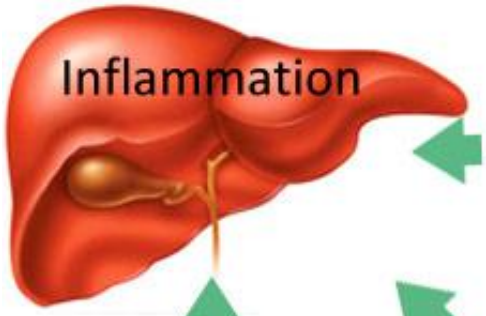
HEPATITIS - inflammation of the liver tissue



Toxic Damage
Alcohol
Drugs
Poisons/Chemicals

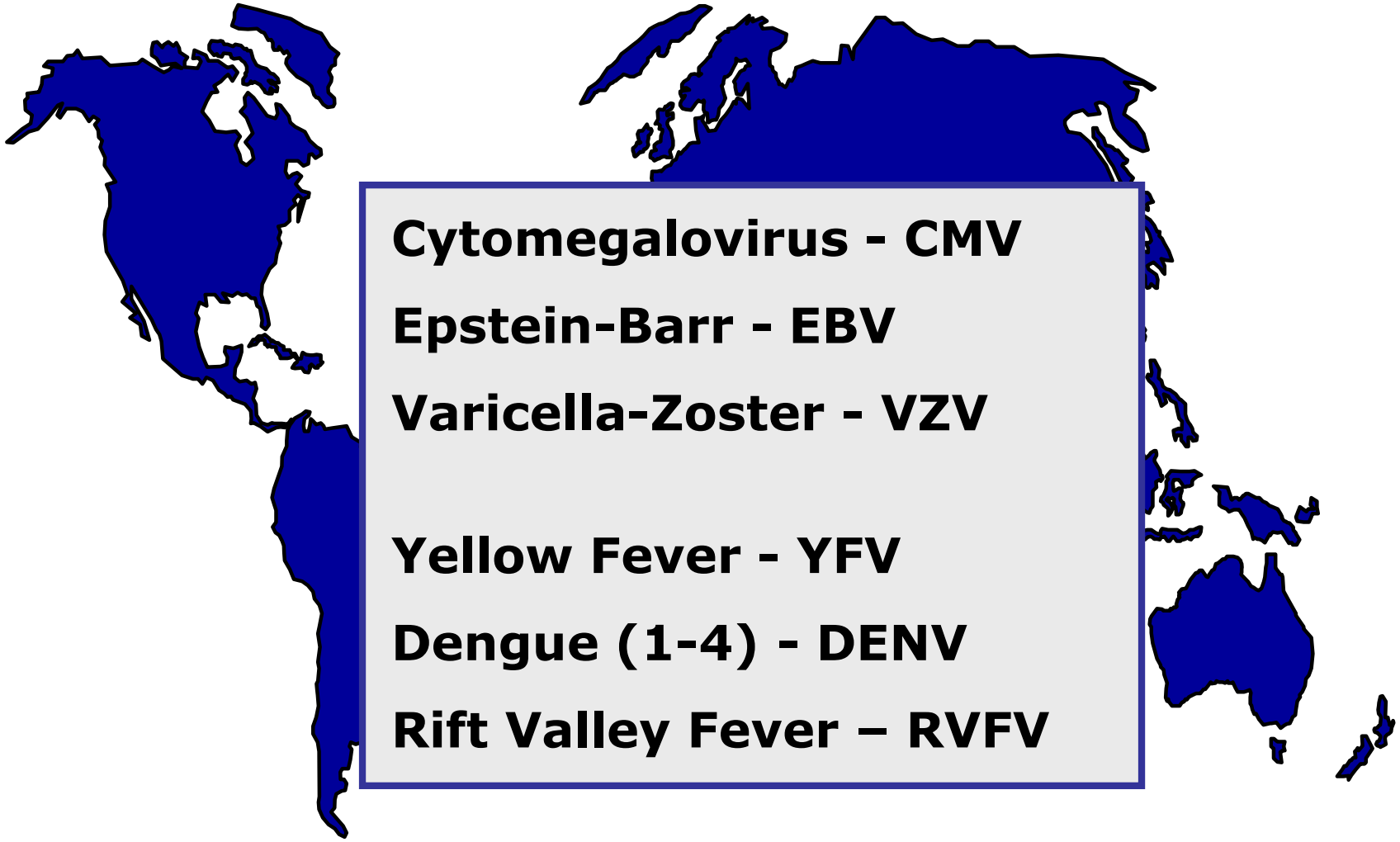
Immunologic Damage

Infections
Viruses
Bacteria
Fung
Protozoa

- **Hepatitis A - HAV**
- **Hepatitis B - HBV**
- **Hepatitis C - HCV**
- **Hepatitis D - HDV**
- **Hepatitis E - HEV**

Differential Diagnosis of Acute Hepatitis	
Infectious	***Noninfectious***
Epstein-Barr virus Cytomegalovirus Herpes simplex virus Yellow fever Leptospirosis Q fever HIV Brucellosis Lyme disease Syphilis	

