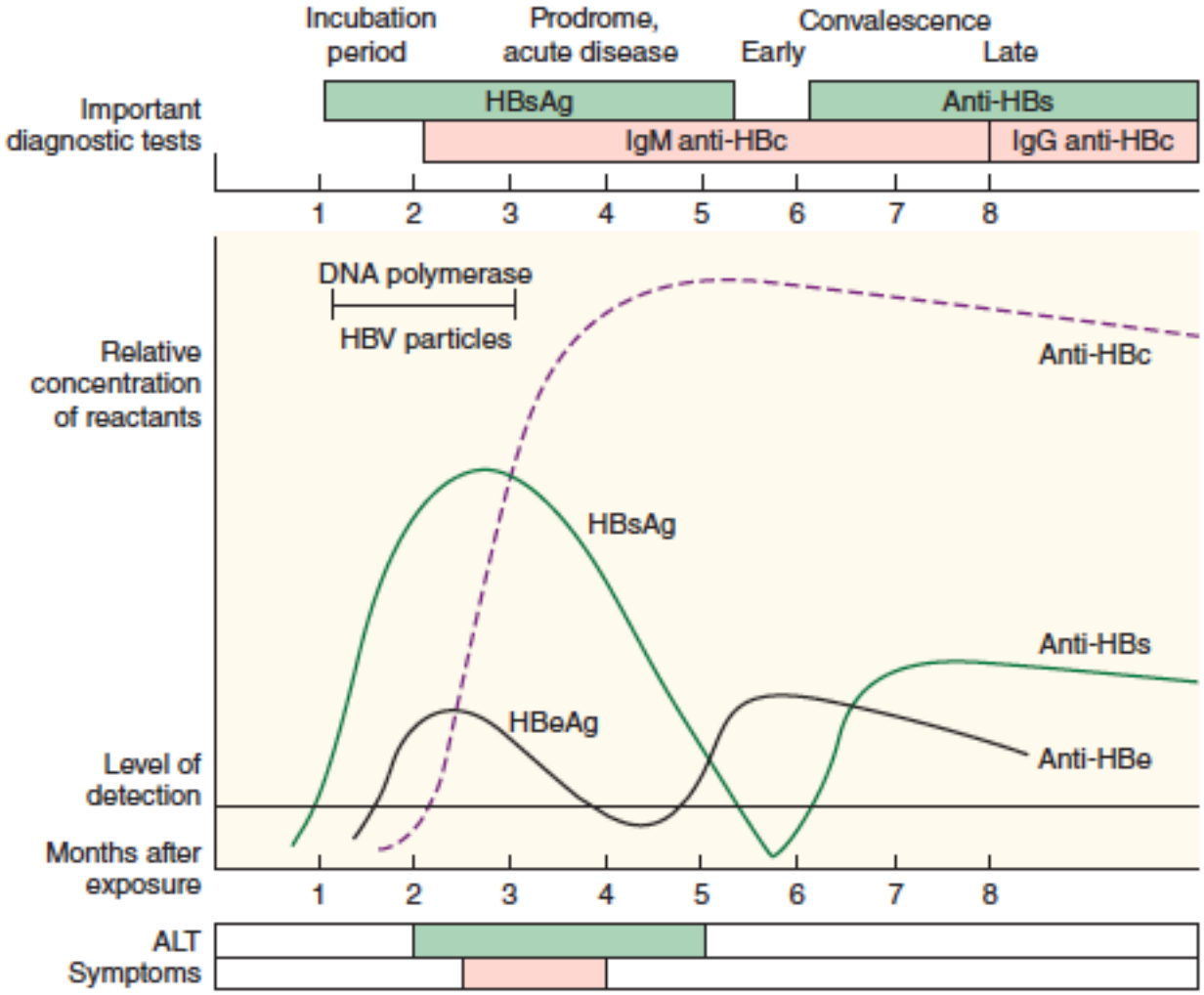
  parenterally, sexually, vertical transmission

- Risk factors:

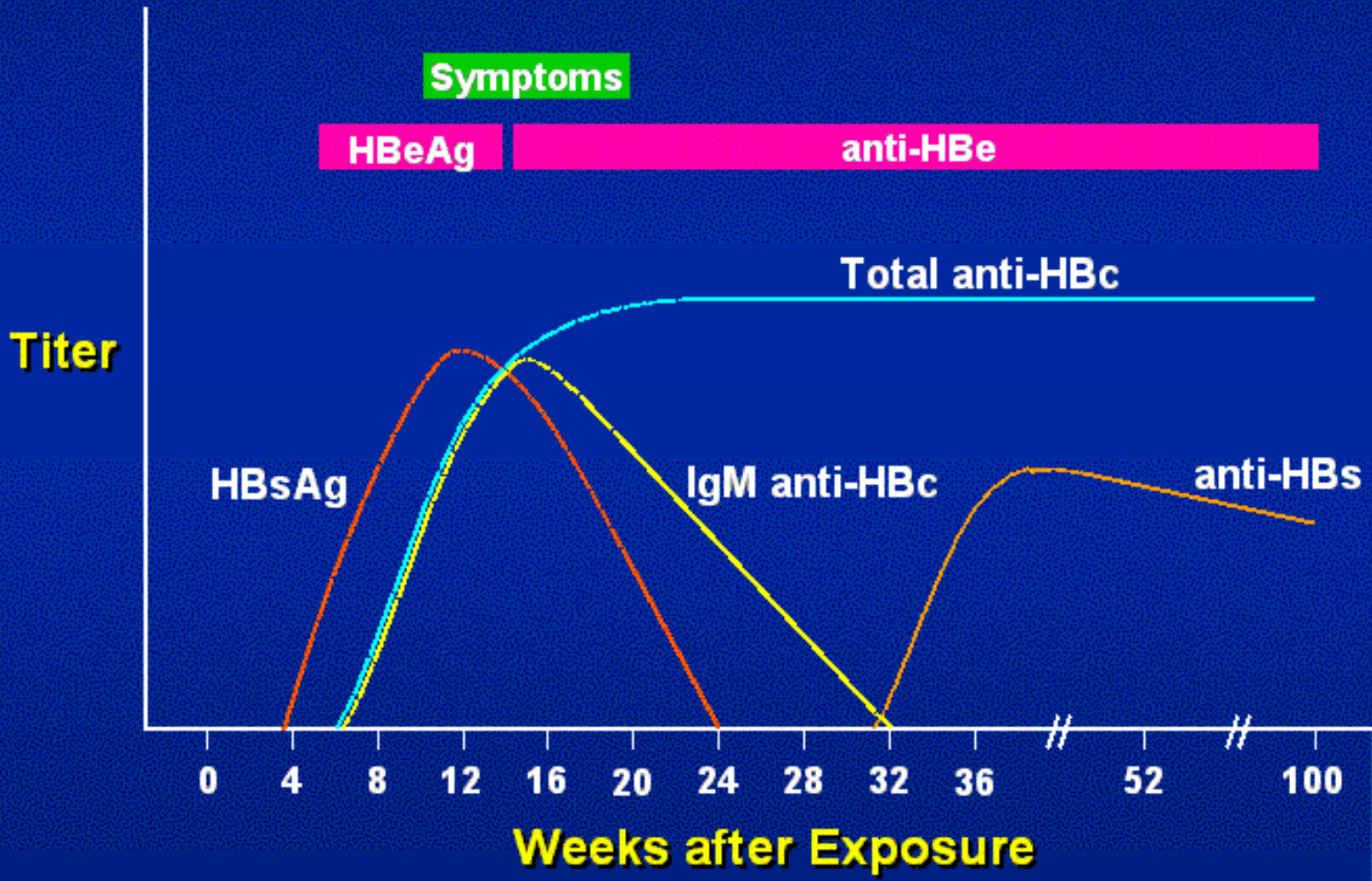
  IV drug use, prostitutes, homosexual men, Asian population, hemodialysis patients, health care workers


Outcome of Hepatitis B Virus Infection by Age at Infection
Chronic Infection (%)
Symptomatic Infection (%)
100
80
60
40
20
0
Chronic Infection
Symptomatic Infection
Birth
1-6 months
7-12 months
1-4 years
Older Children and Adults
Age at Infection
CDC
Centers for Disease Control and Prevention

Clinical and serologic events occurring in a patient with acute hepatitis B virus infection



