HEPATITIS IN PEDIATRICS

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HEPATITIS

- Hepatitis is defined as inflammatory liver injury regardless of the cause.
- Clinical presentation: a spectrum of presentation ranging from asymptomatic to signes of cirrhosis and hepatic failure.
- Non-hepatic causes of elevated liver enzymes should be considered.

Causes of Hepatitis in Children

Infectiuos

Viral

Hepatotropiv viruses

HAV

HBV

HCV

HEV

HDV

Non-A-Eviruses

Systematic infection

Adenovirus

Arbovirus

Coxacckievirus

Cytomegalovirus

Enterovirus

EBV

Herpes simplex

others

Non-viral

Abscess

Amebiasis

Bacterial sepsis

Brucellosis

TB

Non-infectiuos

Autoimmune Hepatitis

Metabolic

Alpha-1_antitrypsin deficiency

Glycogen storage disease

Wilson's disease

Toxic

Drug induced

pesticides

Anatomical

Choledochal cyst

Biliary atresia

Hemodynamic

shock

Congestive heart failure

Hemodynamic

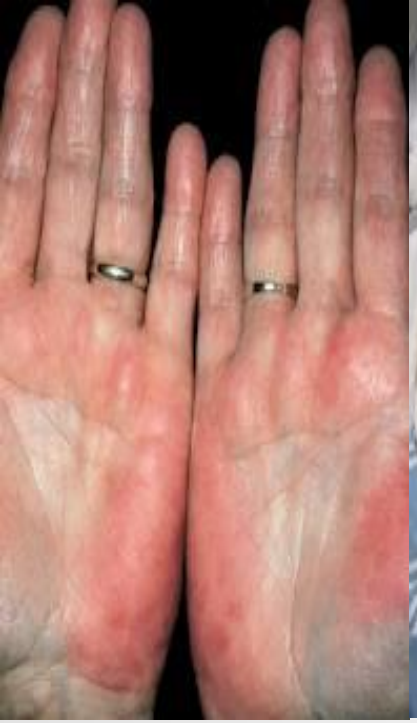
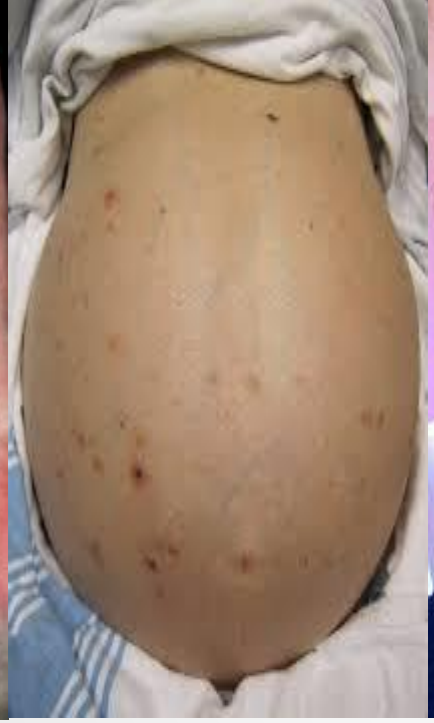
Others

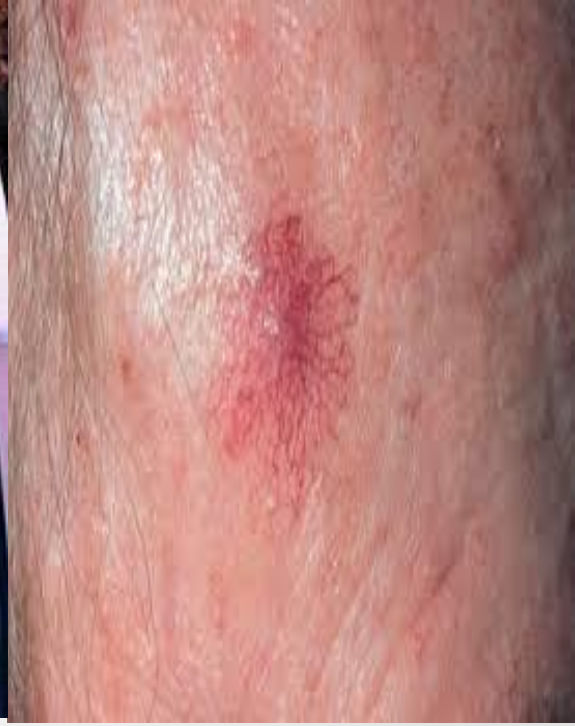
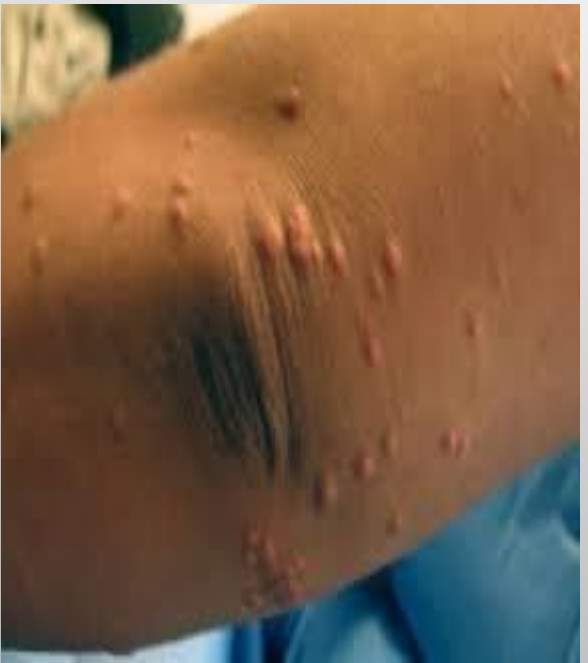
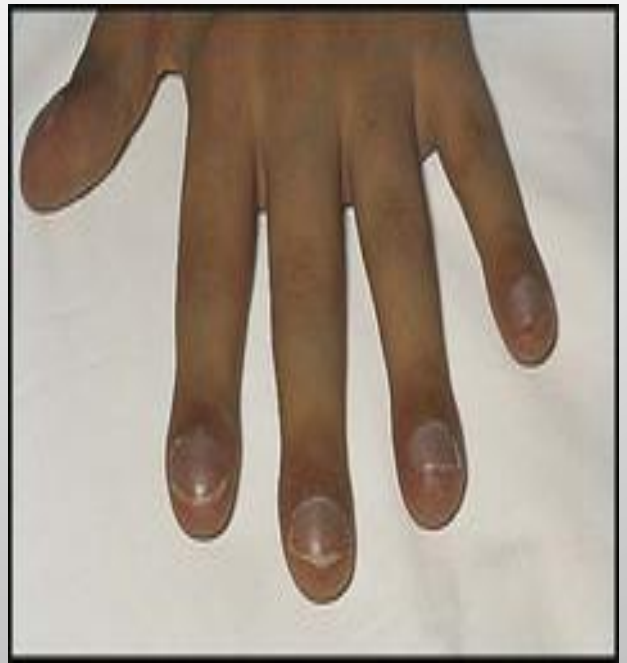
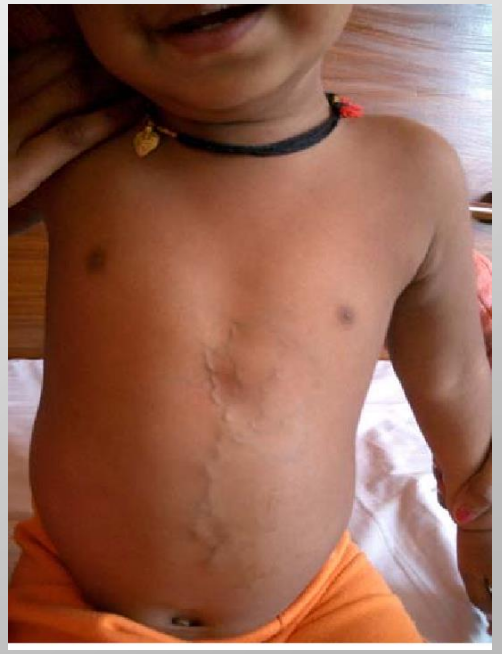
HISTORY AND PHYSICAL SIGNS OF CHRONIC LIVER DISEASE

