



DEPARTAMENTO DE  
**MICROBiologia**  
UNIVERSIDADE DE SÃO PAULO



# Hepatites Virais

**Profa. Patricia C. B. Beltrão Braga**

**Depto de Microbiologia- ICB/USP**

# HEPATITES

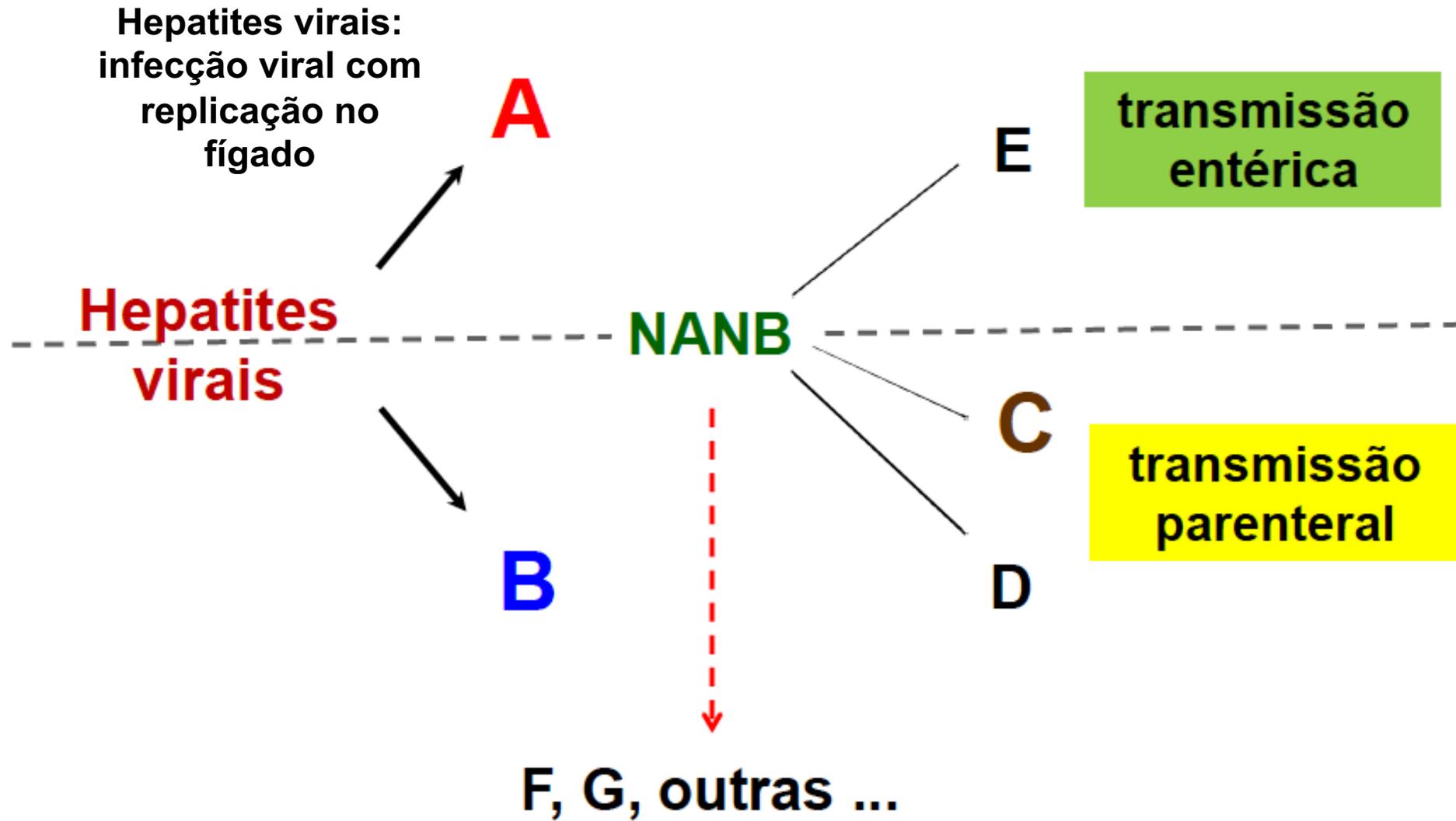


Hepatite designa qualquer inflamação do fígado por causas diversas, sendo as mais frequentes as infecções pelos vírus tipo A, B e C e o abuso do consumo de álcool ou outras substâncias tóxicas (como alguns remédios).

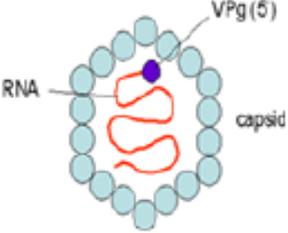
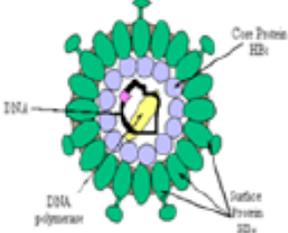
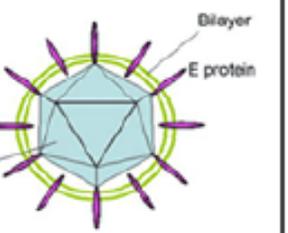
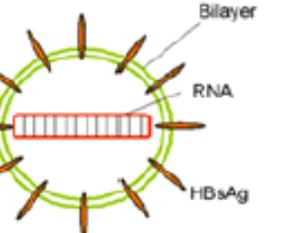
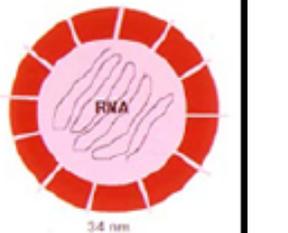
## **HEPATITES VIRAIS**

### *Sinais e sintomas:*

Cansaço, febre, mal-estar, tontura, enjojo, vômitos, dor abdominal, pele e olhos amarelados, urina escura e fezes claras.



# Hepatitis Virais

					
<b>Name of Virus</b>	Hepatitis A Virus (HAV)	Hepatitis B Virus (HBV)	Hepatitis C Virus (HCV)	Hepatitis D Virus (HDV)	Hepatitis E Virus (HEV)
<b>Classification</b>	Picornavirus	Hepadnavirus	Flavivirus	Deltavirus	Hepevirus
<b>Viral genome</b>	ssRNA	dsDNA	ssRNA	-ssRNA (-ve)	ssRNA
<b>Transmission</b>	Enteric	Parental	Parental	Parental	Enteric
<b>Incubation period</b>	15-45 days	45-160 days	15-150 days	30-60 days	15-60 days
<b>Chronic Hepatitis</b>	No.	Yes. 10% chance	Yes. >50% chance	Yes. <5% of coinfectious >80% of superinfectious	No.
<b>Cure?</b>	No cure. Treatments usually tackle the symptoms.	No cure. Treatments usually tackle the symptoms.	No cure. Treatments usually tackle the symptoms.	No cure. Treatment: Alpha interferon for 12 months.	No cure. Treatments usually tackle the symptoms

# Hepatites Virais: impacto nas populações humanas

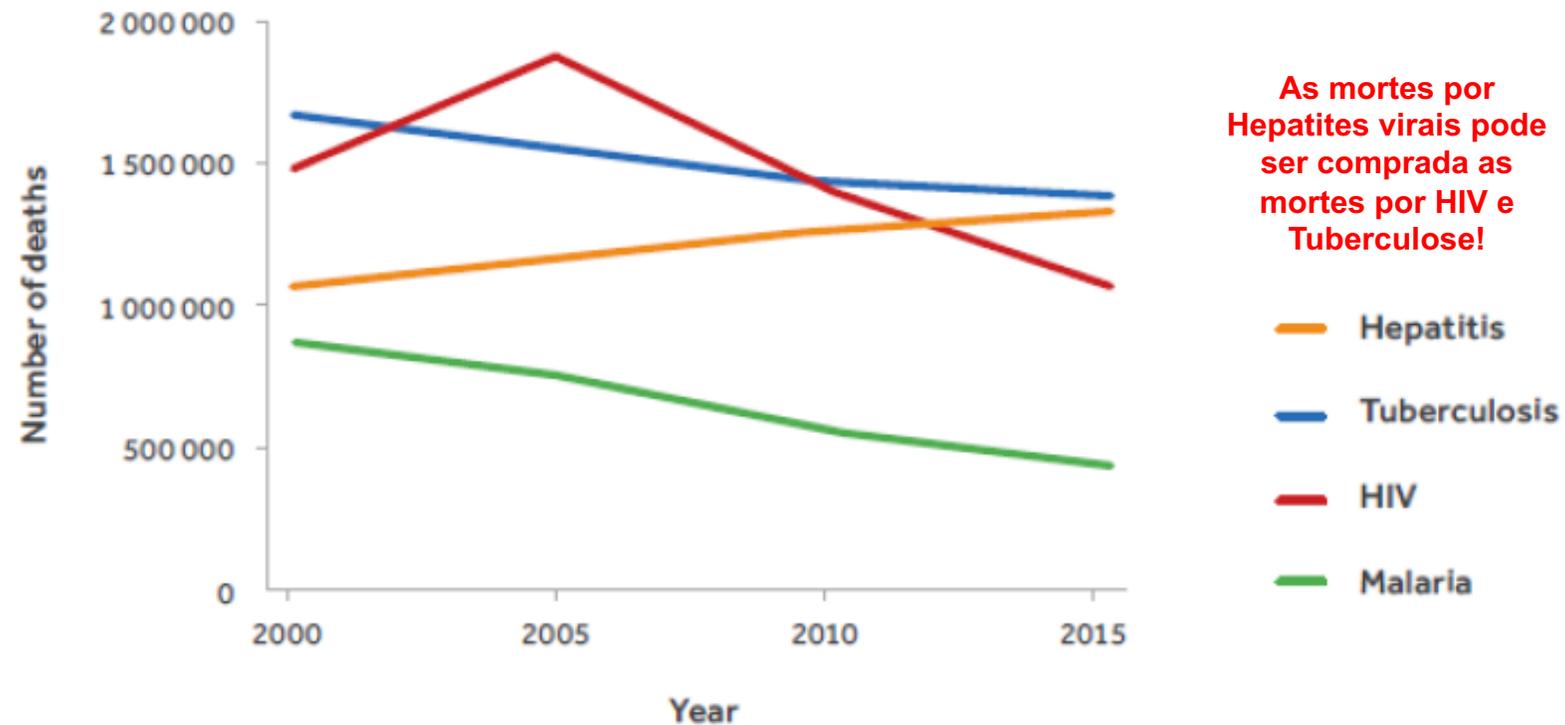
## Estimativas da WHO (2015)

- 257 milhões de pessoas (3.5% da população mundial) estão infectados de maneira crônica pelo HBV.
- 5% das pessoas infectadas por HBV estão infectadas por HDV.
- 71 milhões de pessoas (1.0% da população mundial) estão infectados de maneira crônica pelo HCV.
- 20 milhões de pessoas/ano se infectam com o HEV (44.000 mortes em 2015 [3.3% das mortes por Hepatites virais]).
- Mais de 7.000 mortes por HAV em 2016 (taxa de hepatite fulminante varia de 0.14 – 0.35, portanto, 2 – 5 milhões de casos por ano).

Site do ministério da Saúde (Brasil): 1.4 milhões de mortes por ano no mundo (2024)

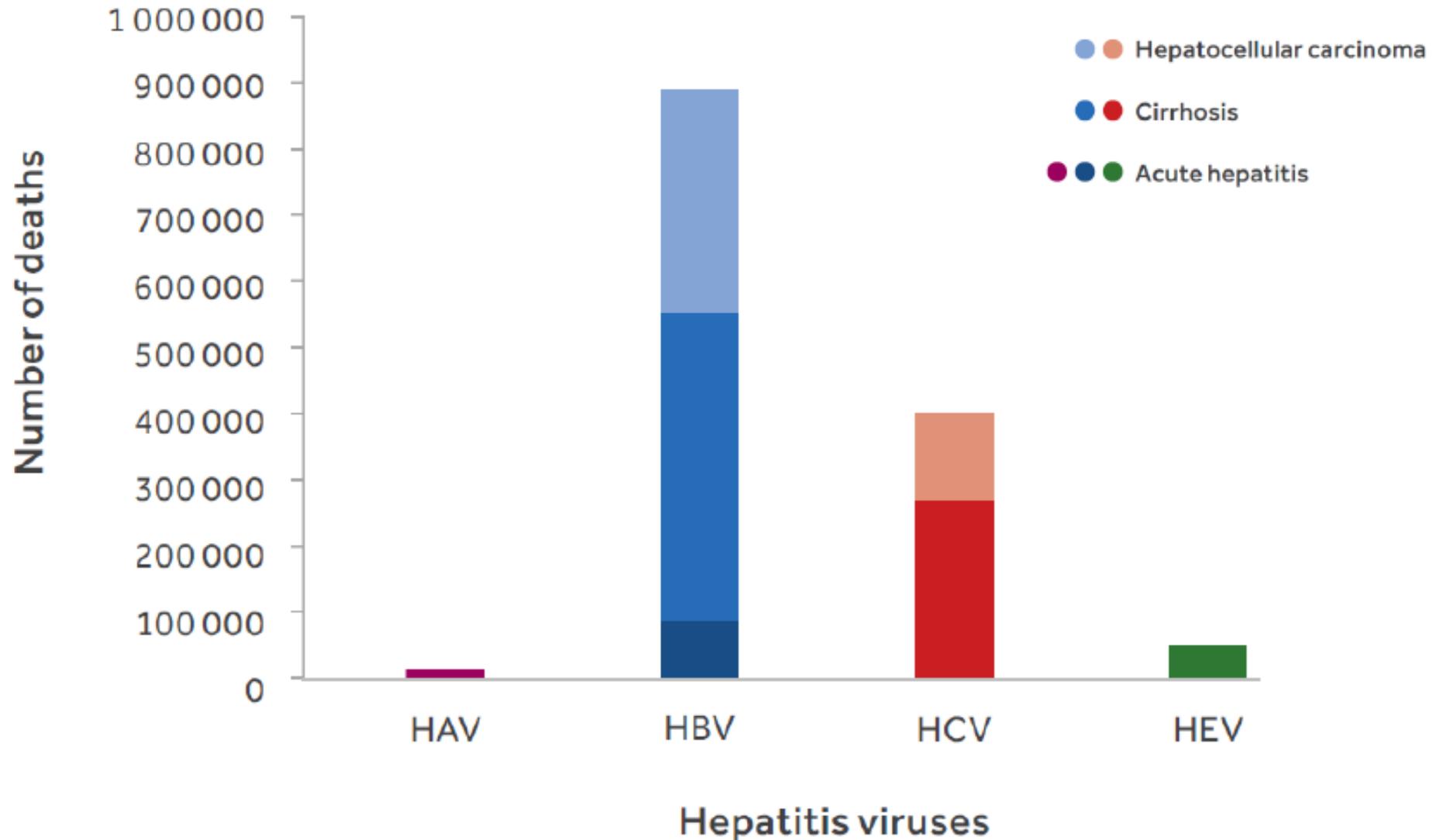
# Hepatites Virais: impacto nas populações humanas

Fig. 2. Global annual mortality from hepatitis, HIV, tuberculosis and malaria, 2000–2015: unlike HIV, tuberculosis and malaria, the trend in mortality from viral hepatitis is increasing



Source: WHO global health estimates (Global Health Estimates 2015: deaths by cause, age, sex, by country and by region, 2000-2015. Geneva: World Health Organization; 2016.)

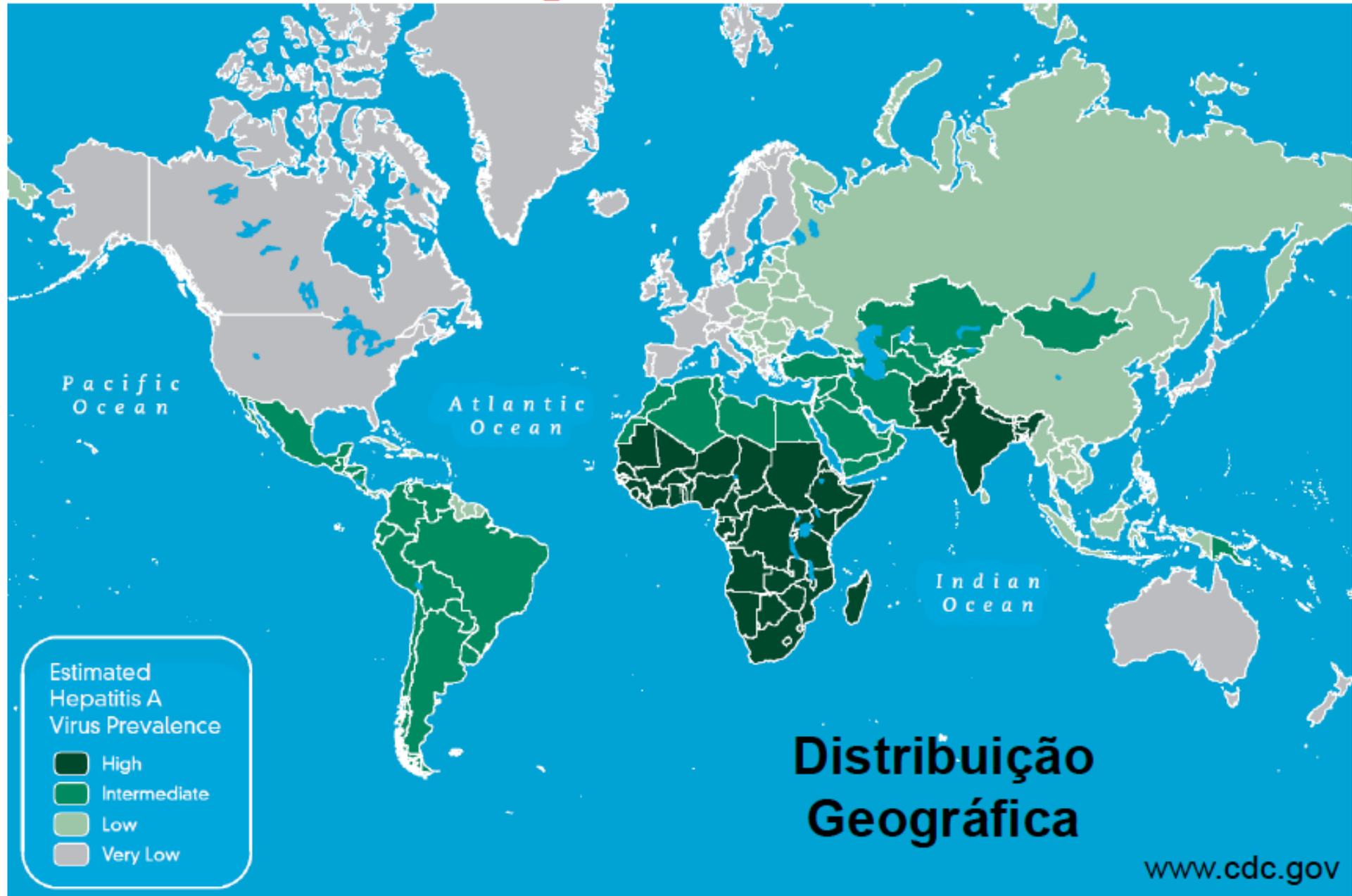
# Hepatites Virais: impacto nas populações humanas



