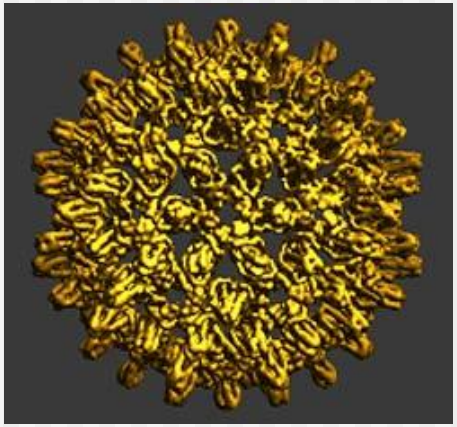
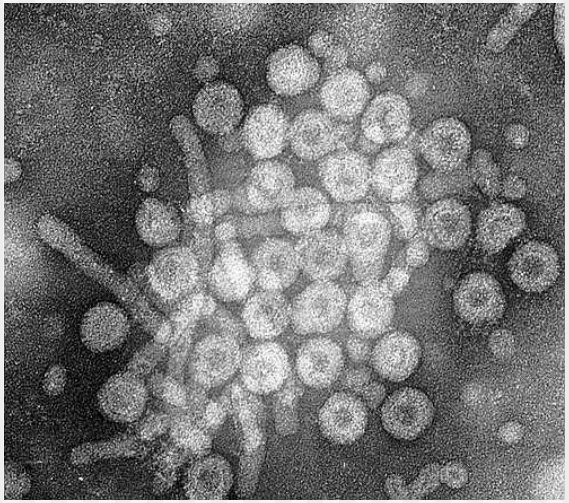
Hepadnaviridae
Hepatitis B



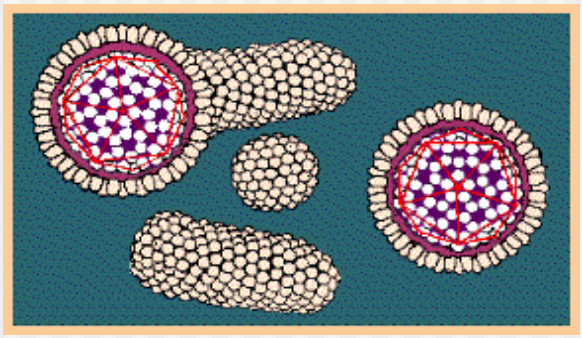
Assistant Professor Dr.
Mushtak T. S. Al-Ouqaili



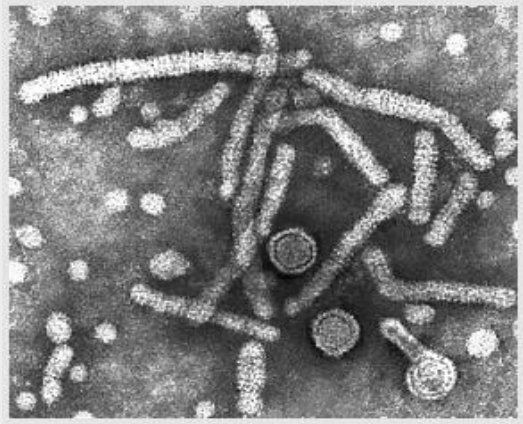
Electron micrograph of serum containing hepatitis B virus after negative staining.

Hepatitis B

- Hepadnaviridae family
  - DNA virus
  - Double-shelled particles
    - Outer lipoprotein envelope (surface Ag)
    - Inner viral nucleocapsid (core)
  - seven genotypes
  - four major subtypes.
  - All HBV subtypes share one common antigenic determinant - "a."
  - Thus, antibodies to the "a" determinant confer protection to all HBV subtypes