HEPATOTROPISM: FREQUENT



Cytomegalovirus - CMV

Epstein-Barr - EBV

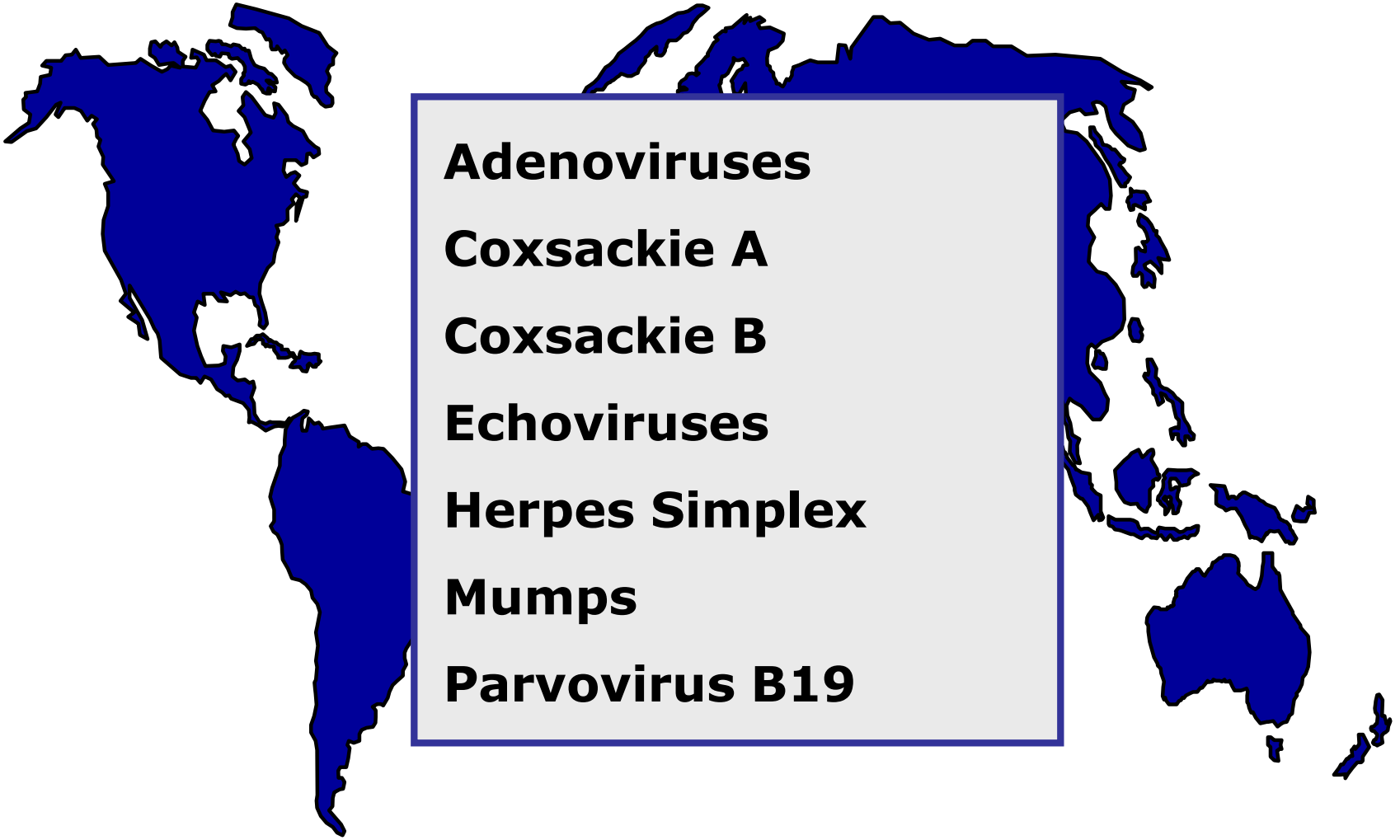
Varicella-Zoster - VZV

Yellow Fever - YFV

Dengue (1-4) - DENV

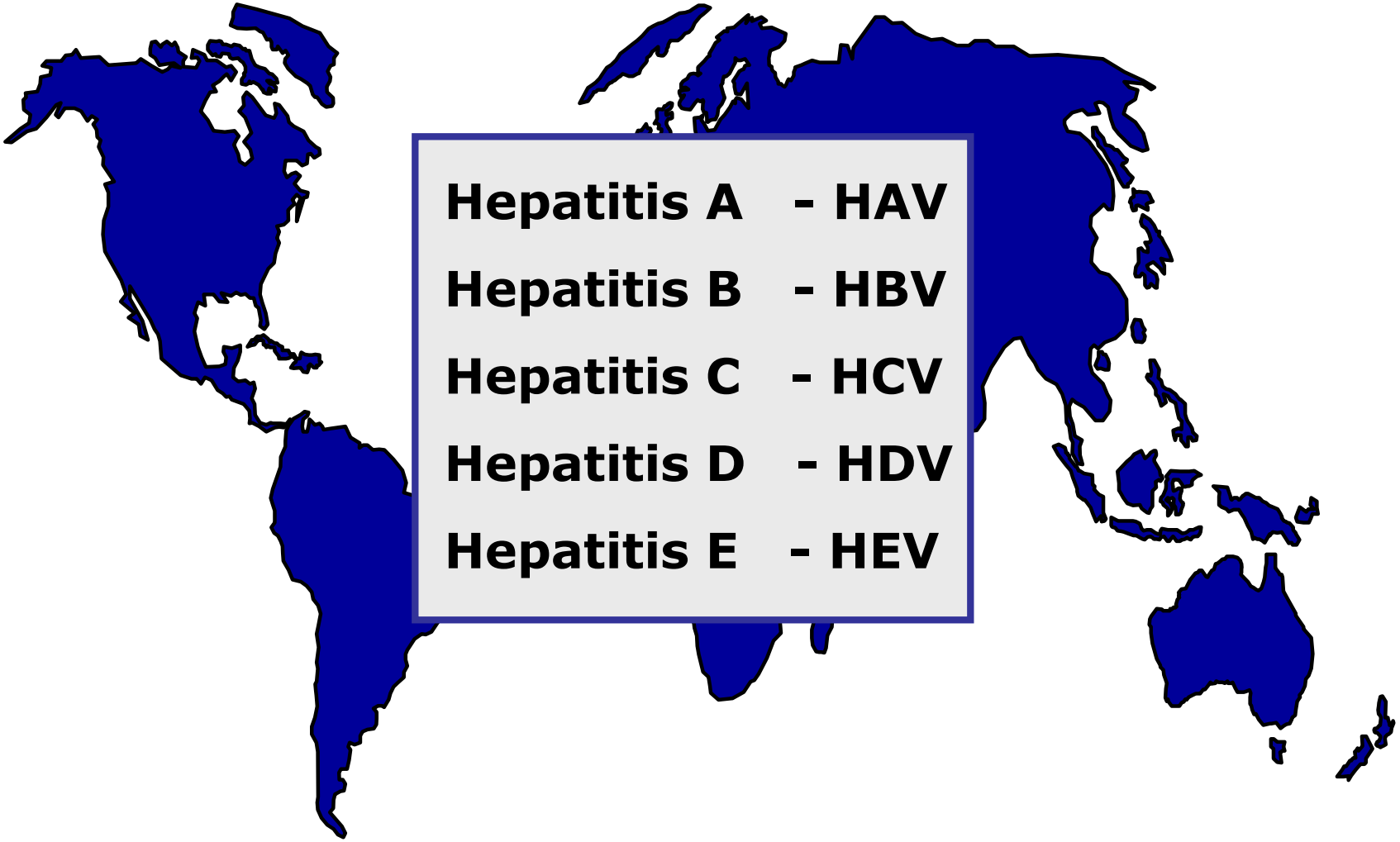
Rift Valley Fever – RVFV

HEPATOTROPISM: SPORADIC



- Adenoviruses
- Coxsackie A
- Coxsackie B
- Echoviruses
- Herpes Simplex
- Mumps
- Parvovirus B19