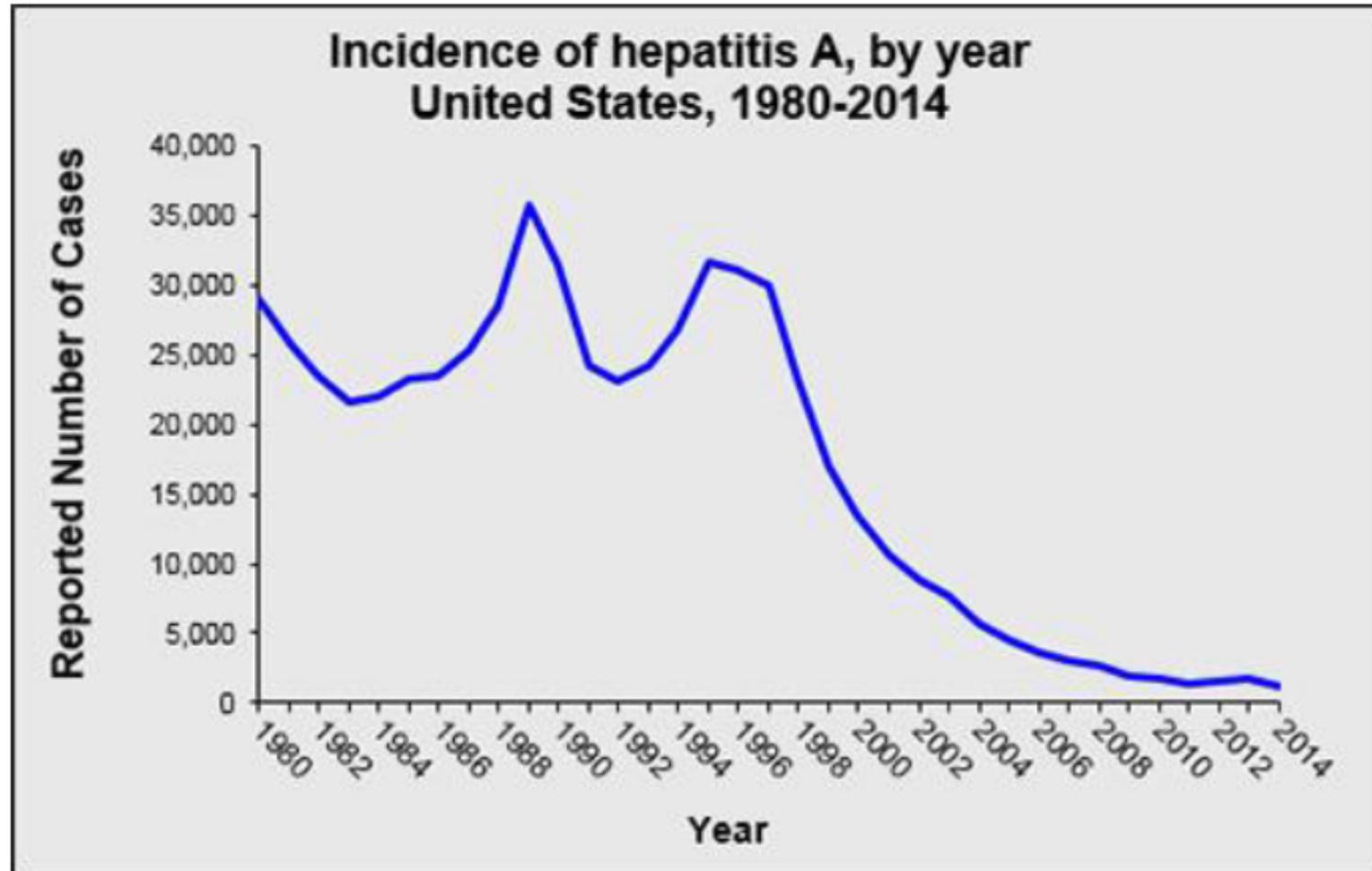
HAV: hepatitis A virus; HBV: hepatitis B virus; HCV: hepatitis C virus; HEV: hepatitis E virus Source: WHO global health estimates for 2015 published in 2016 (Global Health Estimates 2015: deaths by cause, age, sex, by country and by region, 2000–2015. Geneva: World Health Organization; 2016.)

# **Vírus de hepatite de transmissão entérica**

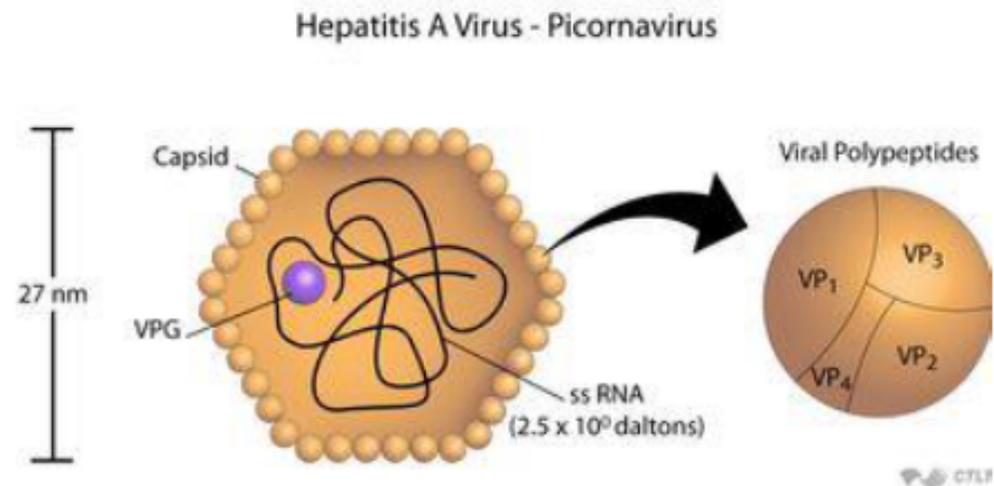
# Hepatite A



# Hepatitis A



# Hepatitis A (HAV)



# Hepatite A

**Família:** *Picornavidae*

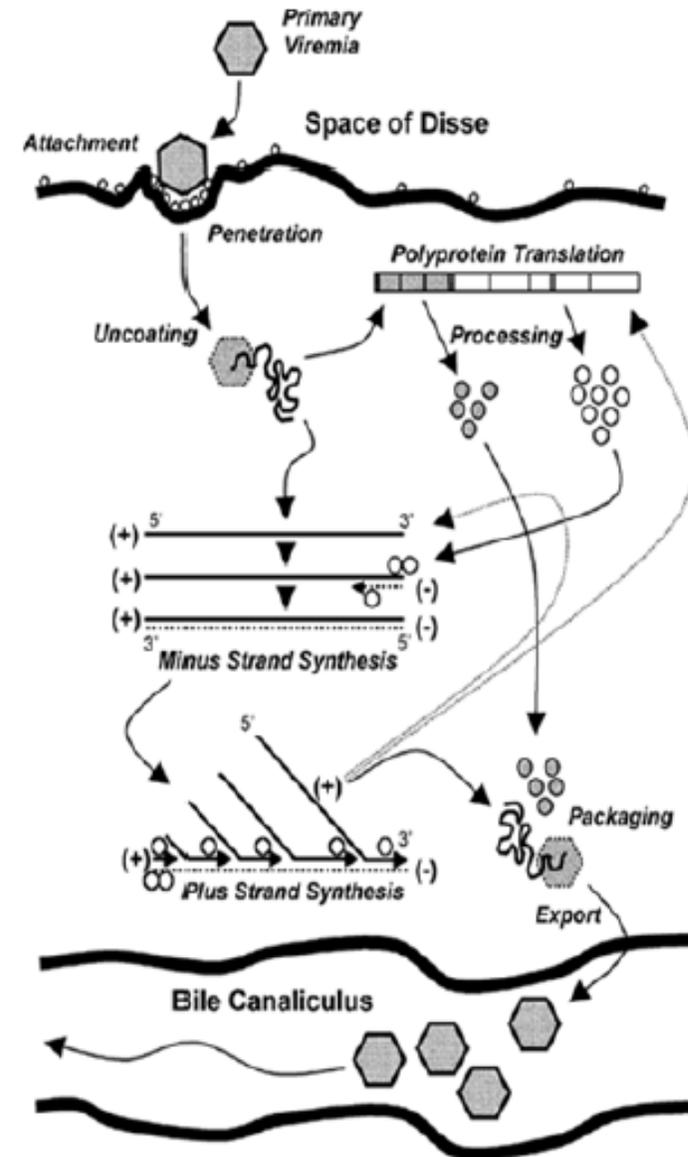
**Gênero:** Hepatovírus

- Capsídeo icosaédrico, não envelopado, de 27-32nm.
- Resistente ao calor, frio, condições ácidas e relativa resistência à desinfecção.
- Genoma de RNA linear, de fita simples, (+).
- Genótipos I,II e III infectam humanos
- Transmissão via oral-fecal e parentérica (Crianças = fonte de infecção)

# Hepatite A

## Multiplicação

- Transmissão por água e alimentos.
- Porta de entrada pela via oral.
- Replicação viral primária no intestino delgado e migração por veia porta até o fígado.
- Excretado por bile e pelas fezes.



# Hepatite A

## Diagnóstico Laboratorial

- Ensaio imunoenzimáticos
  - pesquisa de anticorpos
- Imunomicroscopia eletrônica
  - antígeno nas fezes
- Técnicas de biologia molecular
  - PCR, sequenciamento (tipagem dos vírus circulantes)

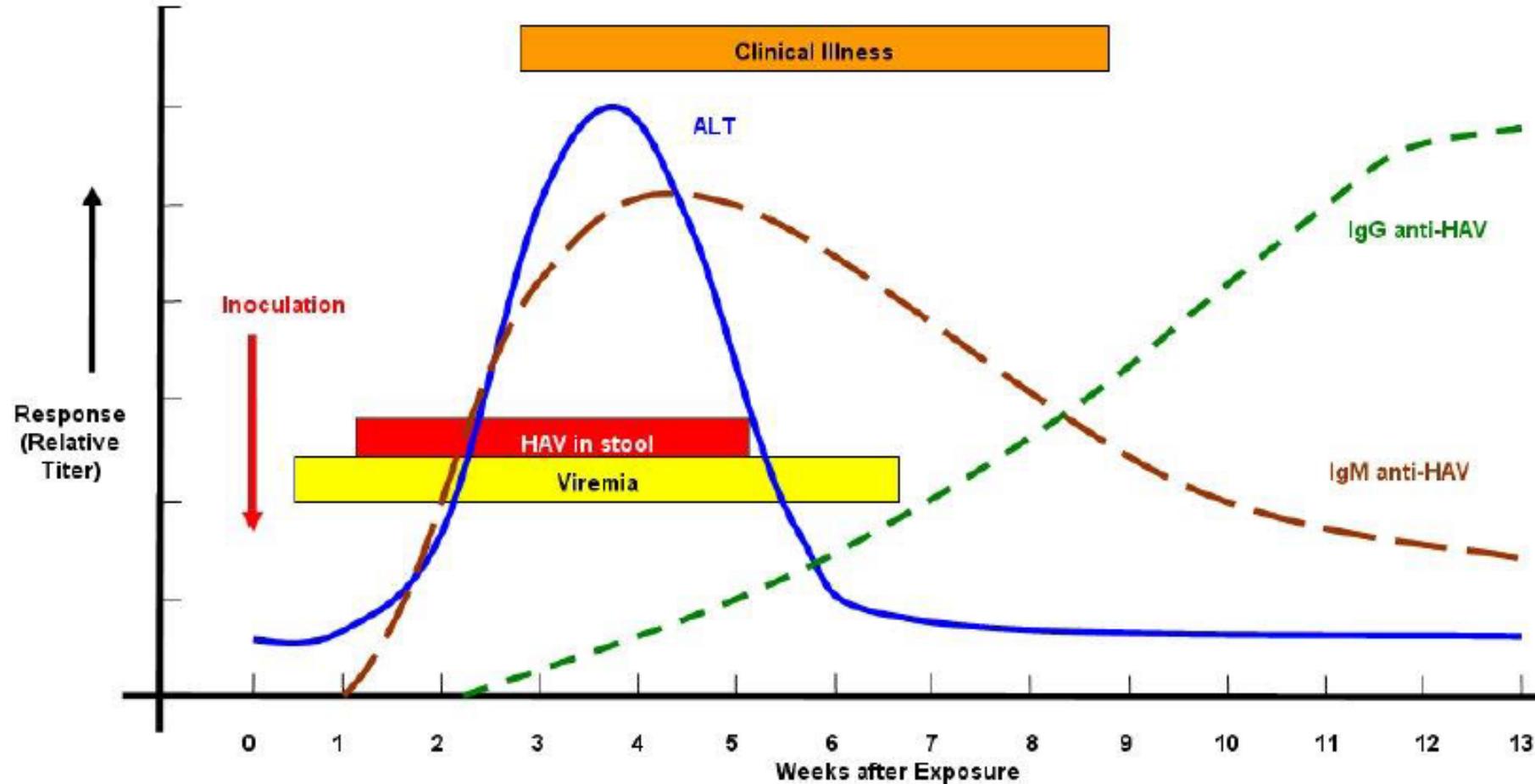
# Hepatite A

## Pesquisa de anticorpos

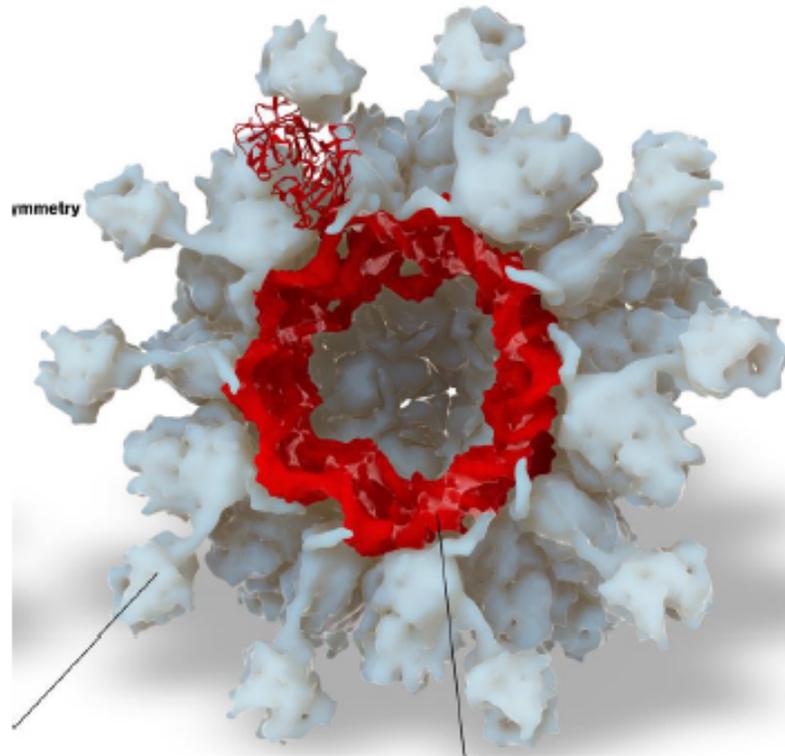
- **anti-VHA IgM**
  - marcador de infecção recente
- **anti-VHA IgG**
  - conferem imunidade duradoura
  - marcador soropidemiológico
  - indicador de contato prévio
- **amostra clínica**
  - soro
  - saliva
  - sangue - polpa digital

# Hepatite A

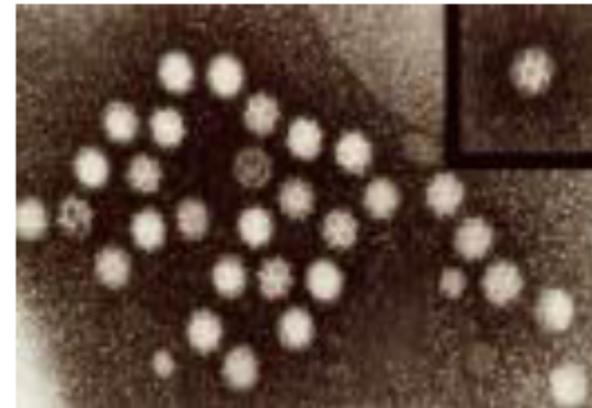
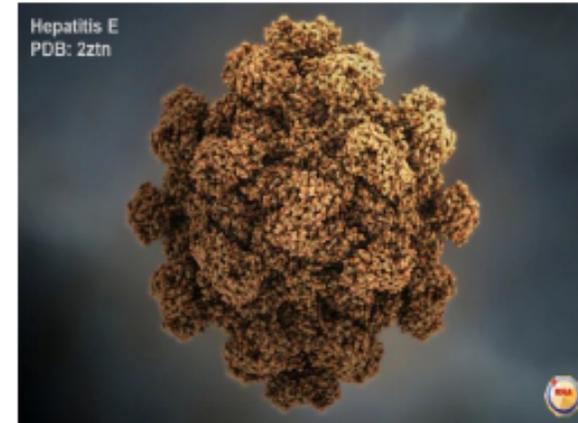
## Sorologia da infecção