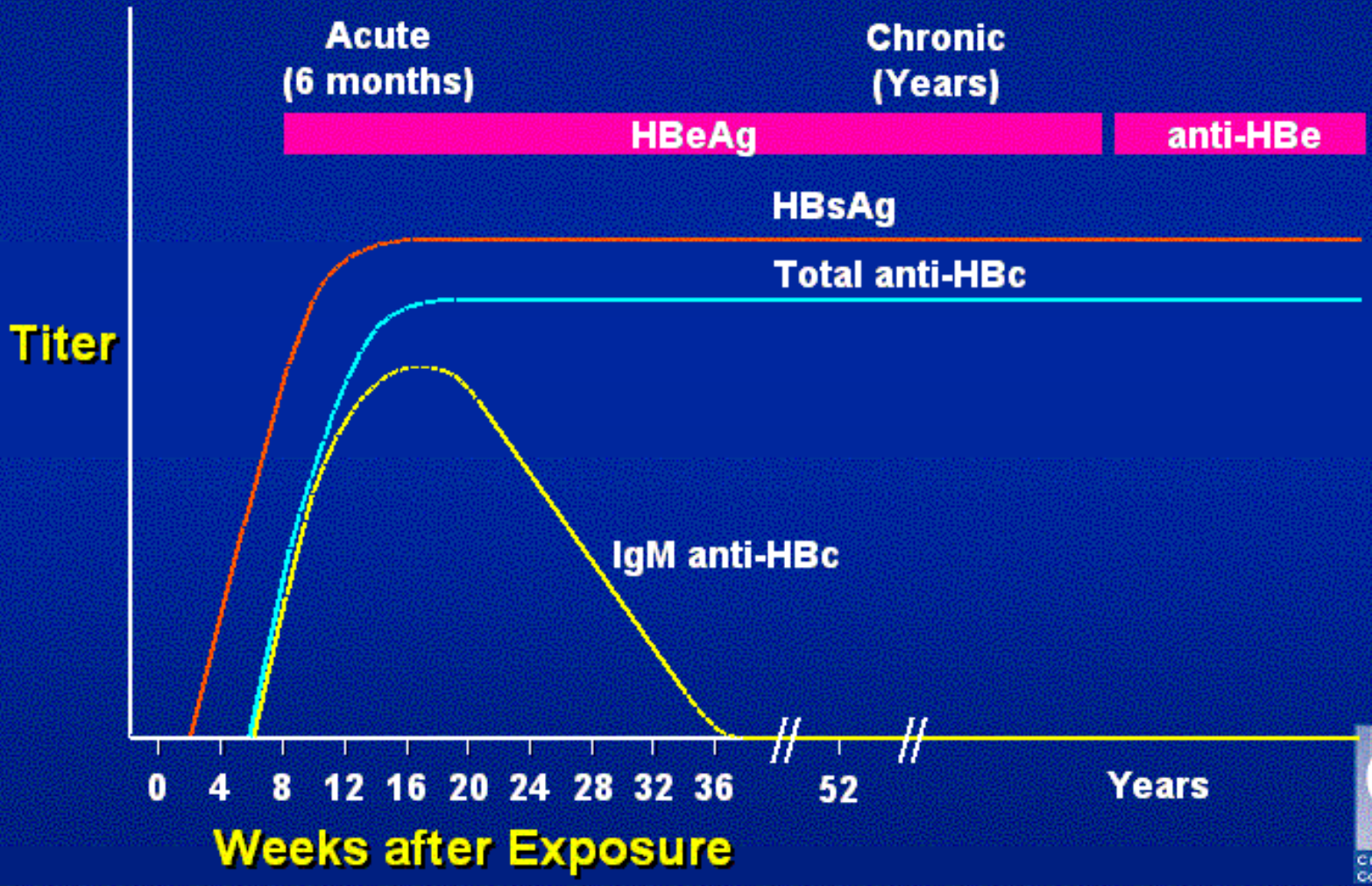
Acute Hepatitis B Virus Infection with Recovery
Typical Serologic Course



CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

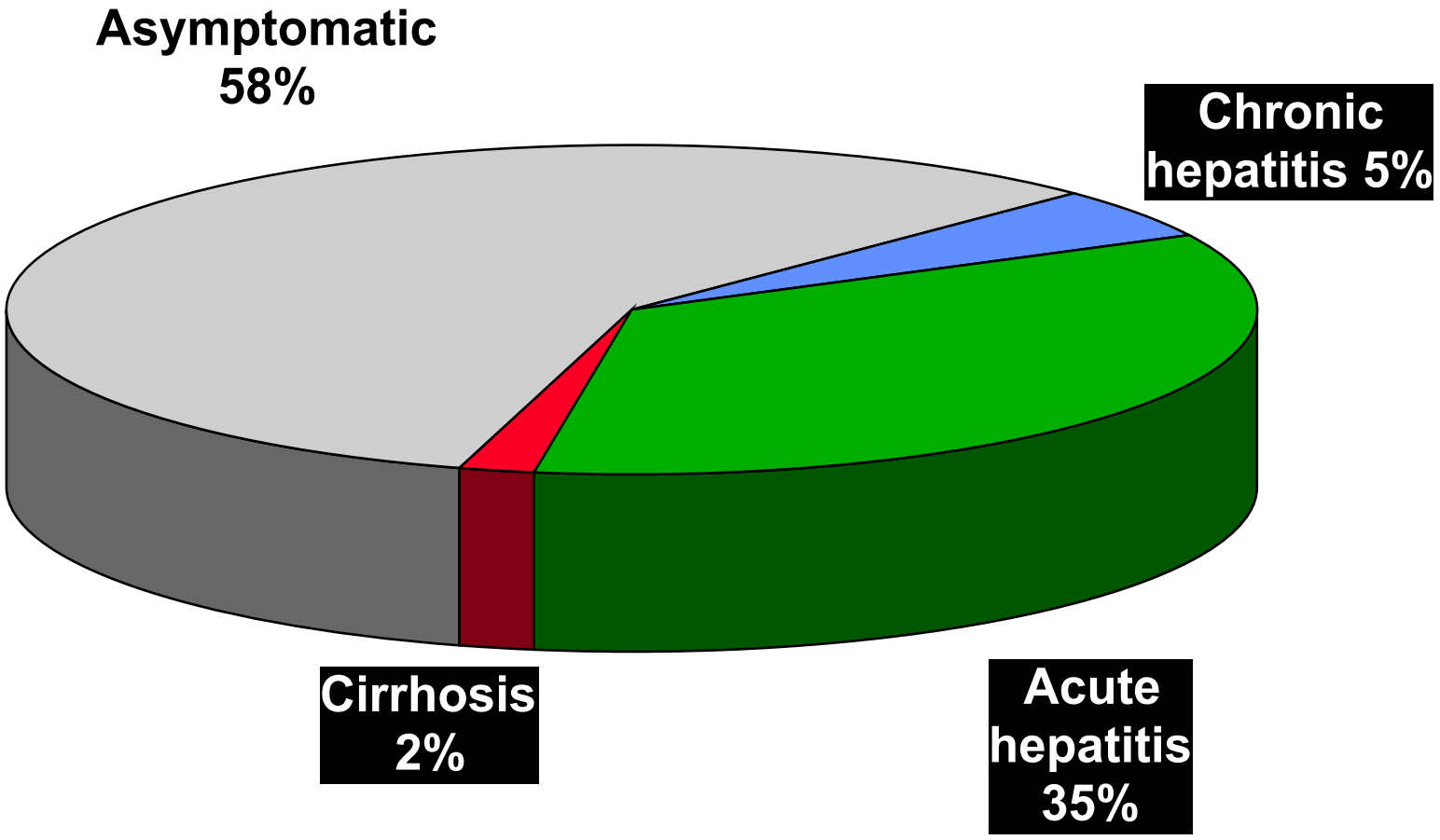
Progression to Chronic Hepatitis B Virus Infection

Typical Serologic Course



CDC
Centers for Disease Control and Prevention

Hepatitis B


Asymptomatic
58%
Chronic
hepatitis 5%
Cirrhosis
2%
Acute
hepatitis
35%

Hepatitis B

Diagnosis

- Laboratory findings:
  - HepBsAg positive
  - HepBcore IgM positive
  - HepBeAg positive
  - HBVDNA positive
- Hep B surface antibody confers immunity