HEPATOTROPISM: broad



World Health Organization

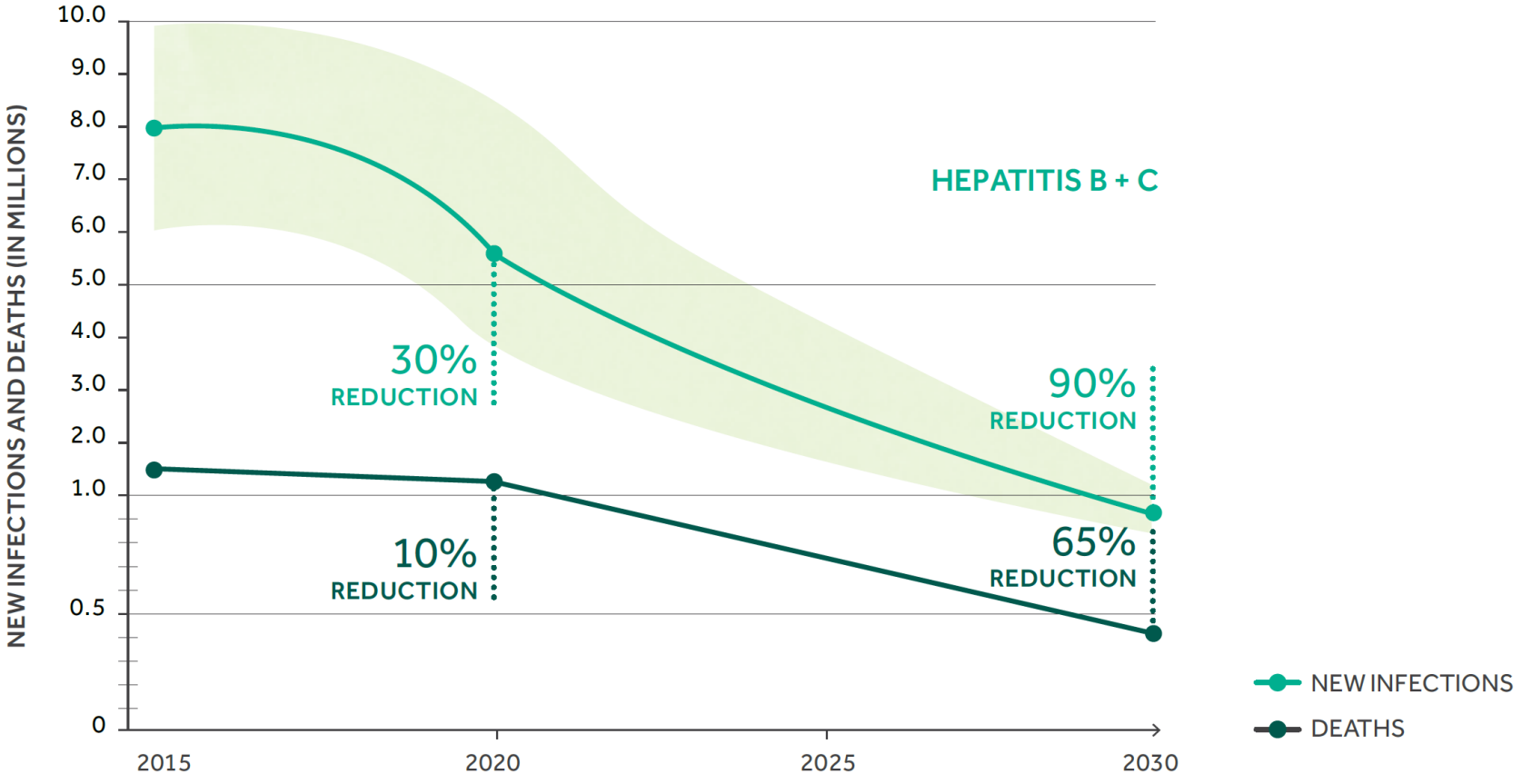
Hepatitis

Overview | Symptoms | Treatment

Hepatitis is an inflammation of the liver that is caused by a variety of infectious viruses and noninfectious agents leading to a range of health problems, some of which can be fatal. There are five main strains of the hepatitis virus, referred to as types A, B, C, D and E. While they all cause liver disease, they differ in important ways including modes of transmission, severity of the illness, geographical distribution and prevention methods. In particular, types B and C lead to chronic disease in hundreds of millions of people and together are the most common cause of liver cirrhosis, liver cancer and viral hepatitis-related deaths. An estimated 354 million people worldwide live with hepatitis B or C, and for most, testing and treatment remain beyond reach.

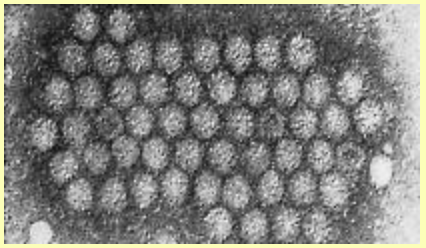
Some types of hepatitis are preventable through vaccination. A WHO study found that an estimated 4.5 million premature deaths could be prevented in low- and middle-income countries by 2030 through vaccination, diagnostic tests, medicines and education campaigns. WHO's global hepatitis strategy, endorsed by all WHO Member States, aims to reduce new hepatitis infections by 90% and deaths by 65% between 2016 and 2030.

Figure 6. Targets for reducing new cases of and deaths from chronic viral hepatitis B and C infection

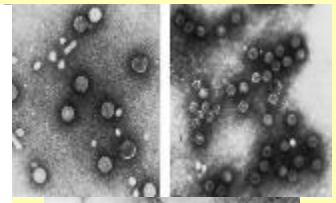


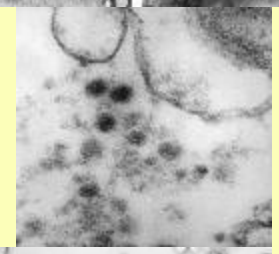
MAJOR HEPATITIC VIRUS

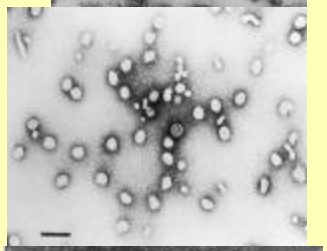
Name	Family	genome
Hepatitis A virus	*Picornaviridae*	RNA +
Hepatitis B virus	*Hepadnaviridae*	DNA
Hepatitis C virus	*Flaviviridae*	RNA+
Hepatitis delta virus	*Deltavirus*	RNA –
Hepatitis E virus	*Caliciviridae- Hepevirus*	*RNA +*