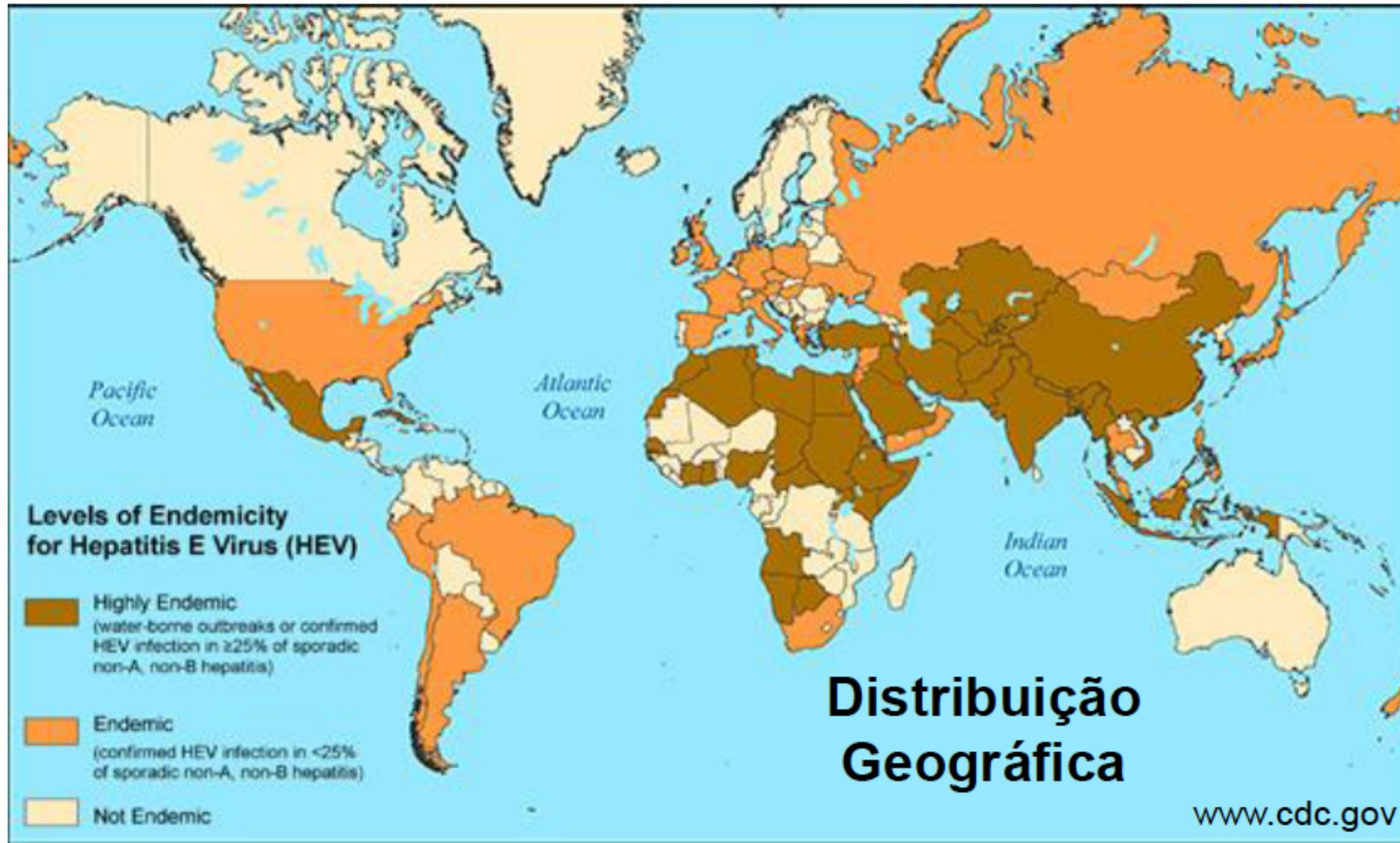
# Hepatite E (HEV)



RNA-vírus simples fita, não envelopados



# Hepatitis E



# Hepatite E

## Epidemiologia

- Maioria dos surtos associados a consumo de água contaminada com fezes
- Transmissão pessoa-a-pessoa mínima
- Casos descritos em áreas endêmicas ou em pessoas que viajaram para estas regiões

# Hepatite E

*A hepatite E não tem dados de prevalência significativos no Brasil, mas é muito comum na Ásia, Índia e África!*

**Família: Hepeviridae**  
**Gênero: Hepevírus**

- Capsídeo: icosaédrico, esférico, não envelopado, 27-34nm.
- Genoma de RNA com leitura positiva com 7,2 kb 3 ORF.
- transmissão fecal-oral e água contaminada (zoonose - suínos).
- Endêmico no Sudeste Asiático e Índia.
- Mortalidade de até 20%, especialmente em grávidas.

# Hepatitis E

**Table 1 Comparison of the four hepatitis E virus genotypes by select characteristics**

Characteristics	Genotype 1	Genotype 2	Genotype3	Genotype 4
Viral discovery	1983	1986	1995	2003
Geographic distribution	Developing countries	Mexico, West Africa	Developed countries	China, Taiwan, Japan
Food-borne transmission	No	No	Yes	Yes
Fecal-oral transmission	Yes	Yes	?	No
Water-borne transmission	Yes	Yes	?	No
Person-to-person transmission	Yes	Unknown	Yes	Unknown
Zoonotic transmission	No	No	Yes	Yes
Occurrence of epidemics	Common	Smaller scale epidemics	No epidemics	Uncommon
Highest attack rate	Young adults	Young adults	Persons $\geq$ 40 yr of age	Young adults
Gender	Male preponderance	Not discriminatory	Mostly male	Not discriminatory
Mortality rate	0.5%-3%	0.5%-3%	Not determined	0.5%-3%
Mortality among pregnant women	High	High	Not determined	High
Chronic infection	None	None	Yes	None
Severe disease among immuno-compromised	Not reported	Not reported	Yes	Not reported
Interspecies transmission	Only humans and non-human primates	Only humans and non-human primates	Humans Pigs	Humans Pigs
Subtypes	5	2	10	7

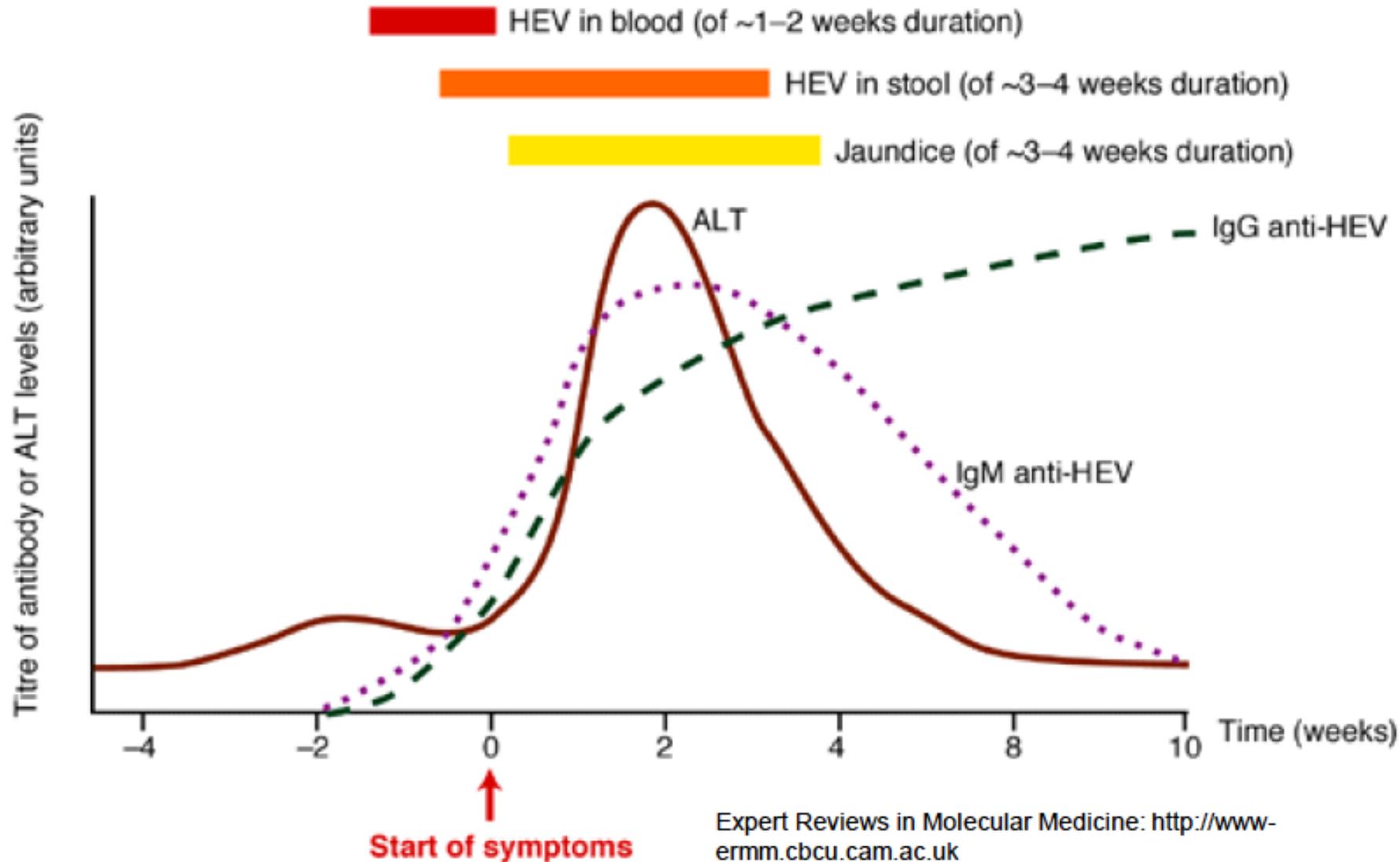
# Hepatite E

## Diagnóstico Laboratorial

- ensaios imunoenzimáticos
  - Pesquisa de anti-VHE (IgM ou IgG) - ELISA
    - ELISA
    - IMUNOBLOT
- técnicas de biologia molecular

# Hepatitis E

## Sorologia da infecção

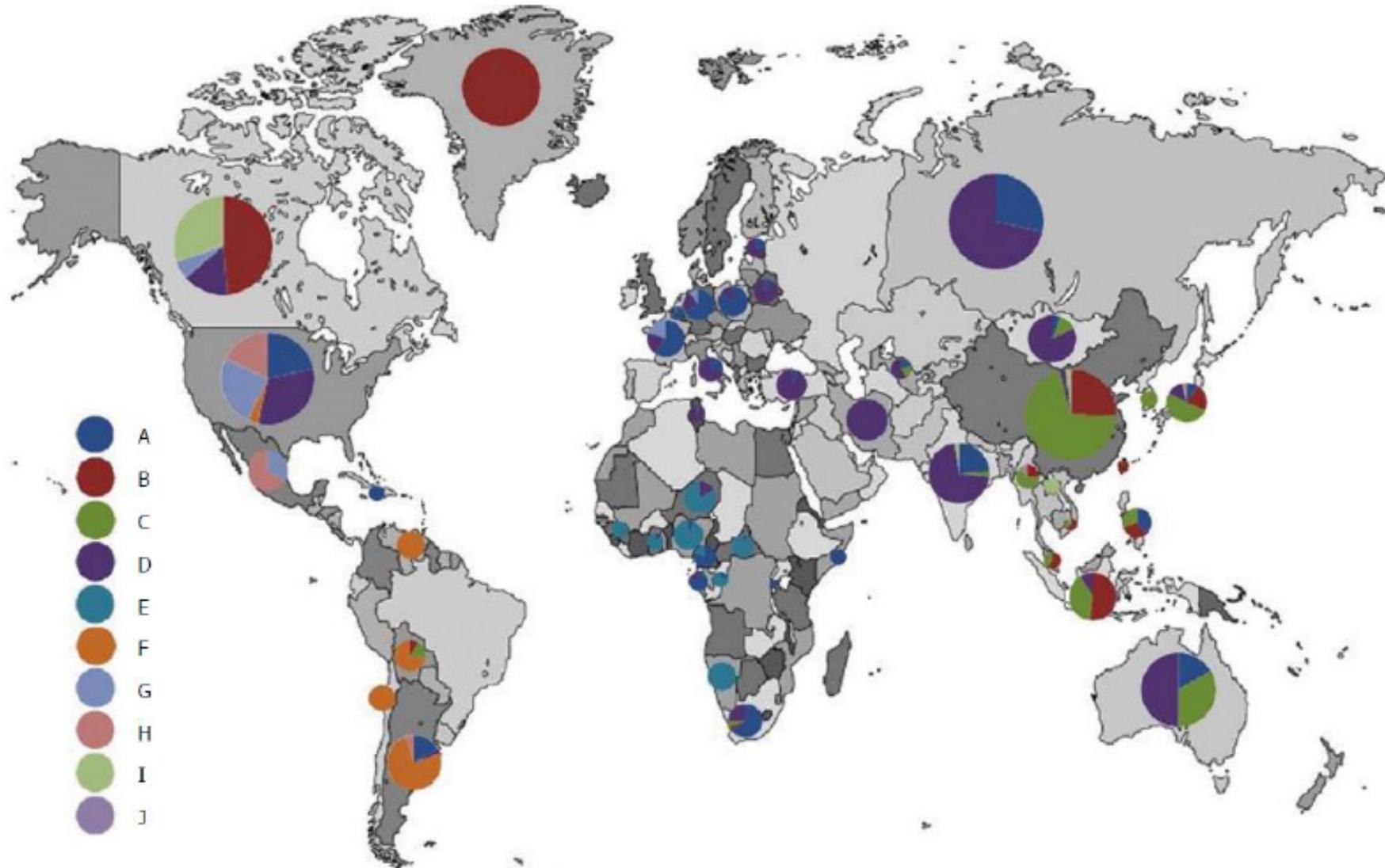


**Vírus de hepatite  
de transmissão  
parenteral  
(sexual?)**

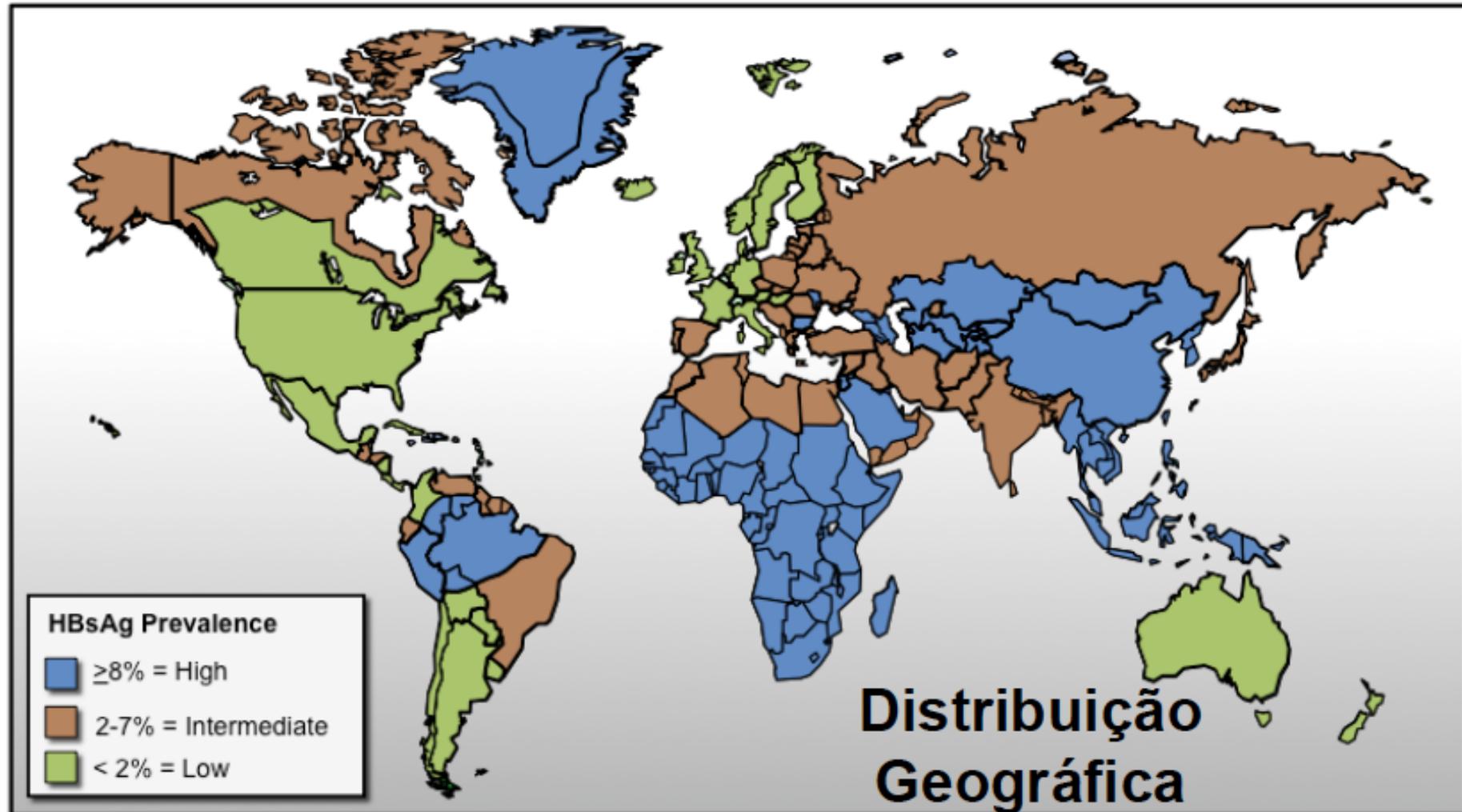
# Hepatitis B (HBV)

# Hepatite B

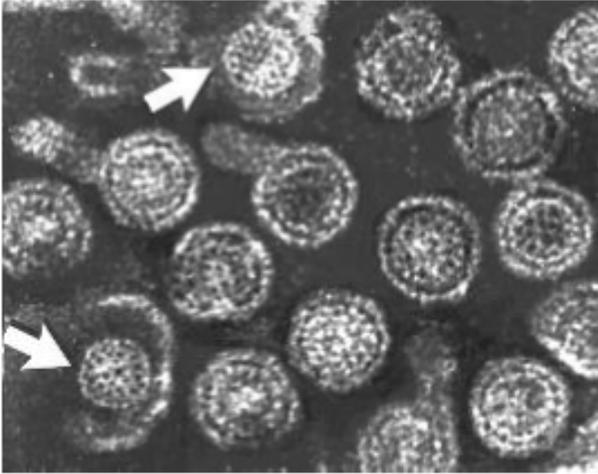
Dez genótipos



# Hepatitis B



# Hepatite B



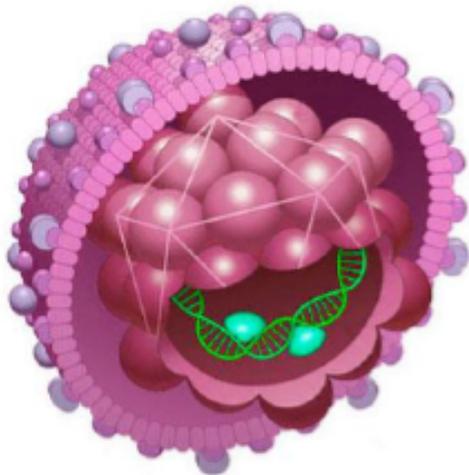
**Familia :** *Hepadnaviridae*  
**Gênero:** *Orthohepadnavírus*

- Pararetrovírus

Vírus pequenos de DNA envelopados (~45 nm)

DNA circular dupla-fita parcial (~3,5 kpb)