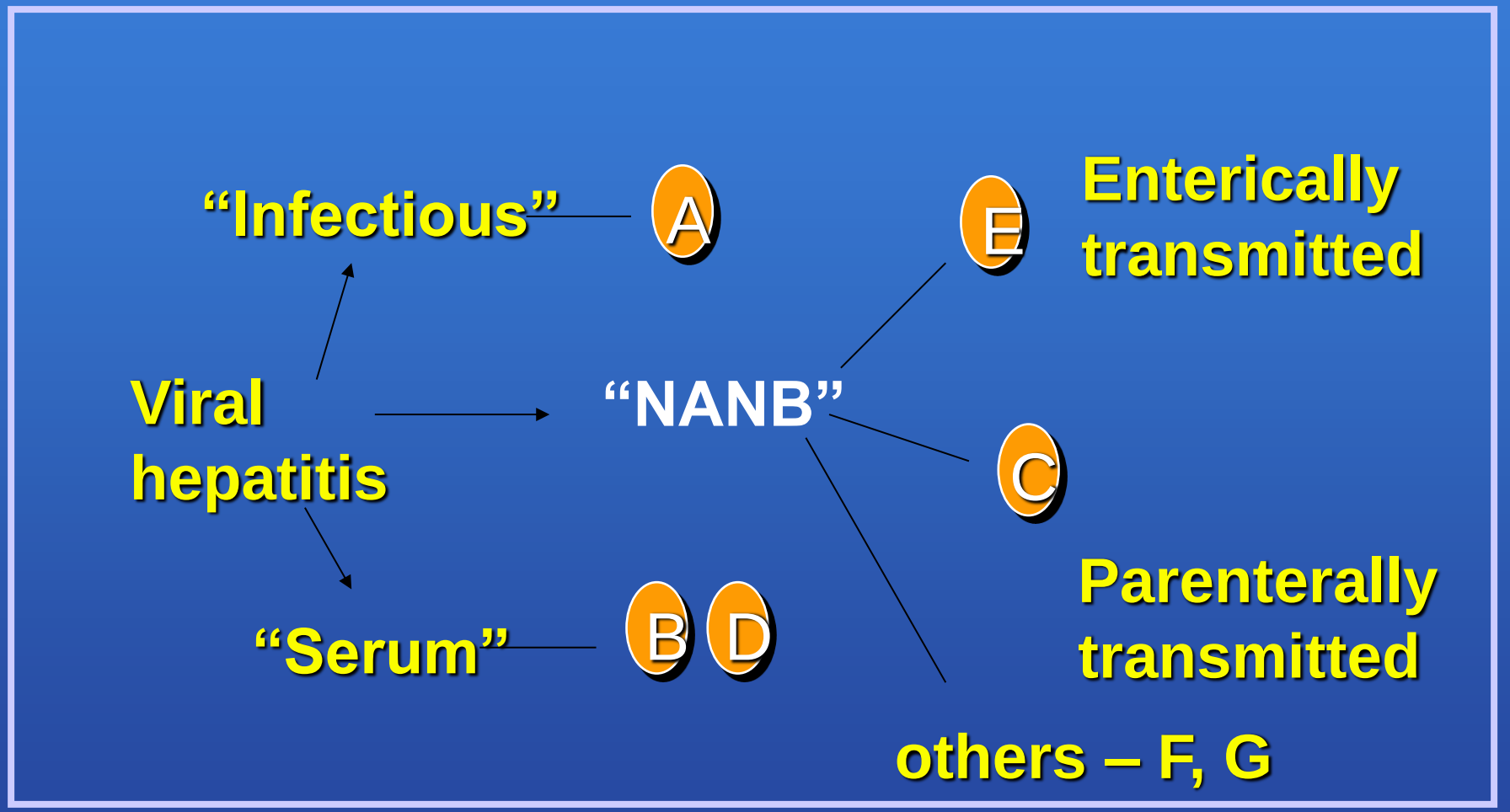


Diagrammatic representation of the hepatitis B virion and the surface antigen components



EM of Hepatitis B viron

Viral Hepatitis – Clinical Classification



Introduction

- Primary infection of liver
- Divided into six types:A, B, C, D, E, G
- Type F : transfusion associated hepatitis
  a mutant (HBx) of HBV.
- All are RNA virus except HBV which is a DNA virus.

Viral Hepatitis Overview

Types of Viral Hepatitis

	A	B	C	D	E
Source of virus	feces	blood/ blood-derived body fluids	blood/ blood-derived body fluids	blood/ blood-derived body fluids	feces
Route of transmission	fecal-oral	percutaneous permucosal	percutaneous permucosal	percutaneous permucosal	fecal-oral
Chronic infection	no	yes	yes	yes	no
Prevention	pre-exposure immunization	pre/post-exposure immunization	blood donor screening; risk behavior modification	pre/post-exposure immunization; risk behavior modification	ensure safe drinking water