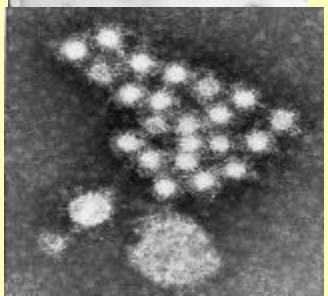


HCV

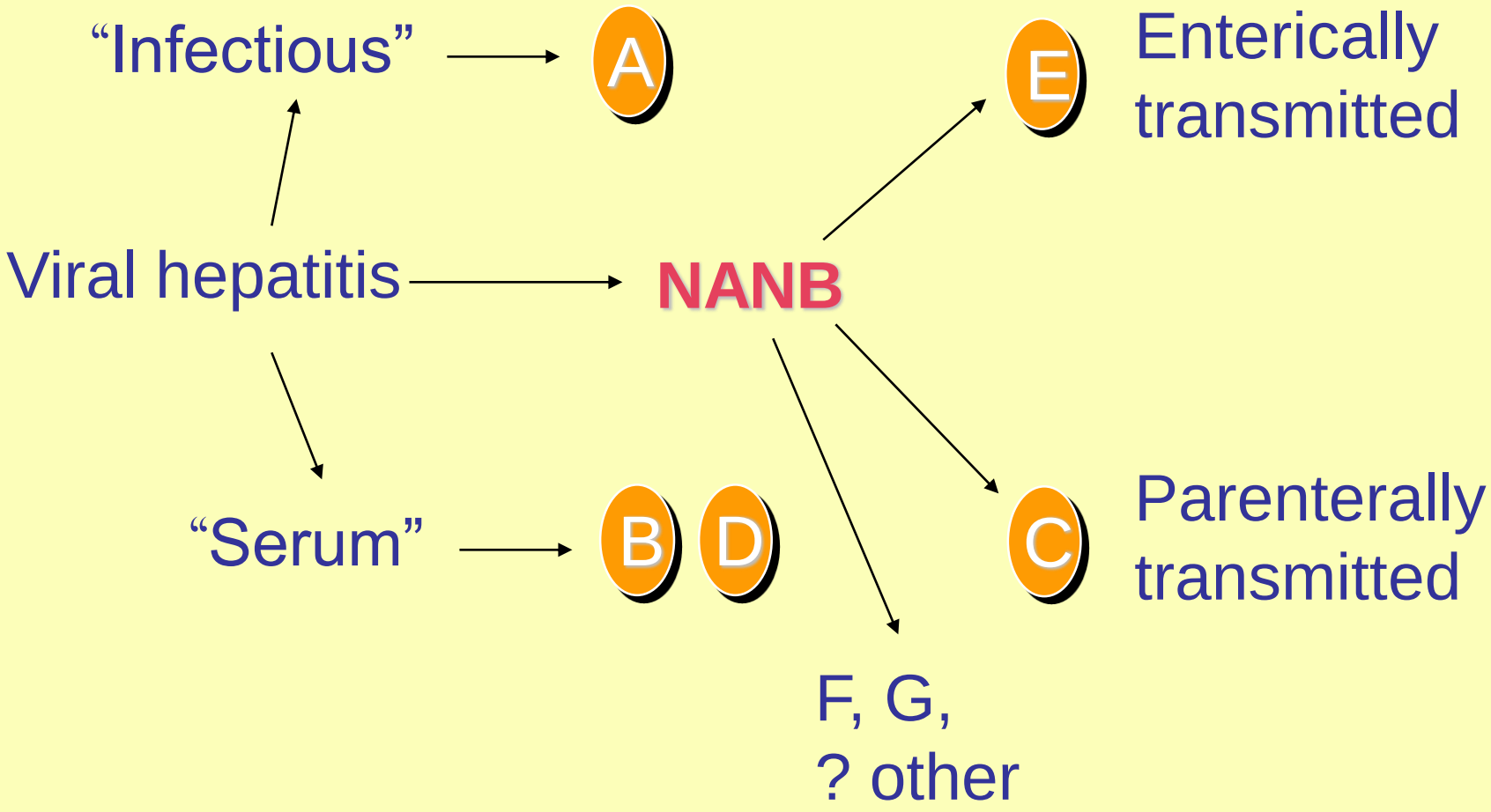




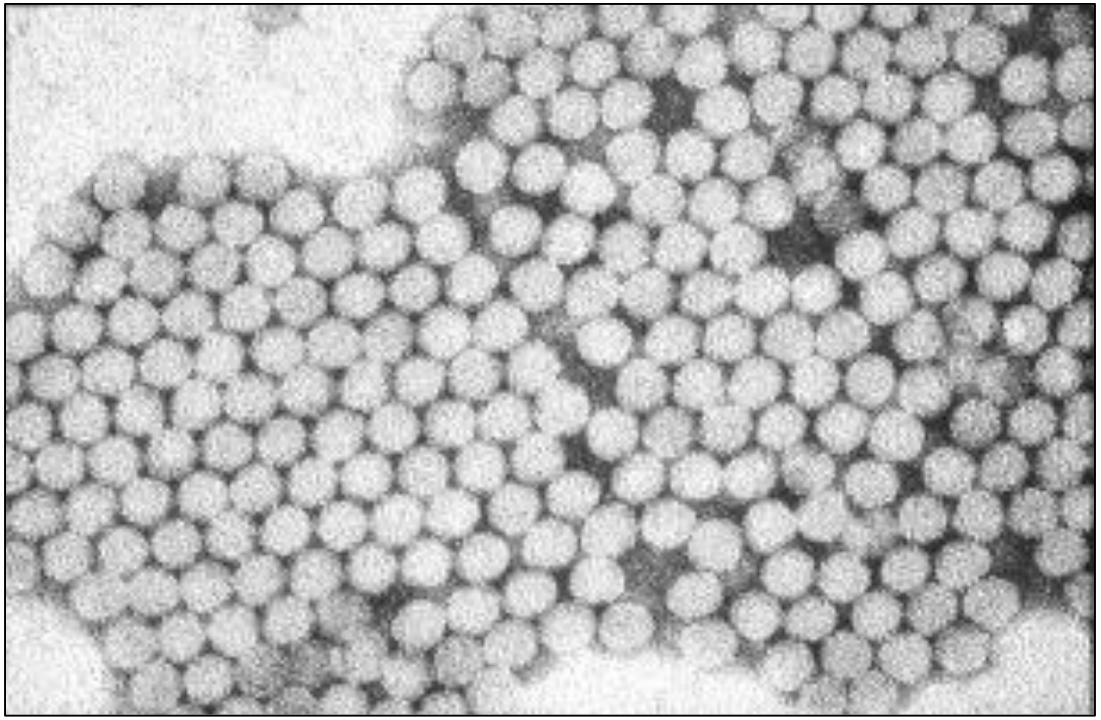




Viral Hepatitis - Historical Perspectives



HEPATITIS A VIRUS



World Health Organization

Hepatitis A

24 June 2022

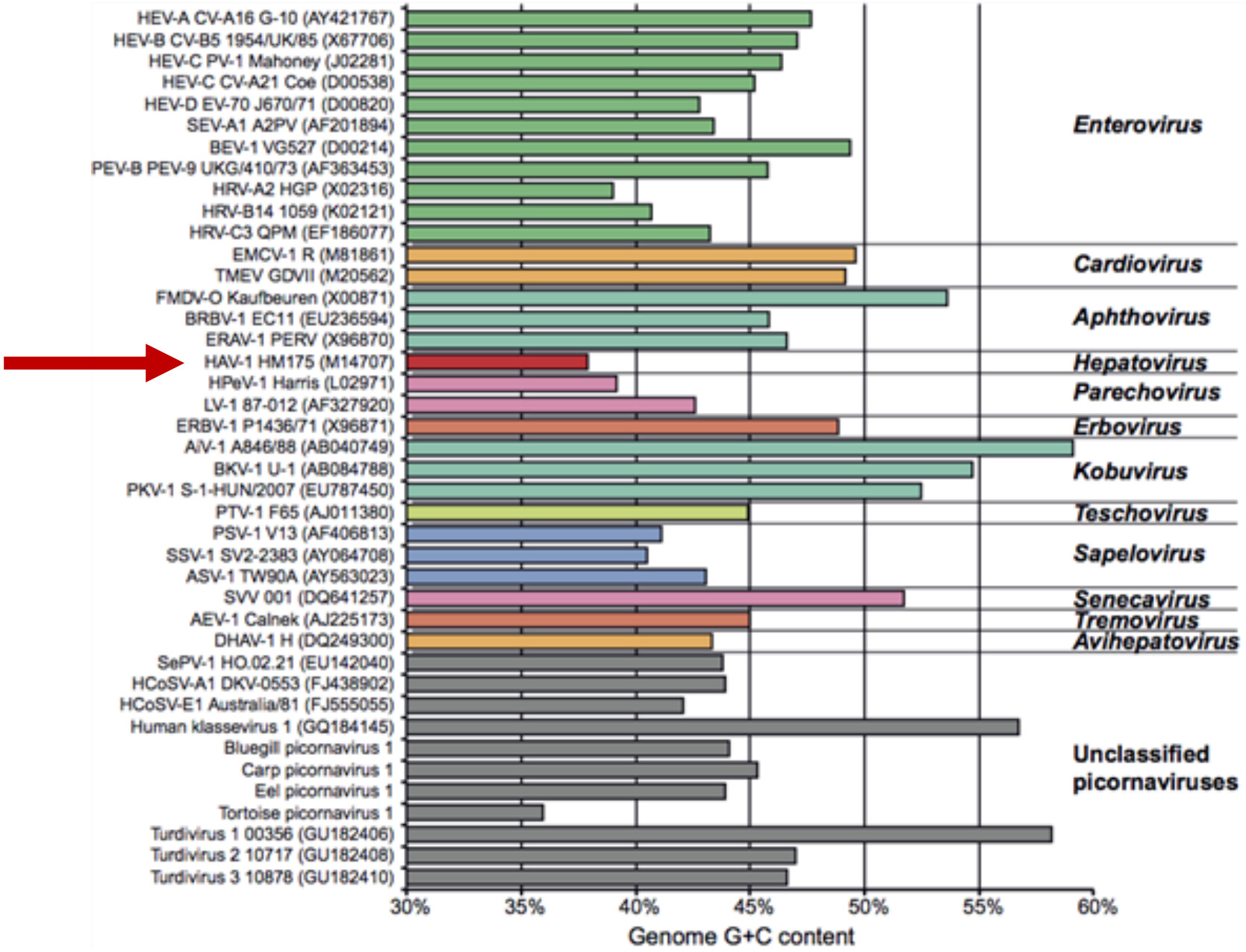
Key facts

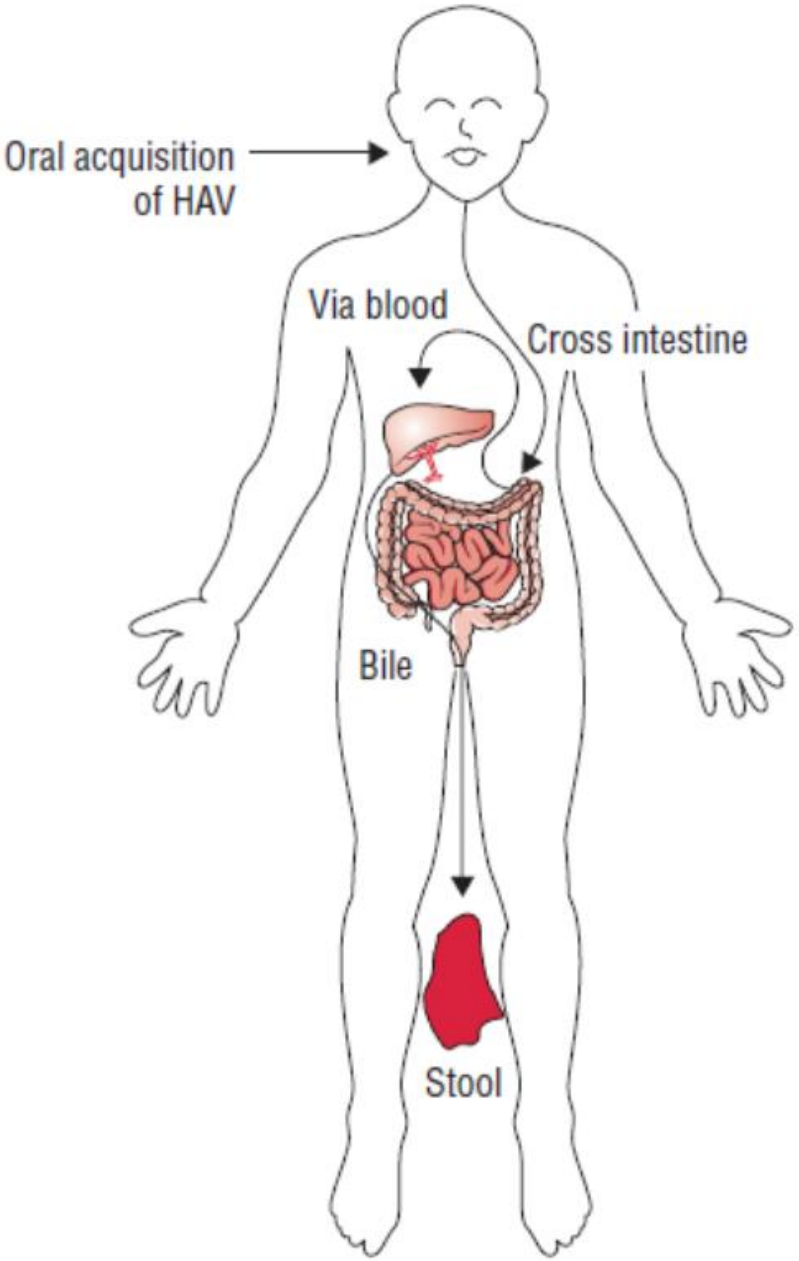
- Hepatitis A is an inflammation of the liver that can cause mild to severe illness.
- The hepatitis A virus (HAV) is transmitted through ingestion of contaminated food and water or through direct contact with an infectious person.
- Almost everyone recovers fully from hepatitis A with a lifelong immunity. However, a very small proportion of people infected with hepatitis A could die from fulminant hepatitis.
- The risk of hepatitis A infection is associated with a lack of safe water and poor sanitation and hygiene (such as contaminated and dirty hands).
- A safe and effective vaccine is available to prevent hepatitis A.

The *Picornaviridae* is a family of small, icosahedral viruses with single-stranded, highly diverse positive-sense RNA genomes.

The family comprises 47 genera containing 110 species, but many viruses are presently awaiting classification.

Picornaviruses may cause subclinical infections of humans and animals or conditions ranging from mild febrile illness to severe diseases of heart, liver and the central nervous system.


HEV-A CV-A16 G-10 (AY421767)
HEV-B CV-B5 1954/UK/85 (X67706)
HEV-C PV-1 Mahoney (J02281)
HEV-C CV-A21 Coe (D00538)
HEV-D EV-70 J670/71 (D00820)
SEV-A1 A2PV (AF201894)
BEV-1 VG527 (D00214)
PEV-B PEV-9 UKG/410/73 (AF363453)
