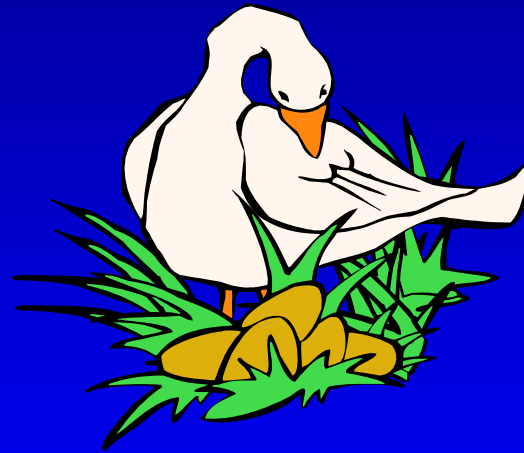


# Viral Hepatitis



Prof. MUDr. Petr Husa, CSc.

Klinika infekčních chorob, FN Brno

# Viral Hepatitis

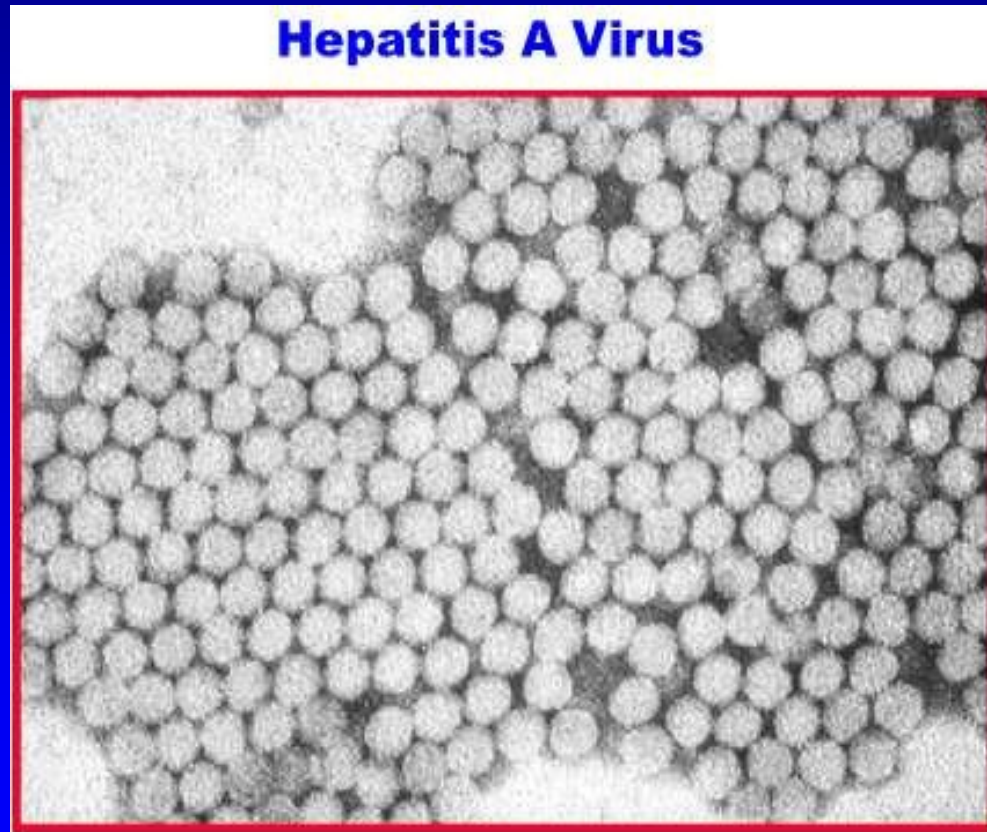
1. Enterically transmitted – no chronic stage
  - VH A
  - VH E
2. Parenterally transmitted – possible chronic stage
  - VH B
  - VH C
  - VH D

# Viral Hepatitis in CR 1999-2009

	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
<b>VH A</b>	933	614	325	127	114	70	322	132	128	1648	1106
<b>VH B</b>	636	604	457	413	370	392	361	304	307	306	247
<b>VH C</b>	634	637	798	858	846	868	844	1022	980	980	843
<b>VH E</b>	5	12	13	12	21	36	37	35	43	62	99

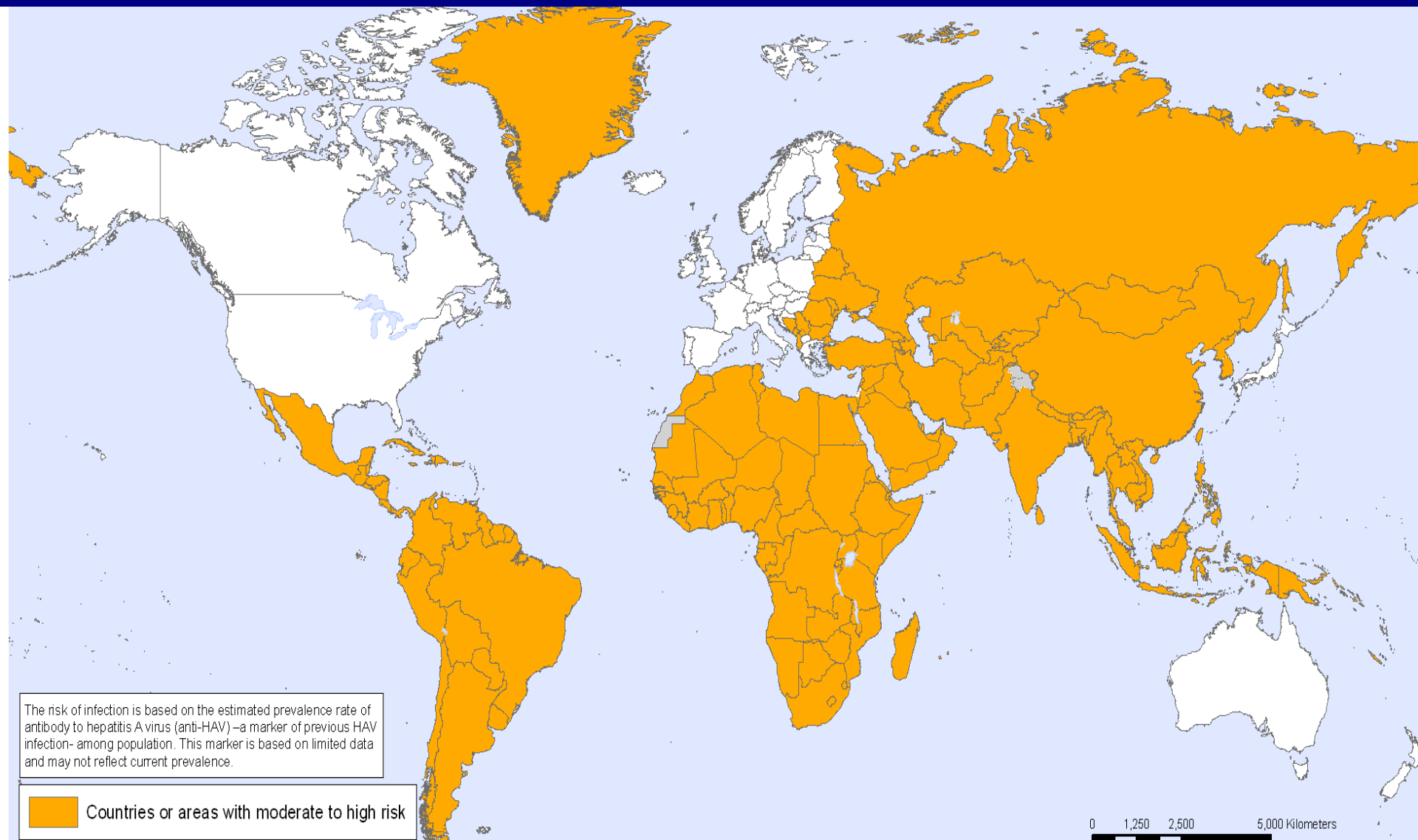
	<b>A</b>	<b>B</b>	<b>C</b>	<b>D</b>	<b>E</b>
<b>Genom</b>	RNA	DNA	RNA	RNA	RNA
<b>Incubation</b>	15-50	30-180	15-180	30-180	15-60
<b>Enteral</b>	Yes	No	No	No	Yes
<b>Parenteral</b>	Rare	Yes	Yes	Yes	No
<b>Sexual</b>	Rare	Yes	Rare	Yes	Rare
<b>Vertical</b>	No	Yes	Rare	Yes	Yes
<b>Chronicity</b>	No	Yes	Yes	Yes	Very rare
<b>Vaccination</b>	Yes	Yes	No	VH B	No
<b>Imunoglob.</b>	Yes	Yes	No	VH B	No

# Hepatitis A



family *Picornaviridae*, genus *Hepatovirus* – non-enveloped RNA, 27 nm

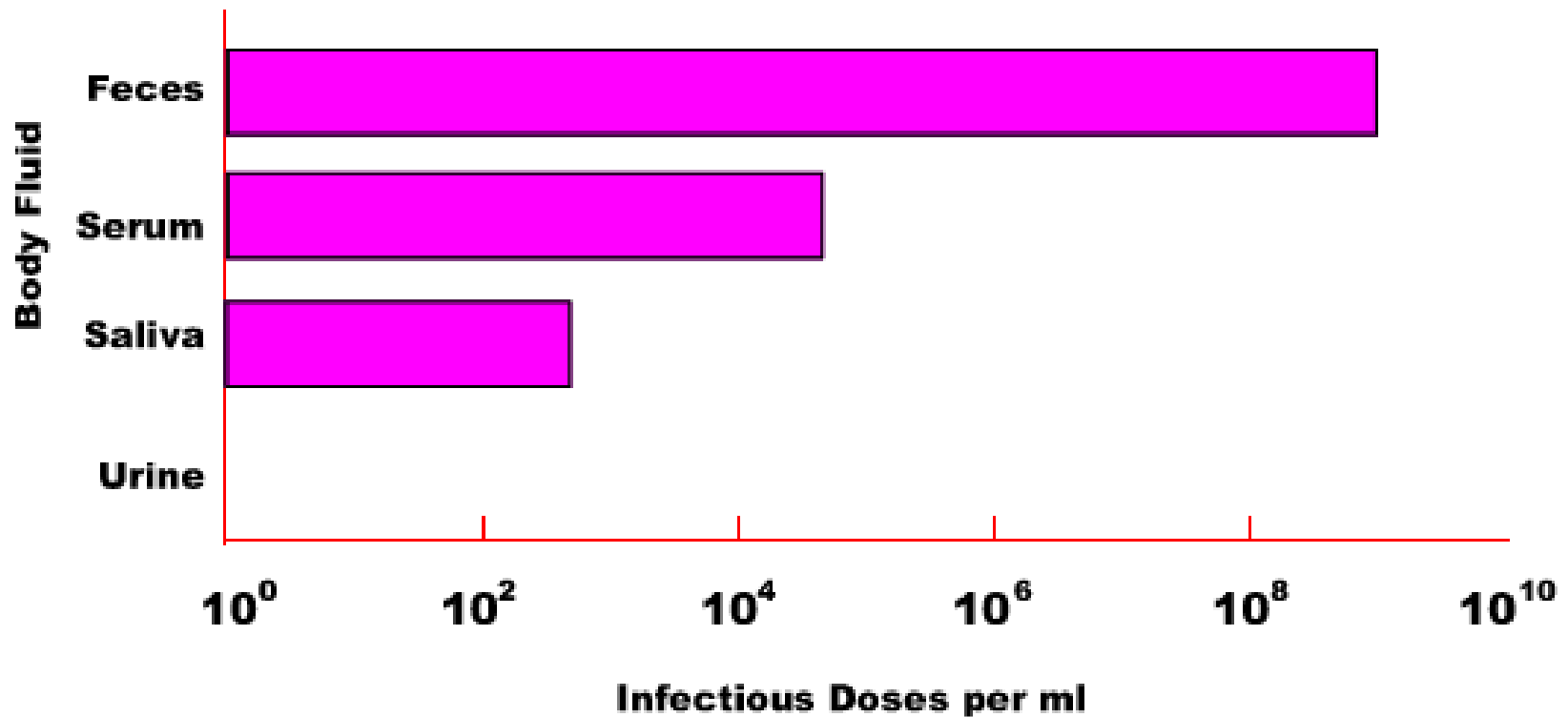
# Hepatitis A



# Epidemiology

- Fecal –oral route of transmission
  - ✓ Contaminated hands or daily used instruments
  - ✓ Contaminated drinking water
  - ✓ Contaminated food
- Vaccination available, recommended especially for travelers to countries with lower standard of hygiene