A, B, Cs of Viral Hepatitis

- **A**
  - fecal-oral spread: hygiene, drug use, men having sex with men, travelers, day care, food
  - vaccine-preventable
- **B**
  - sexually transmitted – 100x more infectious than HIV
  - blood-borne (sex, injection drug use, mother-child, and health care)
  - vaccine-preventable
- **C**
  - blood borne (injection drug use primarily)
  - 4-5 times more common than HIV
  - NOT vaccine-preventable**!**

Acute Hepatitis – Clinical Symptoms

Asymptomatic > Symptomatic > Fulminant Liver Failure > Death

Symptoms (if present) are the same, regardless of cause (e.g., A, B, C, other viruses, toxins)

- Nausea, vomiting
- Abdominal pain
- Loss of appetite
- Fever
- Diarrhea

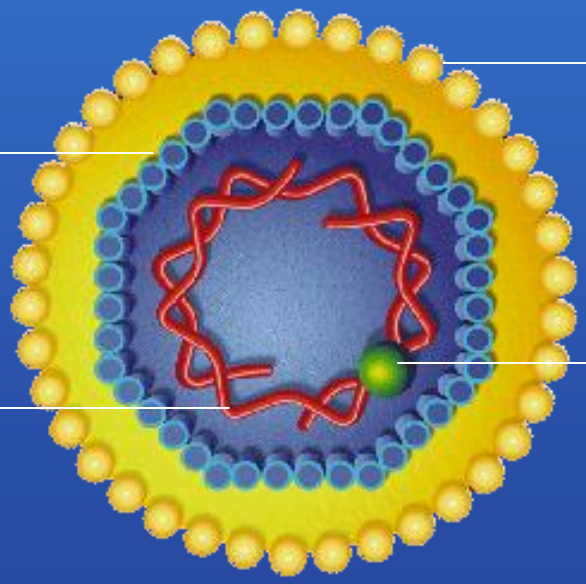
Pre- icteric stage

- Light (clay) colored stools
- Dark urine
- Jaundice (yellowing of eyes, skin)