HRV-A2 HGP (X02316)
HRV-B14 1059 (K02121)
HRV-C3 QPM (EF186077)
EMCV-1 R (M81861)
TMEV GDVII (M20562)
FMDV-O Kaufbeuren (X00871)
BRBV-1 EC11 (EU236594)
ERAV-1 PERV (X96870)
HAV-1 HM175 (M14707)
HPeV-1 Harris (L02971)
LV-1 87-012 (AF327920)
ERBV-1 P1436/71 (X96871)
AiV-1 A846/88 (AB040749)
BKV-1 U-1 (AB084788)
PKV-1 S-1-HUN/2007 (EU787450)
PTV-1 F65 (AJ011380)
PSV-1 V13 (AF406813)
SSV-1 SV2-2383 (AY064708)
ASV-1 TW90A (AY563023)
SVV 001 (DQ641257)
AEV-1 Calnek (AJ225173)
DHAV-1 H (DQ249300)
SePV-1 HO.02.21 (EU142040)
HCoSV-A1 DKV-0553 (FJ438902)
HCoSV-E1 Australia/81 (FJ555055)
Human klassevirus 1 (GQ184145)
Bluegill picornavirus 1
Carp picornavirus 1
Eel picornavirus 1
Tortoise picornavirus 1
Turdivirus 1 00356 (GU182406)
Turdivirus 2 10717 (GU182408)
Turdivirus 3 10878 (GU182410)
Enterovirus
Cardiovirus
Aphthovirus
Hepatovirus
Parechovirus
Erbovirus
Kobuvirus
Teschovirus
Sapelovirus
Senecavirus
Tremovirus
Avihepatovirus
Unclassified picornaviruses
30%
35%
40%
45%
50%
55%
60%
Genome G+C content


Oral acquisition of HAV
Via blood
Cross intestine
Bile
Stool

HEPATITIS A VIRUS

Picornaviridae

- Single serotype
- Endemic worldwide
- Acute disease and asymptomatic infection

Oro-fecal transmission

No chronic infection

- Protective antibodies develop in response to infection - confer lifelong immunity

HEPATITIS A VIRUS - CLINICAL FEATURES

- Jaundice by age group:
  - <6 yrs <10%
  - 6-14 yrs 40%-50%
  - >14 yrs 70%-80%
- Rare complications:
  - Fulminant hepatitis
  - Cholestatic hepatitis
  - Relapsing hepatitis
- Incubation period:
  - 30 days on average
  - Range: 15-50 days
- Chronic sequelae:
  - None