## Concentration of Hepatitis A Virus in Various Body Fluids

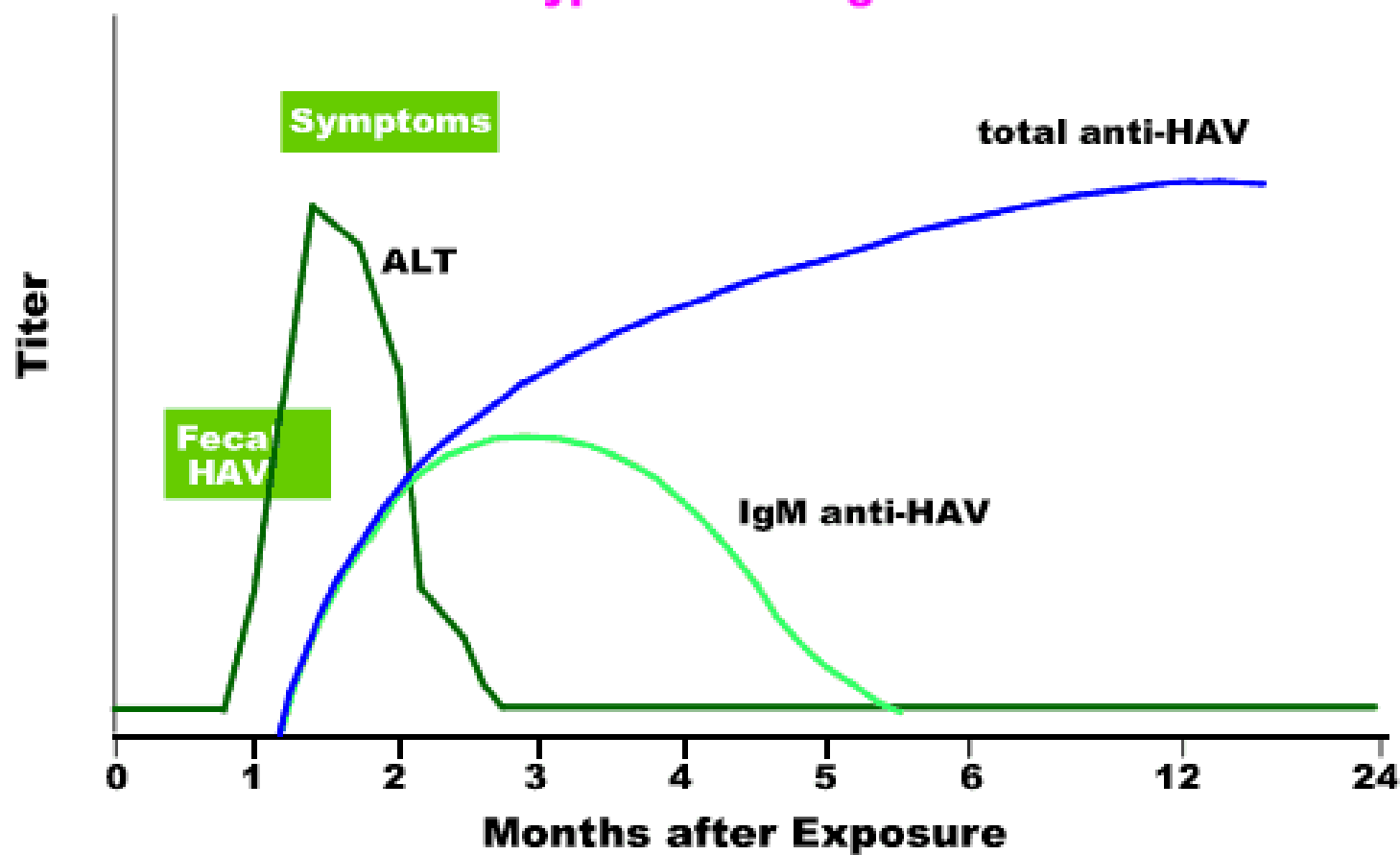


Source: Viral Hepatitis and Liver Disease 1984;9-2  
J Infect Dis 1989; 160:887-890



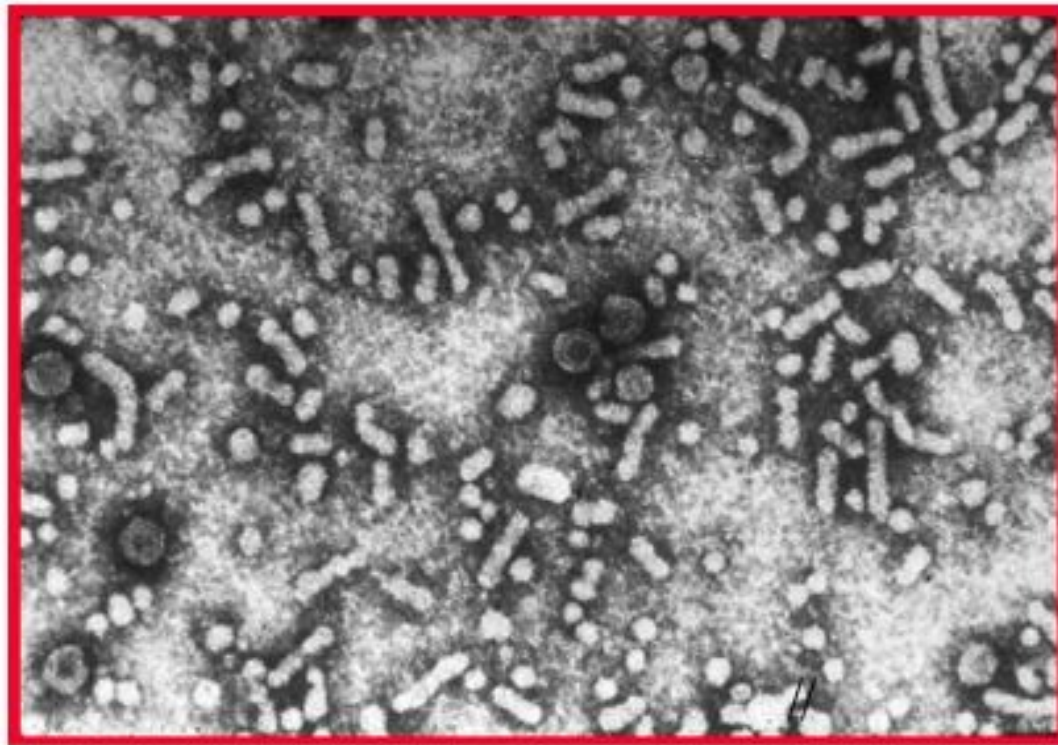
# Hepatitis A Virus Infection

## Typical Serologic Course



# Hepatitis B

## Hepatitis B Virus

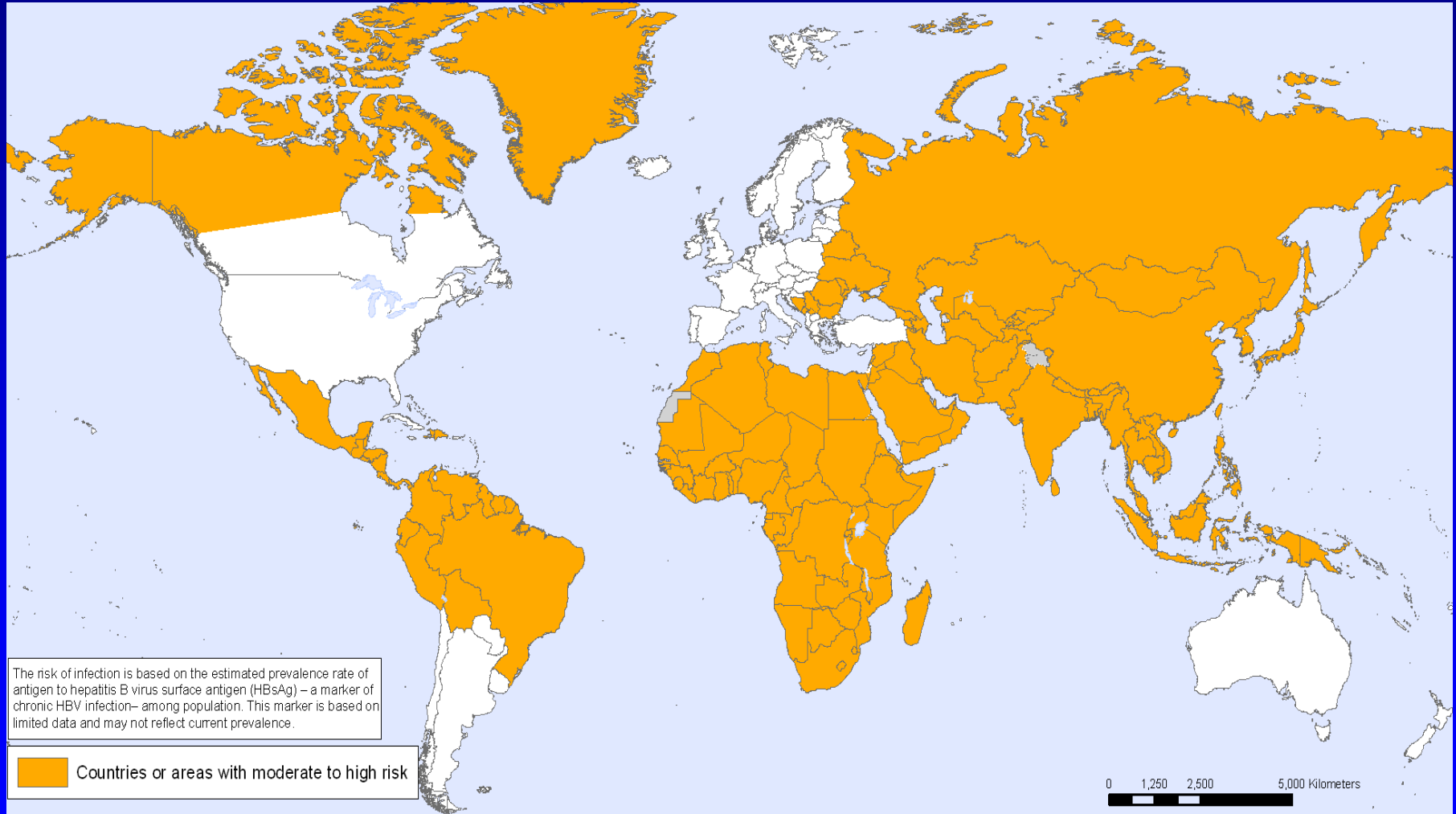


family *Hepadnaviridae*, enveloped DNA virus, 42 nm

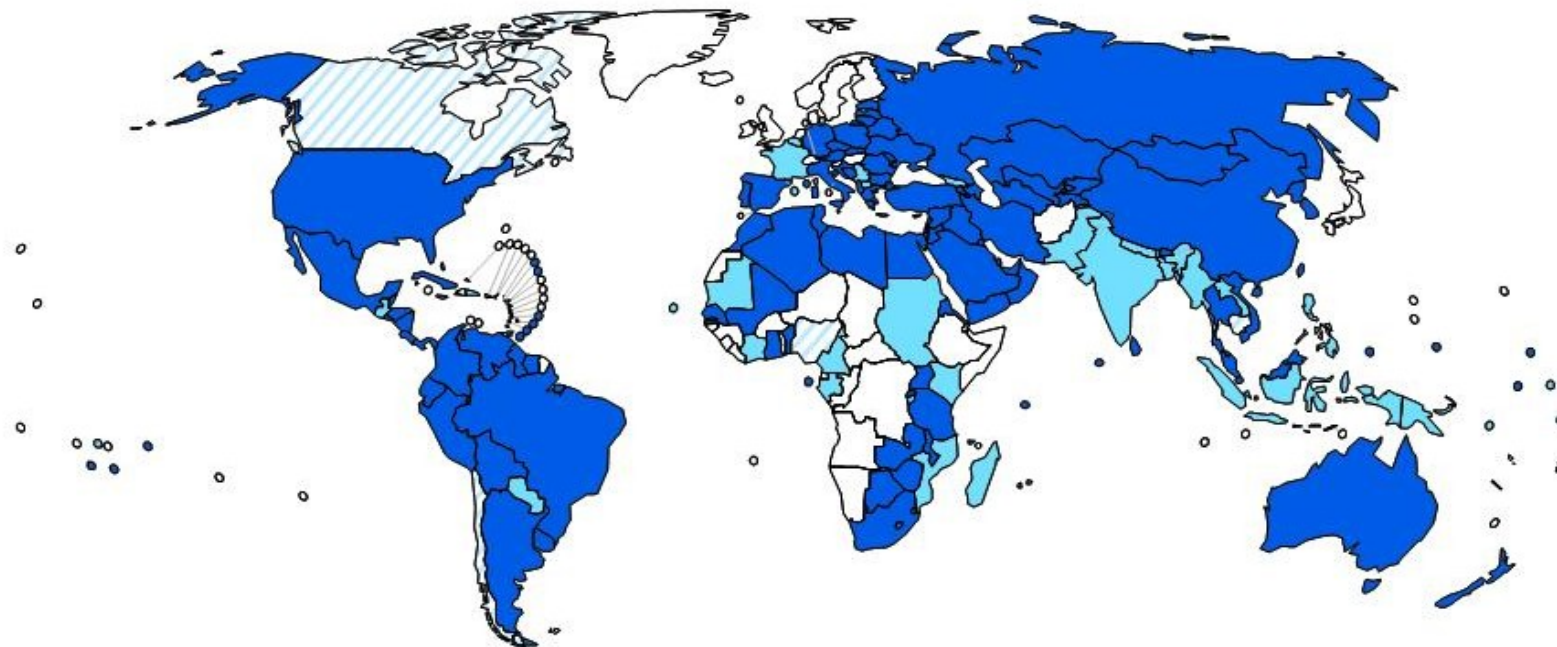
# Global significance of HEP B

- One of the biggest global health problems
  - ✓ More than 2 billions of infections during the life
  - ✓ 350-400 million chronic carriers - China (125 million), Brazil (3,7 million), South Korea (2,6 million), Japan (1,7 million), USA (more than 1 million), Italy (900 thousand).
  - ✓ 25-40 % chronic carriers have LC or HCC, 0,5-1,0 million death due to decompensated LC or HCC
  - ✓ 50 thousand death annually due to fulminant hepatitis
  - ✓ Global vaccination in 158 countries

# Hepatitis B



# Global vaccination against HBV- 2005



158 countries introduced in national infant immunization schedule

■ HepB3  $\geq$  80% (119 countries or 62%)

■ HepB3 < 80% (36 countries or 19%)

▨ HepB vaccine introduced but no coverage data reported (3 countries or 1%)

□ HepB\* vaccine not introduced (34 countries or 18%)

\* 4 countries introduced HepB in adolescent immunization schedule

Source: WHO/UNICEF coverage estimates 1980-2005, August 2006

Date of slide: 5 September 2006

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.  
© WHO 2006. All rights reserved.