- Acute vs. chronic hepatitis
- Exposure to hepatotoxic drugs
- Elicit specific mode of transmission in infectious causes
- Family history of liver disease or liver transplantation
- History to suggest viral hepatitis
- Consanguinity for inherited disorders

HISTORY AND PHYSICAL SIGNS OF CHRONIC LIVER DISEASE

- Non-specific
- Failure to thrive
- Pruritus
- Jaundice
- Pallor
- Clubbing
- Symptoms of portal hypertension
- Hepatomegaly vs. shrunken liver
- Neurological signs

COMPLICATIONS OF HEPAPTITIS

- **Hepatic encephalopathy**

	STAGES			
	I	II	III	IV
Symptoms	Periods of lethargy, euphoria; reversal of day-night sleeping; may be alert	Drowsiness, inappropriate behavior, agitation, wide mood swings, disorientation	Stupor but arousable, confused, incoherent speech	Coma IVa responds to noxious stimuli IVb no response
Signs	Trouble drawing figures, performing mental tasks	Asterixis, fetor hepaticus, incontinence	Asterixis, hyperreflexia, extensor reflexes, rigidity	Areflexia, no asterixis, flaccidity
Electroencephalogram	Normal	Generalized slowing, q waves	Markedly abnormal, triphasic waves	Markedly abnormal bilateral slowing, d waves, electric-cortical silence

COMPLICATIONS OF HEPATITIS

- Cirrhosis
- Hepatorenal syndrome
- Hepatopulmonary syndrome
- Hepatocellular carcinoma

HEPATITIS A

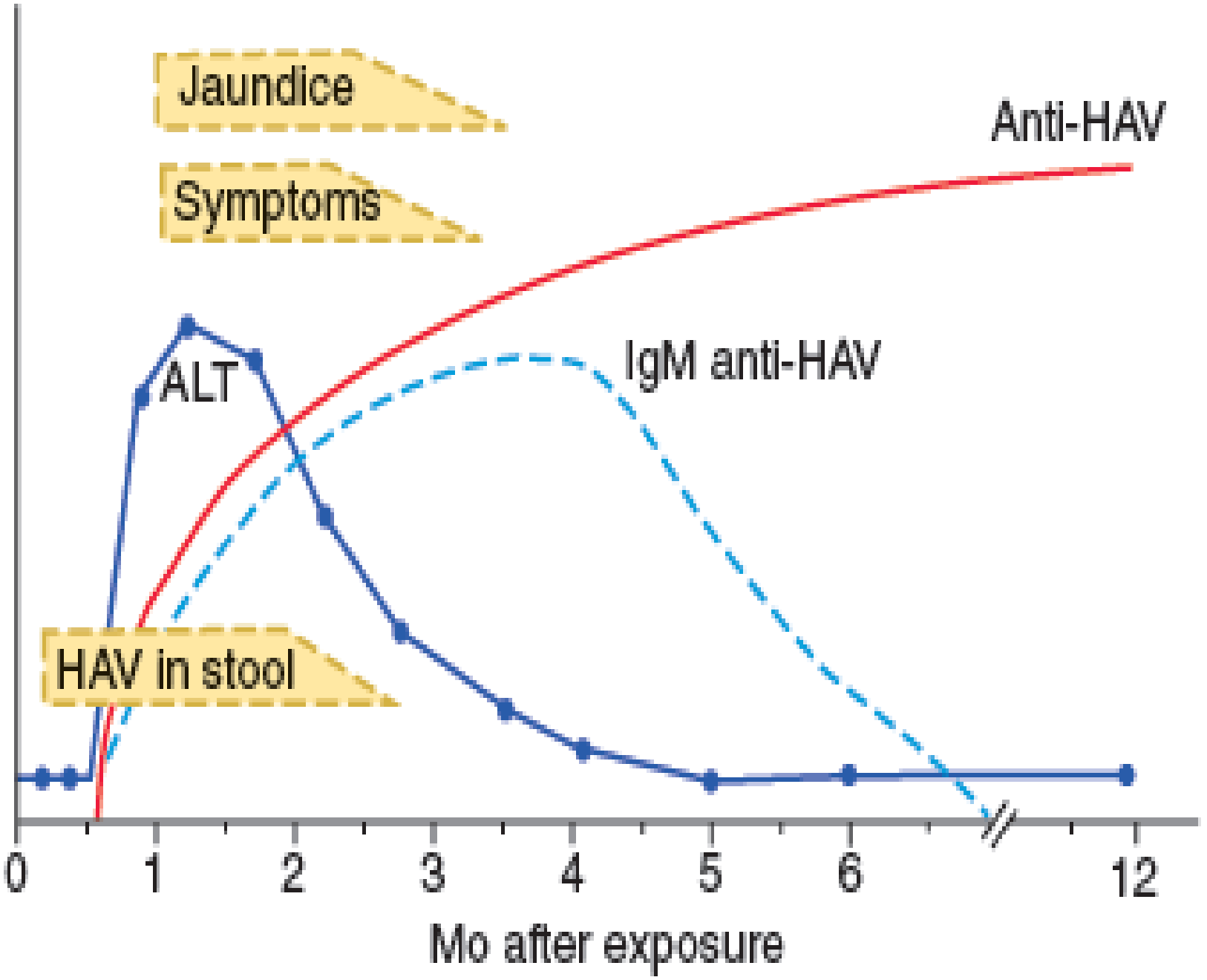
- Acute and benign hepatitis.
- A member of the picornavirus family.
- Humans are the only natural hosts
- Hepatitis is the result of direct cytolytic ad immune-mediated effect of HAV.

HEPATITIS A

- Transmission is either by direct contact or by contaminated food and water.
- The incubation period for HAV is ~4 weeks (14-49 days).
- Fecal excretion of the virus 2-3 weeks before and 1 week after the onset of jaundice.