Icteric stage

Structure of HBV

- Hepadnaviridae family
- 42 nm DNA virus with an outer envelope and inner core



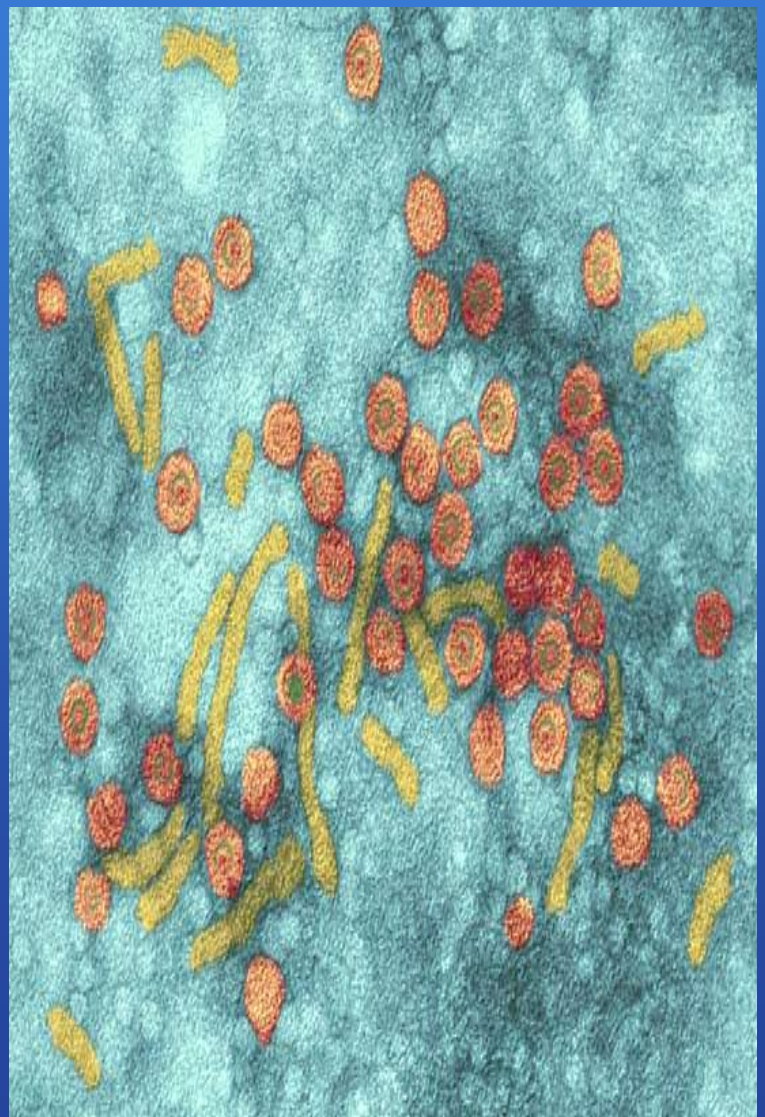
Structure of HBV

- **Exists in 3 different forms in serum of infected individuals:**

1. **Spherical particle – 22nm, most abundant**

2. **Tubular or filamentous particle – 22nm**

3. **Dane particle – 42nm, few in no, double walled spherical structure, true infectious form of HBV.**



Hepatitis B Antigens

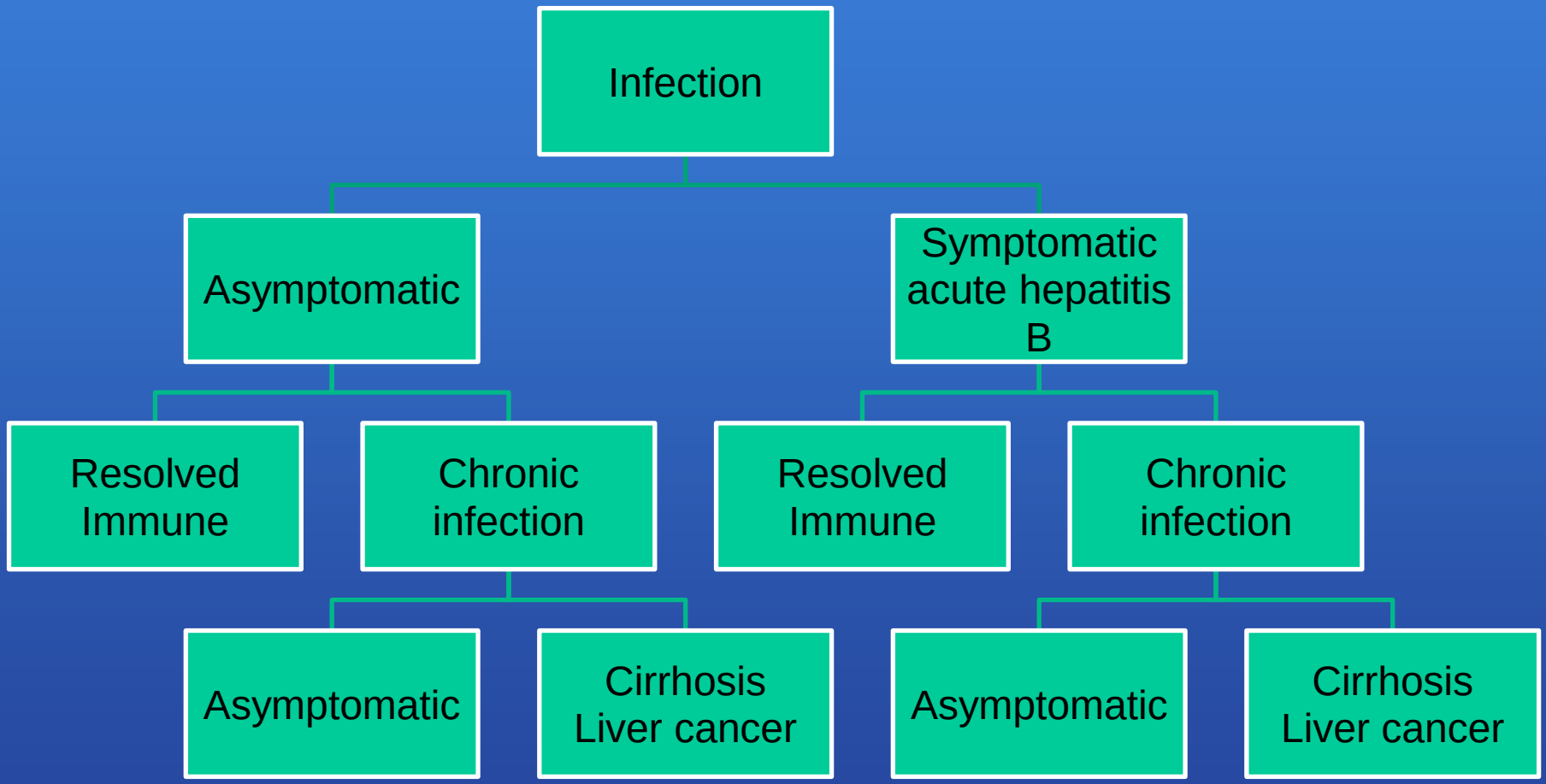
- Hepatitis B surface antigen(S): HBs Ag – the envelope protein – detectable in blood
- Hepatitis B core antigen (HBcAg) – not detectable in blood.
- Hepatitis B e antigen (HBeAg) - Detectable in blood during active viral multiplication, generally at the same time as HBsAg