Célula alvo: hepatócitos

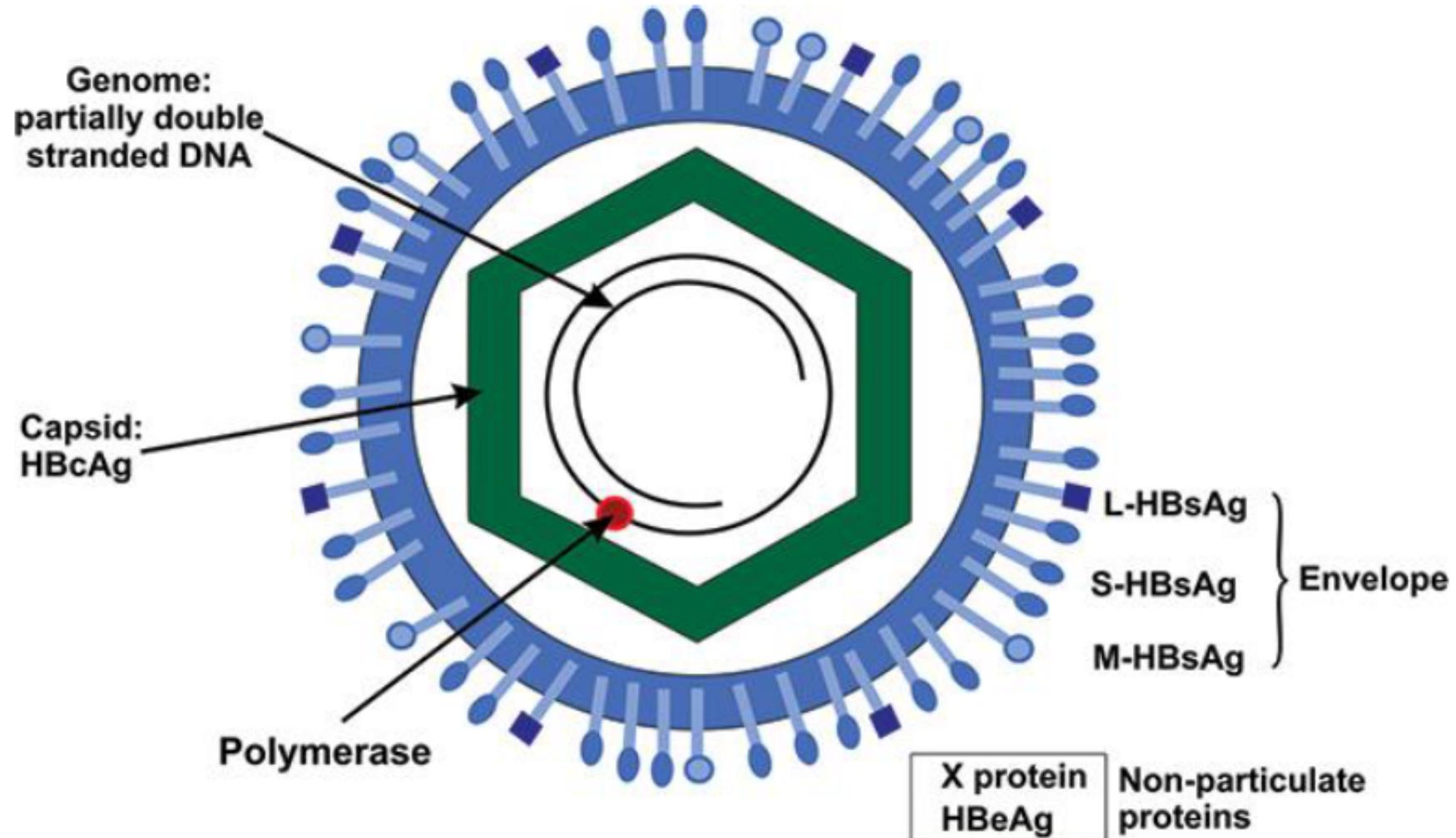


Etiologicamente associado com:

- Hepatite
- Cirrose
- Carcinoma hepatocelular

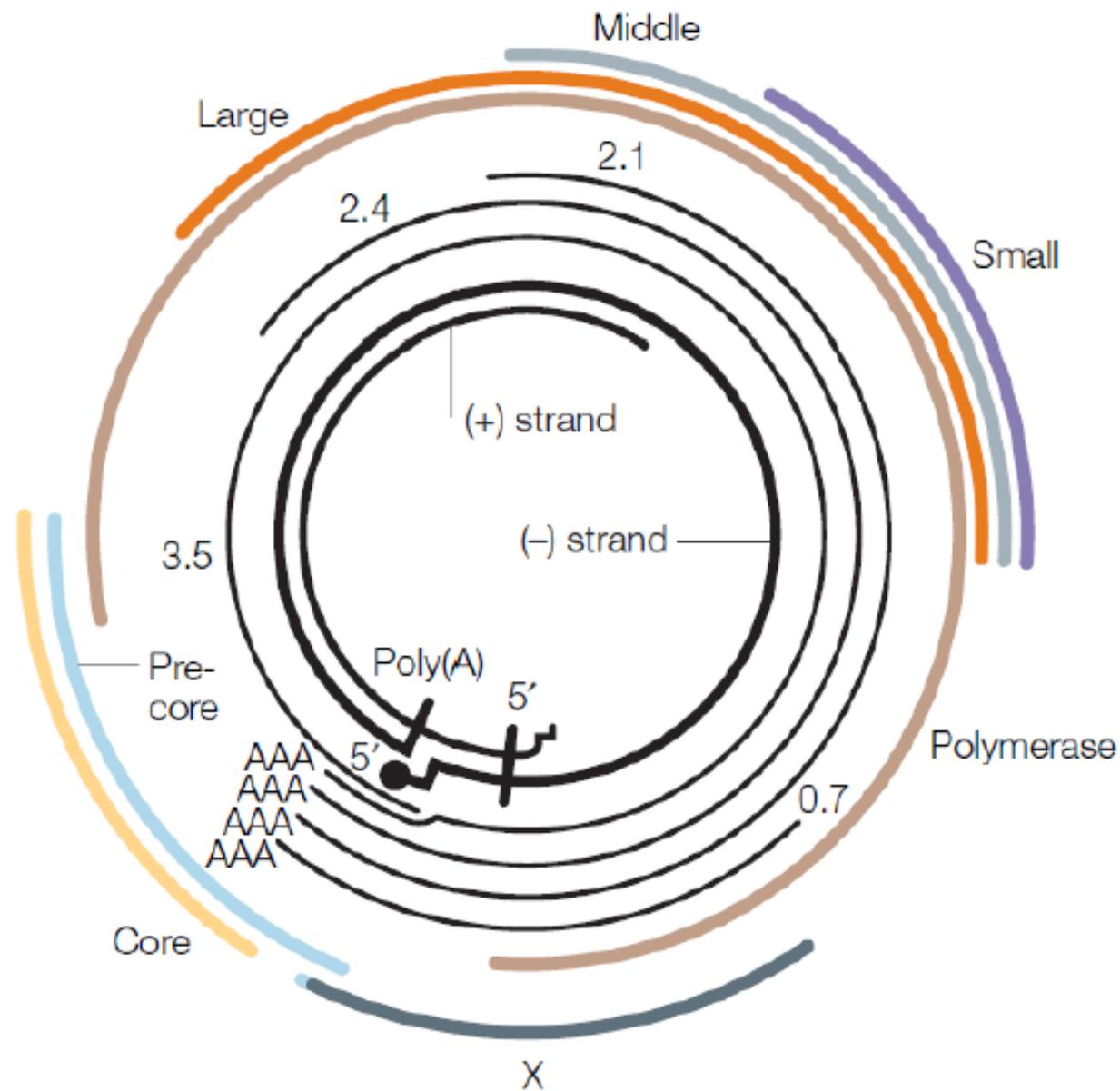
# Hepatitis B

## Antígenos virais



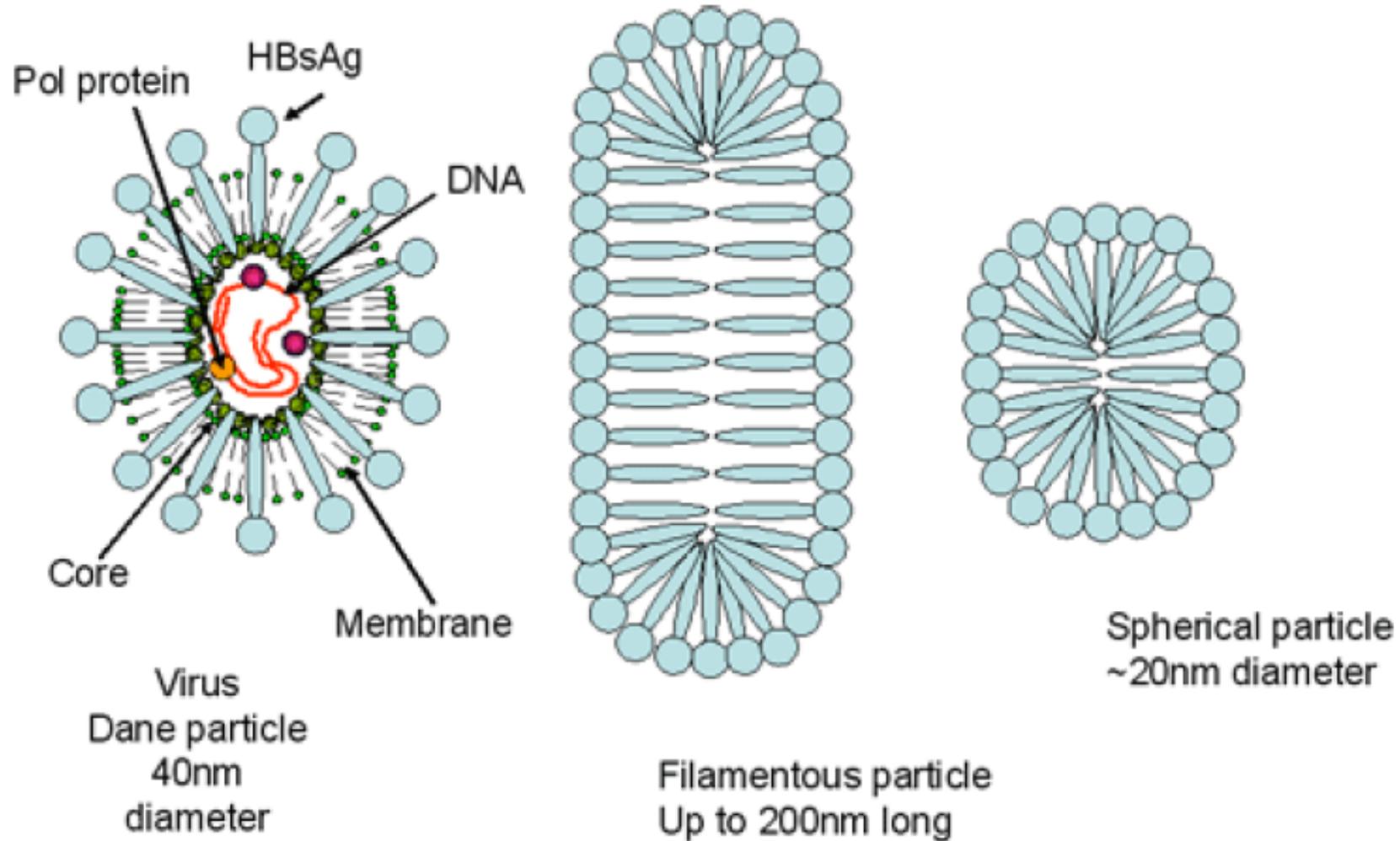
# Hepatitis B

## Organização genômica



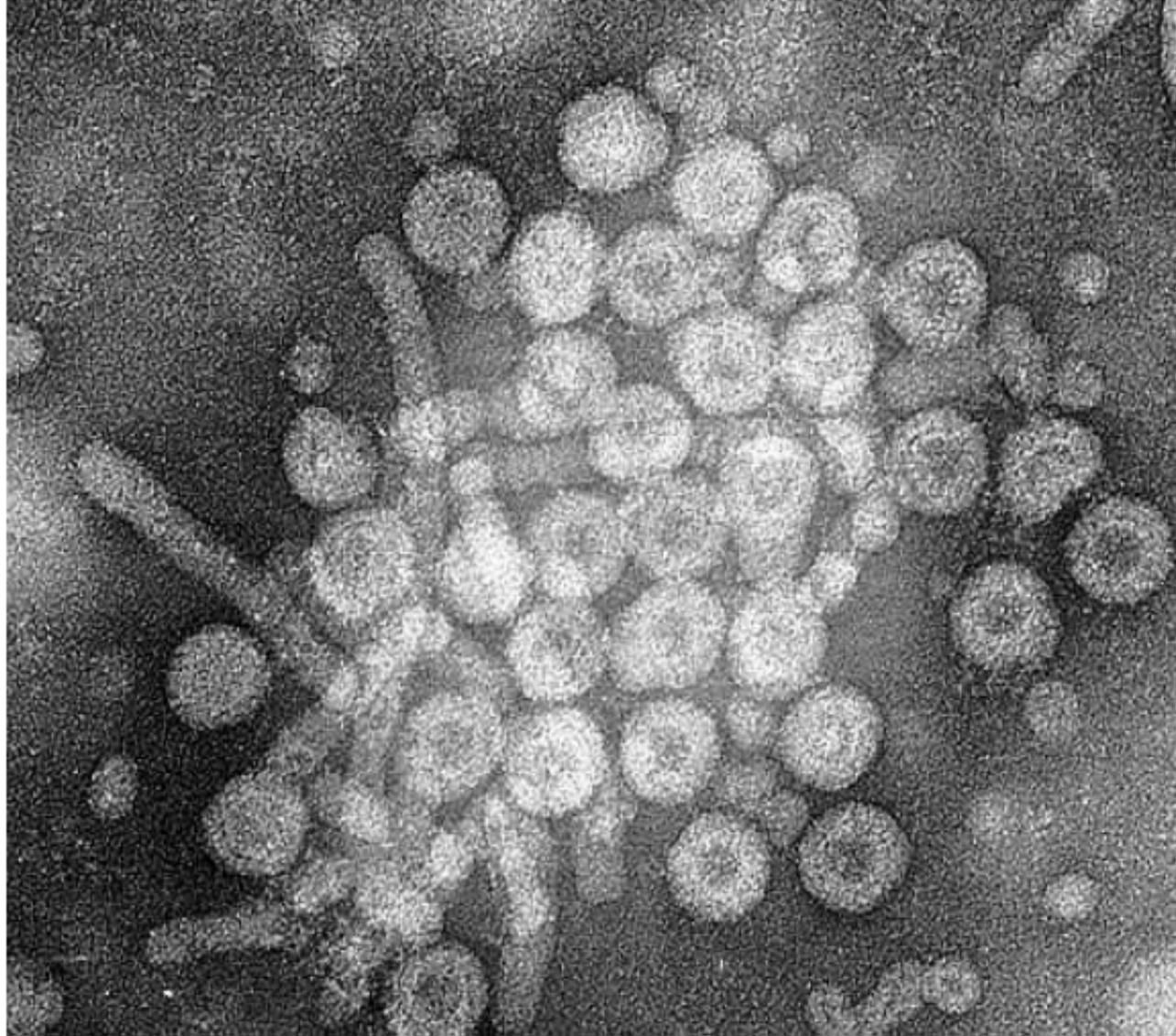
# Hepatitis B

## Antígenos virais



# Hepatitis B

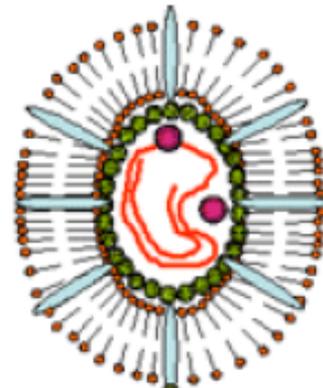
Antígenos virais



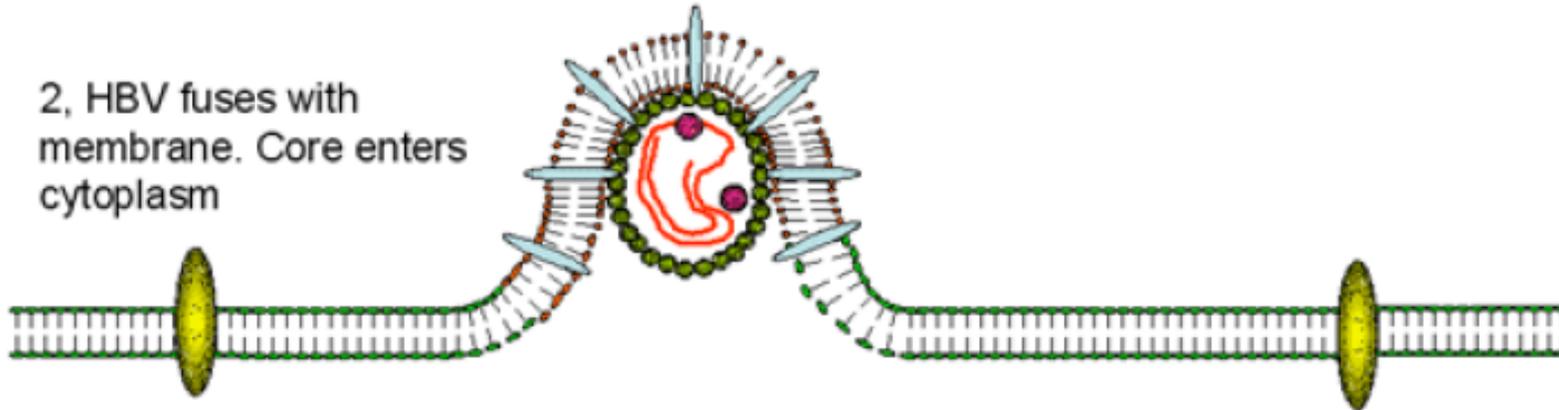
# Hepatitis B

## Ciclo Viral

1. HBV fuses binds to host cell membrane



2. HBV fuses with membrane. Core enters cytoplasm



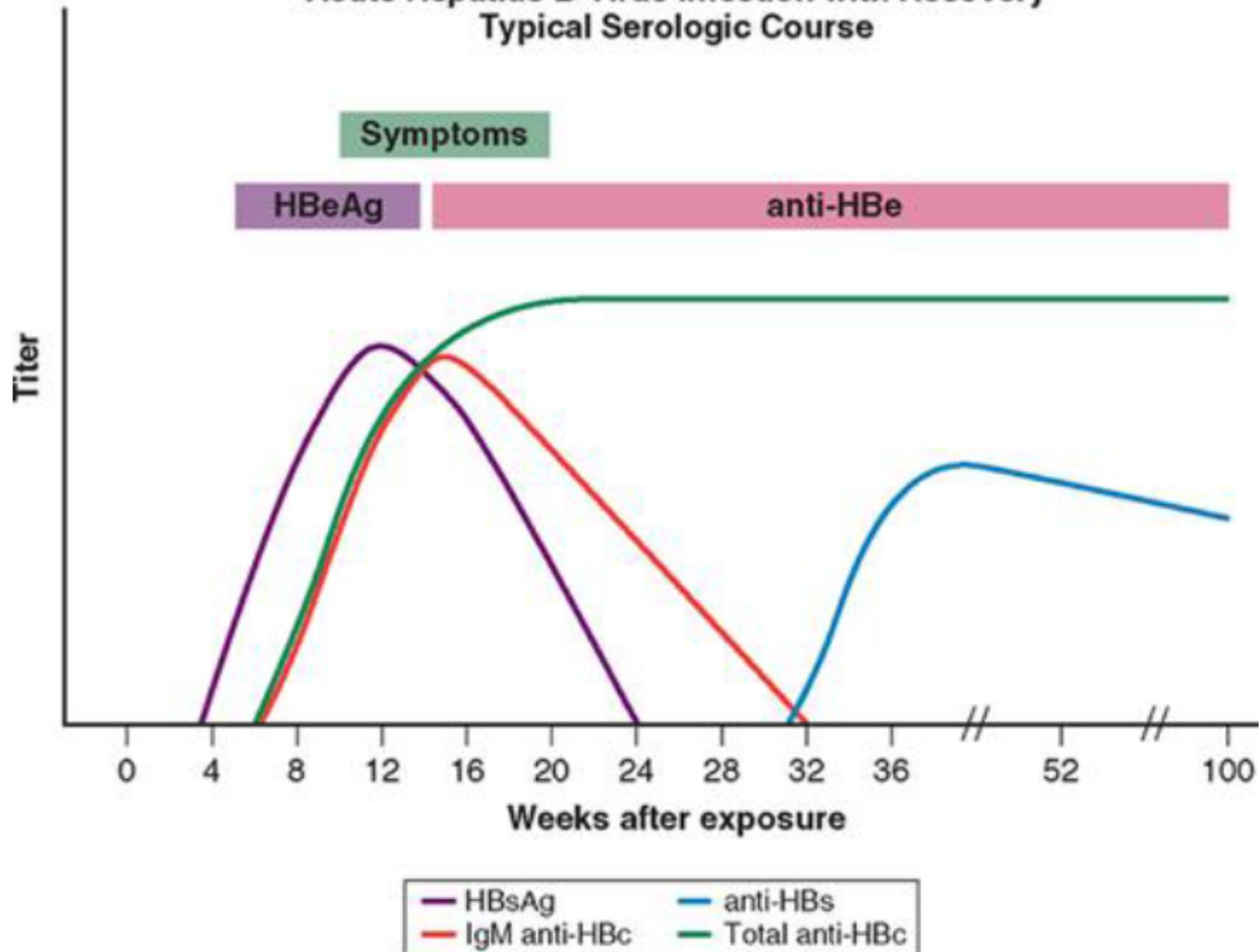
3. Double stranded genome is completed by enzymes contained with the core