# Hepatitis B in Czech Republic

- Still important infection but incidence and prevalence are gradually decreasing
  - ✓ Prevalence of chronic carriers was 0.56 % (2001)
  - ✓ Prevalence of historical antibodies anti-HBc total was 5,59% (2001)
  - ✓ Decrease of prevalence and incidence due to vaccination of high-risk persons (health care workers, newborns of HBsAg-positive mothers, before hemodialysis)
  - ✓ Global vaccination of all newborns and 12-years old children since 2001

# Epidemiology of HEP B

- **Transmission**
  - ✓ blood and blood products
  - ✓ sexual intercourse
  - ✓ organ and tissue transplant recipients
  - ✓ vertically from mother to newborn
- **Who is in the highest risk in well-developed countries?**
  - ✓ intravenous drug abusers
  - ✓ persons with multiple sexual partners

# Clinical pictures of acute HEP B

- IP: 30–180 days (mostly 2–3 months)
- Prodomal stage - flu-like syndrome
- Icteric form: < 5 years < 10 %, > 5 years (30–50 %)
- Chronicity: newborns > 90 %, children 30-40 %, adults 5–10 %
- Fulminant hepatitis: < 1 %
- Chronic HBV infection mortality: 15 – 25 %



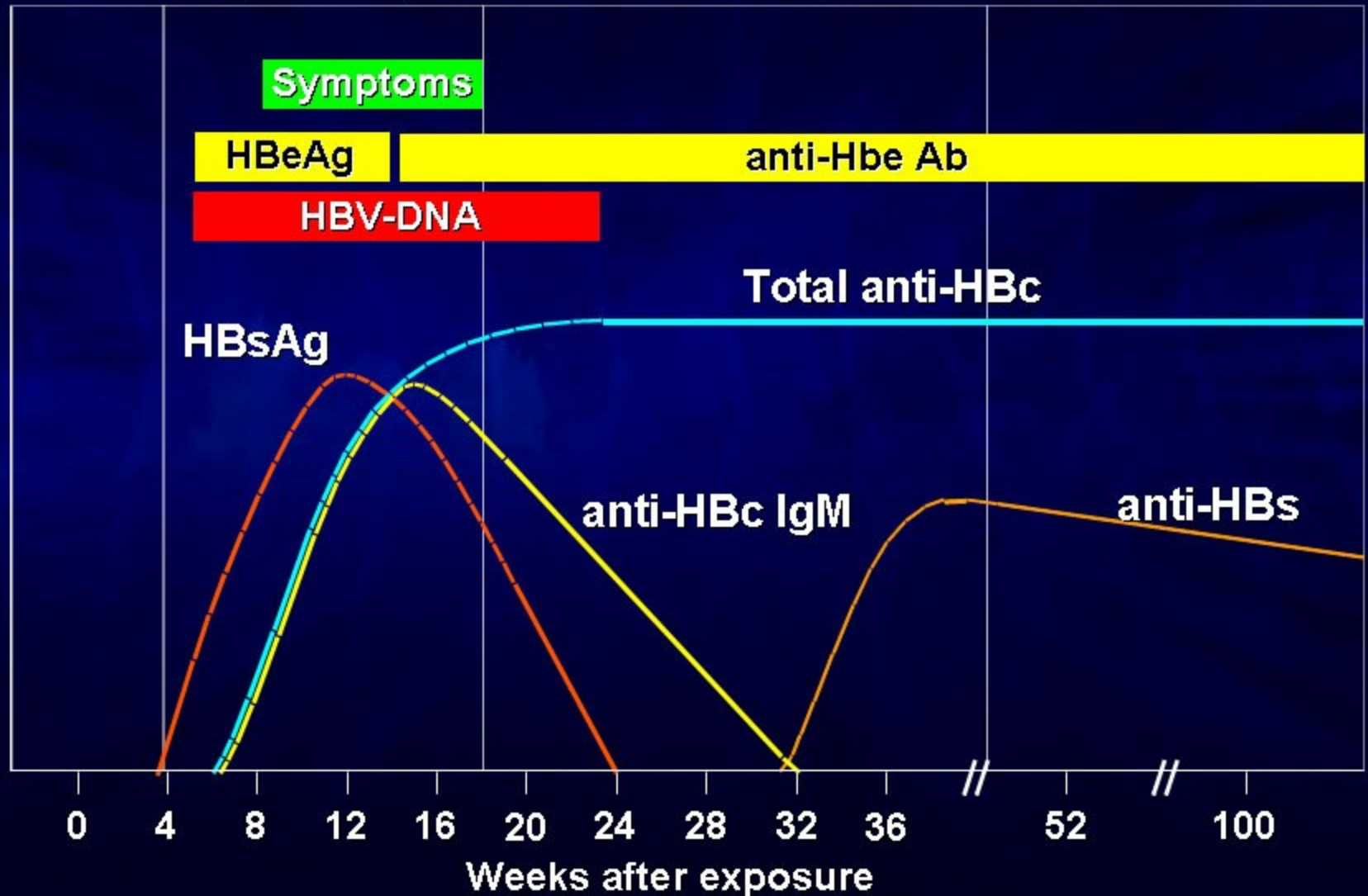
# Acute Hepatitis B

Incubation  
4-12 weeks

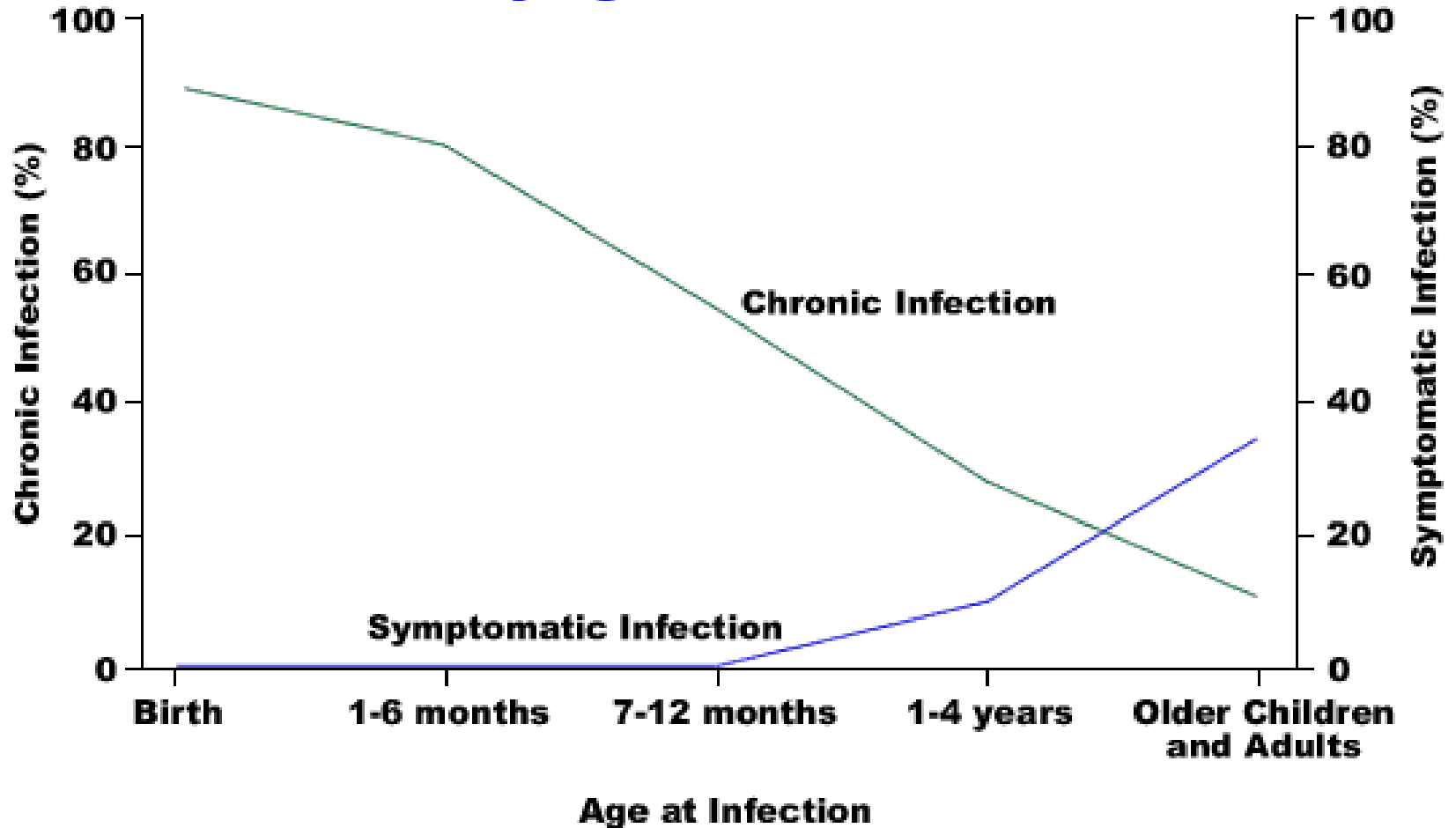
Acute infection  
(2-12 weeks)

Early recovery  
(12-24 weeks)

Recovery  
(24-48 weeks)



## Outcome of Hepatitis B Virus Infection by Age at Infection

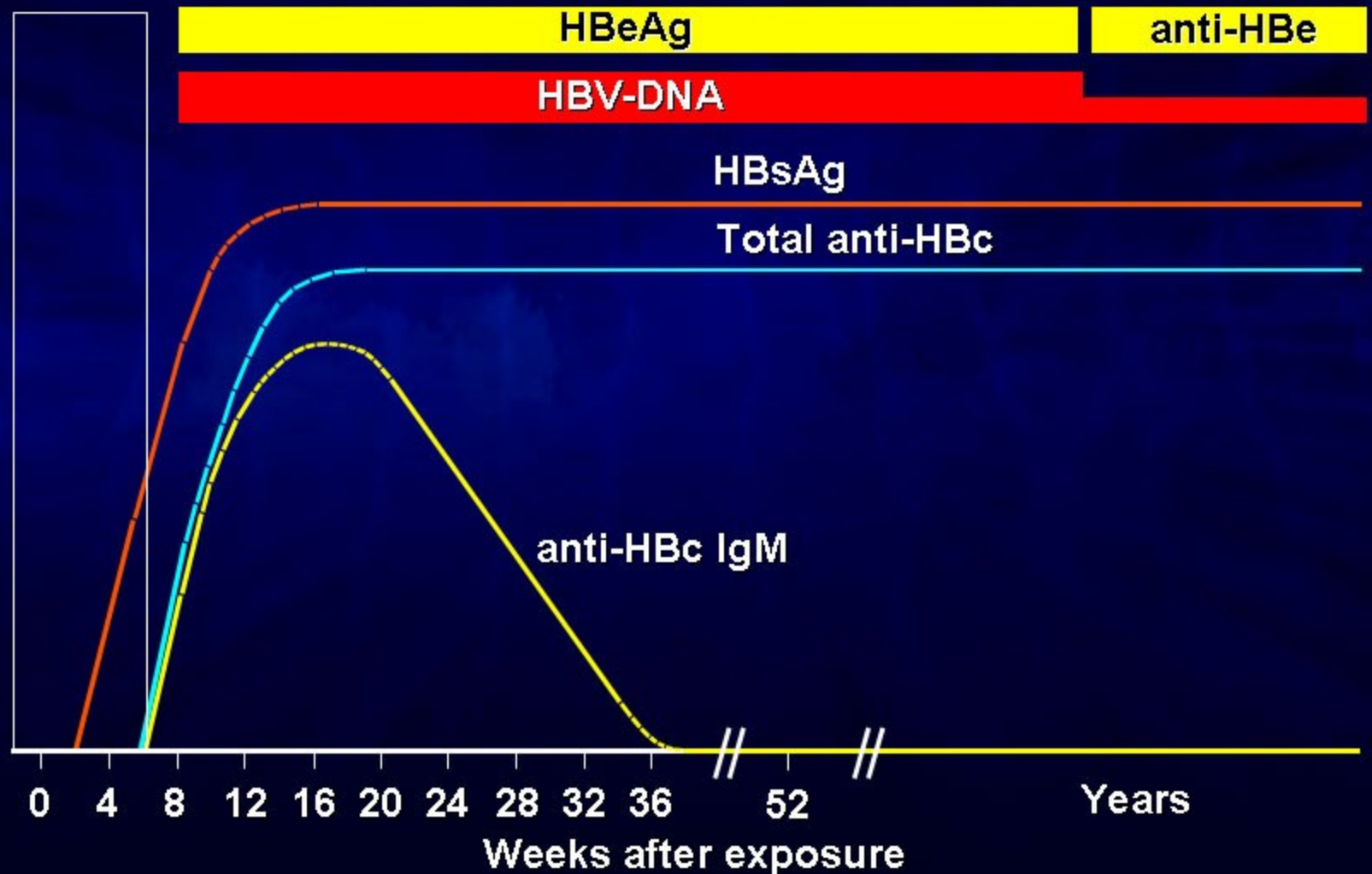


# Chronic Hepatitis B (HBeAg+)

Incubation  
(4-12 wk)

Acute  
(6 months)

Chronic  
(Years)