Hepatitis B – Clinical Features

- **Incubation period:** long Average 60- 90 days

  Range 45-180 days
- Fever is not prominent
- 90- 95% with acute hepatitis recover within 1-2 months of onset.
- Mortality in about 0.5-2 % of cases.
- 1-10% develop chronic infection.

Outcome of HBV Infection



Epidemiology

- Natural infection occurs only in humans.
- Virus maintained in carriers.
- Largest carrier pool in China followed by India.
- Carrier – a person with detectable HBsAg in blood for more than 6 months.
- Carrier state is more common in males.
- Carriers - two types:

1. Super carriers – high titre HBsAg, along with HBeAg, DNA polymerase and HBV in circulation, with elevated transaminases.
2. Simple carriers – low infectivity & low titres of HBsAg.

Epidemiology

- Prevalence of hepatitis carriers- varies in different countries

1. High endemicity: carrier rate >8% as in SE Asia, China, parts of S. America

2. Intermediate: 2 to 7 % as in ME Asia, India, S. Asia

3. Low endemicity: <2% as in Western Europe, N. America, Australia

HBV Modes of Transmission

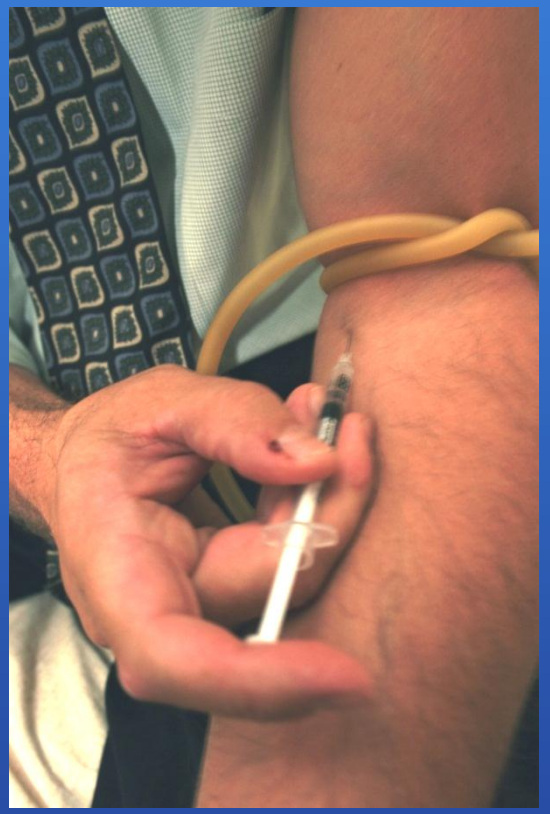
- Sexual
- Parenteral
- Perinatal

Concentration of HBV in Various Body Fluids

High	Moderate	Low/Not Detectable
blood	semen	urine
serum	vaginal fluid	feces
wound exudates	saliva	sweat
		tears
		breast milk

Risk Factors Associated with Transmission of HBV

- **IV drug abuse** – HBV transmission is Four times more common than HIV
- **Transfusion or transplant** from infected donor
- **Occupational exposure** to blood - Mostly needle sticks
- **Iatrogenic** – dialysis, unsafe injection practices (reuse of needles/syringes, contaminated multiple dose medication vials), dental procedures, blood bank



Risk Factors Associated with Transmission of HBV

- **Transmission from Carrier mothers**
  - by contact of maternal blood with the skin & mucosa of the fetus during birth
  - Very high (60-90%) if the mother is HBeAg +ve and low (5-15%) if negative