Hepatitis B

Prognosis

- <1% develop fulminant hepatic failure
- 5-10% develop chronic hepatitis
- 30% of chronically infected develop cirrhosis

Hepatitis B

Prevention

- Early recognition and education
- Adequate hygiene and universal precautions
- Vaccination- health care workers, high risk groups, children born to infected mothers (HBIG)

Interpretation of common serological patterns in HBV infection

Virus/Antibody markers					Interpretation
HBsAg	HBeAg	Anti-HBc	Anti-HBs	Anti-HBe	
+	+	IgM	-	-	Acute HBV infection; highly infectious
+	+	IgG	-	-	Late/Chronic HBV infection or carrier state; highly infectivity
+	-	IgG	-	+/-	Late/Chronic HBV infection or carrier state; low infectivity
-	+/-	IgM	-	+/-	Seen rarely in early acute HBV infection; infectious
-	-	IgG	+/-	+/-	Remote HBV infection; infectivity nil or very low
-	-	-	+	-	Immunity following HBV vaccine

Treatment

- Interferon Alfa (Intron A)
  Response rate is 30 to 40%
- Lamivudine (Epivir HBV)
  (relapse ,drug resistance)
- Adefovir dipivoxil (Hepsera)

Hepatitis C

- Caused by the hepatitis C virus (HCV)
- Infection is often asymptomatic
- Chronic infection can lead to cirrhosis
- 150–200 million people, or ~3% of the world's population, are living with chronic hepatitis C
- About 50 to 80 % of patients progress to chronic hepatitis

Incubation Period

40-120 days

Mode of Transmission

- Intravenous drug use
- Healthcare Exposure: Blood Transfusion, transfusion of Blood products, Organ Transplant without HCV screening carry significant risk of infection.
- Hemodialysis
- Accidental injuries with needles/sharps
- Sexual/household exposure to anti-HCV-positive contact
- Multiple sex partners
- Vertical Transmission: Vertical transmission of hepatitis C from an infected
mother to her child

Diagnosis

- HCV antibody – ELISA
  - Not useful in the acute phase
  - takes at least 4 weeks after infection before antibody appears
- HCV-RNA –
  - diagnose HCV infection in the acute phase.
  - monitoring the response to antiviral therapy
- HCV-antigen –
  - EIA for HCV antigen is available
  - much easier to carry out

Prevention

- Only General Prophylaxis,
- No specific active or passive immunizing agent is available

Treatment

Interferon –

Considered for patients with chronic active hepatitis.

Response rate is around 50% but 50% of responders will relapse upon withdrawal of treatment

Ribavirin –

Recent studies suggest that a combination of interferon and ribavirin is more effective than interferon alone

Hepatitis D

- **Hepatitis D**
- Classified as *Hepatitis delta virus*
- small circular enveloped RNA virus.
- HDV is considered to be a subviral satellite because it can propagate only in the presence of the hepatitis B virus (HBV)

Hepatitis E

- Caused by infection with a virus called hepatitis E virus
- Spread mainly by the fecal-oral route
- Causes an acute and self-limiting infection with low mortality rates
- Fatal out come is about 2% of High risk of developing chronic hepatitis in immunocompromised patients
- In pregnant women the disease is more often severe and is associated with a clinical syndrome called fulminant hepatic failure

Hepatitis G

- Member of *Flaviviridae* family
- HGV RNA has been found in patients with acute, chronic and fulminant hepatitis, hemophiliacs, patients with multiple transfusions and hemodialysis, intravenous drug addicts and blood donors

Summery

- Six different viruses are causative agents of hepatitis
  - hepatitis A virus (HAV)
  - hepatitis B virus (HBV)
  - hepatitis C virus (HCV)
  - Hepatitis D virus (HDV)
  - hepatitis E virus (HEV)
  - Hepatitis G virus (HEV)

- HAV, HEV and HGV transmitted by fecal–oral route
- HBV, HCV, and HDV are transmitted by parenteral
- routes

Summery

- HBV, HCV, and HDV establish chronic infections, HAV and HEV do not
- Individuals infected with HBV as infants develop chronic infections and are at risk for liver disease as adults
- HBV and HCV causes of liver cancer
- Virus vaccines are available against HAV and HBV