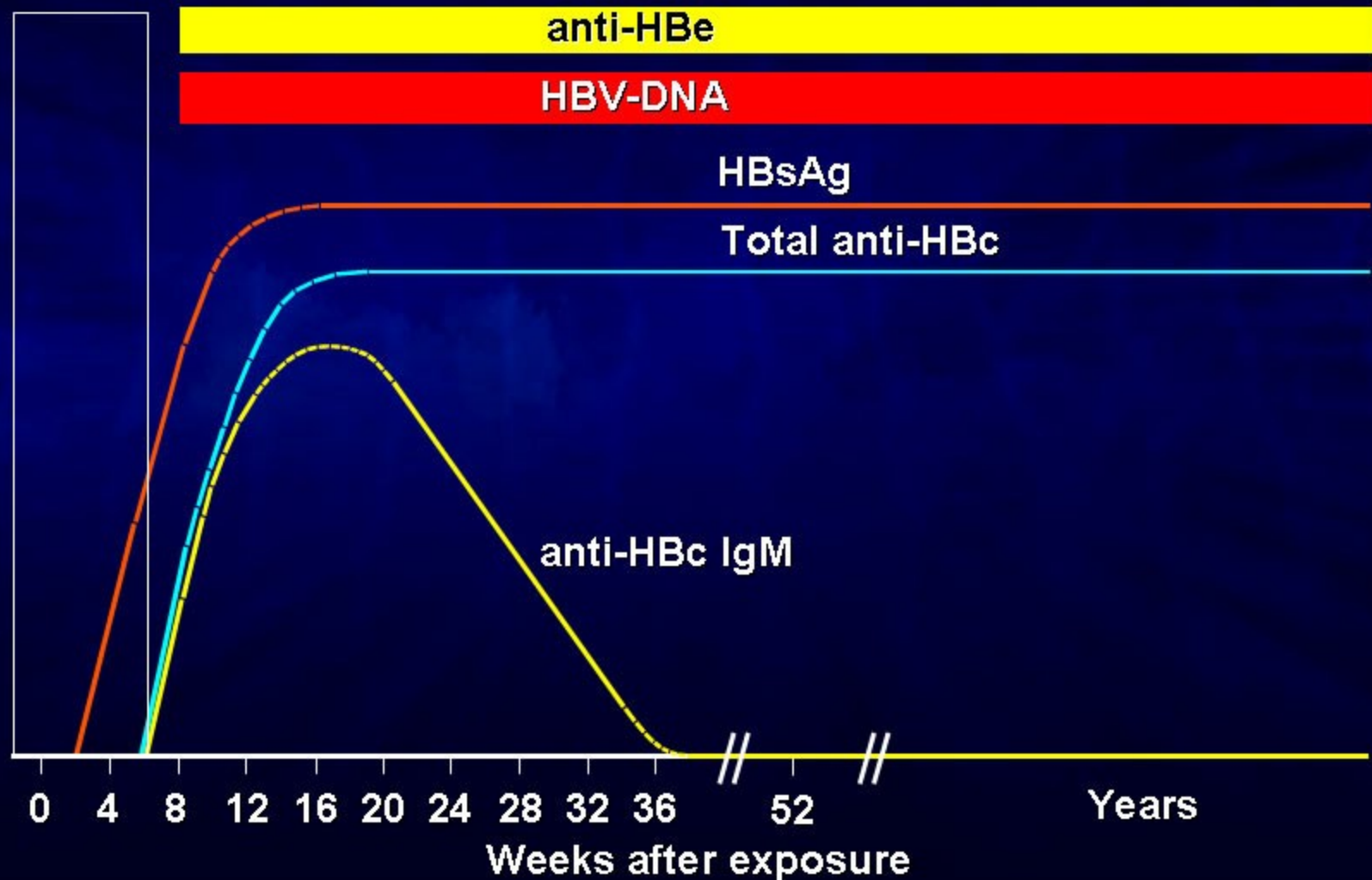


# Chronic Hepatitis B (HBeAg-)

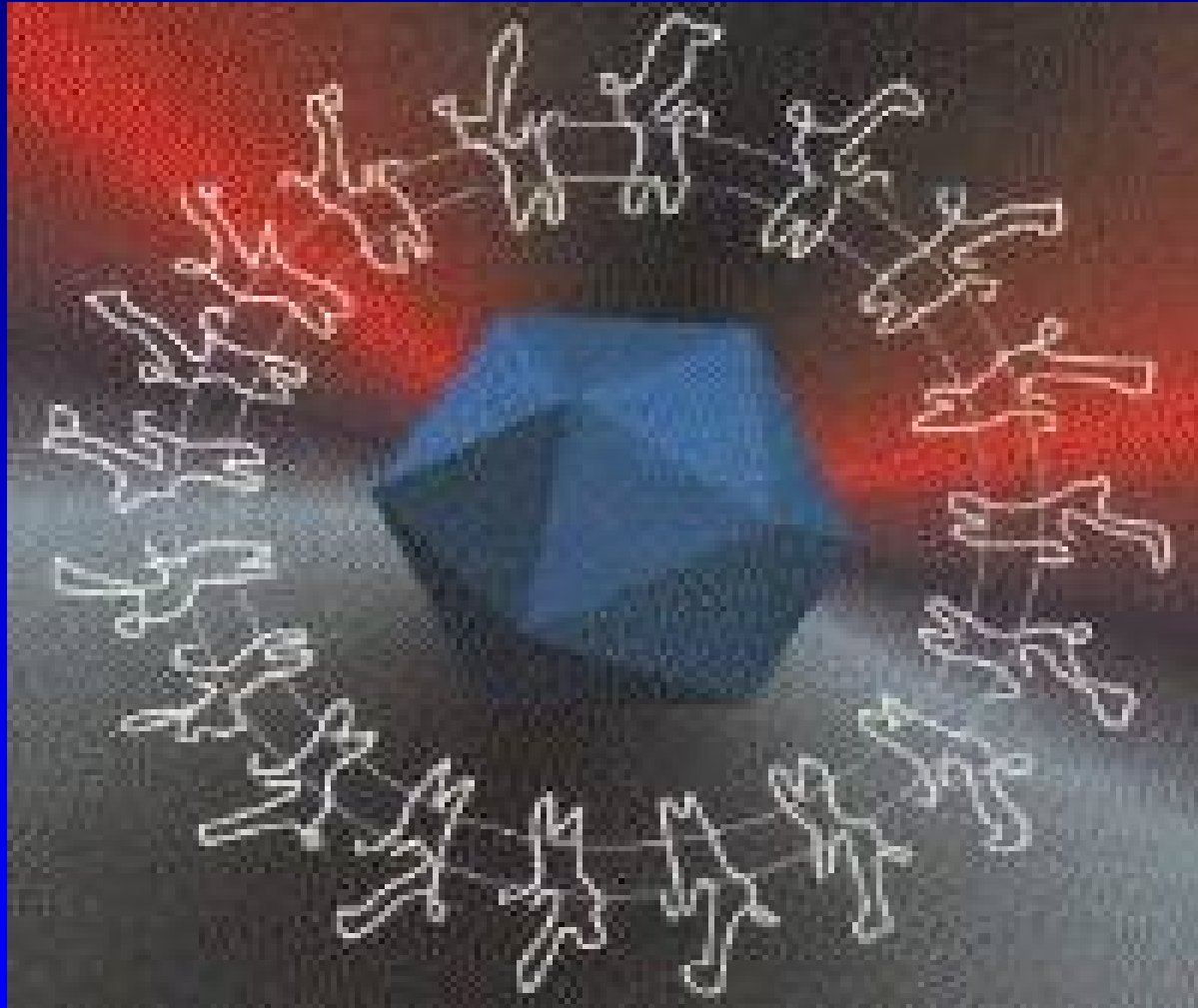
Incubation  
(4-12 wk)

Acute  
(6 months)

Chronic  
(Years)

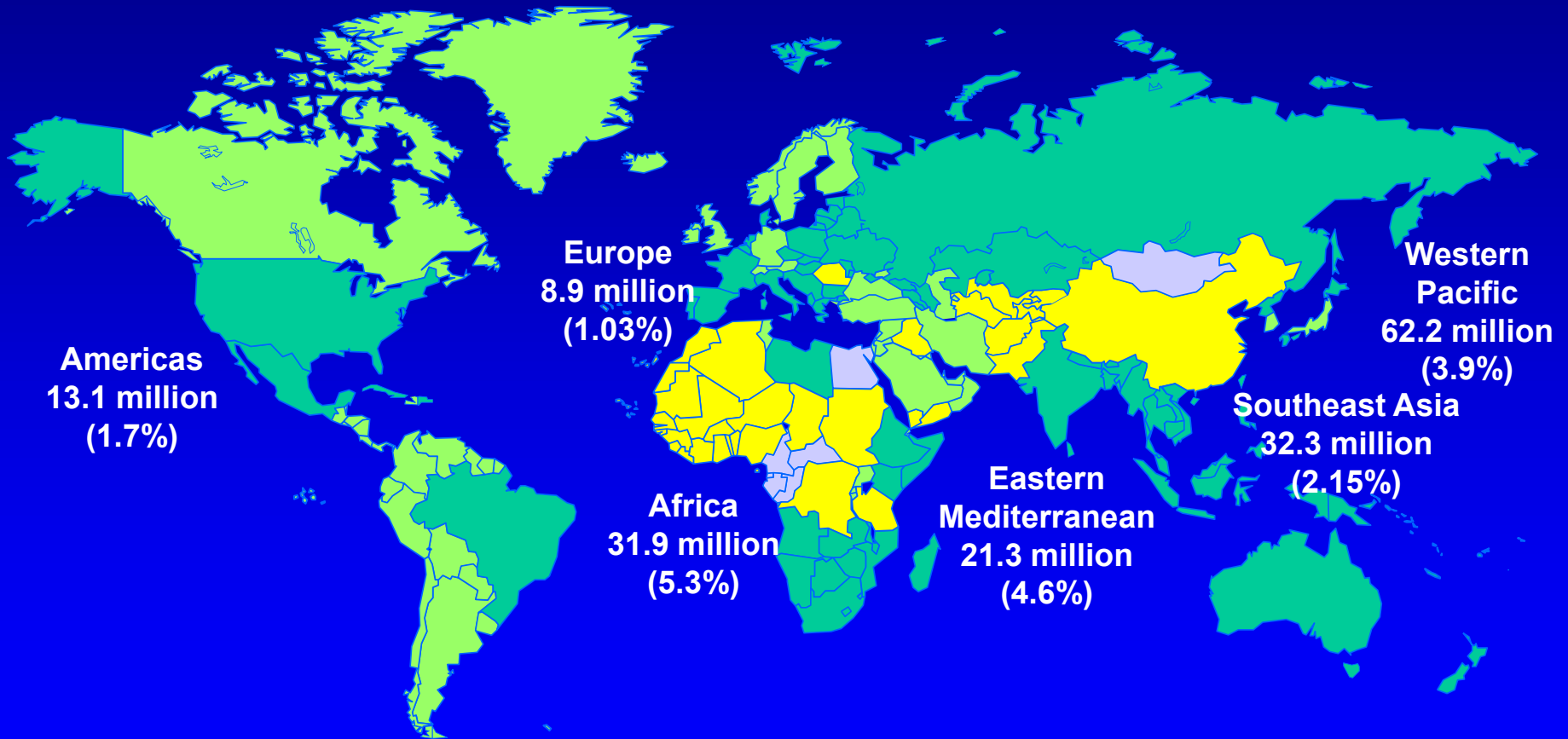


# Hepatitis C



*family Flaviviridae, genus Hepacivirus, enveloped RNA virus 60 nm*

# Hepatitis C



World Health Organization. Wkly Epid Rec .1999;74:425-427. World Health Organization. Hepatitis C: Global Prevalence: Update. 2003. Farci P, et al. Semin Liver Dis. 2000;20:103-126. Wasley A, et al. Semin Liver Dis. 2000;20:1-16.

# Distribution of HCV genotypes



# Hepatitis C

- Significant global health problem
  - ✓ about 3 % of the world population are chronically infected with HCV
  - ✓ In well-developed countries about 20 % of all acute hepatitis, 70 % chronic hepatitis, 40 % cirrhosis, 60 % HCC and indication to 30 % liver transplantations
- In Czech Republic
  - ✓ prevalence 0,2 % (2001)
- No vaccine, no hyper-immune immunoglobulin



# Epidemiology of HEP C

- **Transmission:**
  - ✓ blood and blood products
  - ✓ sharing of used injection needles and syringes
  - ✓ sexually (rare)
  - ✓ vertically (rare)
- **Who is in the highest risk of HCV infection at present?**
  - ✓ intravenous drug abusers
- **Infection is frequently diagnosed in chronic stage**

# Patients with higher risk of HCV infection

- ✓ Intravenous drug abusers (sharing of injection needles and syringes)
- ✓ Recipients of blood transfusions before the year 1992 (especially hemophiliacs)
- ✓ Persons with tattoo or piercing

# Clinical course of HEP C

- Acute hepatitis is mostly asymptomatic
- Probability of chronicity is high (40-50% till 90-100%).

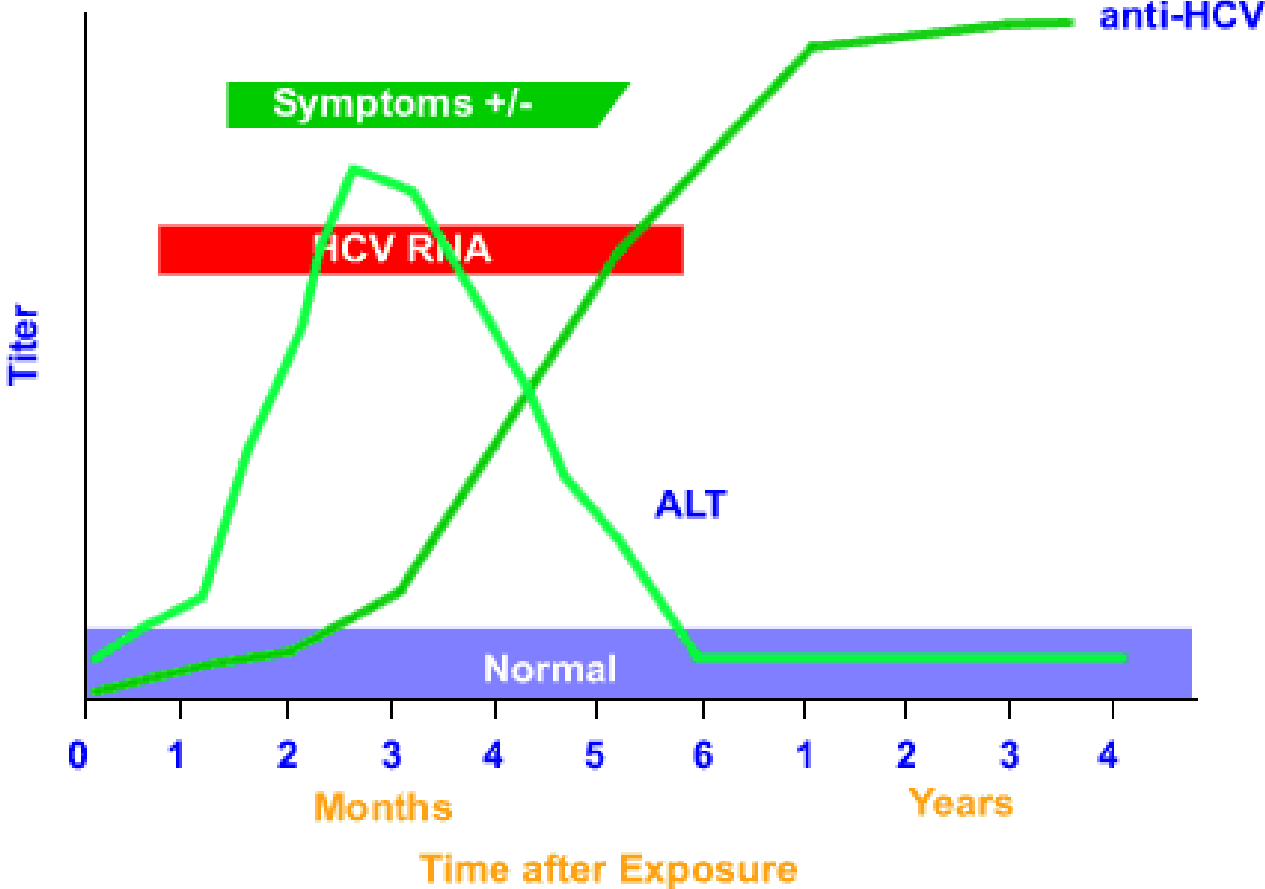
## Higher probability of chronicity:

- ⇒ Older persons
- ⇒ Higher initial infection dose (transfusion versus needles)
- ⇒ HBV, HIV co-infection
- ⇒ abusus of alcohol
- ⇒ immunodeficiency

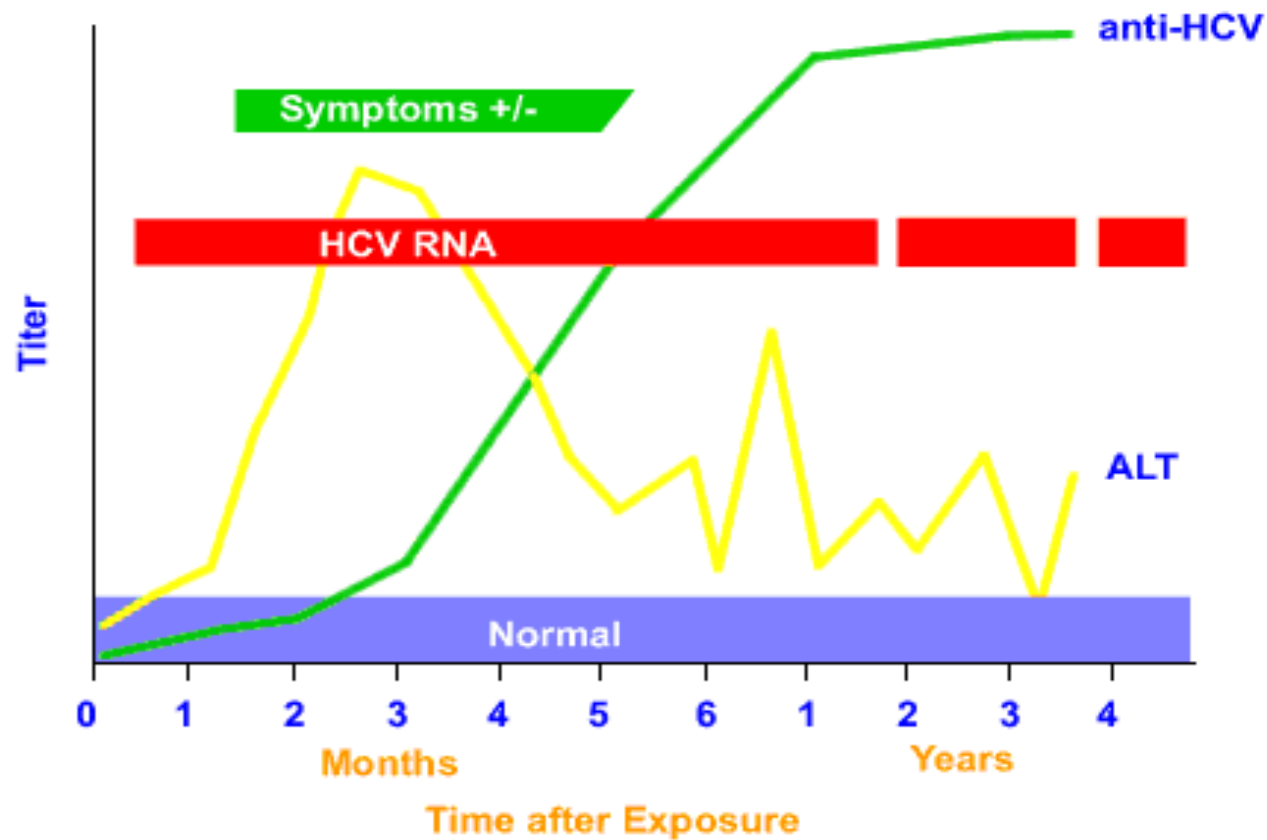
# Clinical course of HEP C

- LC in about 20 % patients with chronic HCV infection
- HCC annually in 1-4 % patients with LC
- Progression to HCC depends on:
  - ✓ age (more rapid progression in older persons)
  - ✓ alcohol abuse
  - ✓ HIV co-infection
  - ✓ HBV co-infection

# Serologic Pattern of Acute HCV Infection with Recovery

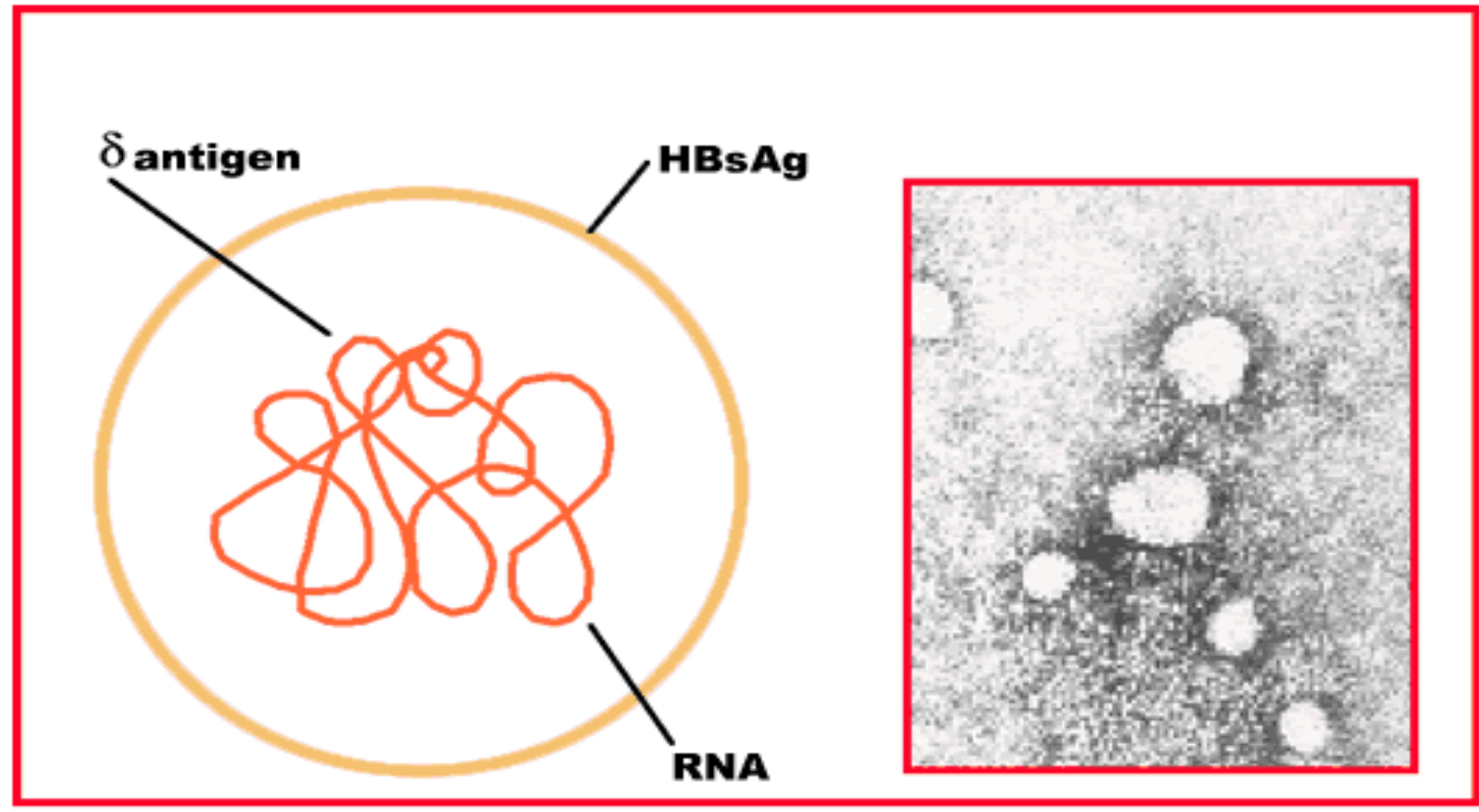


## Serologic Pattern of Acute HCV Infection with Progression to Chronic Infection



# Hepatitis D

## Hepatitis D (Delta) Virus



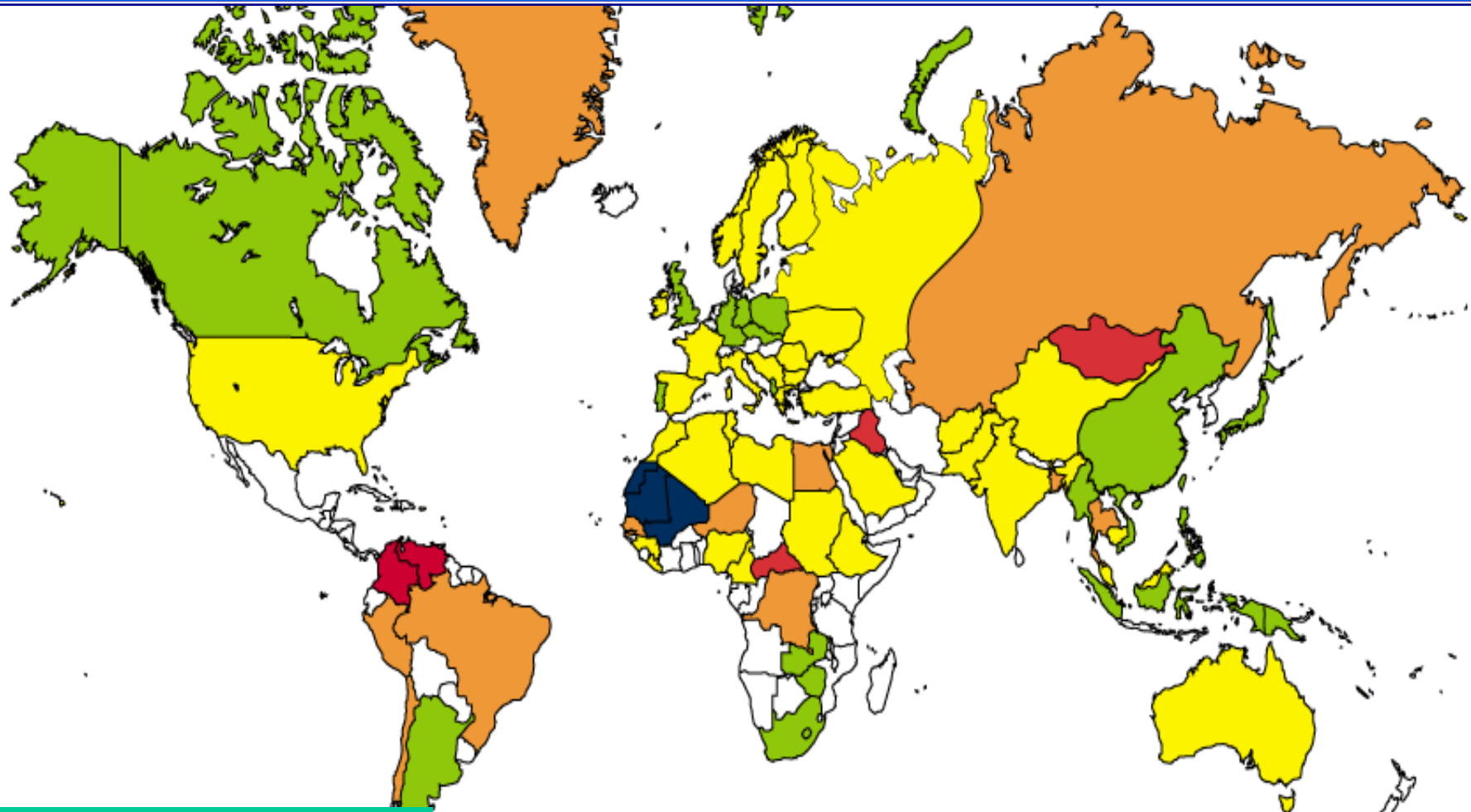
Satellite virus, family *Deltaviridae*, enveloped RNA, 40 nm

# Hepatitis D

- Ability of replication only in presence of HBV infection
- ✓ Co-infection (better prognosis)
- ✓ Super-infection (worse prognosis)
- **Endemic** in South America, Mediterranean Region, Romania, Central Africa
- **Very low prevalence in CR**