HEPATITIS A

- Clinical expression is age dependent.
- Jaundice, dehydration, enlarged tender liver.
- Liver enzymes are 20-100 times normal upper level.
- Only 1 in 12 children develops jaundice


Jaundice
Symptoms
Anti-HAV
ALT
IgM anti-HAV
HAV in stool
0
1
2
3
4
5
6
12
Mo after exposure

HEPATITIS A

- **Complications:**
  - Prologed jaundice: may last 12 weeks
  - Relapse : 3-20% 0F CASES
  - Meningioencephalitis
  - Arthritis
  - Fulminant hepatitis: 0.1%

HEPATITIS A

- **Diagnosis:**
  - Positive total anti-hepatitis A antibodies (IgG): current or past infection, passive antibody acquisition, or vaccination.
  - Positive anti-hepatitis A IgM antibodies: current or recent infection.
- **Management:**
  - Supportive
- **Indication for admission:**
  - Ecephalopathy
  - Coagulopathy
  - Decreased oral intake

HEPATITIS A

- Passive immunoprophylaxis should be given no more than two weeks after exposure in case of traveling to endemic areas, immunocompromised children, or household members.
- Active immunoprophylaxis:
  - formalin-inactivated virus
  - Two doses 6-12 months apart in children older than one year.

HEPATITIS B VIRUS

It is a hepadnavirus.

The intact virus is double-shelled:

The external shell expresses the surface antigen HBsAg.

The inner shell expresses the core antigen HBcAg.

Inside the core reside the viral genome, a reverse transcriptase, and a third antigen HBeAg.

EPIDEMIOLOGY AND NATURAL HISTORY

- The number of cases of chronic HBV infection has been estimated at almost 400 million worldwide (~5% of world's population).
- HBV has 8 genotypes (a–h) which are associated with moderate differences in response to therapy
- Maternal-fetal transmission is currently the most common route of HBV transmission because meticulous screening for HBV has been performed in individuals receiving transfusion of blood products.
- Perinatal transmission occurs at or close to the time of birth
- Infants born to mothers positive for HBeAg and mothers with very high serum DNA levels ((>= 109 copies per ml) are at risk for acquiring HBV despite receiving active and passive immunization within 24 hours postpartum.

EPIDEMIOLOGY AND NATURAL HISTORY

- Although hbsag and HBV DNA can be detected in the colostrum and breast milk of hbv-infected mothers, several studies have shown that there is no additional risk of transmission of HBV to breast-fed infants of infected mothers, provided that completed active and passive immunoprophylaxis is received.
- The mode of delivery does not likely influence hbv transmission. A higher incidence of low birth weight and prematurity has been reported in infants born to mothers infected with HBV compared to those born to uninfected mothers.

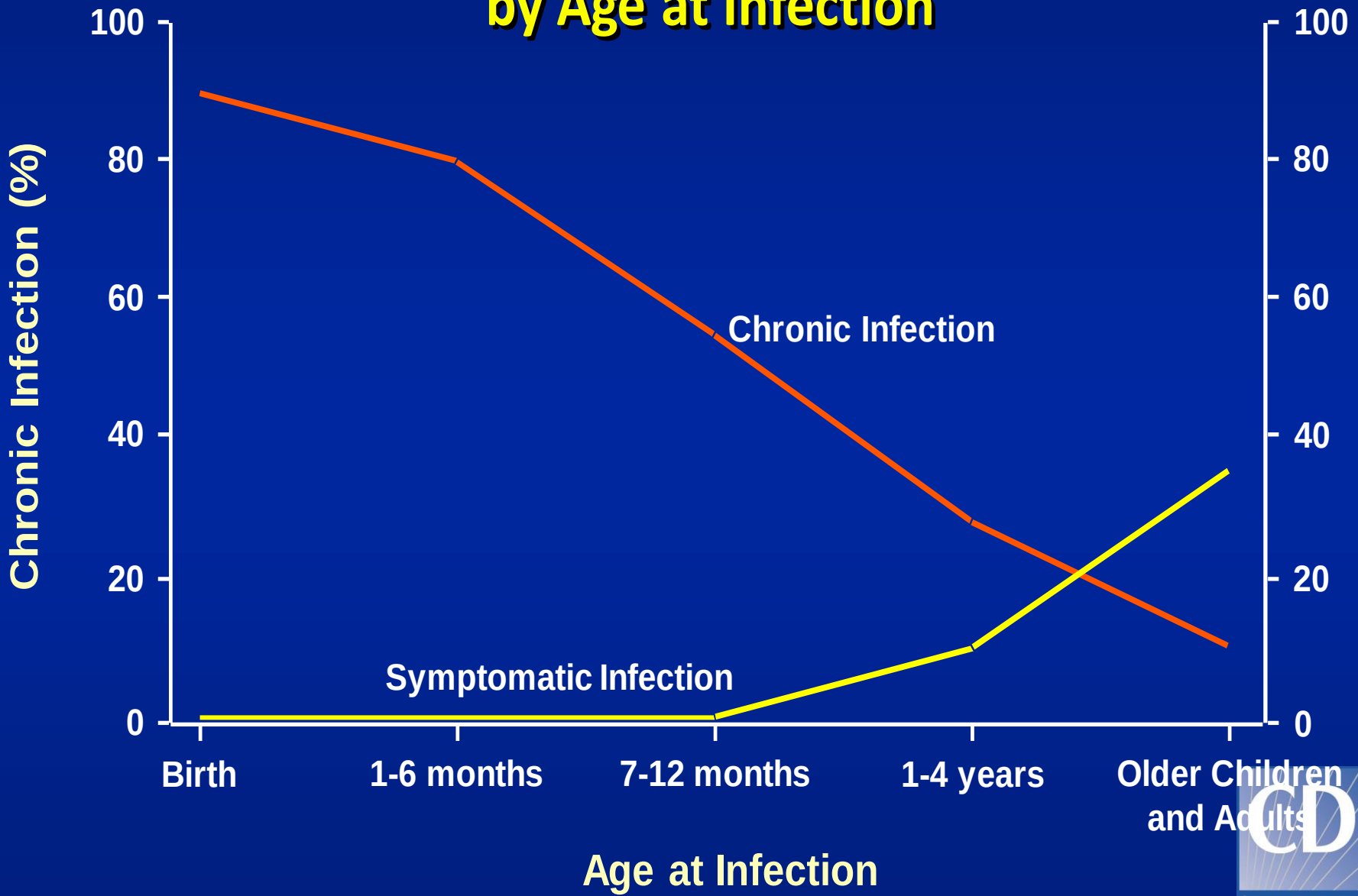
EPIDEMIOLOGY AND NATURAL HISTORY

- About 1/3 of older children and adolescents with acute HBV infection will develop classical symptoms of hepatitis.
- Cirrhosis and hepatocellular carcinoma, mostly in adulthood, may be anticipated in about 25% of those who acquire HBV infection during infancy or childhood.

HEPATITIS B TRANSMISSION

- The hepatitis B virus cannot penetrate unbroken skin and is killed by the digestive juices in the stomach if it is swallowed.
- There is a 95% chance that a mother with chronic hepatitis b will pass it on to her baby
- Babies born to hepatitis b positive mothers can be given vaccination and hepatitis B immunoglobulin at birth, which reduces the risk of hepatitis b transmission to only 5%
- Overall, the risk of acquiring hepatitis B from needle-stick (or sharps) injury in a health care setting is around 30%.