- **High risk Sexual behaviour -** Multiple sex partners, homosexuals & those diagnosed with STDs like HIV, gonorrhea etc

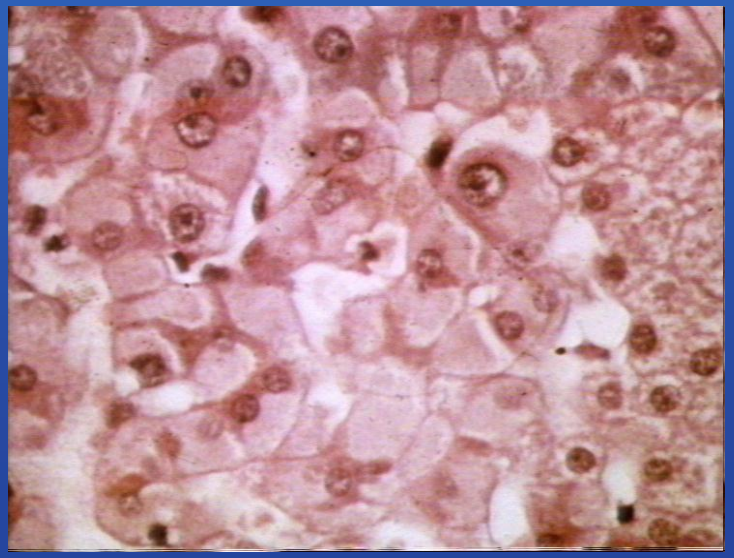
Laboratory Diagnosis

- Serology – specific diagnosis, demonstration of serological markers

- HBV DNA levels – indicator of viral replication & great infectivity

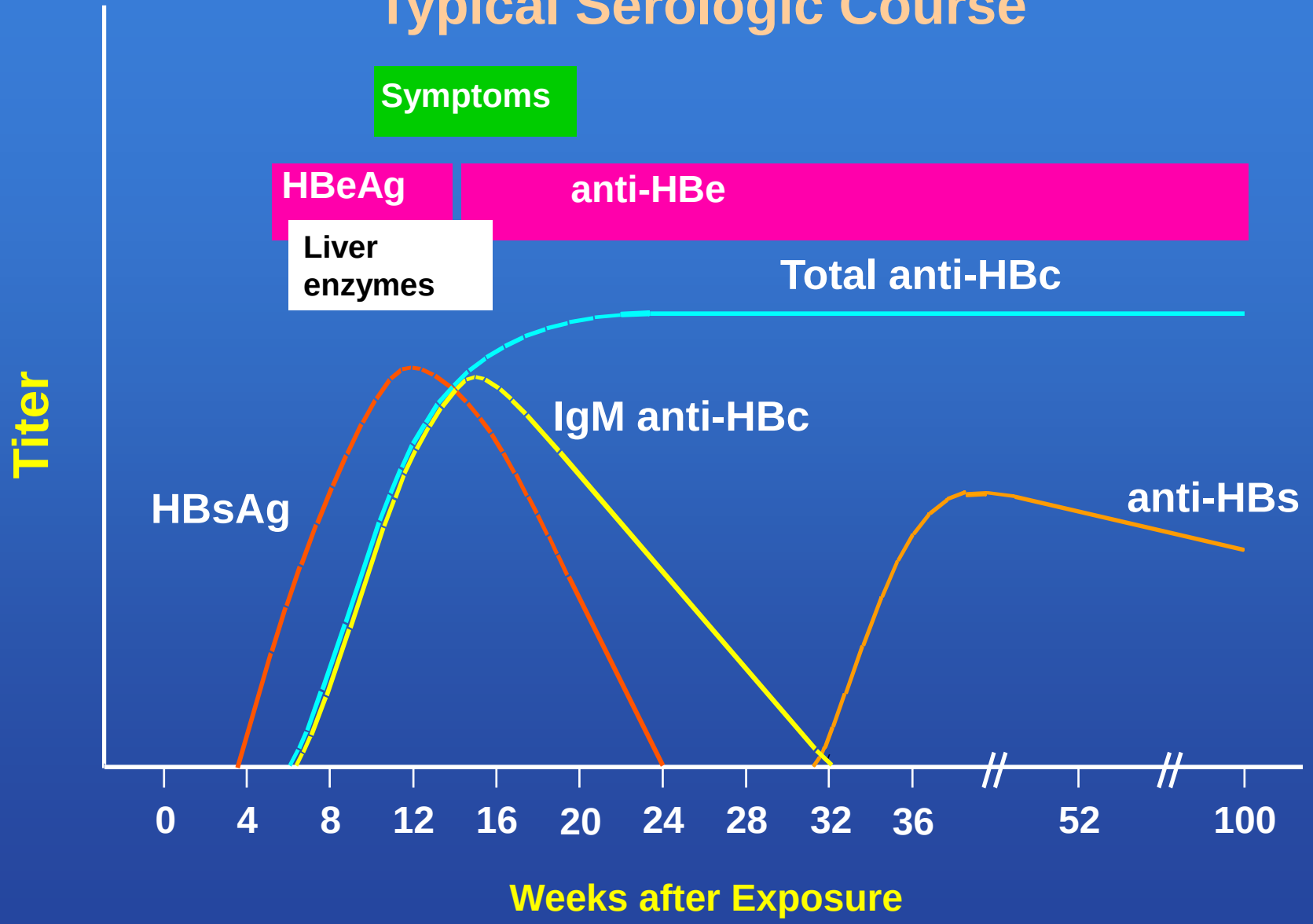
  - measured by PCR, DNA:DNA hybridization.