# Anti-HDV prevalence in HBsAg-positive (approximately 15 000 000 persons)

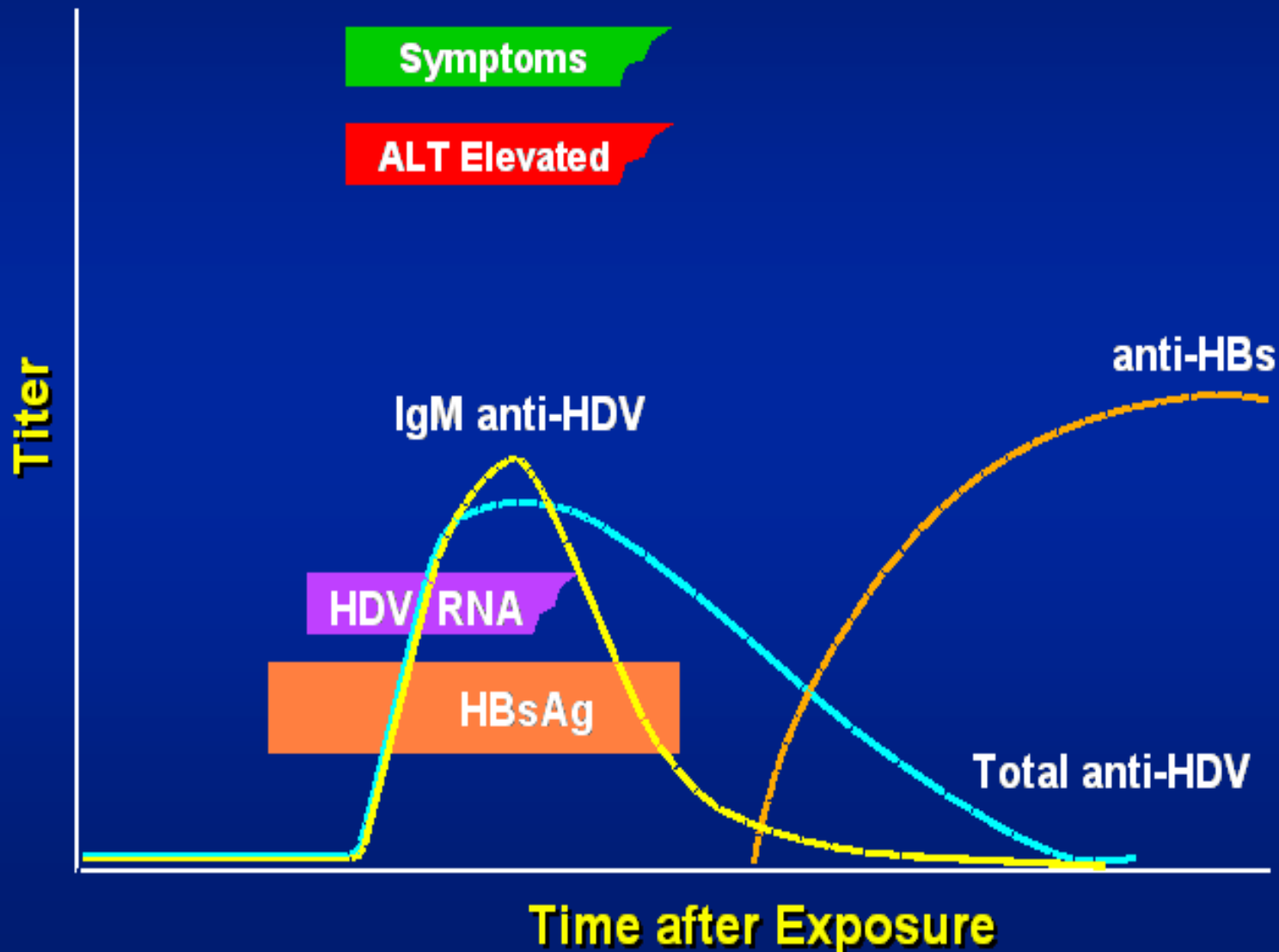


## HDV

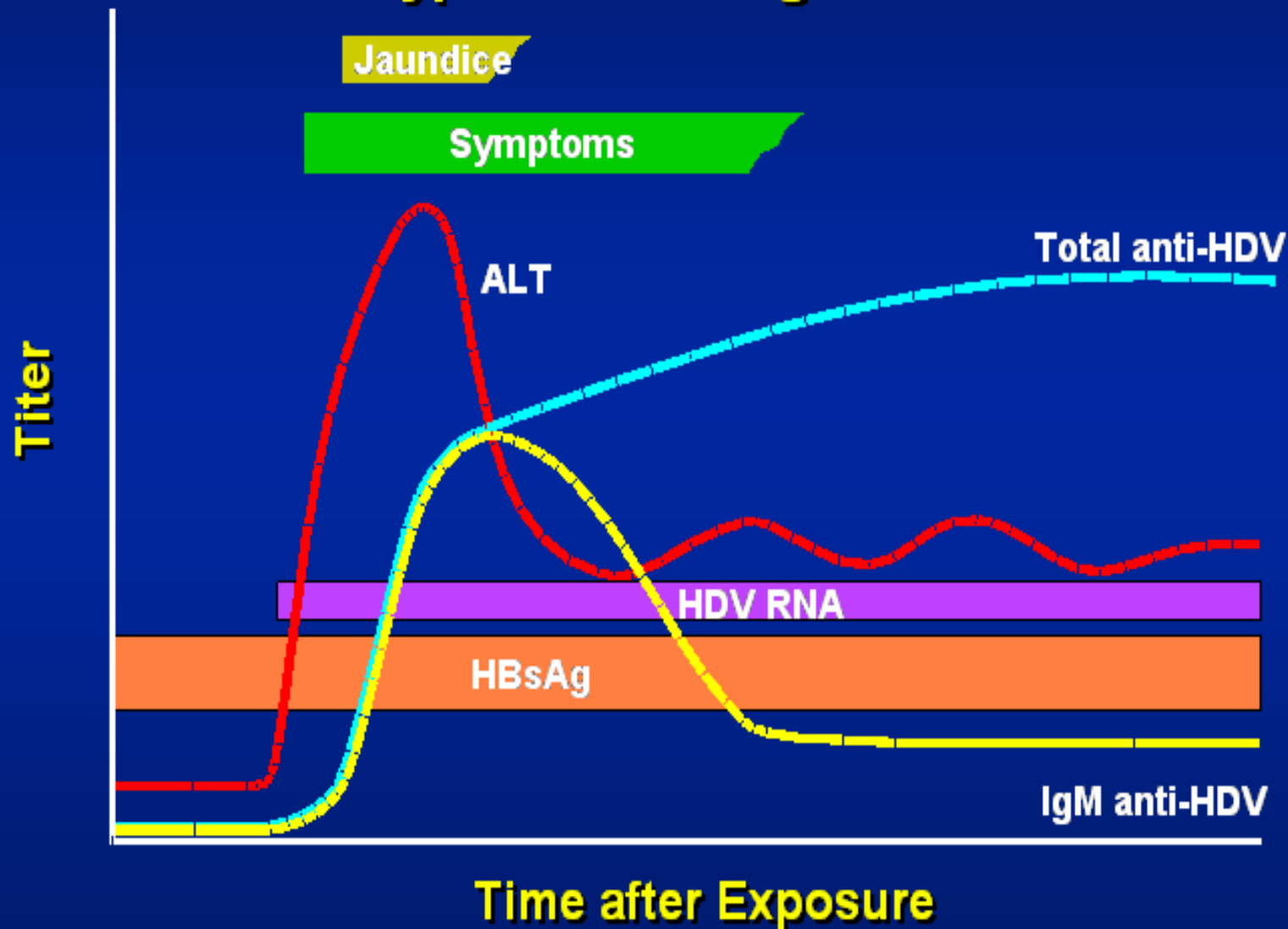
Anti-HD(HBsAg (+))  ?  0-5%  6-20%  21-60%  >60%

Rizzetto M. *EASL 2009*

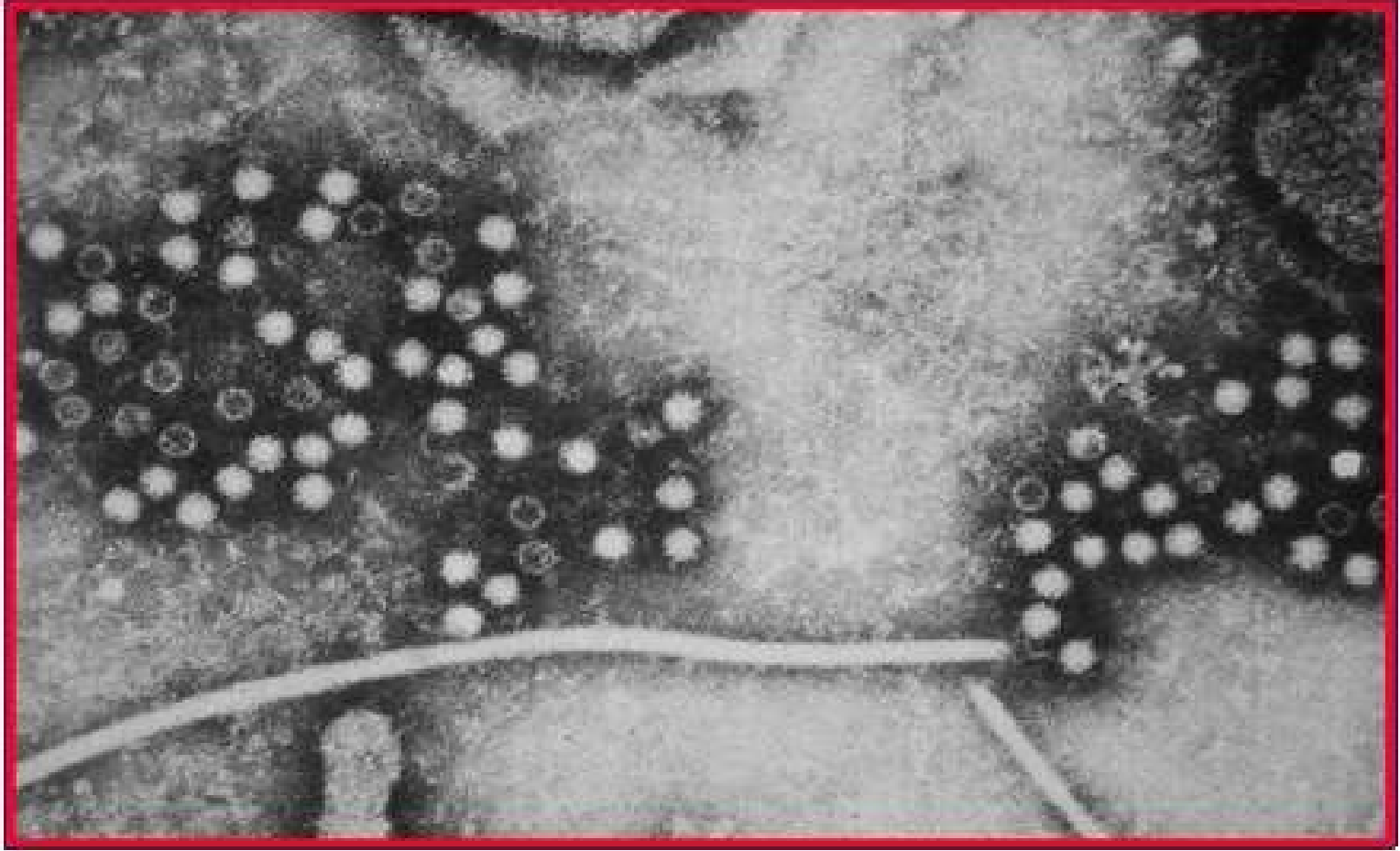
# HBV - HDV Coinfection Typical Serologic Course