Outcome of Hepatitis B Virus Infection by Age at Infection



CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

THE OUTCOME OF HEPATITIS B VIRUS INFECTION BY THE AGE OF INFECTION

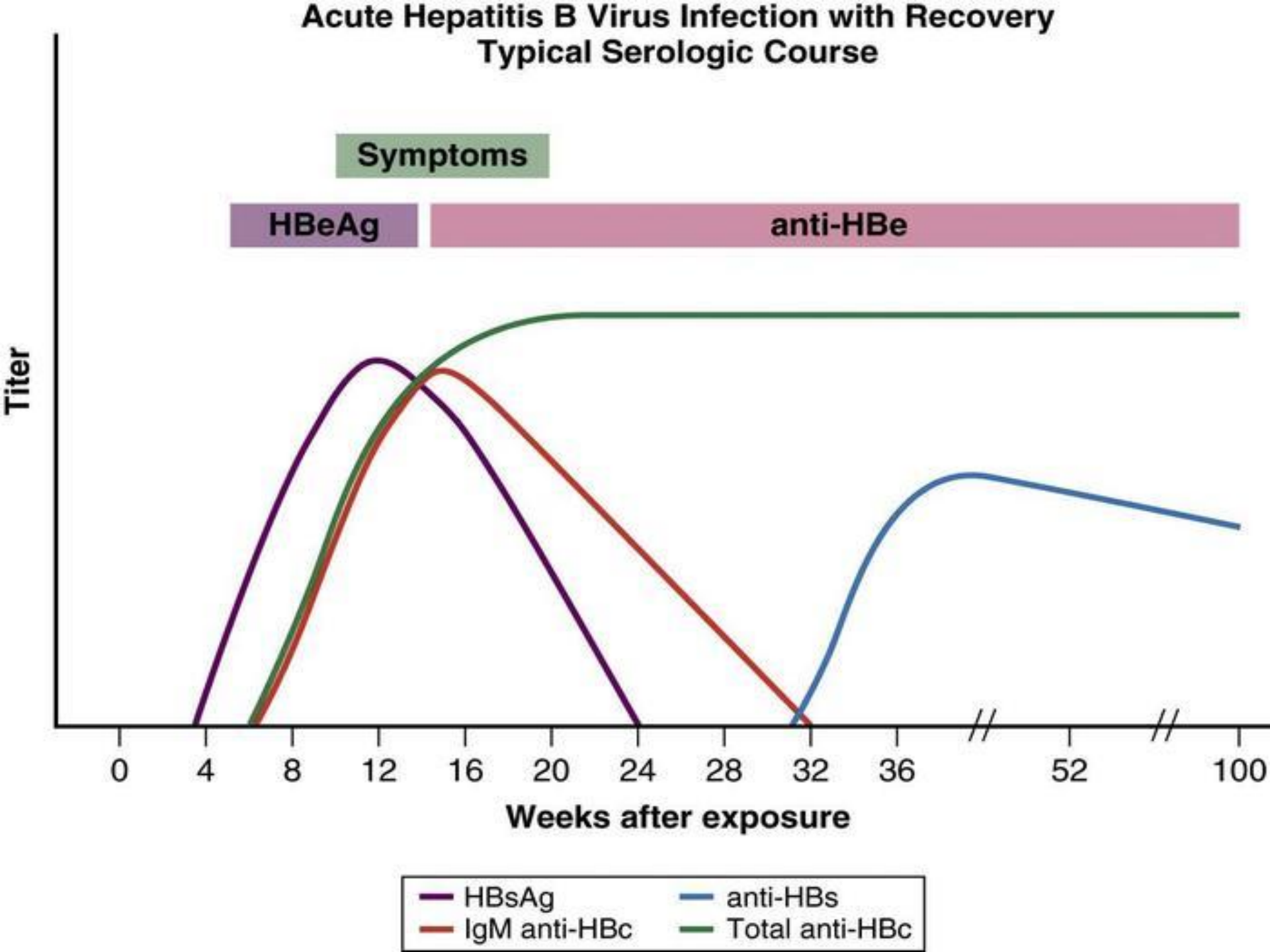
- Approximately 90% of children infected as infants will develop chronic HBV infection (CHB).
- The risk falls to 25 – 50% for children who become infected after early infancy but before age 5 years and to only 5 – 10% for children who become infected in adolescents or adulthood.
- Anti-HBs and HBsAg should be tested at 9 to 12 months of age or one to two months after the last dose of hepatitis B vaccine given to an at-risk infant.