- Histopathology – ground glass appearance of infected hepatocytes due to HBsAg.



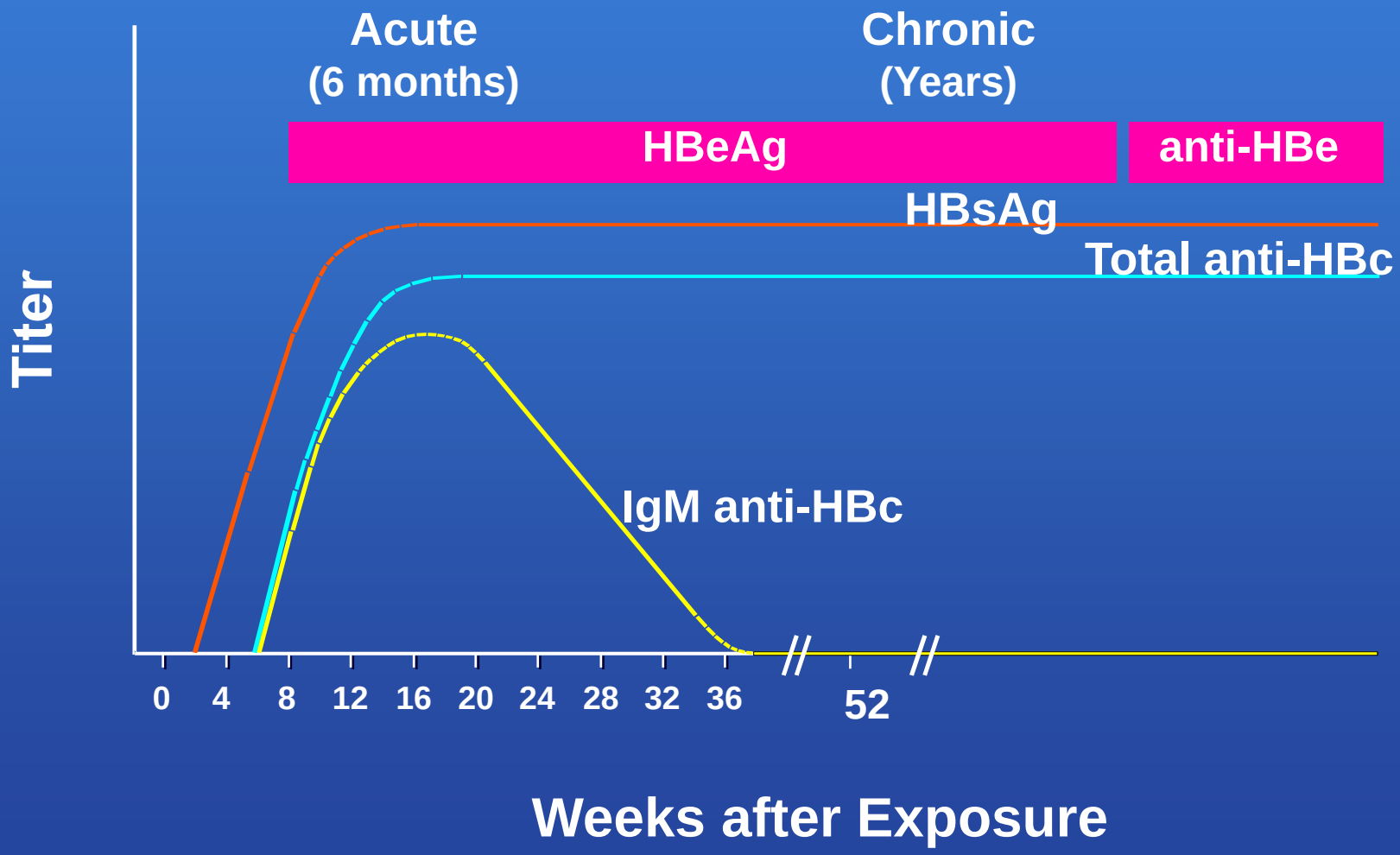
Acute Hepatitis B Virus Infection with Recovery