# HBV - HDV Superinfection Typical Serologic Course

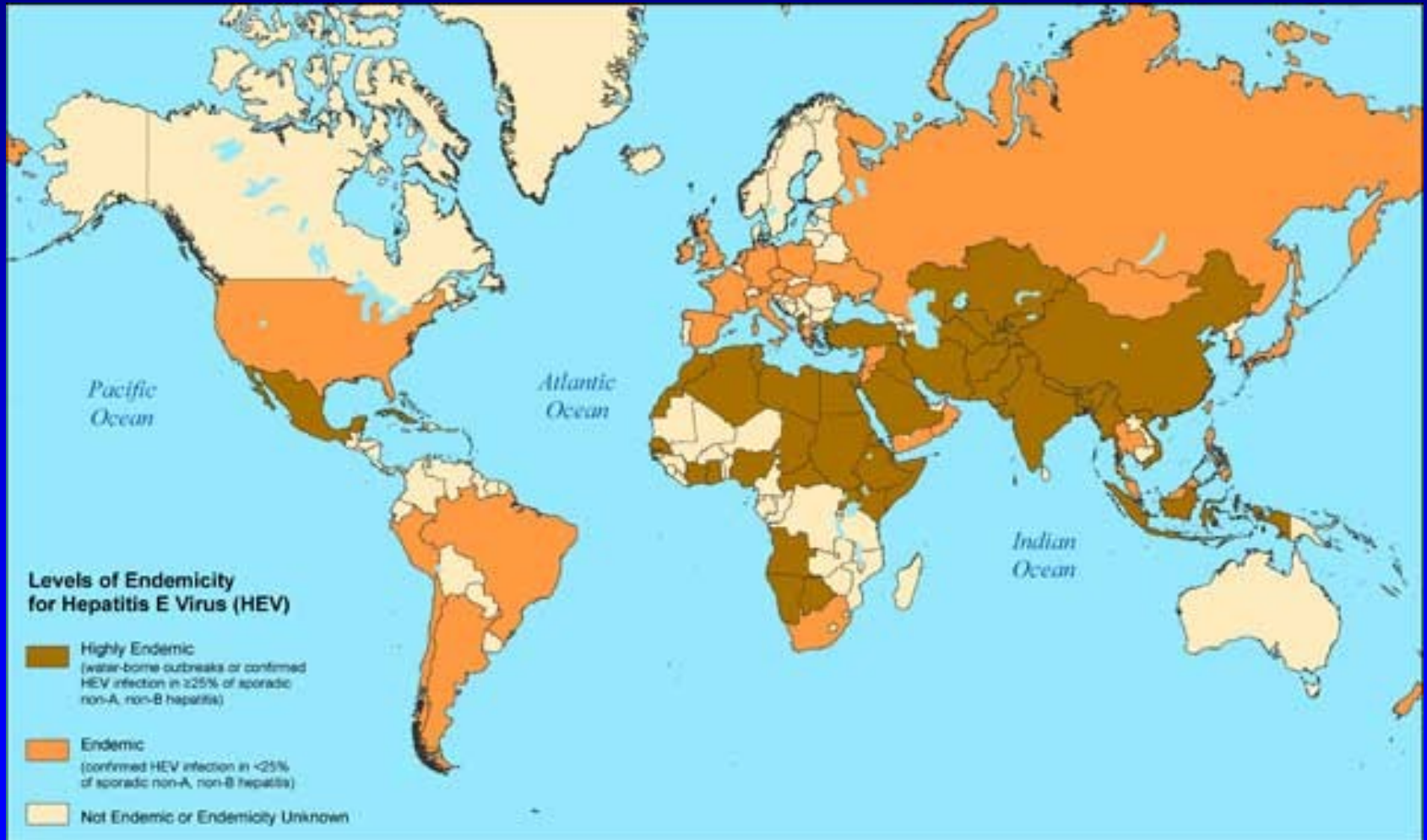


# Hepatitis E Virus



Family *Hepeviridae*, genus *Hepevirus*, non-enveloped RNA virus,  
27-34 nm

# Hepatitis E



Source: *CDC*

# HEV genotypes

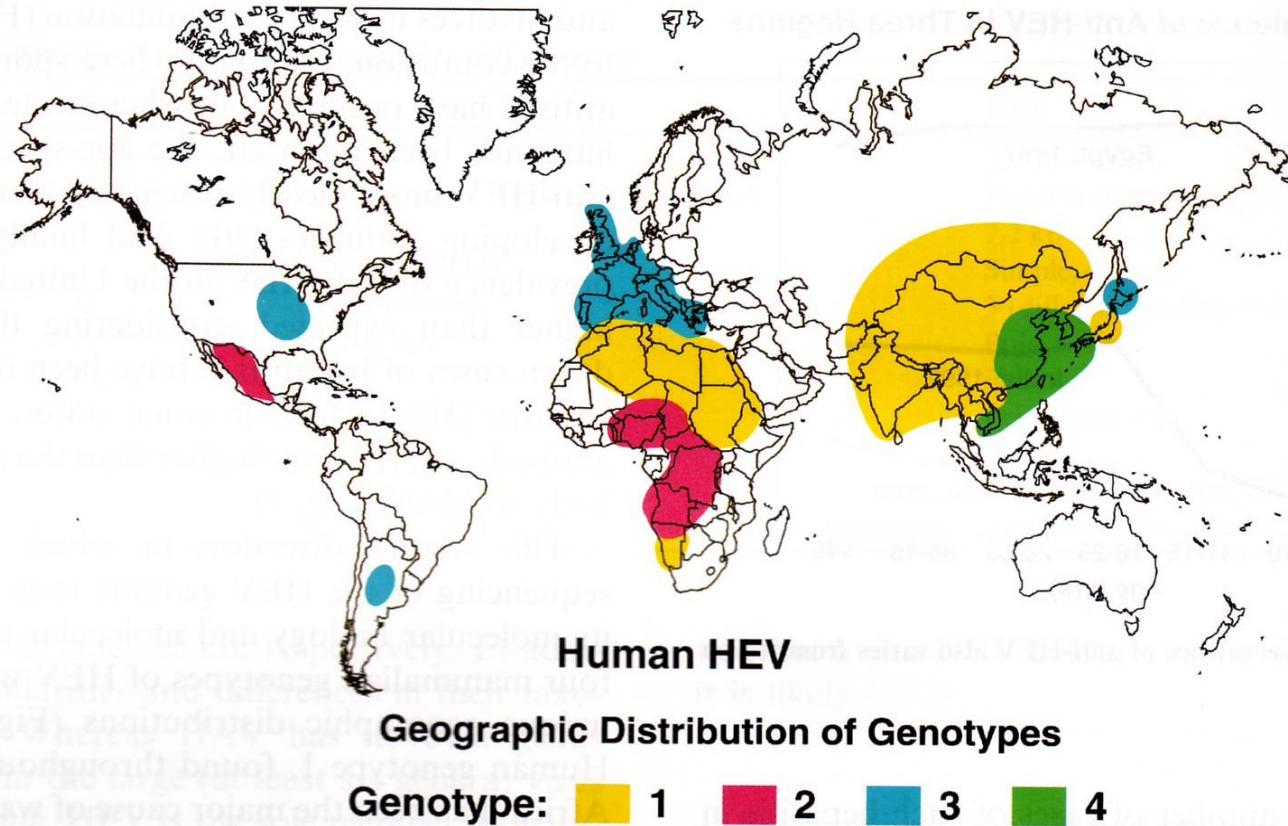
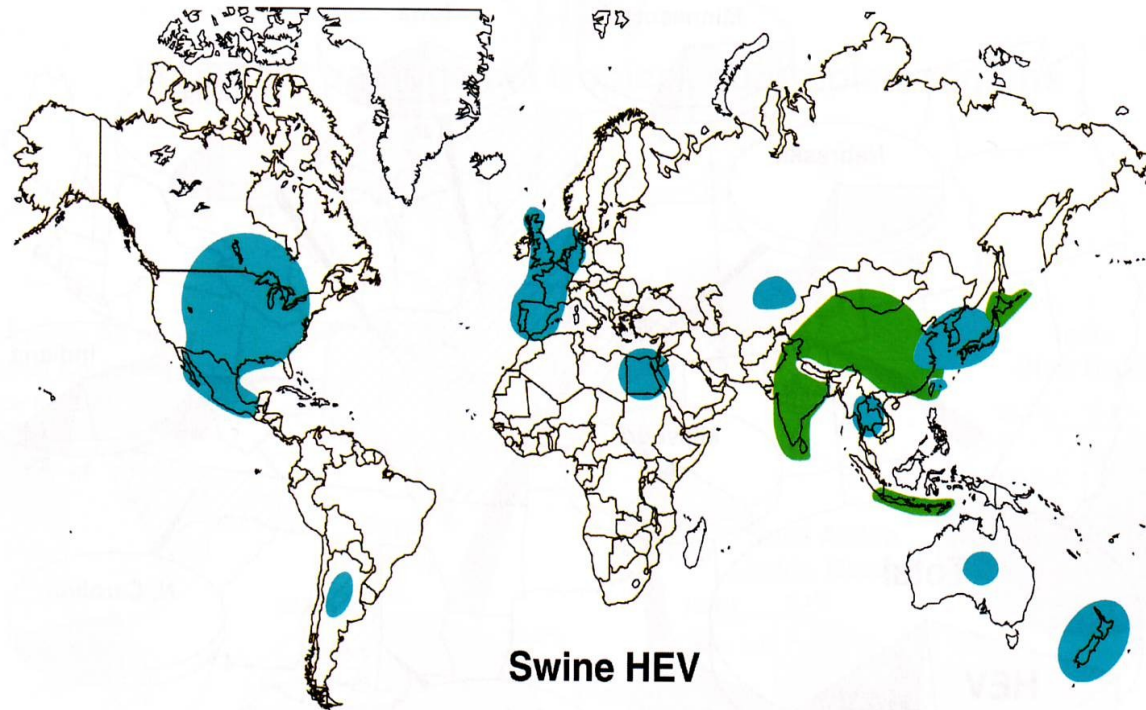


Fig. 4. Each of the four genotypes of HEV that infect humans has a distinct, and in some cases, overlapping geographic distribution.

# Genotypes of swine HEV



Swine HEV

Geographic Distribution of Genotypes

Genotype: ■ 3 ■ 4

Fig. 5. HEV genotypes 3 and 4, which infect both humans and swine, have been recovered from pigs in regions that roughly parallel the distribution of these viruses in human infections. However, there are exceptions.



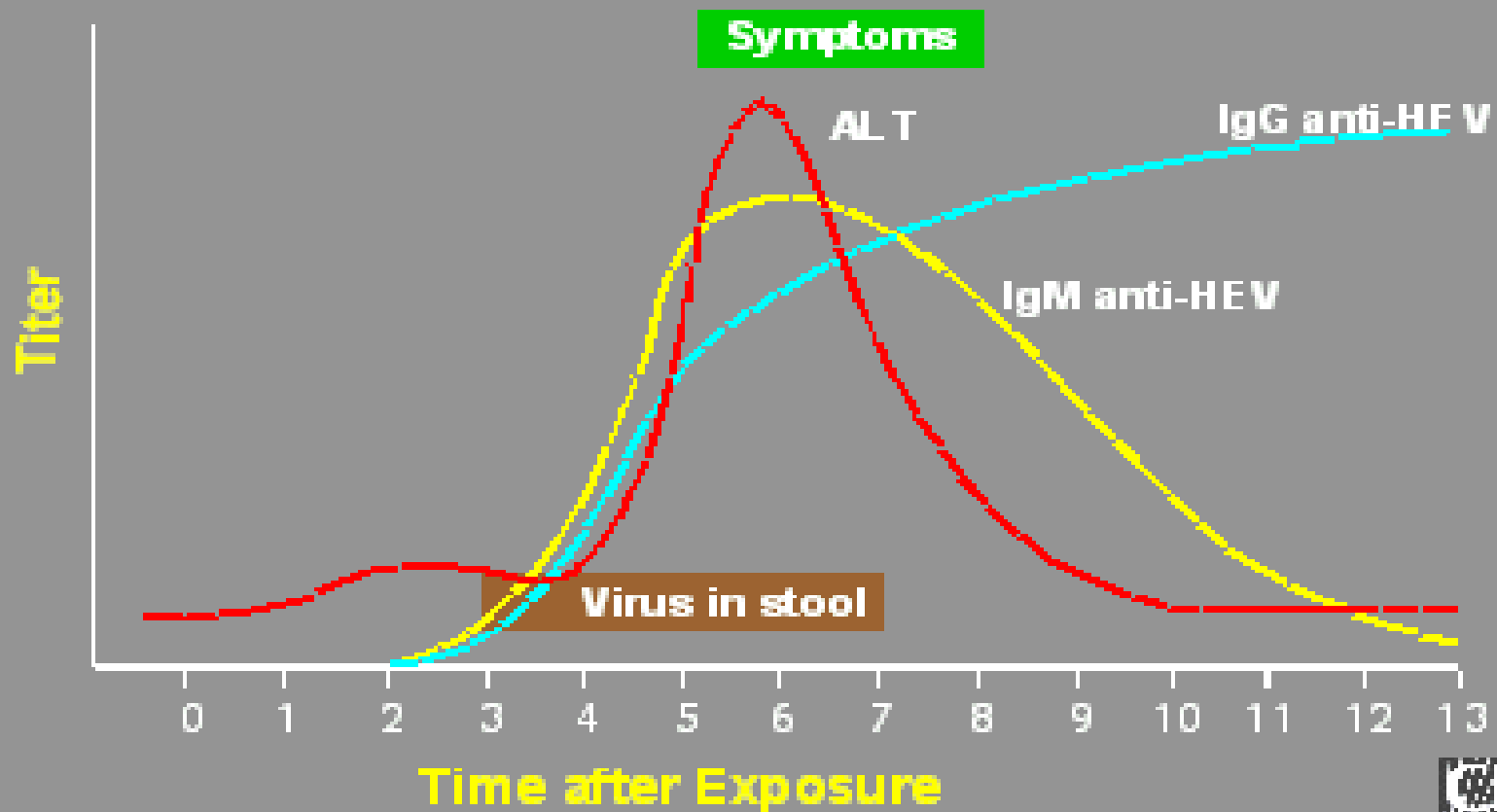
# Hepatitis E

- Travel-related disease especially
- Infection is possible to acquire in CR as well (pork, sea food)
- Main route of transmission by drinking water
- Extremely serious clinical course in late pregnancy (mortality above 20 %)
- Repeated infection may be possible
- Rare cases of chronic hepatitis E in seriously immunosuppressed patients (organ recipients...)