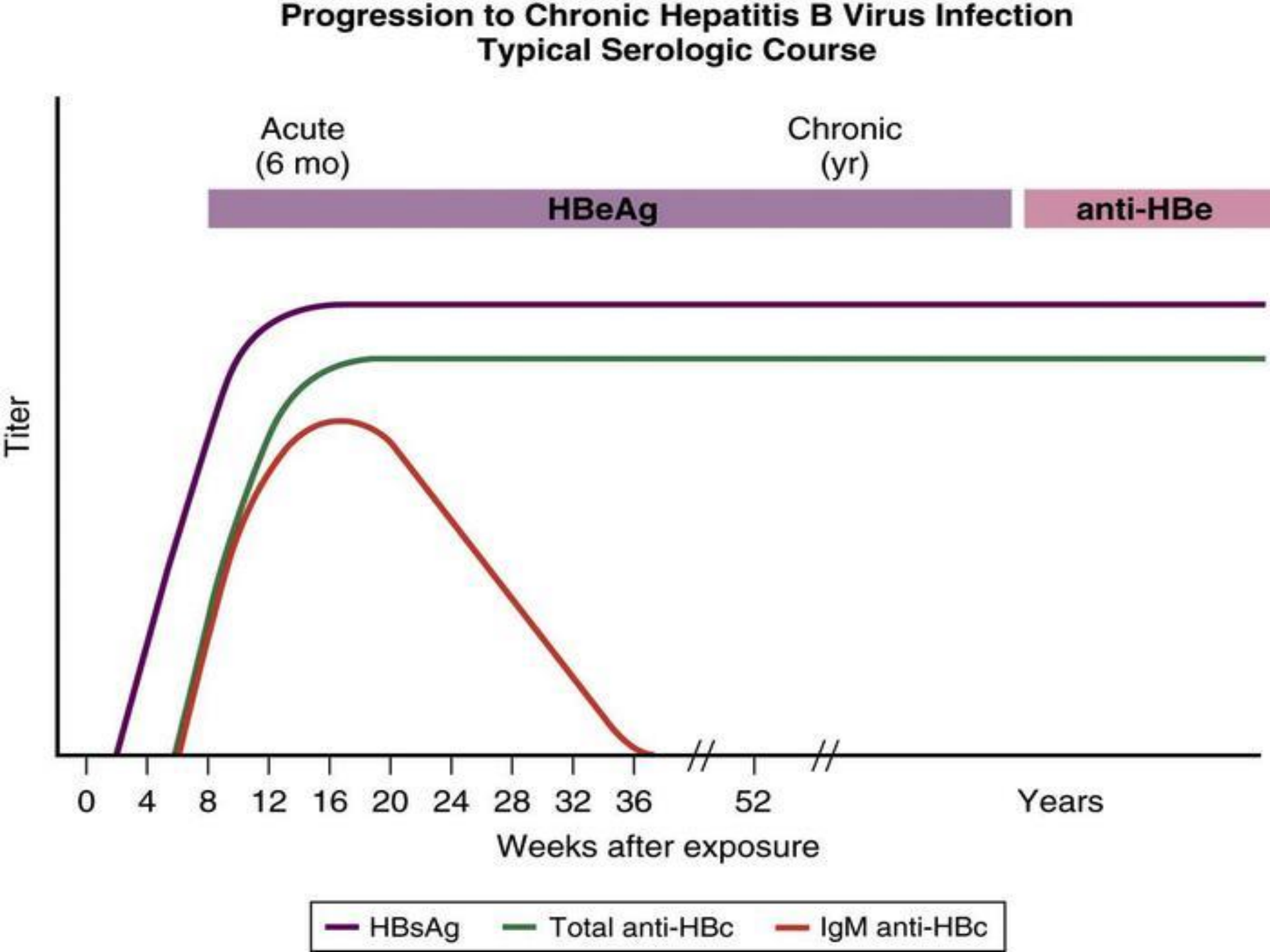
RISK FACTORS FOR HBV INFECTION

- Intravenous drugs or blood products
- Acupuncture or tattoos
- Sexual contact
- Institutional care and intimate contact with carriers.
- Occupational exposure (health care workers)
- Perinatal exposure to HBsAg positive mother
- No risk factors are identified in ~40% of cases.

SEROLOGY OF HBV

- Acute hepatitis: positive HBsAg and HBcAb IgM for < 6 months
- HbeAg: correlate with high infectivity and viral replication
- HBcAb IgG remains positive after the infection regardless of the outcome (resolved or carrier or chronic phase)
- Chronic HBV= persistence of HBsAg > 6 months


Acute Hepatitis B Virus Infection with Recovery
Typical Serologic Course
Symptoms
HBeAg
anti-HBe
Titer
0
4
8
12
16
20
24
28
32
36
52
100
Weeks after exposure
HBsAg
IgM anti-HBc
anti-HBs
Total anti-HBc


Progression to Chronic Hepatitis B Virus Infection
Typical Serologic Course
Acute
(6 mo)
Chronic
(yr)
HBeAg
anti-HBe
Titer
0
4
8
12
16
20
24
28
32
36
52
Years
Weeks after exposure
HBsAg
Total anti-HBc
IgM anti-HBc

Phases	Immune Tolerant	Immune active	Immune inactive
Serum Aminotransferase	normal or mildly elevated (ALT <2 times the upper limit of normal)	elevated serum aminotransferases (ALT>1.5 to 2 times the upper limit of normal)	Normal
HBV Replication	Active	Active	Inactive
HBV DNA	>20,000 IU/mL or 10^5 copies/mL	>20,000 IU/mL or 10^5 copies/mL	low or undetectable levels
HBsAg	Positive	Positive	Positive
HBeAg	Positive	Positive	Negative
Anti HBs	Negative	Negative	Negative
Spontaneous clearance	Less likely	Possible	possible
Response to antiviral therapy	Less likely	Highly possible	possible

PREVENTION AND TREATMENT

- The combination vaccination strategy (HBIG and HBV vaccine series) for high-risk neonates significantly prevents vertical transmission to neonates born to HBV-infected mothers.
- Children and adolescents with CHB should be immunized against hepatitis A, if not already immune.
- Not all children with CHB would benefit from antiviral therapy due to potential side effects and the development of antiviral resistance.
- Treatment should be considered for children with immune active CHB regardless of HBsAg status or if the liver er biopsy shows moderate to severe inflammation or the presence of fibrosis.
- The goal of treatment for CHB is to suppress HBV replication, reduce liver inflammation, reverse hepatic fibrosis, and prevent the development of cirrhosis and HCC.

PREVENTION OF HEPATITIS B INFECTION

- **Hepatitis B vaccine**
  - 3 doses (0, 1 month, 6-12 months)
  - Preterm
- **Hepatitis B- specific immunoglobulin**

  Contaminated needle-stick exposure

  Perinatal exposure for newborns of positive HBsAg mothers within 12 hours after birth (in addition to the first dose of HBV vaccine)

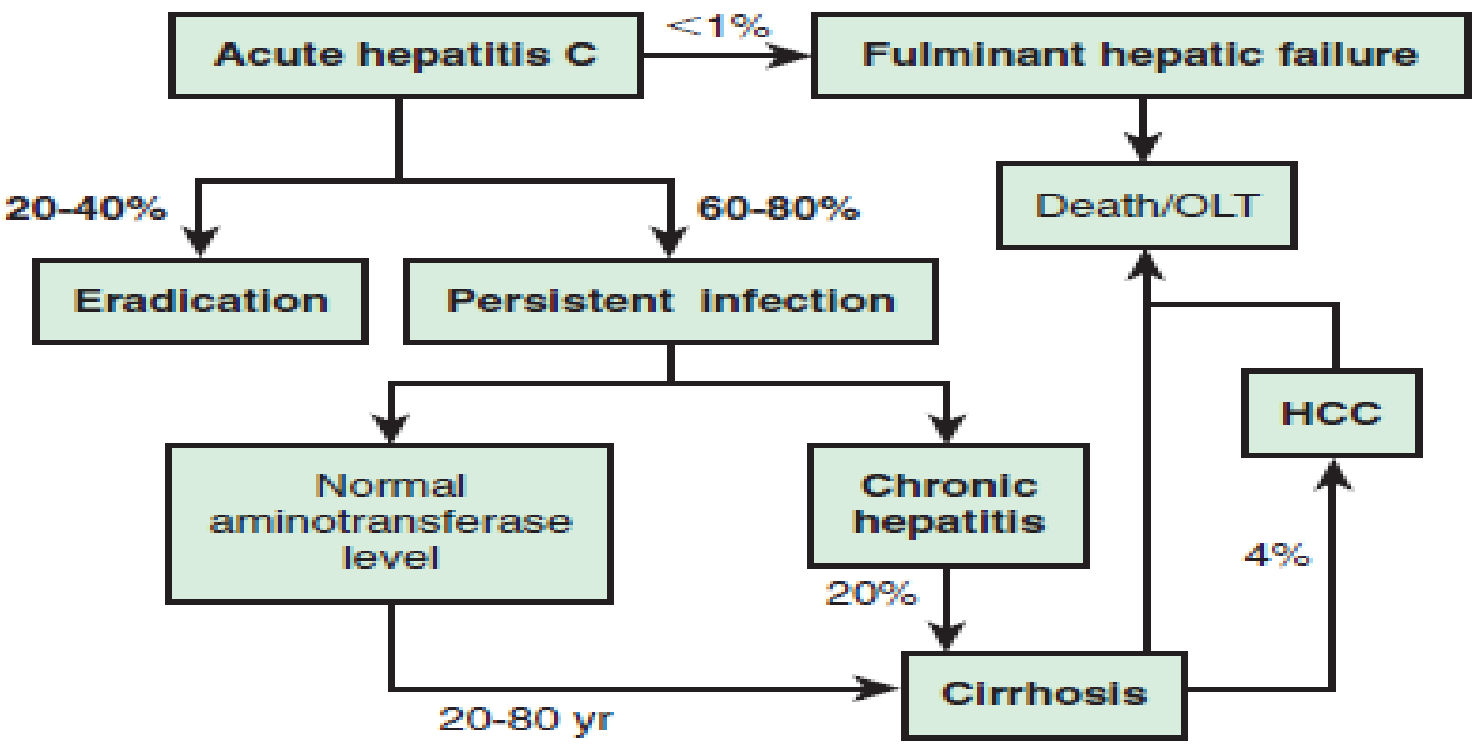
  Pre and post liver transplant for HBsAg patient