Typical Serologic Course



Progression to Chronic Hep. B Virus Infection

Typical Serologic Course



Interpretation of serological markers

Virus/ Antibody markers					Interpretation
HBsAg	HBeAg	Anti-HBc	Anti-HBs	Anti-HBe	
+	+	Ig M	-	-	**Acute infection, highly infectious**
+	+	Ig G	-	-	**Late/chronic or carrier state, highly infectious**
+	-	Ig G	-	+/ -	**Late/chronic or carrier state, low infectivity**
-	+/ -	Ig M	-	+/ -	**Infectious,rarely seen, window phase**
-	-	Ig G	+/ -	+/ -	**Remote infection, nil or very low infectivity**
-	-	-	+	-	**Following vaccination**

Reduce or Eliminate Risks for Acquiring HBV Infection

- **Screening and testing donors of blood, organs, and tissues**
- **Virus inactivation of plasma-derived products**
- **Risk-reduction counselling and services**
  - Obtain history of high-risk drug and sex behaviors
  - Provide information on minimizing risky behavior, including referral to other services
  - Vaccinate against hepatitis A and/or hepatitis B
- **Infection control practices**
- **Blood and body fluid precautions**

Passive Immunisation

- Hyperimmune hepatitis B immune globulin (HBIG) given soon after exposure to infection
- 300-500 IU I.M., single dose
- Prepared from human volunteers with high titres of anti-HBs
- Also given to protect patient from severe recurrent HBV infection following liver transplantation
- Protects against illness & carrier state, may not prevent infection.

New Vaccine

- Special vaccine containing all antigenic components (S, Pre S1 & Pre S2) of HBsAg.

- Gives greater seroconversion.

Post Exposure Prophylaxis (PEP)

- For non immune persons exposed to HBV:
  1. Percutaneous or mucosal exposure to HBsAg +ve blood
  2. Sexual exposure to HBsAg +ve person
  3. Perinatal exposure of an infant to HBsAg +ve mother.

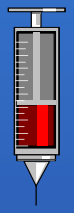
- PEP includes HBIG + full course of Hep B vaccine.

Baby Shots for Hepatitis B

if the mother has Hepatitis B

Birth

Hepatitis B Vaccine

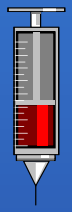


+

H-BIG

1 - 2 months old

Hepatitis B Vaccine

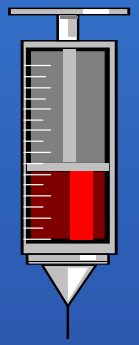


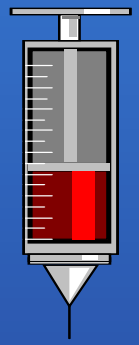
6 months old

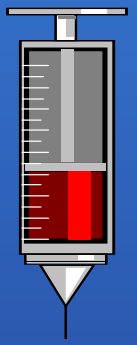
Hepatitis B Vaccine

Hepatitis B can be prevented!

If you have never had hepatitis B,
you can get 3 shots . . .

1 

2 

3 

. . . and get long lasting protection.

Treatment

- Supportive care
- Therapy

1. IFN alpha 2b – mimics cells natural defense mechanisms

2. Adevofir Dipivoxil – inhibits HBV DNA polymerase, chronic hepatitis

3. Lamivudine – inhibits reverse transcriptase