HAV Diagnosis

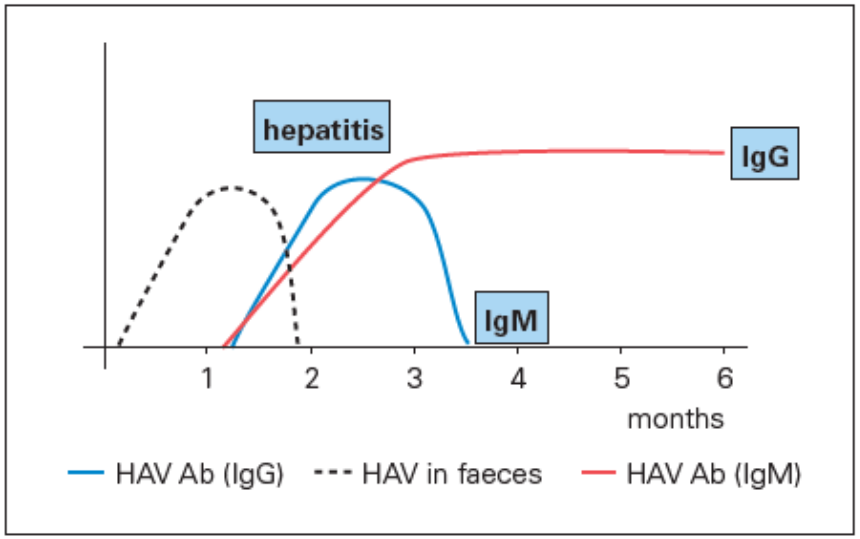
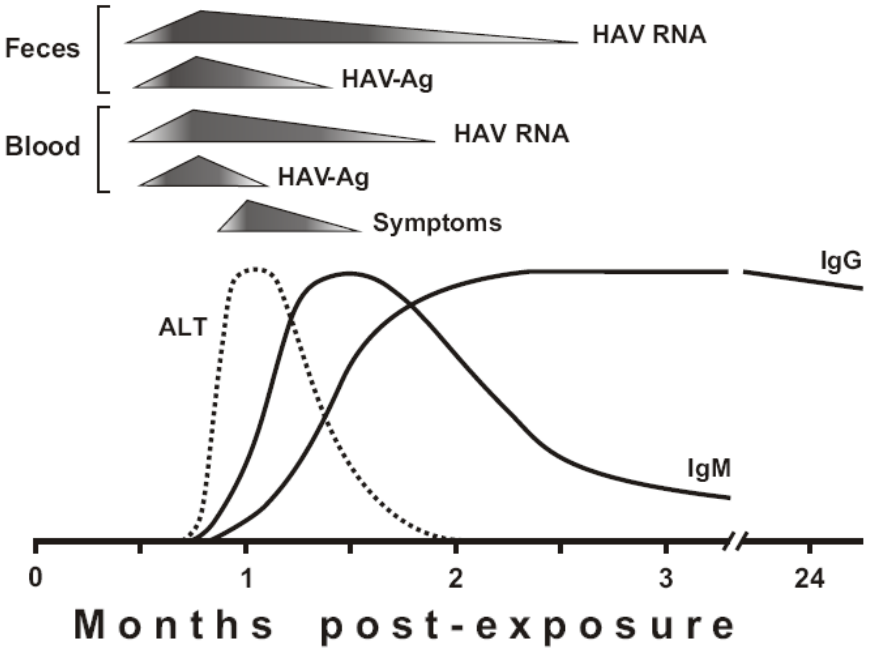


Figure 23.43 The clinical and virological course of hepatitis A virus (HAV). Ab, antibody; Ig, immunoglobulin.

The best laboratory method for the diagnosis of acute infection is the detection of HAV-specific IgM in serum



Bendinelli, Pistello *et al.*, **Manual of Clinical Laboratory Immunology**, Rose et al. eds, American Society for Microbiology, VIIth ed., *in press*.

HEPATITIS B VIRUS

World Health Organization

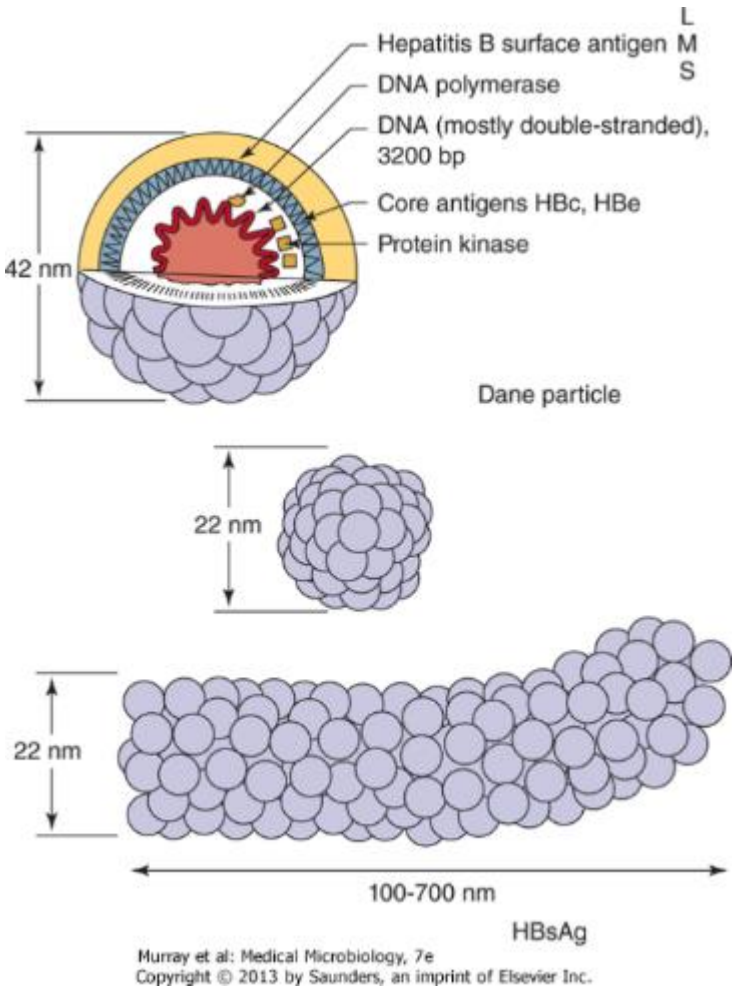
Hepatitis B

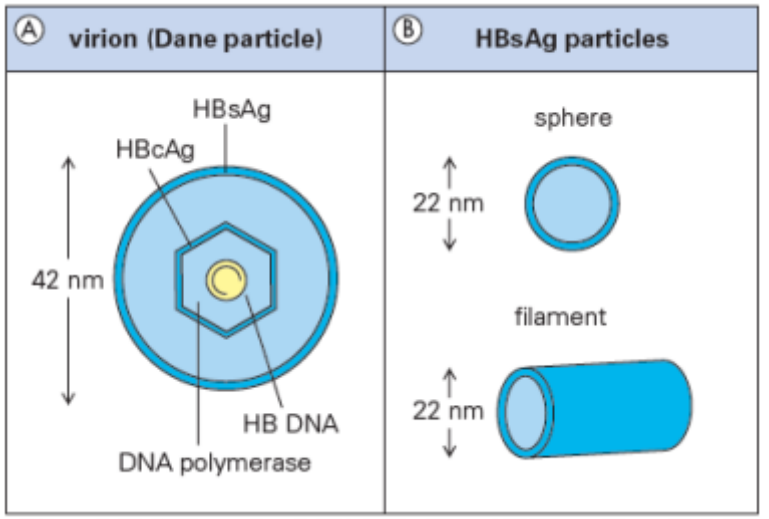
24 June 2022

Key facts

- **Hepatitis B is a viral infection that attacks the liver and can cause both acute and chronic disease.**
- **The virus is most commonly transmitted from mother to child during birth and delivery, as well as through contact with blood or other body fluids during sex with an infected partner, unsafe injections or exposures to sharp instruments.**
- **WHO estimates that 296 million people were living with chronic hepatitis B infection in 2019, with 1.5 million new infections each year.**
- **In 2019, hepatitis B resulted in an estimated 820 000 deaths, mostly from cirrhosis and hepatocellular carcinoma (primary liver cancer).**
- **Hepatitis B can be prevented by vaccines that are safe, available and effective.**