HEPATITIS C VIRUS

HEPATITIS C VIRUS

- RNA VIRUS
- 6 GENOTYPES
- 85% OF INFECTED CASES REMAINED CHRONIC

NATURAL HISTORY OF HCV INFECTION



RISK FACTORS FOR HCV TRANSMISSION

- BLOOD TRANSFUSION
- ILLEGAL DRUG USE
- EXPOSURE TO BLOOD OR BLOOD PRODUCTS
- SEXUAL TRANSMISSION
- OCCUPATIONAL EXPOSURE
- 10% OF NEW INFECTIONS HAS NO KNOWN TRANSMISSION SOURCE.

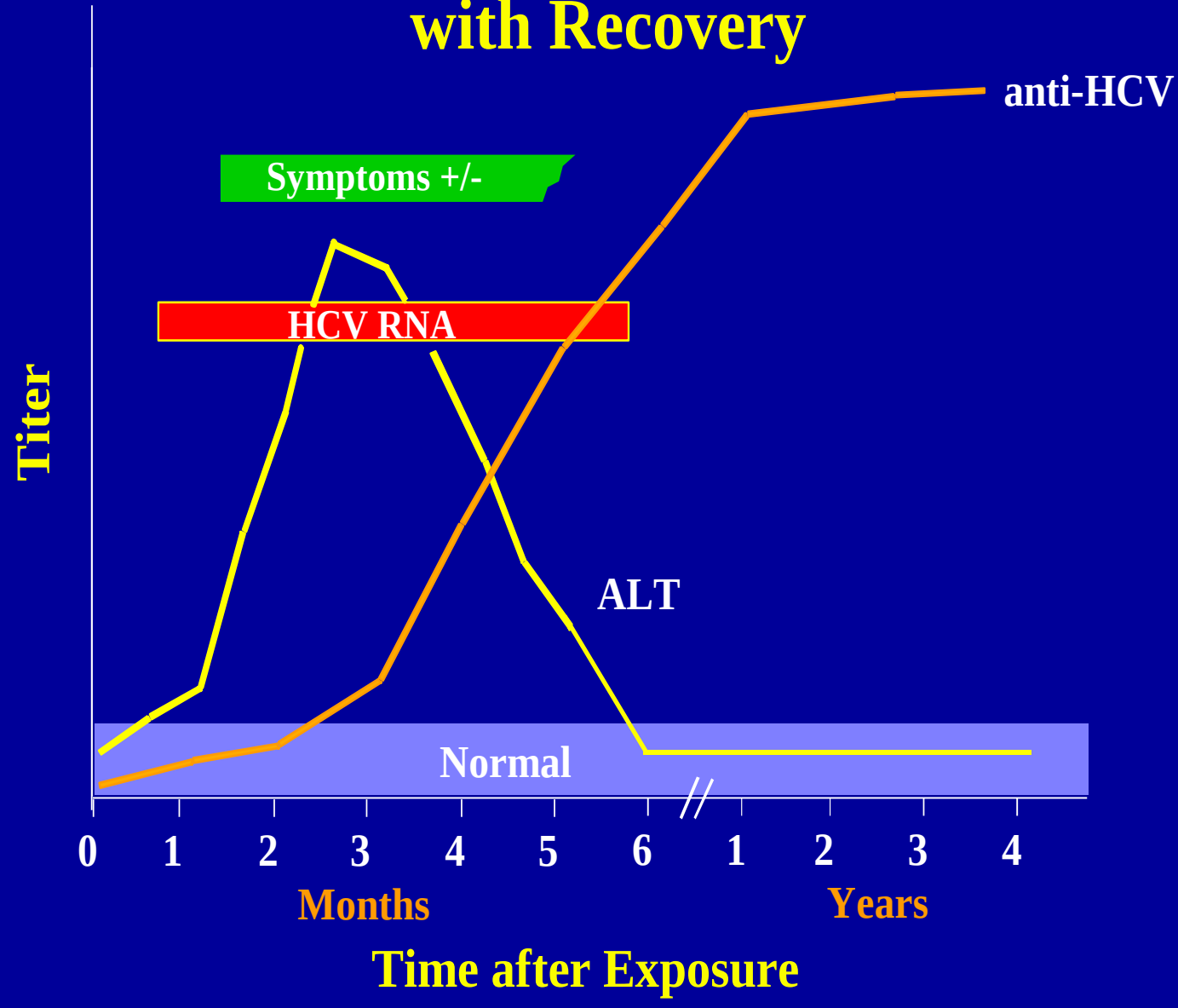
DIAGNOSIS OF HCV INFECTION

- HCV ANTIBODIES
- HCV BY PCR

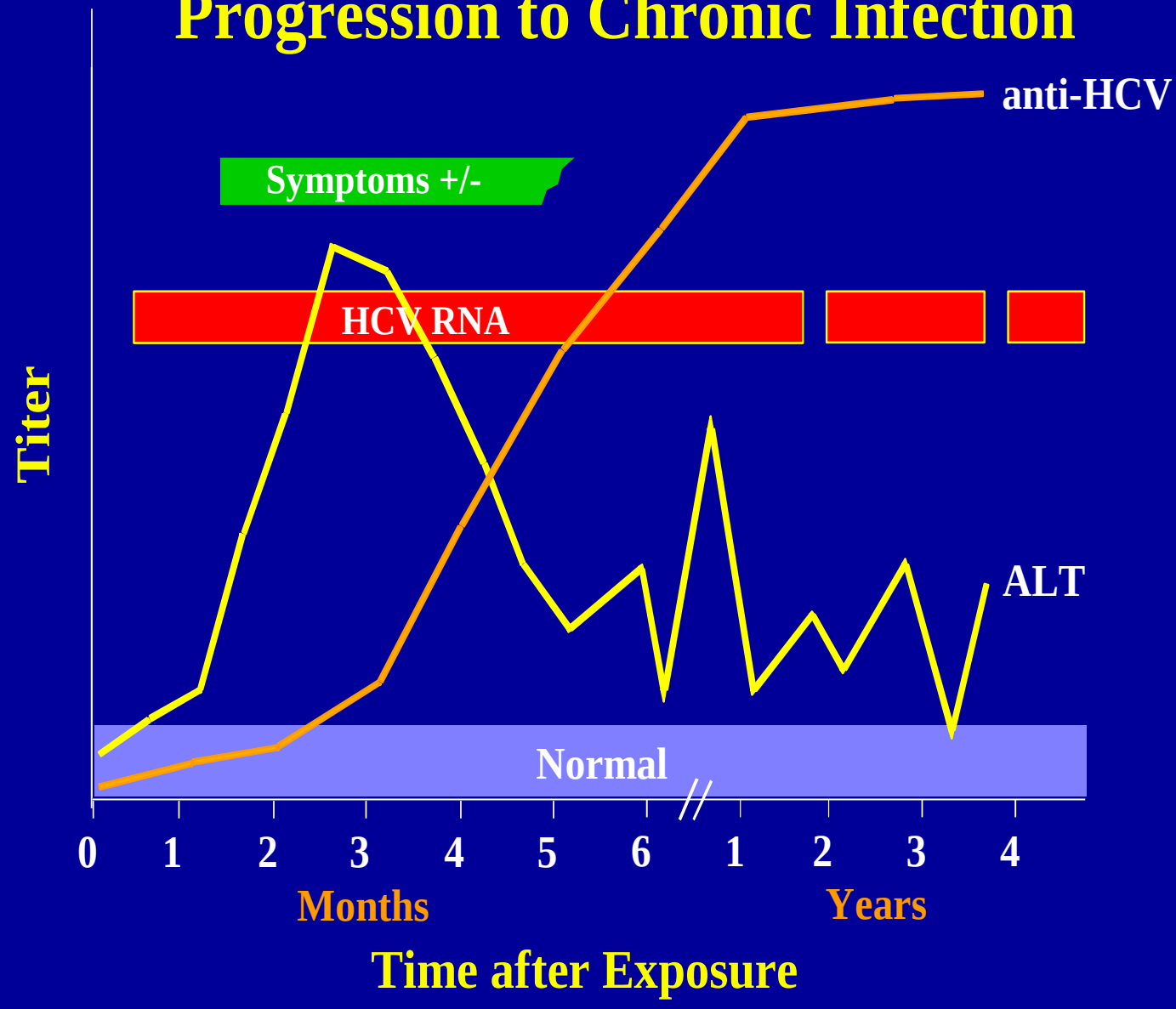
SEROLOGY OF HCV

- POSITIVE HCV ANTIBODIES