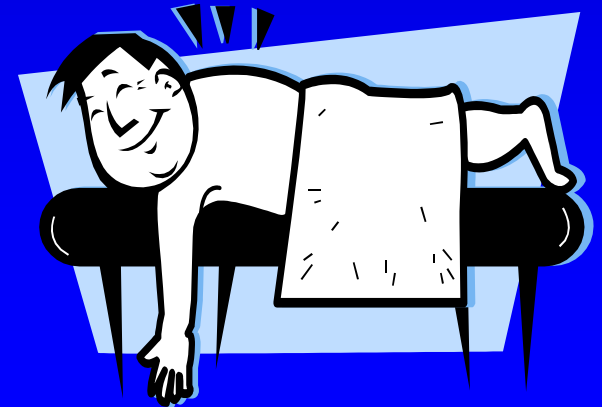
# Hepatitis E Virus Infection

## Typical Serological Course

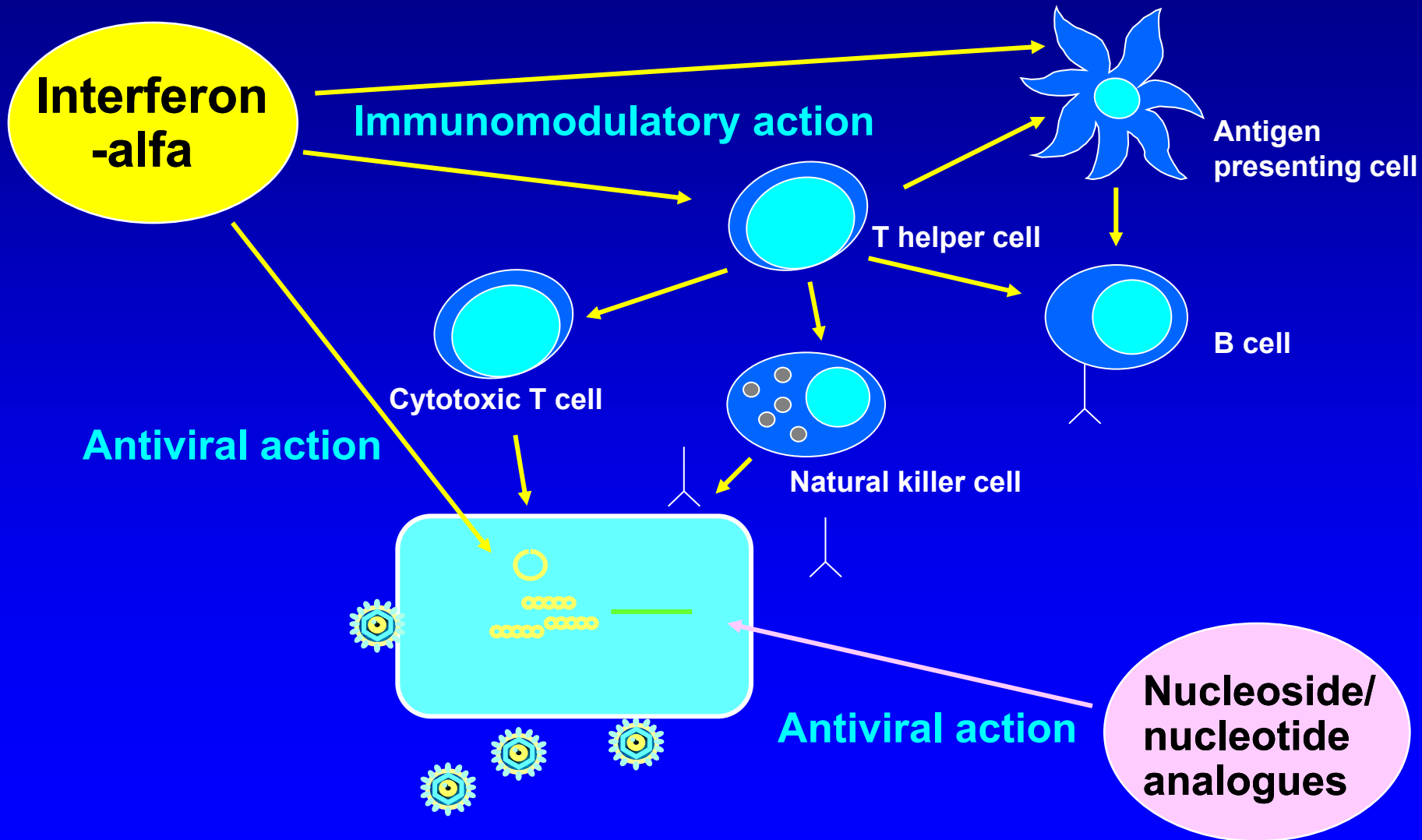


# Treatment of acute hepatitis

- **Symptomatic for all types**
  - ✓ physical and mental rest
  - ✓ diet
  - ✓ no alcohol, no hepatotoxic drugs
  - ✓ supportive treatment (silymarin, essential phospholipids)



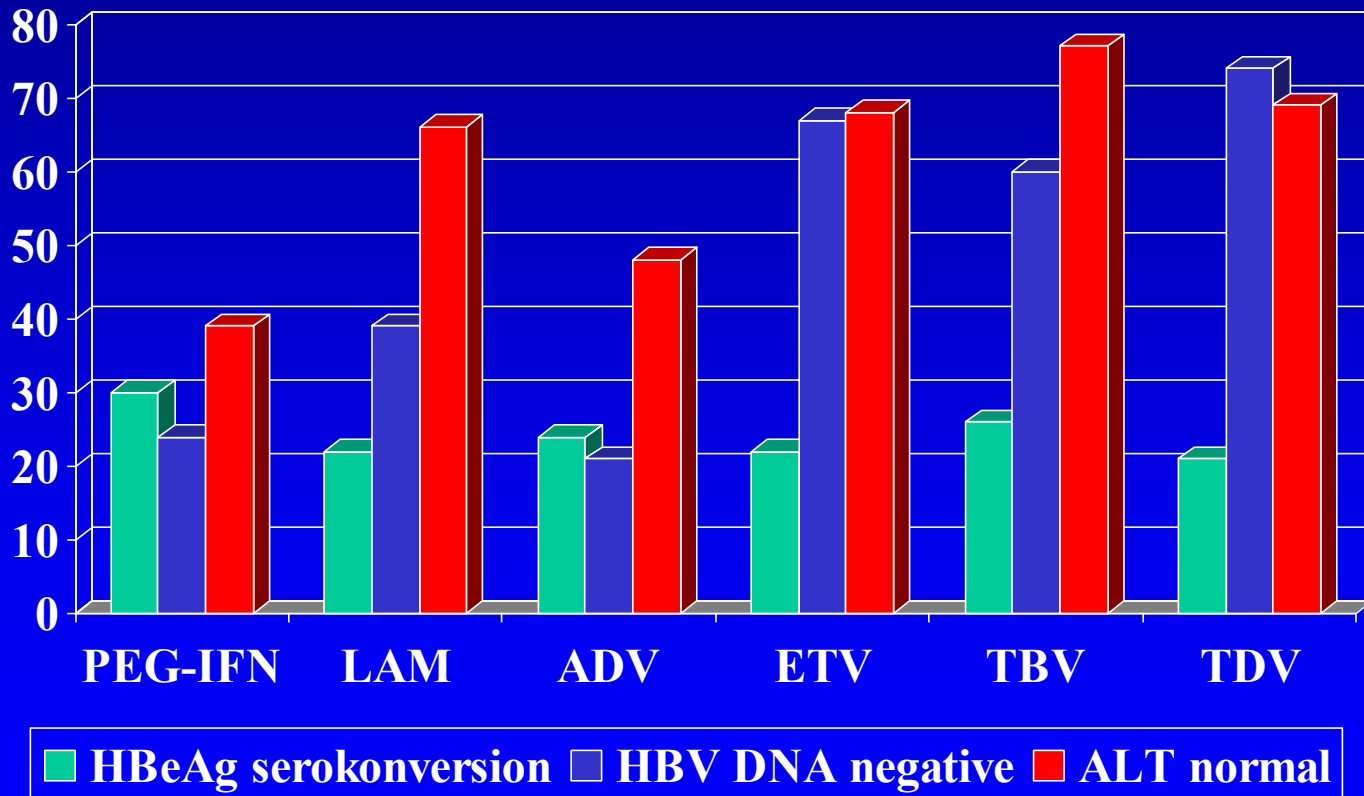
# Treatment options for chronic hepatitis B



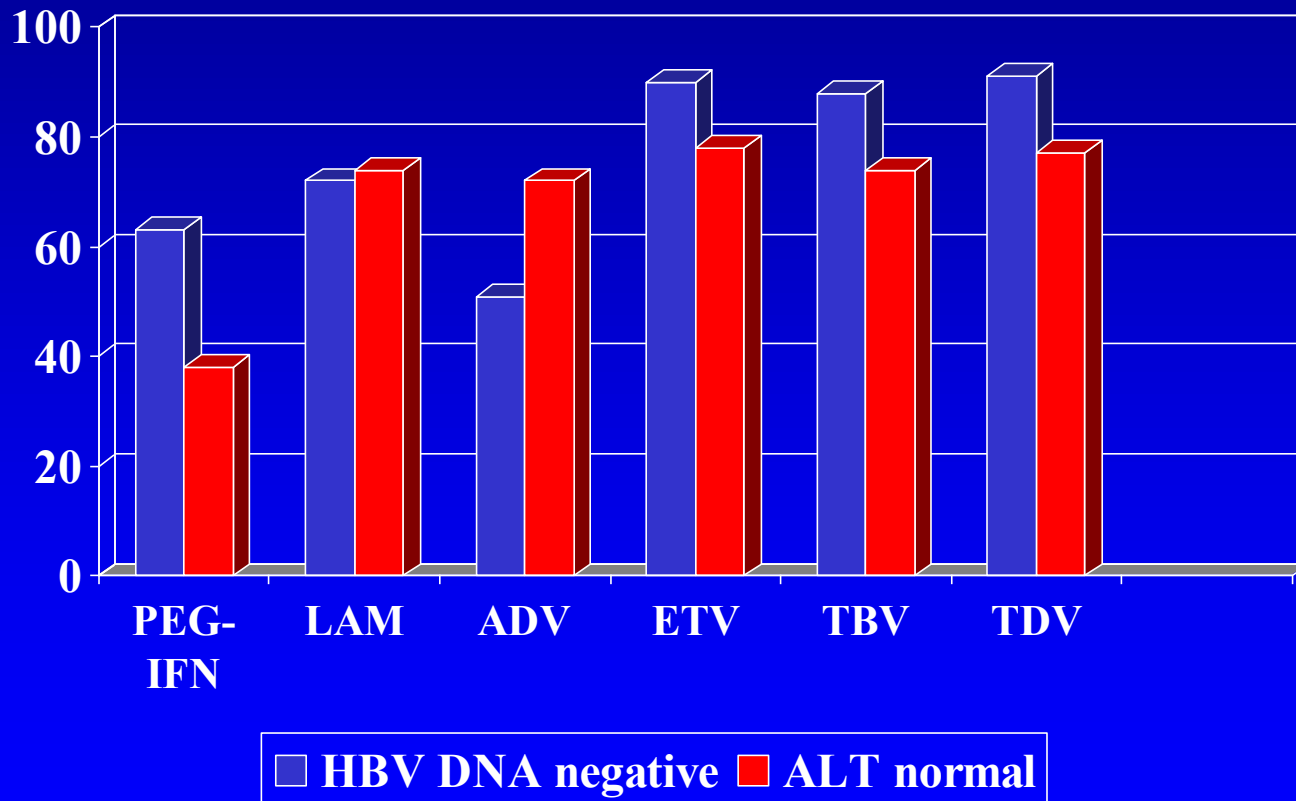
# Current possibilities of treatment of chronic HBV infection

- pegylated interferon alfa-2a – 48 weeks
- conventional interferon alfa-2a or alfa-2b
- lamivudine - long-term treatment (years), mostly temporary effect only, high risk of resistance
- adefovir dipivoxil – for lamivudine-resistant mutants only, long-term treatment (years), mostly temporary effect only
- entecavir
- tenofovir
- telbivudine

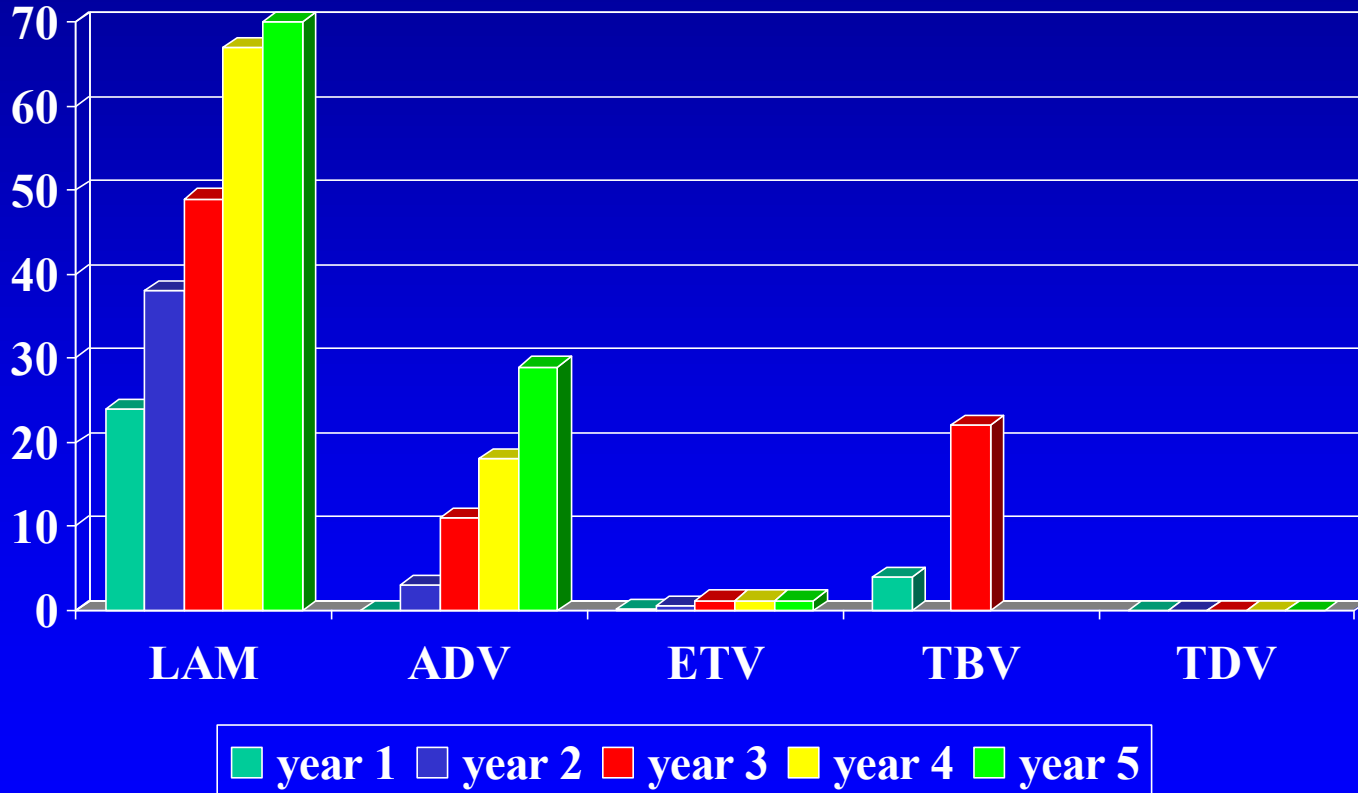
# Efficacy of treatment after 1 year – HBeAg positive



# Efficacy of treatment after 1 year – HBeAg negative



# Resistance to NUCs



# Current possibilities of treatment of chronic HCV infection

- Pegylated interferon alfa-2a or alfa-2b + ribavirin
  - ✓ Genotype 1 – 48 weeks, SVR about 60 %
  - ✓ Genotype 2 or 3 – 24 weeks, SVR about 85 %



# Development of chronic hepatitis C treatment efficacy