# Hepatitis B

## Antígenos virais

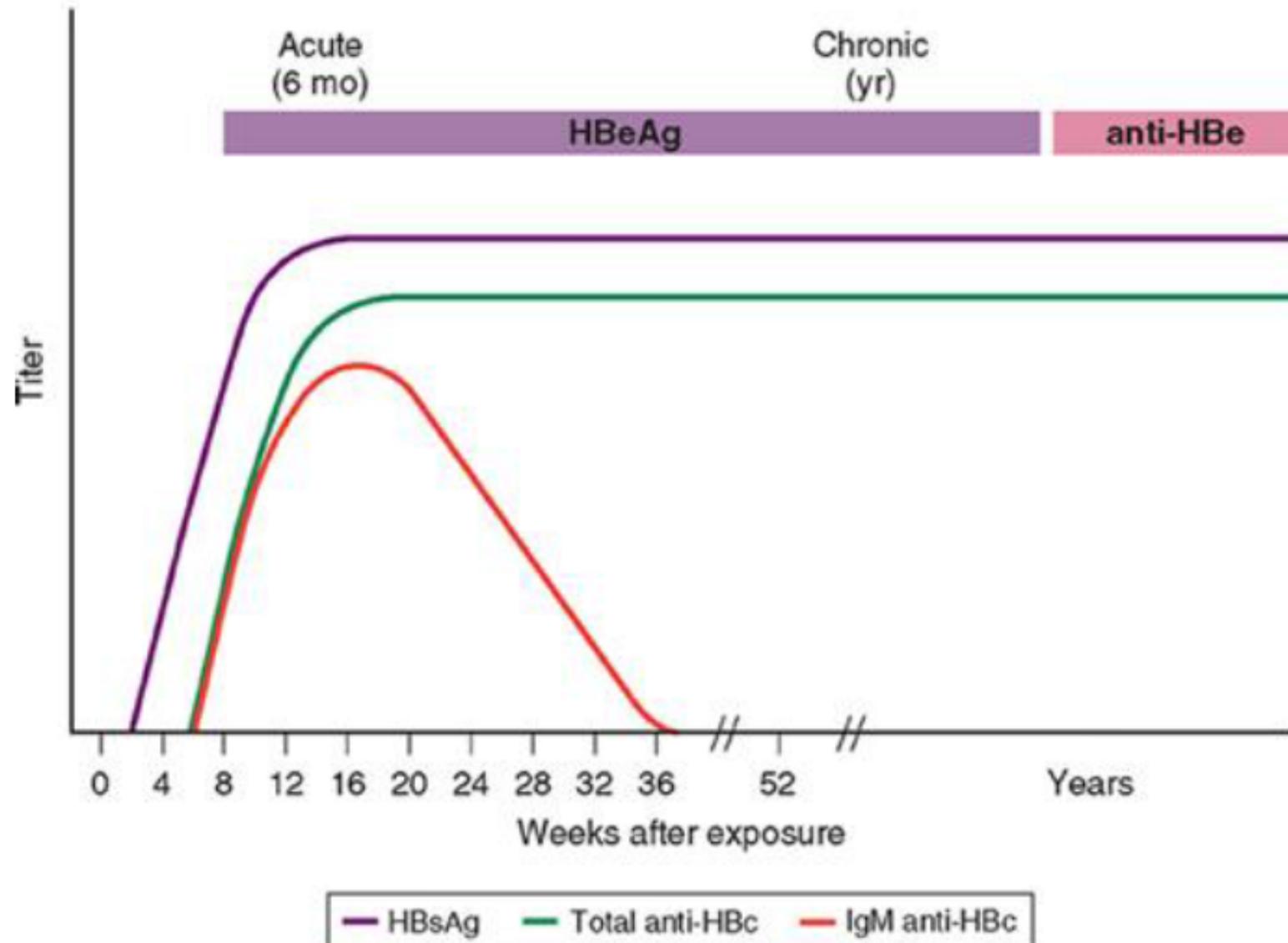
Acute Hepatitis B Virus Infection with Recovery  
Typical Serologic Course



# Hepatitis B

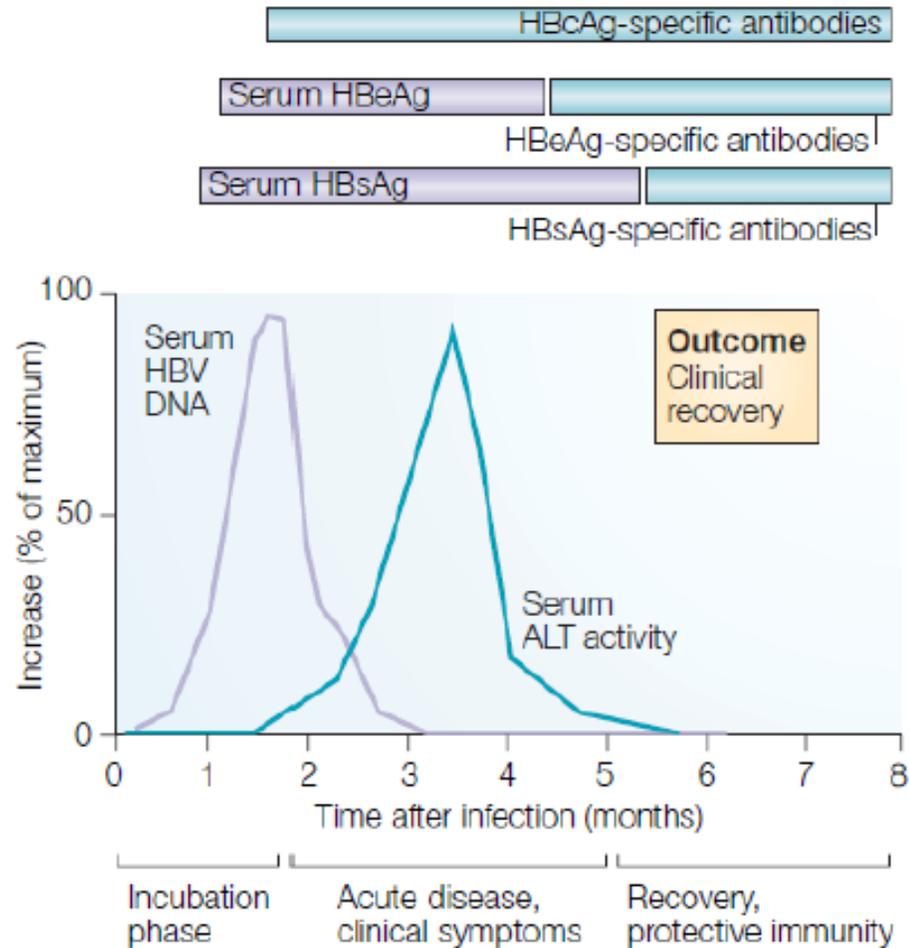
## Antígenos virais

Progression to Chronic Hepatitis B Virus Infection  
Typical Serologic Course



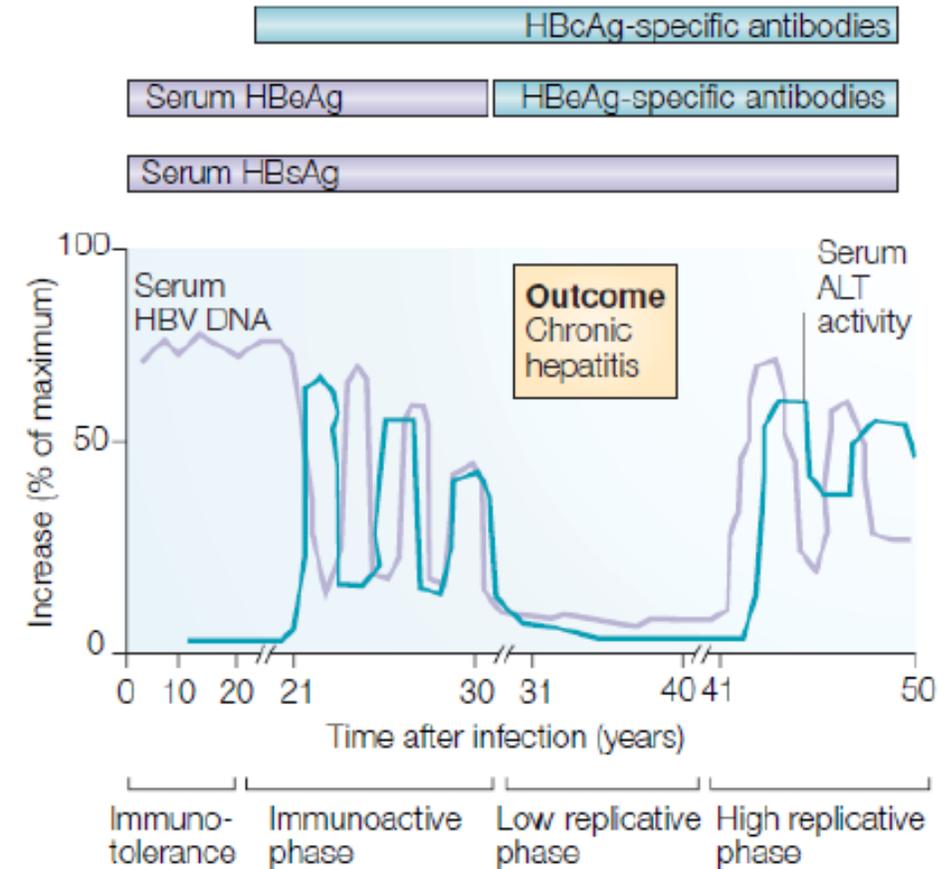
# Hepatitis B

**a Hepatitis B (acute)**

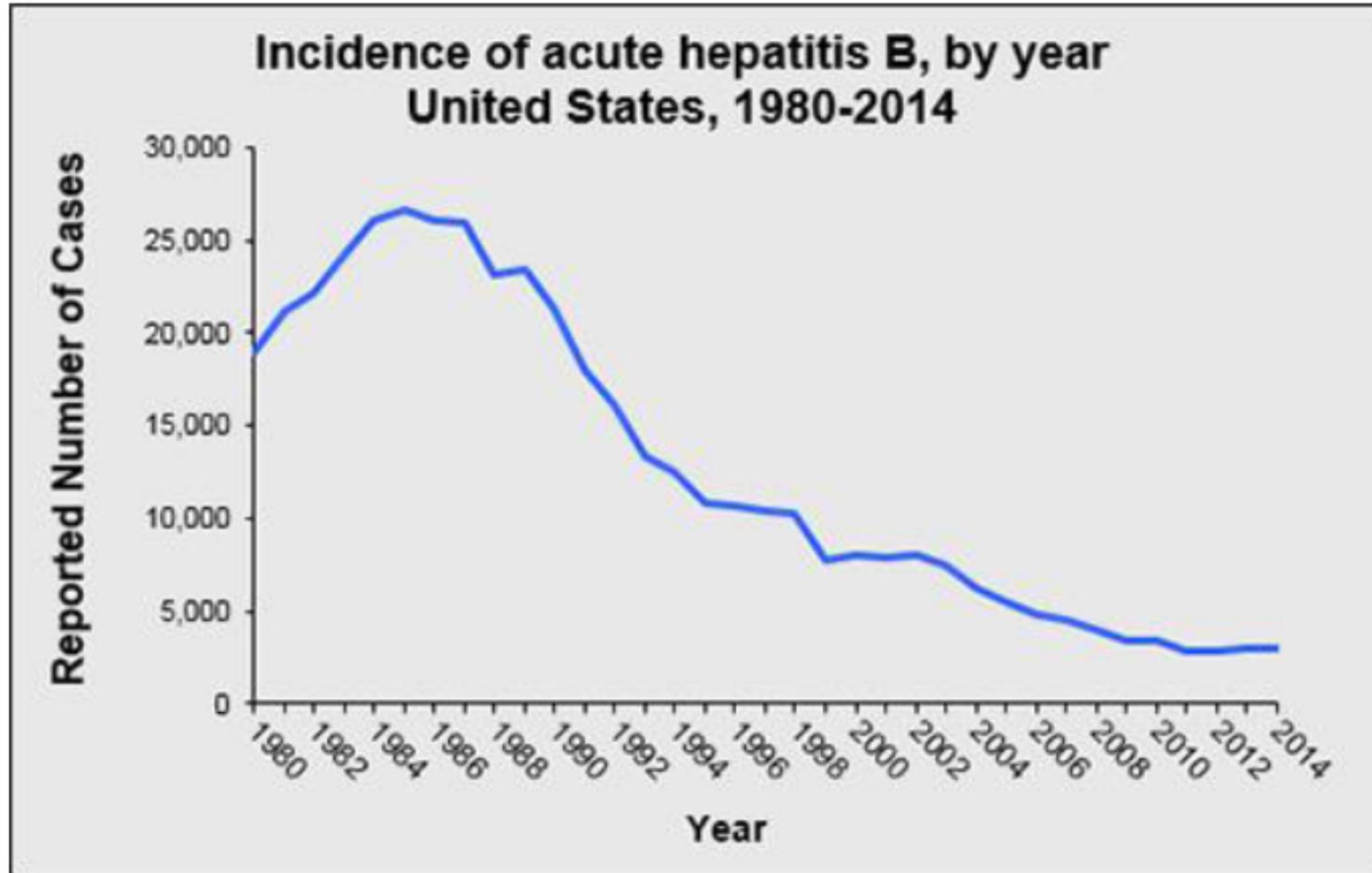


# Antígenos virais

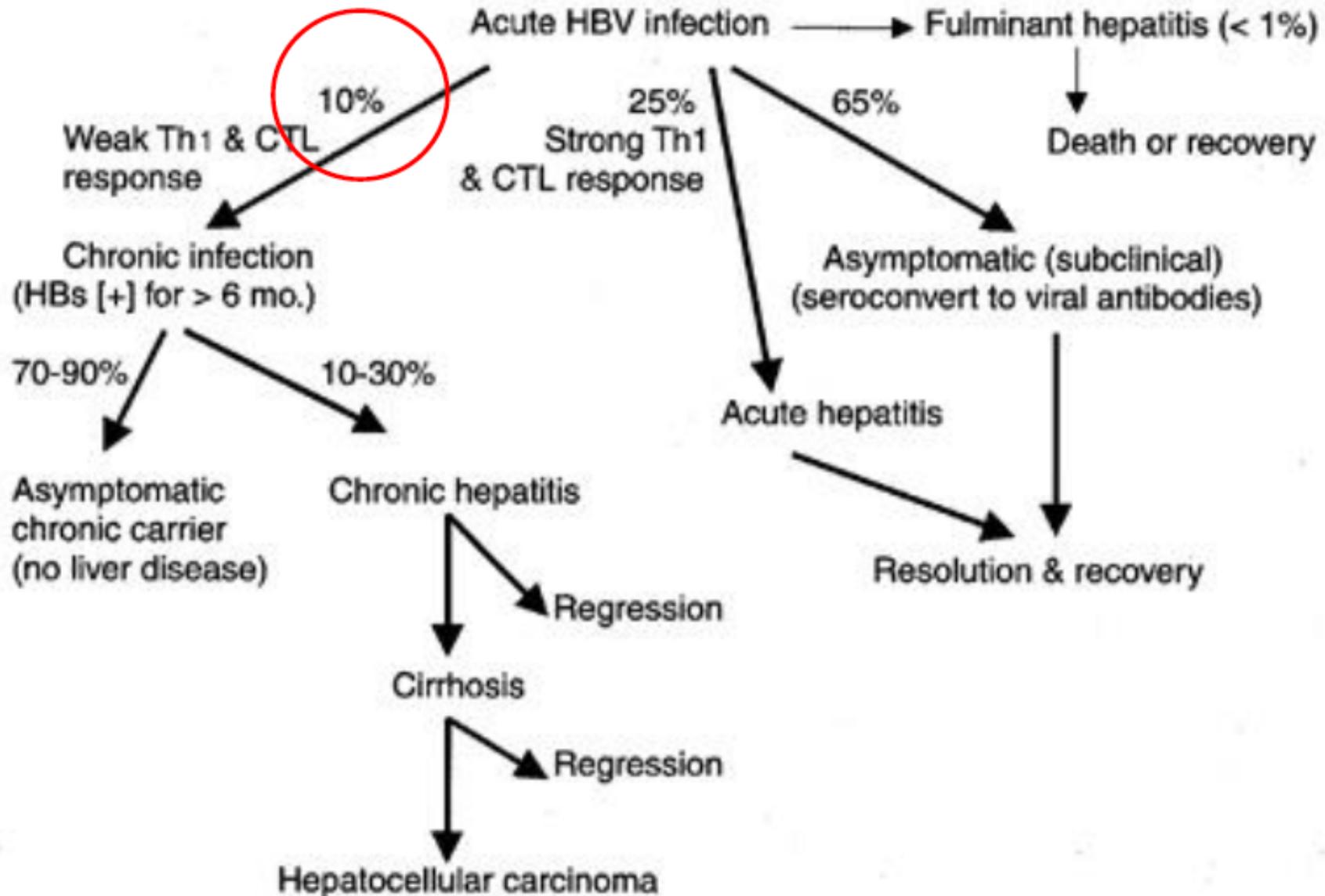
**b Hepatitis B (chronically evolving)**