- ACUTE INFECTION
- CHRONIC INFECTION
- RESOLVED INFECTION

Serologic Pattern of Acute HCV Infection with Recovery



Serologic Pattern of Acute HCV Infection with Progression to Chronic Infection



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PREVENTION OF HEPATITIS C VIRUS INFECTION

- NO PROTECTIVE IMMUNOGLOBULIN
- NO VACCINE AVAILABLE
- PRECAUTIONS , BEHAVIORAL MODIFICATIONS
- PREVENTION BY SCREENING DONATED BLOOD

TREATMENT OF HEPATITIS C VIRUS

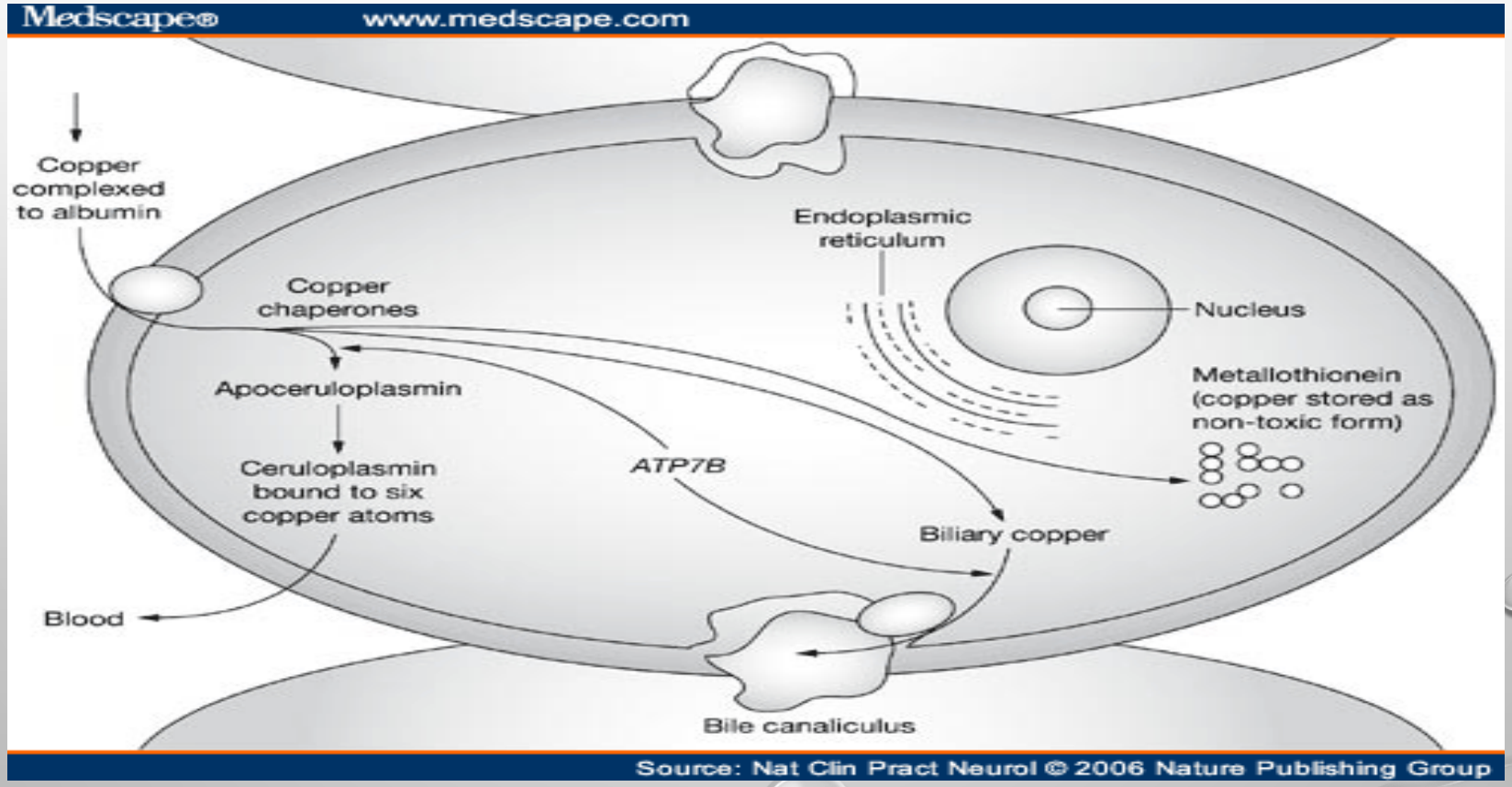
INDICATIONS FOR TREATMENT:

- DETECTABLE HCV- RNA BY PCR > 6 MO
- ELEVATED ALT
- EVIDENCE OF CHRONIC HEPATITIS AND FIBROSIS BY LIVER BIOPSY

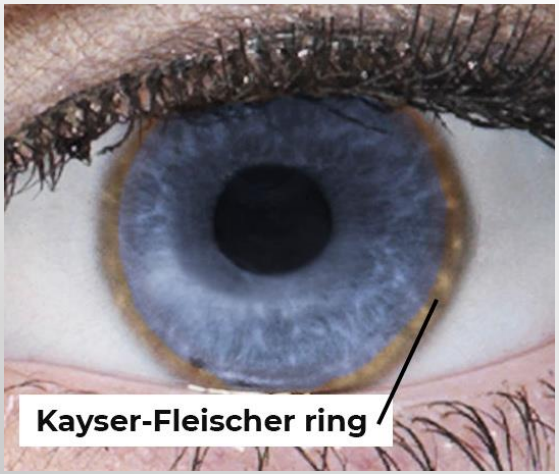
NON-VIRAL CHRONIC HEPATITIS

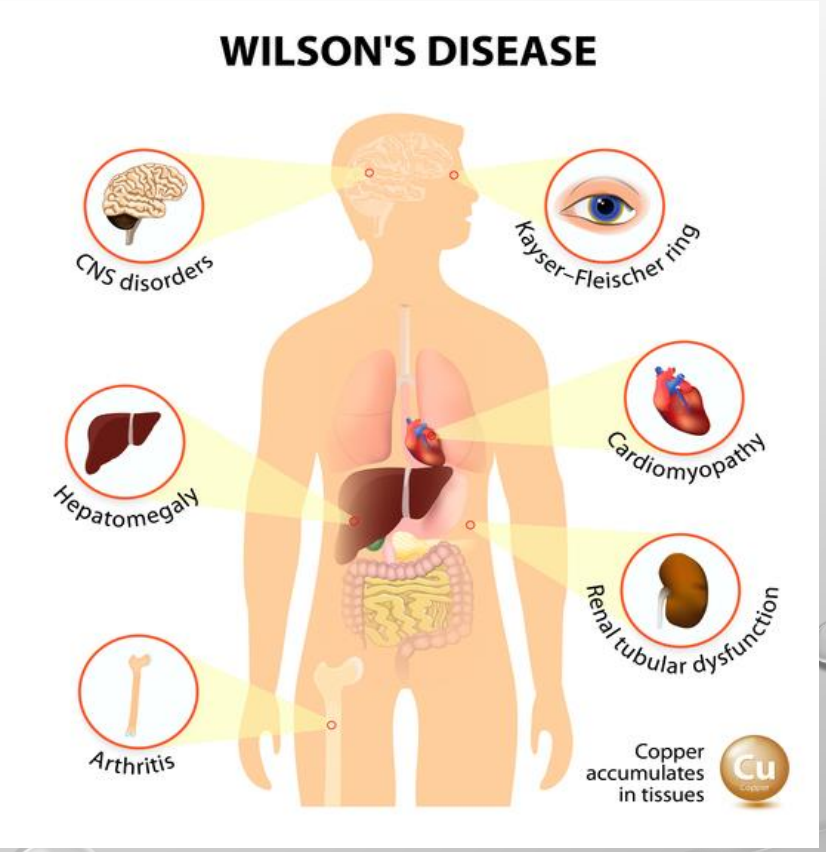
WILSON DISEASE (HEPATOLENTICULAR DEGENERATION)

WILSON'S DISEASE PATHOPHYSIOLOGY



WILSON'S DISEASE CLINICAL MANIFESTATIONS





WILSON DISEASE

DIAGNOSIS

- LOW SERUM CERULOPLASMIN
- ELEVATED SERUM COPPER
- HIGH 24 HR URINE COPPER
- QUANTITATIVE COPPER IN LIVER BIOPSY IS THE DEFINITIVE DIAGNOSTIC TEST

MANAGEMENT OF WILSON DISEASE

- COMPENSATED LIVER DISEASE
- DECOMPENSATED CIRRHOSIS OR FULMINANT LIVER FAILURE
- SCREEN THE SIBLINGS WITH CERULOPLASMIN OR GENETIC MUTATION IF IT IS KNOWN FROM PROBAND CASE

AUTOIMMUNE HEPATITIS

AUTOIMMUNE HEPATITIS (AIH)

- AUTOIMMUNE HEPATITIS IS……..
  - ELEVATED SERUM AMINOTRANSAMINASE CONCENTRATIONS,
  - LIVER-ASSOCIATED SERUM AUTOANTIBODIES,
  - +/- HYPERGAMMAGLOBULINEMIA.
- MIGHT BE ASSOCIATED WITH OTHER AUTOIMMUNE DISEASES

AUTOIMMUNE HEPATITIS (AIH)

CLINICAL PICTURE

- ASYMPTOMATIC ELEVATION OF LIVER ENZYMES
- NON-SPECIFIC
- JAUNDICE
- AMENORRHEA
- STIGMATA OF CHRONIC LIVER DISEASE
- EXTRAHEPATIC MANIFESTATIONS
- FEATURES OF CIRRHOSIS

Table 354-2 CLASSIFICATION OF AUTOIMMUNE HEPATITIS

VARIABLE	TYPE 1 AUTOIMMUNE HEPATITIS	TYPE 2 AUTOIMMUNE HEPATITIS
Characteristic autoantibodies	Antinuclear antibody*	Antibody against liver-kidney microsome 1*
	Smooth-muscle antibody*	
	Antiactin antibody‡	Antibody against liver cytosol 1*
	Autoantibodies against soluble liver antigen and liver-pancreas antigen‡	
	Atypical perinuclear antineutrophil cytoplasmic antibody	
Geographic variation	Worldwide	Worldwide; rare in North America
Age at presentation	Any age	Predominantly childhood and young adulthood
Sex of patients	Female in ~75% of cases	Female in ~95% of cases
Association with other autoimmune diseases	Common	Common§
Clinical severity	Broad range	Generally severe
Histopathologic features at presentation	Broad range	Generally advanced
Treatment failure	Infrequent	Frequent
Relapse after drug withdrawal	Variable	Common
Need for long-term maintenance	Variable	~100%

DIAGNOSIS OF AIH

- ELEVATION OF TRANSAMINASES
- ELEVATED GAMMA-GLOBULIN LEVELS
- THE PRESENCE OF AUTOANTIBODIES
- CHARACTERISTIC HISTOLOGIC FINDINGS

TREATMENT OF AIH

- PREDNISONE
- AZATHIOPRINE OR 6-MERCAPTOPURINE
- LIVER TRANSPLANTATION FOR PATIENTS WITH END-STAGE LIVER DISEASE
- DISEASE CAN RECUR AFTER LIVER TRANSPLANTATION

DIG UP

- HOW DO WE SCREEN BLOOD FOR HRPATITIS B ?
- WHAT MEDICATIONS ARE USED TO TREATMENT OF HEPATITIS B?
- WHAT MEDICATIONS ARE USED TO TREATMENT OF HEPATITIS C?
- HOW TO FOLLOW UP PATIENTS WITH HEPATITIS C?