Hepatitis B Virus





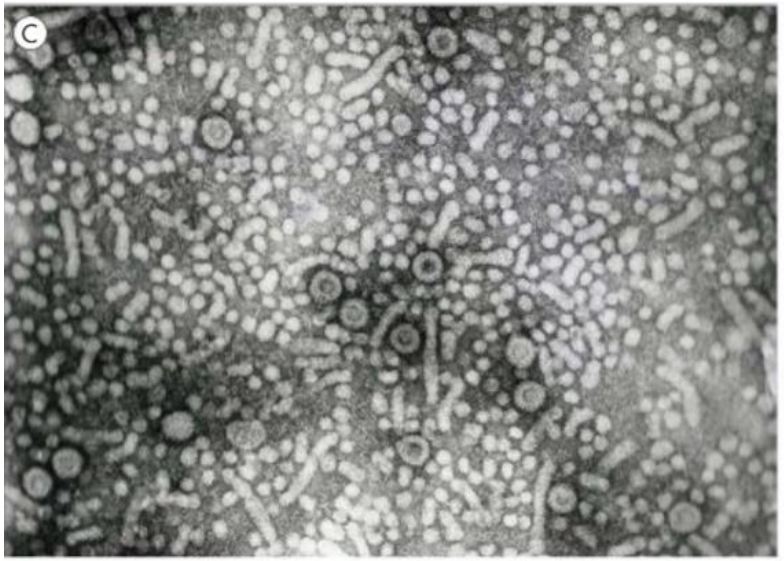
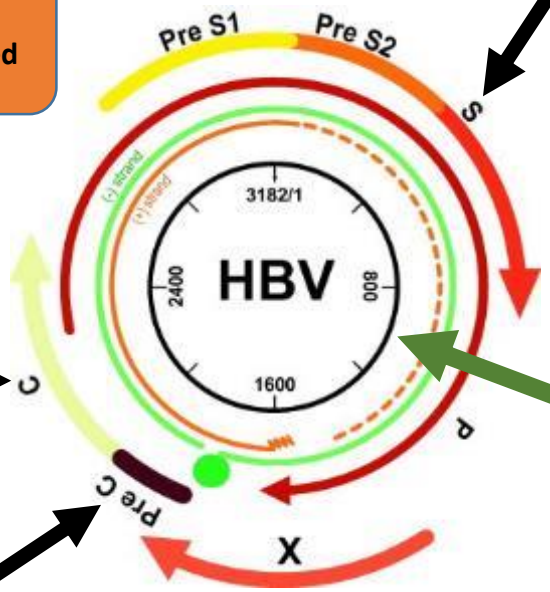


Figure 23.44 During acute infection, and in some carriers there are 10^6–10^7 infectious (Dane) particles/mL of serum (A), and as many as 10^{12} hepatitis B surface antigen (HBsAg) particles/mL (B). (C) Electron micrograph showing Dane particles and HBsAg particles.

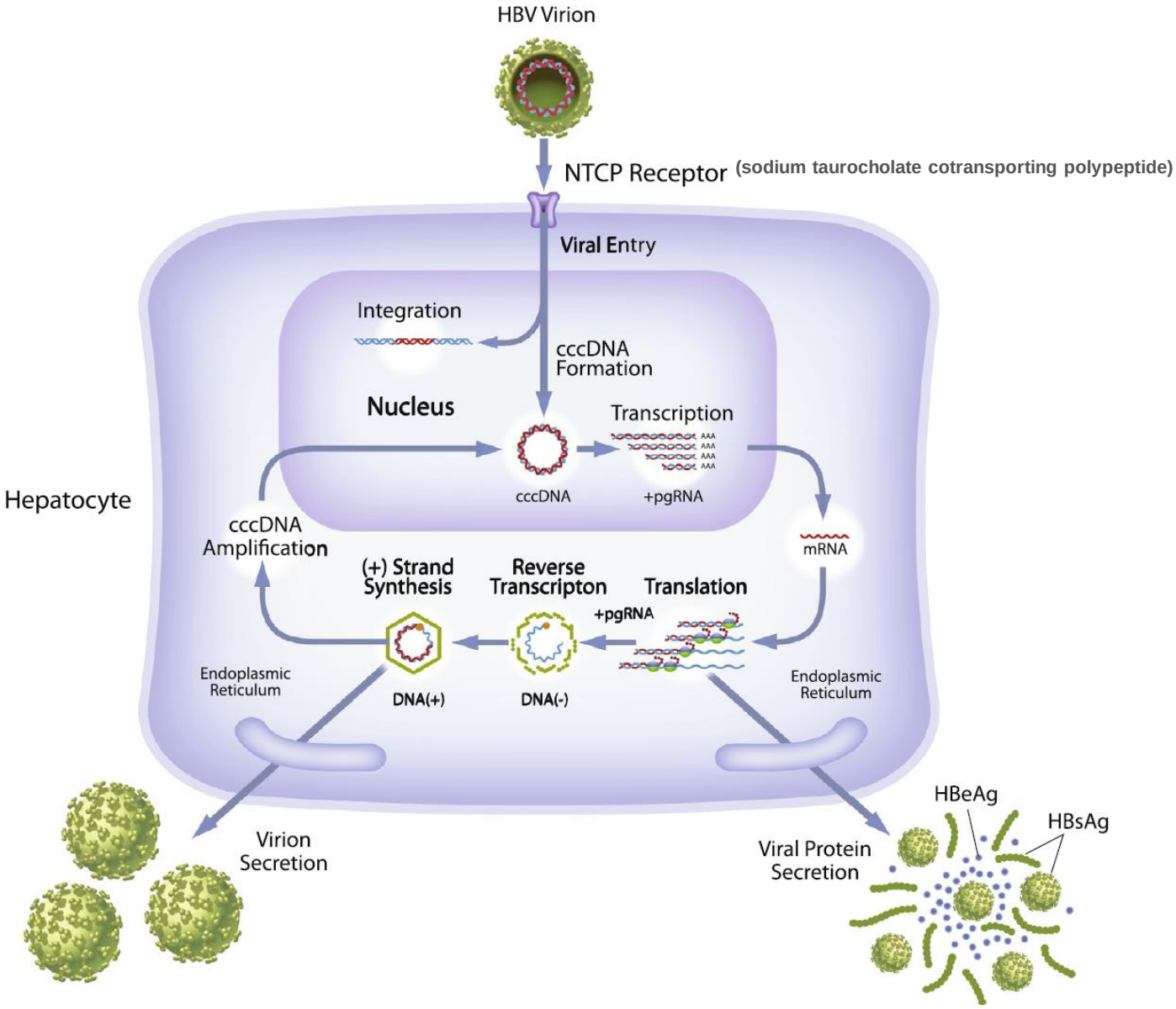
The Hepatitis surface antigen (HbsAg) and the related antibody (Anti-Hbs)

The particulate nucleocapsid antigen (HbcAg) and the related antibody (Anti-HbC)



HBV DNA

The antigen structurally related to HbcAg, namely hepatitis B e antigen (HBeAg) and the related antibody (Anti-Hbe)


HBV Virion
NTCP Receptor (sodium taurocholate cotransporting polypeptide)
Viral Entry
Integration
cccDNA Formation
Nucleus
Transcription
cccDNA
+pgRNA
Hepatocyte
cccDNA Amplification
(+) Strand Synthesis
Reverse Transcripton
Translation
+pgRNA
mRNA
Endoplasmic Reticulum
DNA(+)
DNA(-)
Endoplasmic Reticulum
Virion Secretion
HBeAg
HBsAg
Viral Protein Secretion