# Hepatitis B



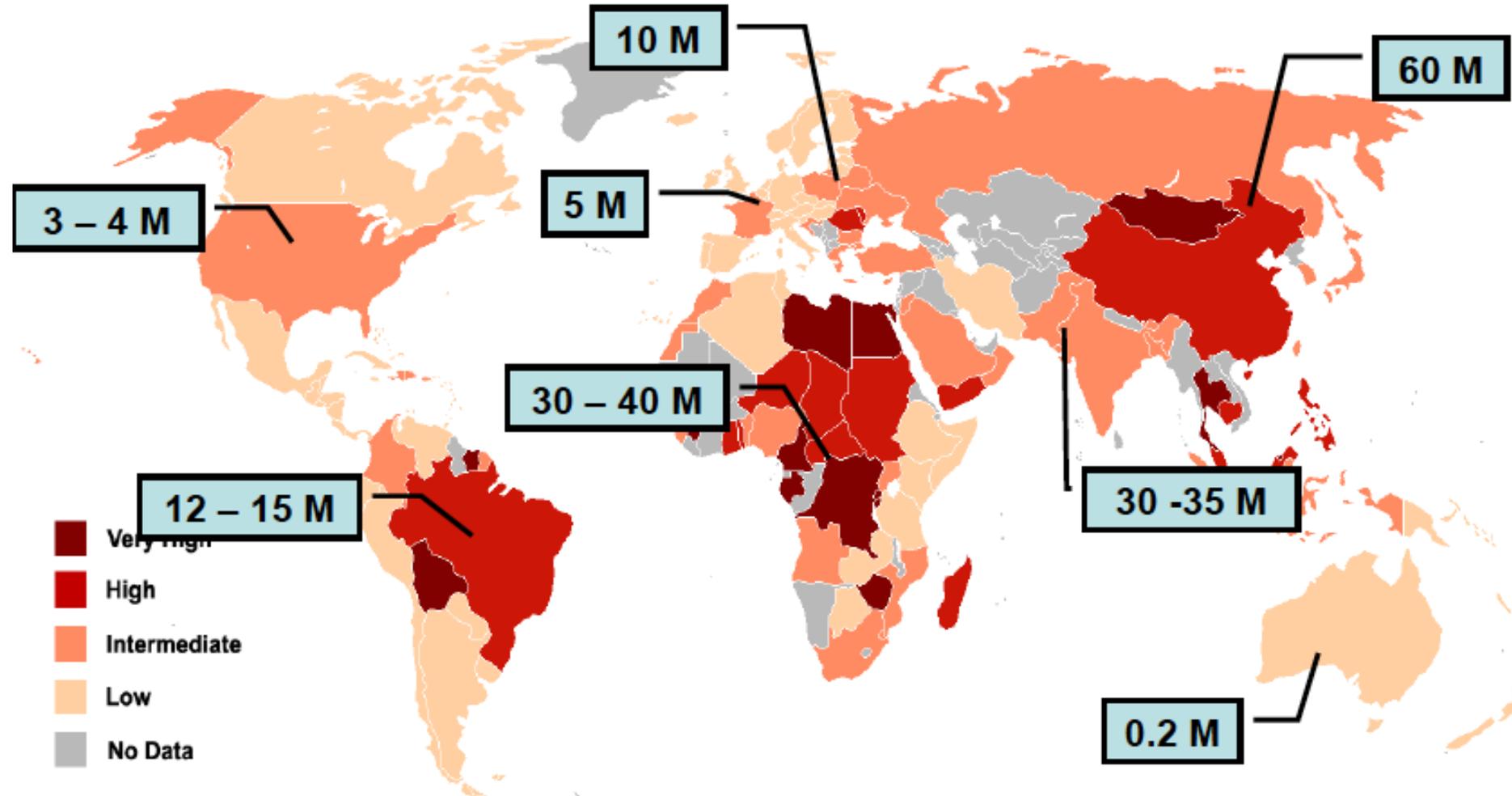
# Hepatitis B



# Hepatitis C (HCV)

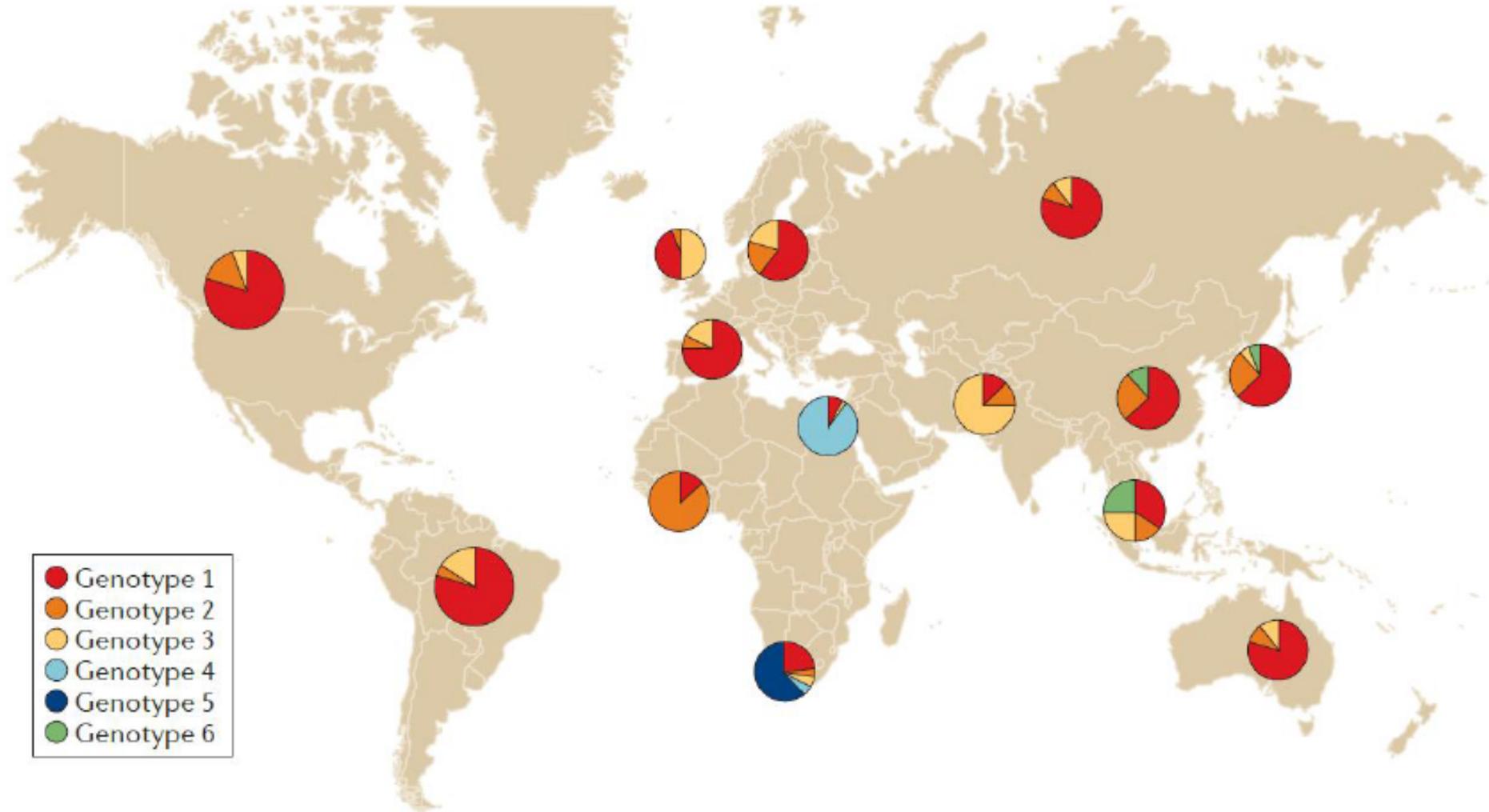
# Hepatite C

170 – 200 milhões de portadores no Mundo todo

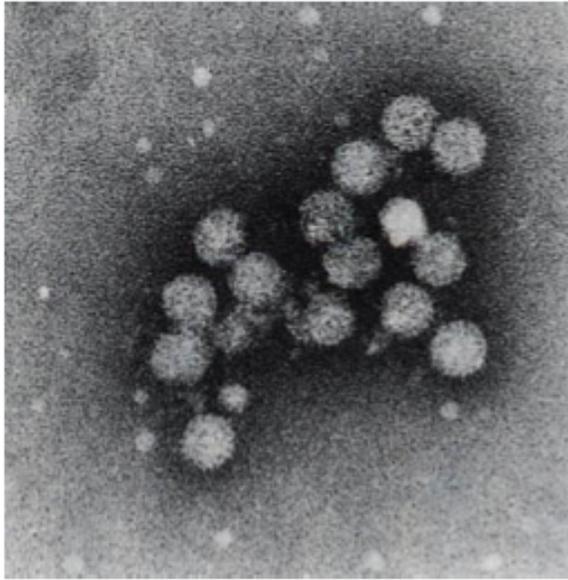


# Hepatite C

170 – 200 milhões de portadores no Mundo todo



# Hepatite C

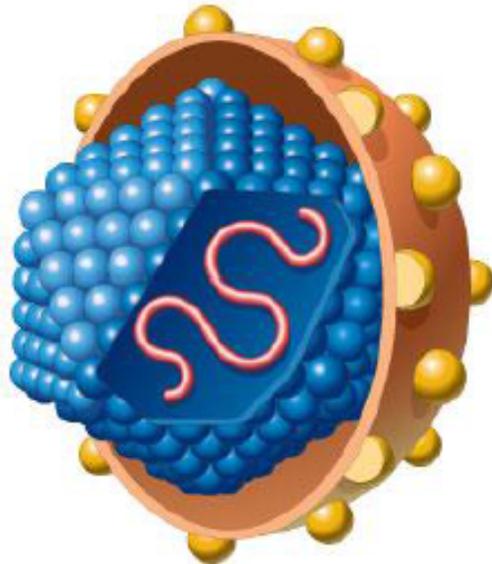


Familia : *Flaviviridae*  
Gênero: *Hepacivírus*

Vírus pequenos de RNA envelopados (~45 nm)

RNA linear simples-fita (~9,4 kpb)

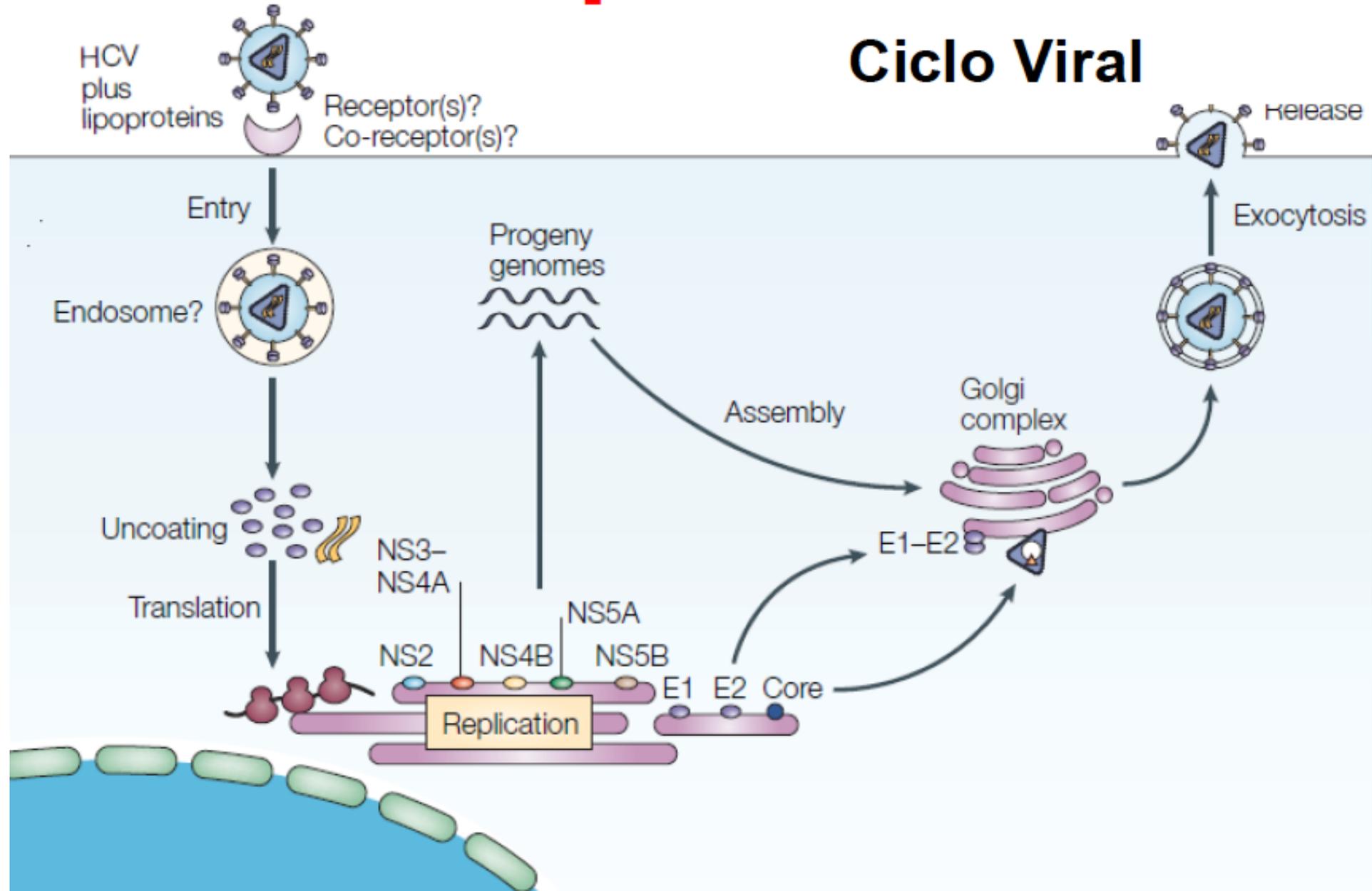
Célular alvo: hepatócitos



Etiologicamente associado com:

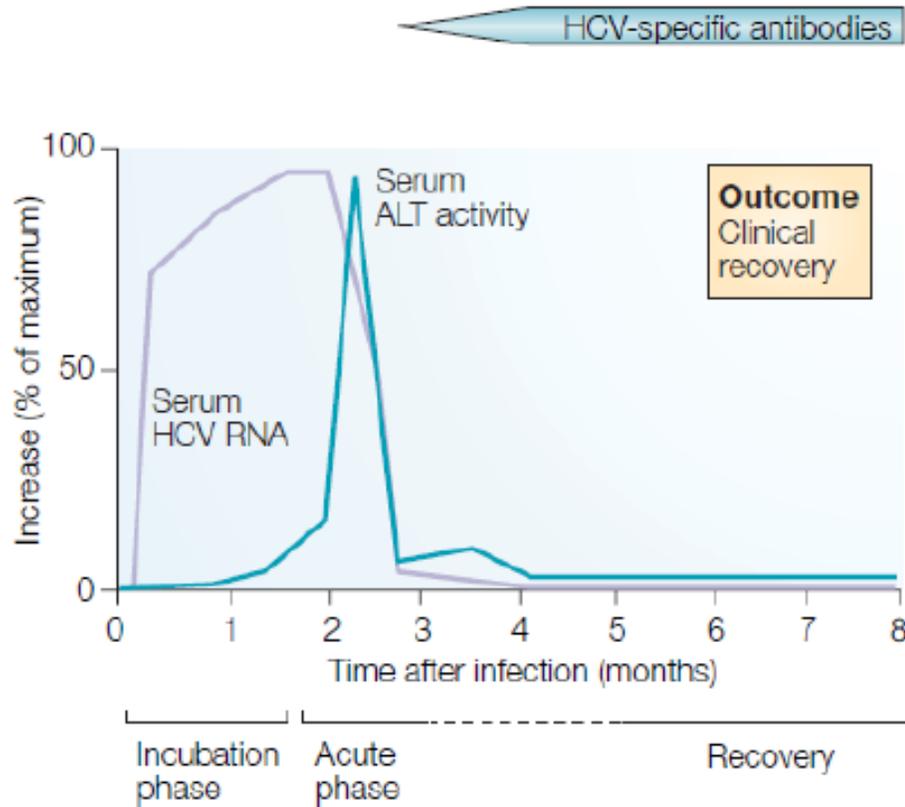
- Hepatite
- Cirrose
- Carcinoma hepatocelular

# Hepatitis C



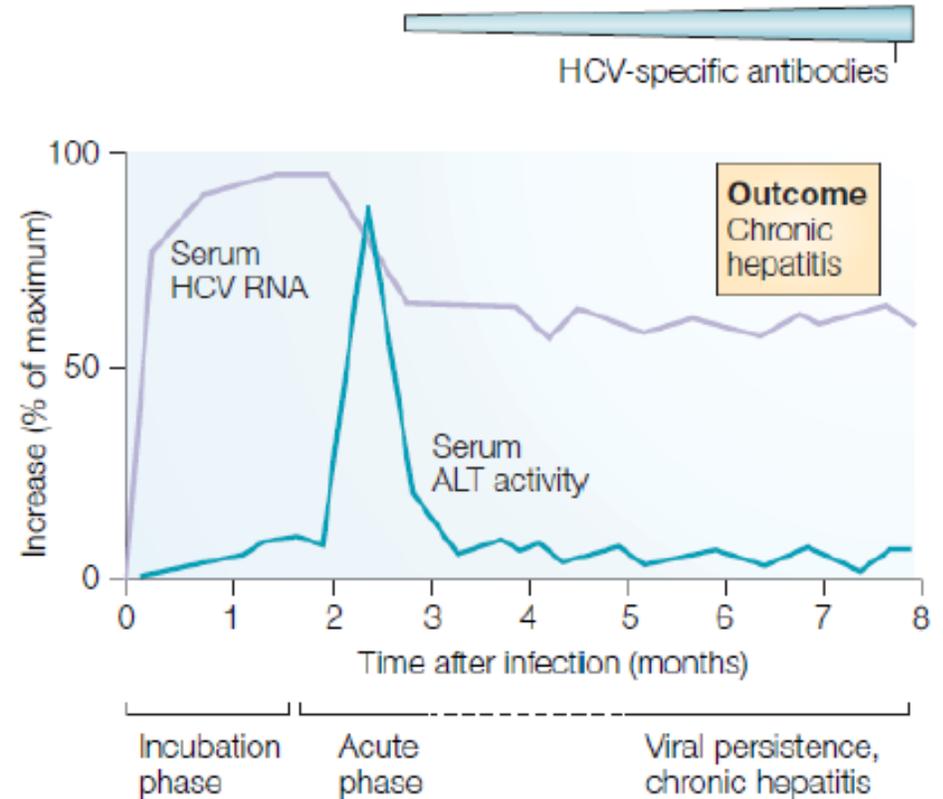
# Hepatitis C

c Hepatitis C (acute)



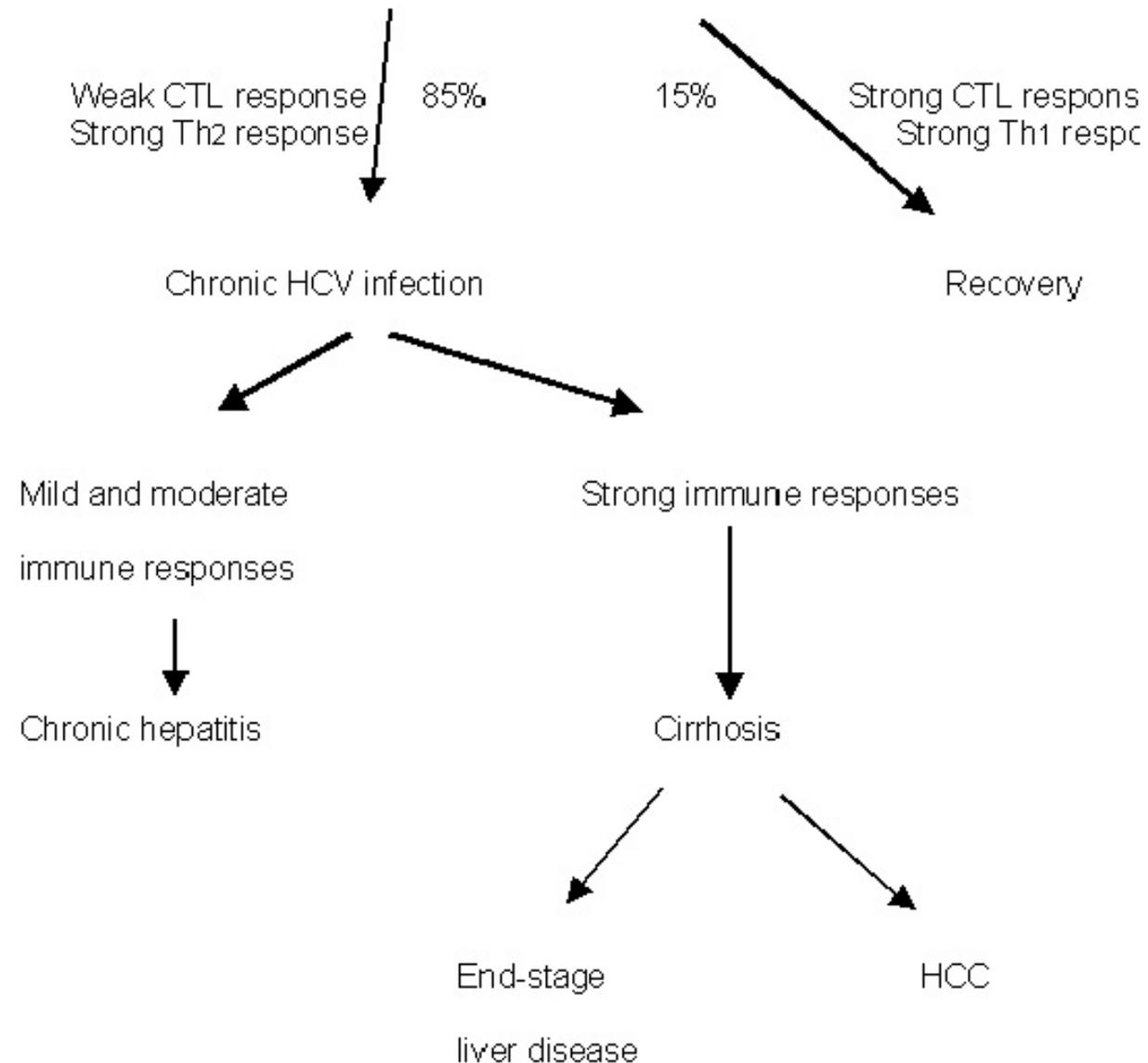
# Antígenos virais

d Hepatitis C (chronically evolving)



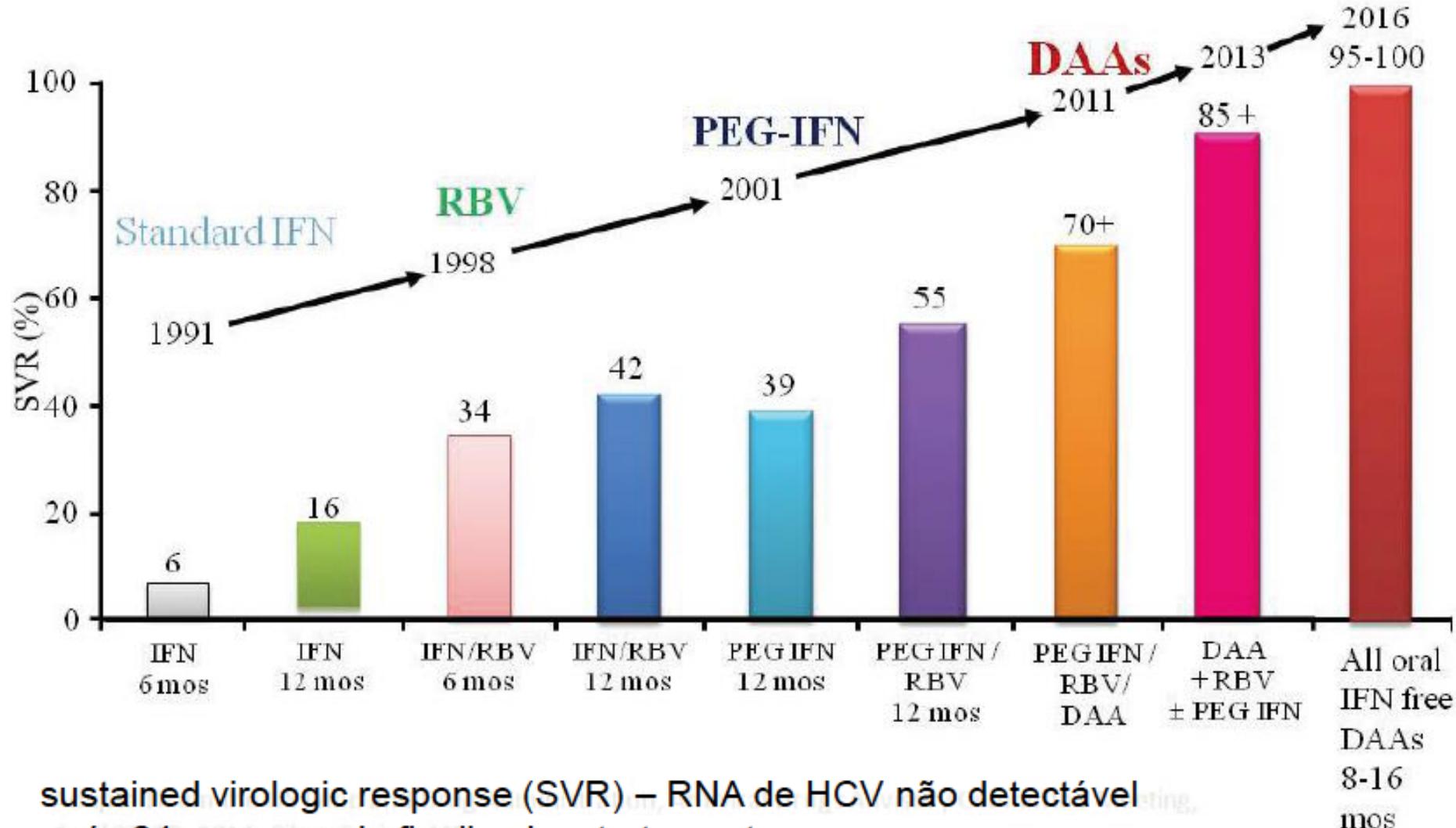
# Hepatitis C

Acute HCV infection



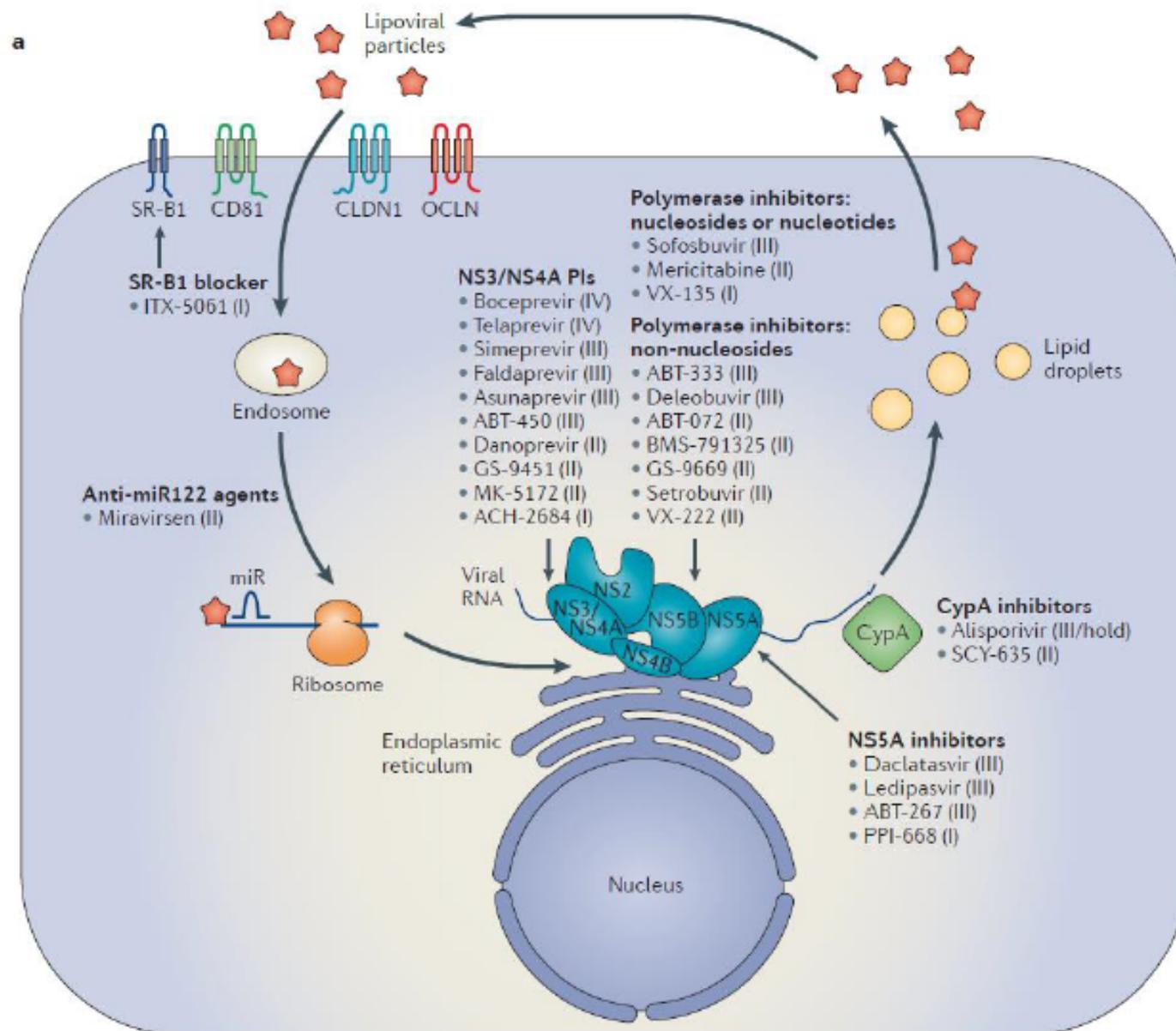
# Hepatite C

## Evolução das terapias contra HCV

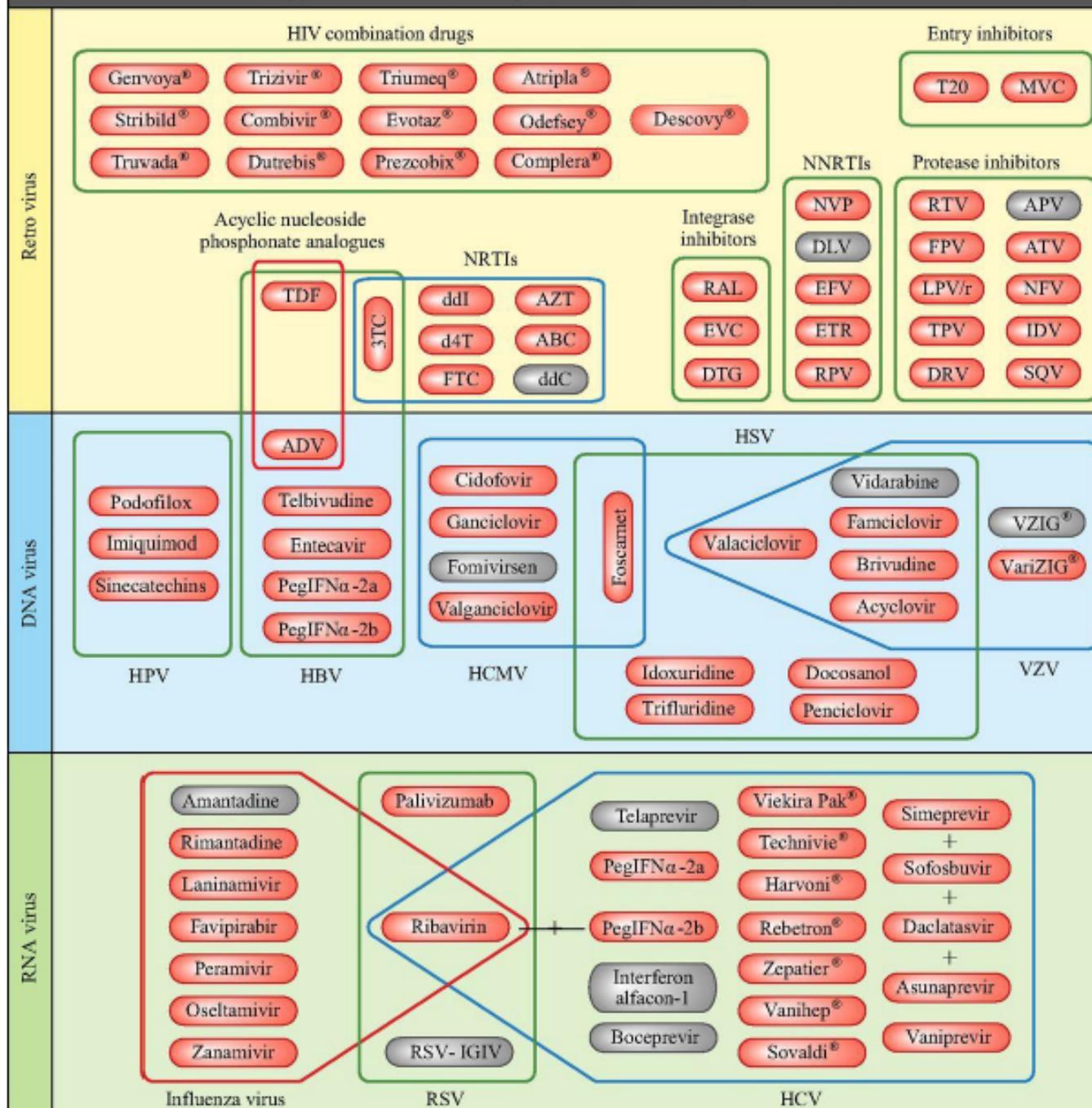


sustained virologic response (SVR) – RNA de HCV não detectável após 24 semanas de finalizado o tratamento.

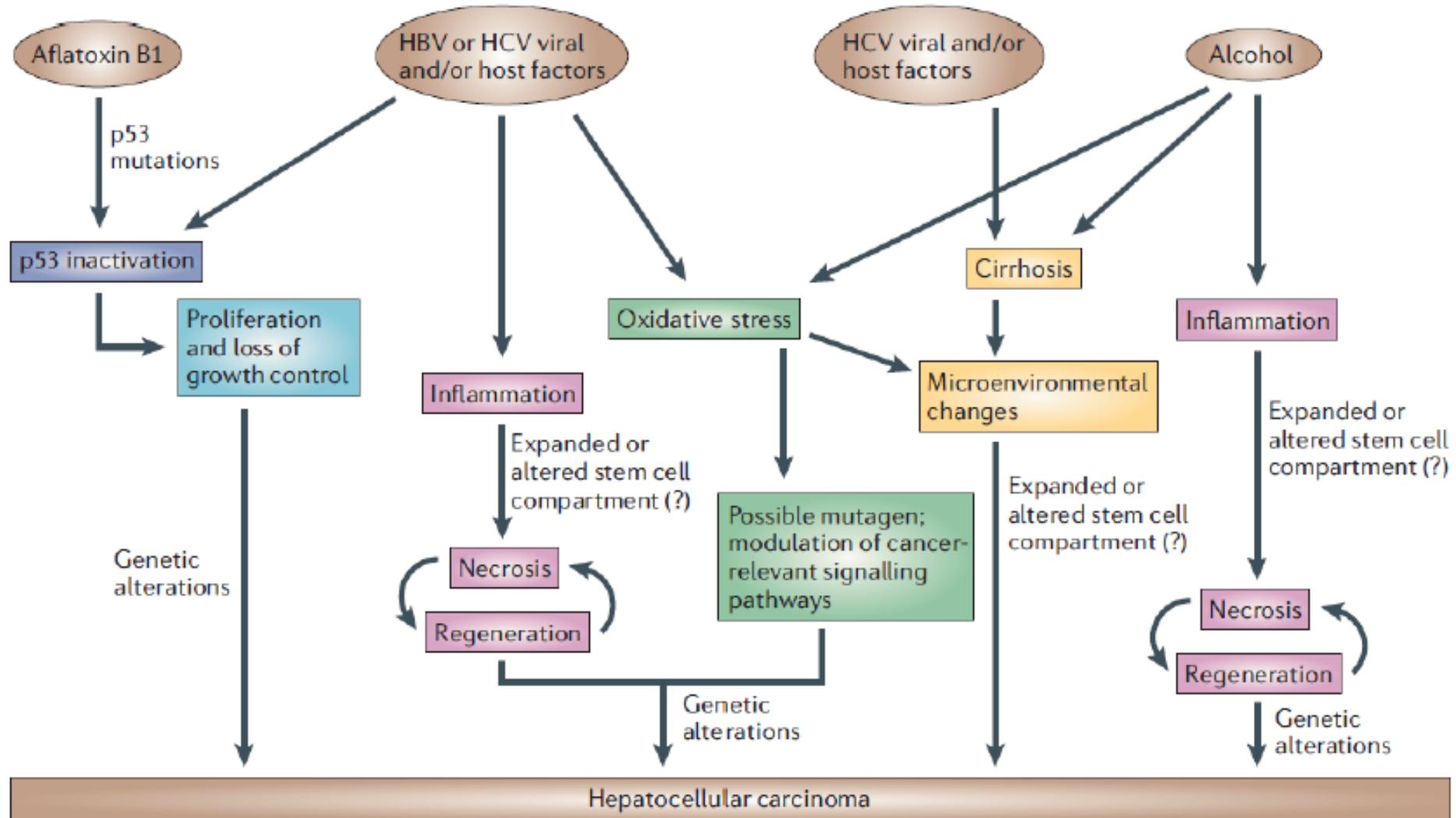
# Hepatitis C Profilaxia



Approved antiviral drugs ( January 1959 - April 2016 )



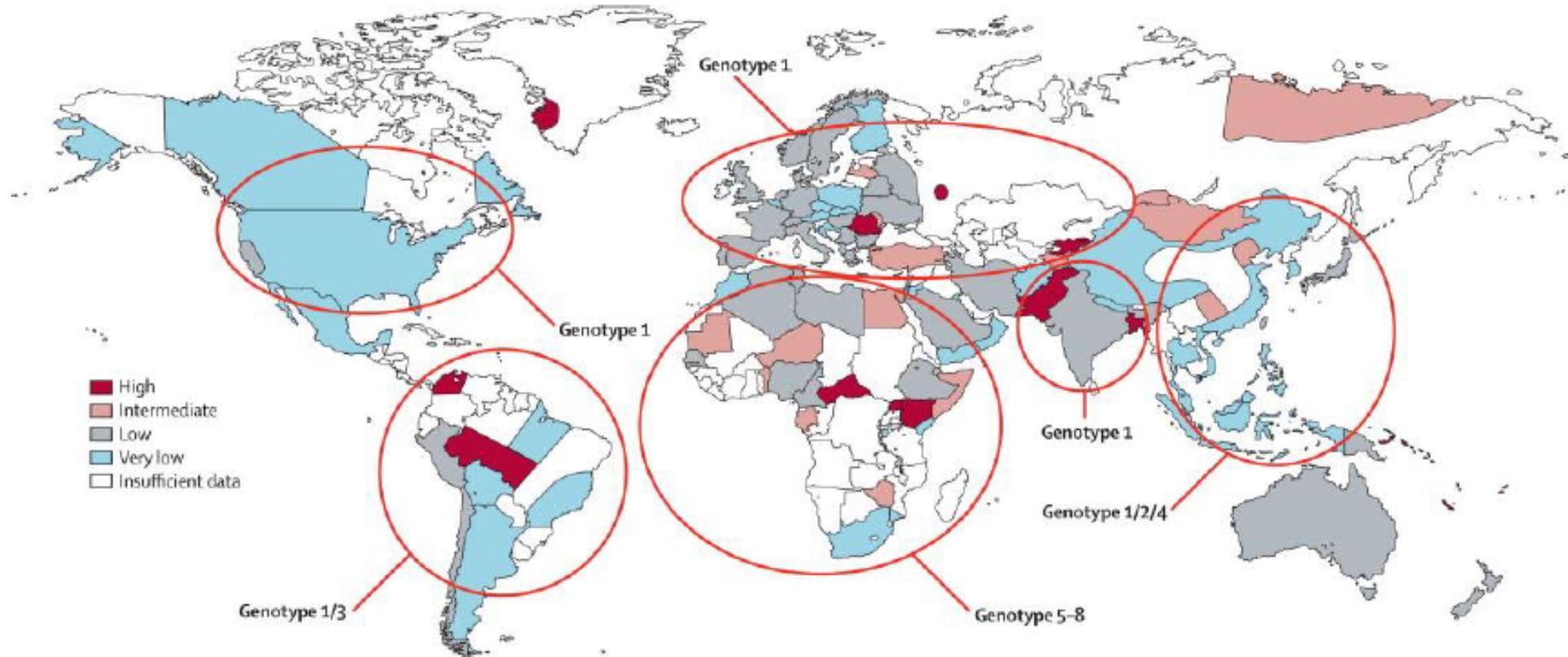
# HCC: Co-fatores



# Hepatitis Delta (HDV)

# Hepatite D

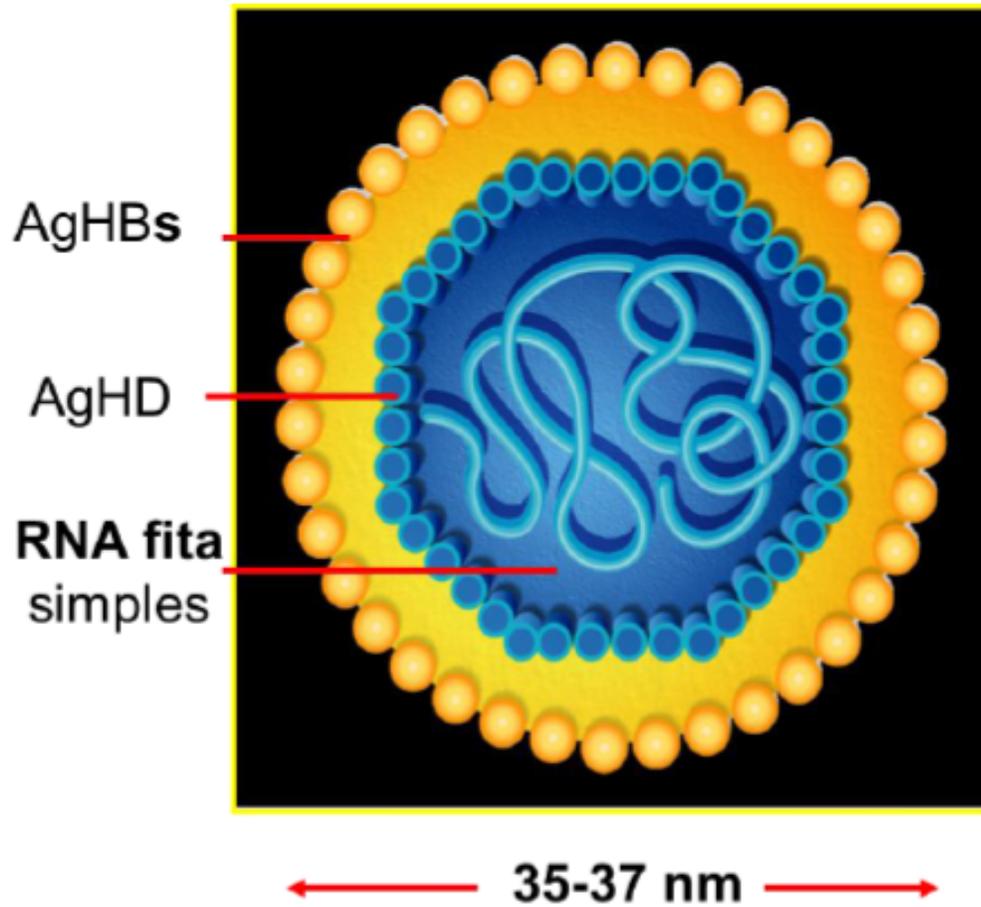
Oito genótipos



# Hepatite D

- Similar a viróides de plantas
- codifica proteínas (S-HDAg/replicação e L-HDAg/montagem)
- RNA com 1,7Kb, circular, negativo, dobrado sobre si mesmo
- Infecção concomitante com HBV, mas com multiplicação independente
- Citopático, 3 genótipos
- Antígeno + RNA envelopado por capsídeo codificada por HBsAg

# Hepatitis D

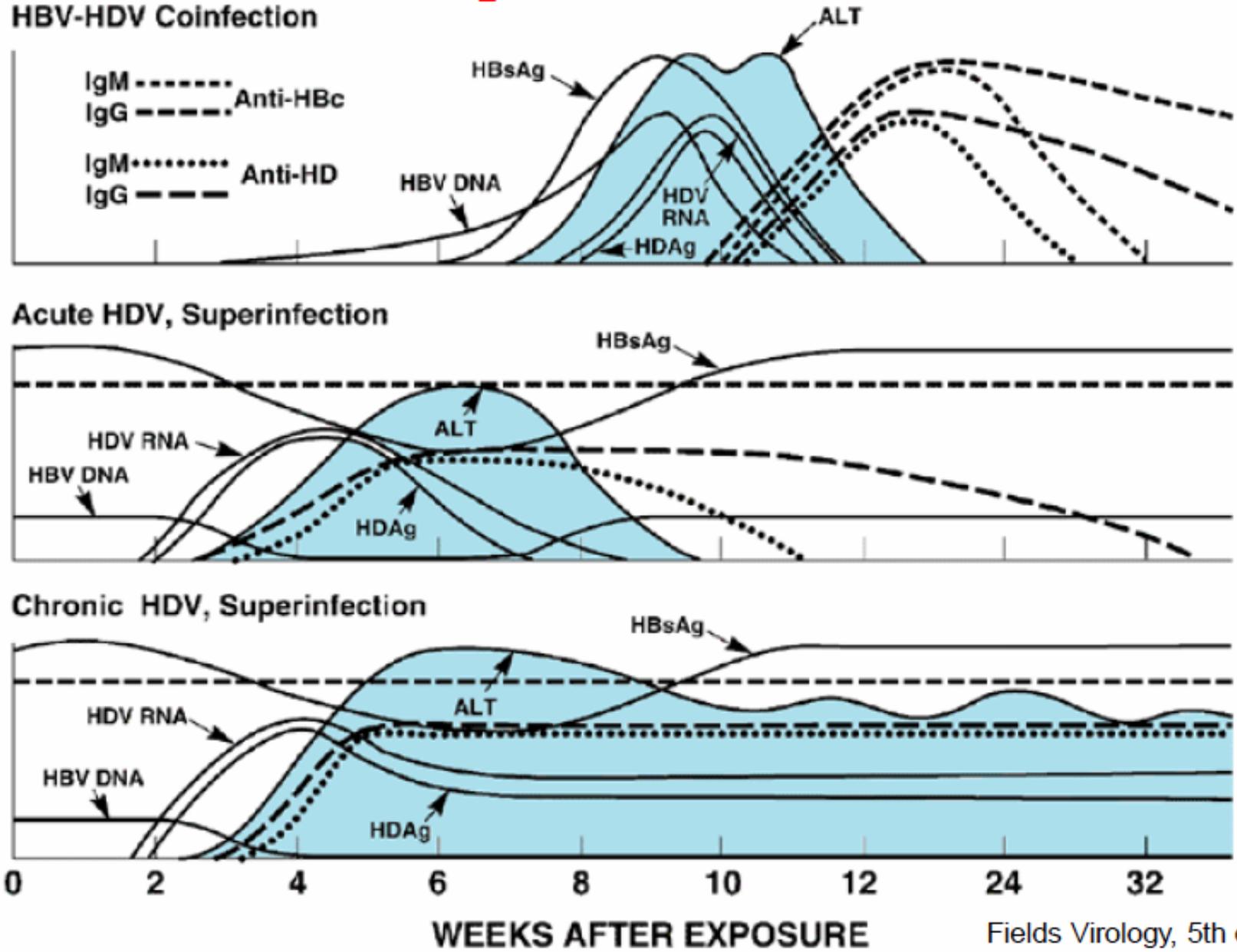


# Hepatite D

## Características clínicas

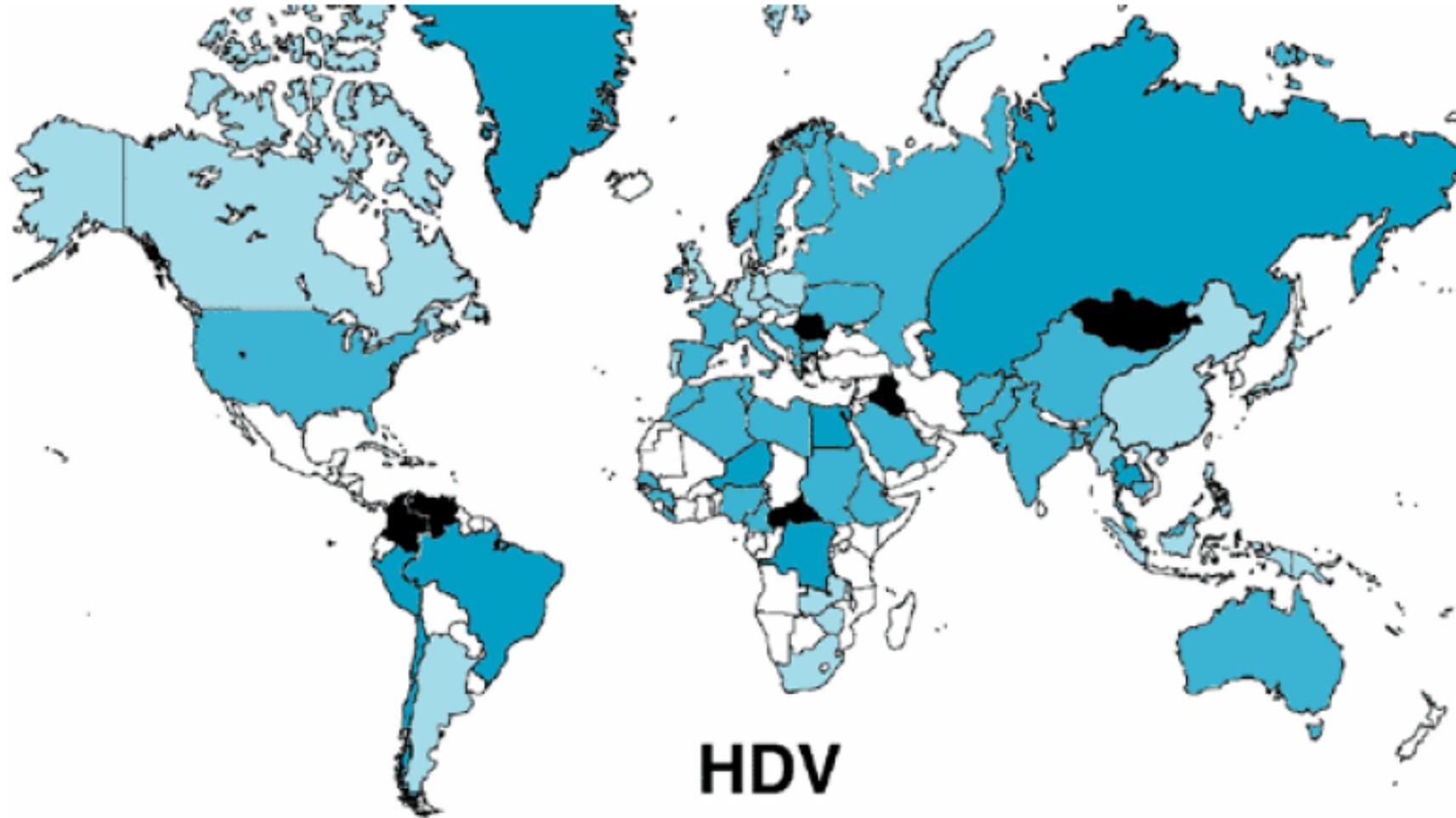
- Co-infecção
  - Doença aguda severa - hepatite fulminante
  - Baixo risco de infecção crônica
  
- Super-infecção
  - Geralmente desenvolve infecção crônica por HDV
  - Alto risco de doença crônica grave

# Hepatitis D



# Hepatite D

Prevalência de anti-HD em indivíduos positivos para HBsAg



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

# Hepatite D

## Diagnóstico Laboratorial

- Marcador Sorológico:
  - VHB (Ag e Ac)
  - Anti-VHD IgM
  - Anti-VHD IgG
  
- Marcador Molecular: RNA
  - RT-PCR / “nested” PCR

**Table 1** | A summary of diagnostic tests for the evaluation of patients with HDV infection

Test	Purpose	Remarks
Anti-HDV IgG antibody	Detects IgG antibodies against HDV, indicates previous or ongoing contact with HDV	Should be the first diagnostic screening test employed and should be performed in all HBsAg-positive patients
Anti-HDV IgM antibody	Detects IgM antibodies against HDV, indicates acute HDV infection or chronic HDV infection with disease activity	Can be used to determine disease activity in patients who test positive for anti-HDV IgG antibodies. Available tests are not standardized
HDV RNA qualitative	Detects HDV RNA Indicates HDV replication and active infection	Gold standard to determine HDV infection. Test can be false-negative if primers are not optimized for all HDV genotypes
HDV RNA quantitative	Determines the level of HDV RNA in the blood	Can be useful in the context of antiviral treatment to predict treatment response. There is no association between serum HDV RNA levels and the grade or stage of liver disease
HDV genotyping	Determines the HDV genotype	Different HDV genotypes may be associated with distinct clinical courses
HBsAg quantitative	Determines the level of HBsAg in the blood	HBsAg is associated with HDV RNA levels. HBsAg clearance is associated with HDV eradication and thus HBsAg monitoring can be useful during antiviral treatment
HBeAg/anti-HBe antibody	Determines the presence of the HBeAg and the presence of anti-HBe antibodies	About 15–20% of patients with HDV infection test positive for HBeAg, which can be associated with HBV replication. Treatment with HBV polymerase inhibitors might be indicated if IFN- $\alpha$ treatment is not possible
HBV DNA quantitative	Determines the level of HBV DNA in the blood	Indication for treatment with HBV polymerase inhibitors depends on the amount of HBV DNA detectable in the blood
Anti-HCV antibody/HCV RNA	Determines the presence of the antibodies against HCV and the presence of HCV RNA	Up to one third of patients in Europe with HDV infection are coinfecting with HCV. Screening for HCV should be performed at least once. HCV RNA is frequently suppressed by coinfection
Liver biopsy	Histological evaluation of and grading or staging of liver disease	Should be performed in all patients with hepatitis D as noninvasive markers of liver fibrosis are not proven to be able to accurately predict the stage of liver disease in patients with HDV infection

Abbreviations: HBsAg, hepatitis B surface antigen; HBe; hepatitis B early antigen; HBeAg, hepatitis B e antigen; HDV, hepatitis D virus.