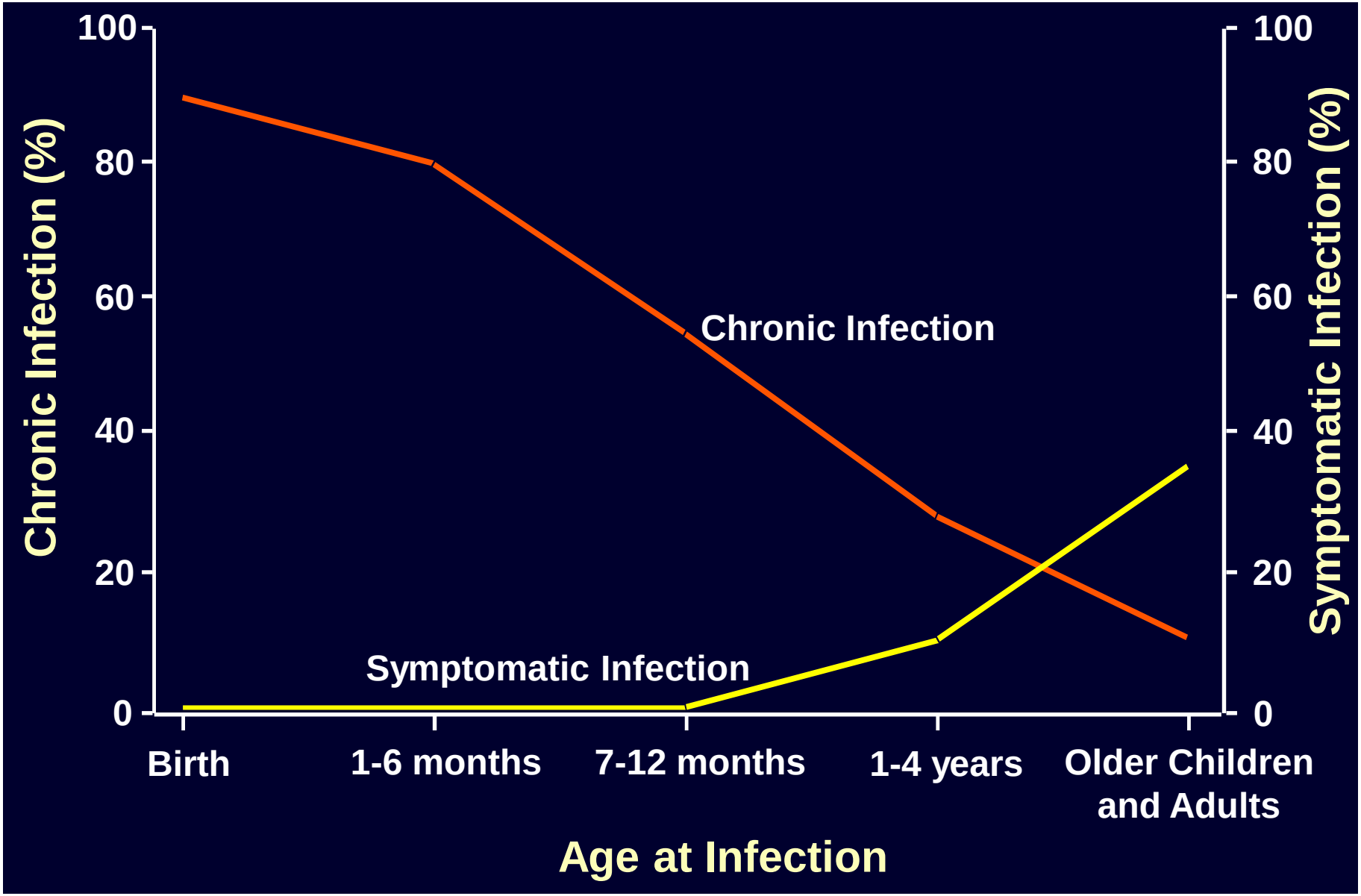
Key role of HBV covalently closed circular (ccc) DNA in viral persistence and chronic hepatitis B

- cccDNA is the template for viral RNAs and subsequent generation of progeny virions
- A few copies of cccDNA per liver can (re)initiate full-blown infection.
- ***HBV persistence is mediated by an intranuclear, episomal form of cccDNA***
- ***cccDNA is not targeted by current treatments and a cure of chronic hepatitis B requires elimination of cccDNA***

HBV - Clinical Features

Incubation period:	Average 60-90 days Range 45-180 days
Clinical illness (jaundice):	<5 yrs, <10% >5 yrs, 30%-50%
Acute case-fatality rate:	0.5%-1%
Chronic infection:	<5 yrs, 30%-90% >5 yrs, 2%-10%
Premature mortality from chronic liver disease:	15%-25%

Outcome of Hepatitis B Virus Infection by Age at Infection



HBV - Diagnosis

Characteristics of hepatitis B virus antigens (Ag) and antibodies (Ab)

HBsAg	Envelope (surface) antigen of HBV particle also occurs as free particles (spheres and filaments) in blood; indicates infectivity of blood
HBsAb	Antibody to HBsAg; post-hepatitis B vaccine response; appears late after resolved HBV infection (not in carriers)
HBcAb (total)	Antibody to HB core antigen; appears early; includes HB core IgM
HBc IgM	Appears in acute HBV infection; can last for 3 months and is a marker of acute HBV infection if it has resolved; seen in HBeAg-positive carriers with high viral replication; seen in HBeAg HBeAb reversion
HBeAg	Antigen derived from HBV core; indicates high transmissibility
HBeAb	Antibody to the HBV core

HBV - Diagnosis

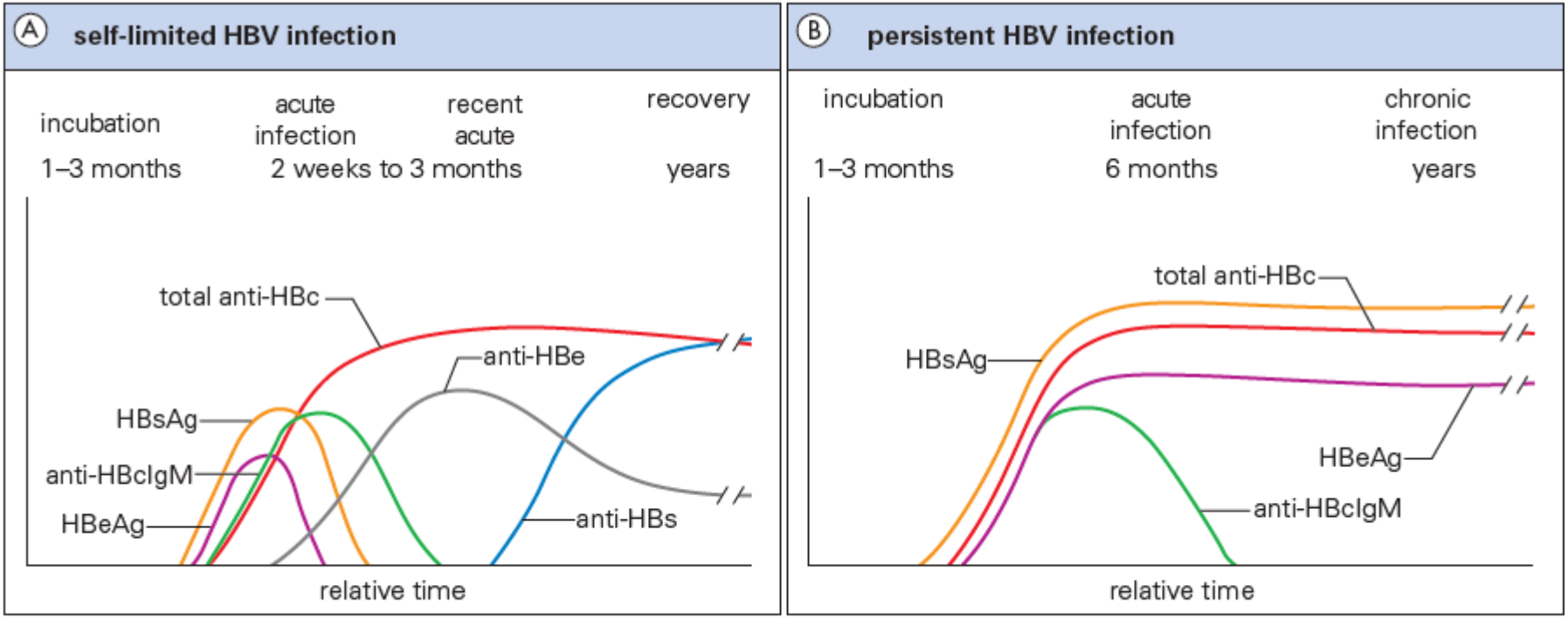


Figure 23.45 (A) Clinical and virological course of hepatitis B virus (HBV) infection, with recovery. (B) Clinical and virological course in a carrier of hepatitis B.

HBV - Diagnosis

INTERPRETATION OF SEROLOGICAL RESULTS

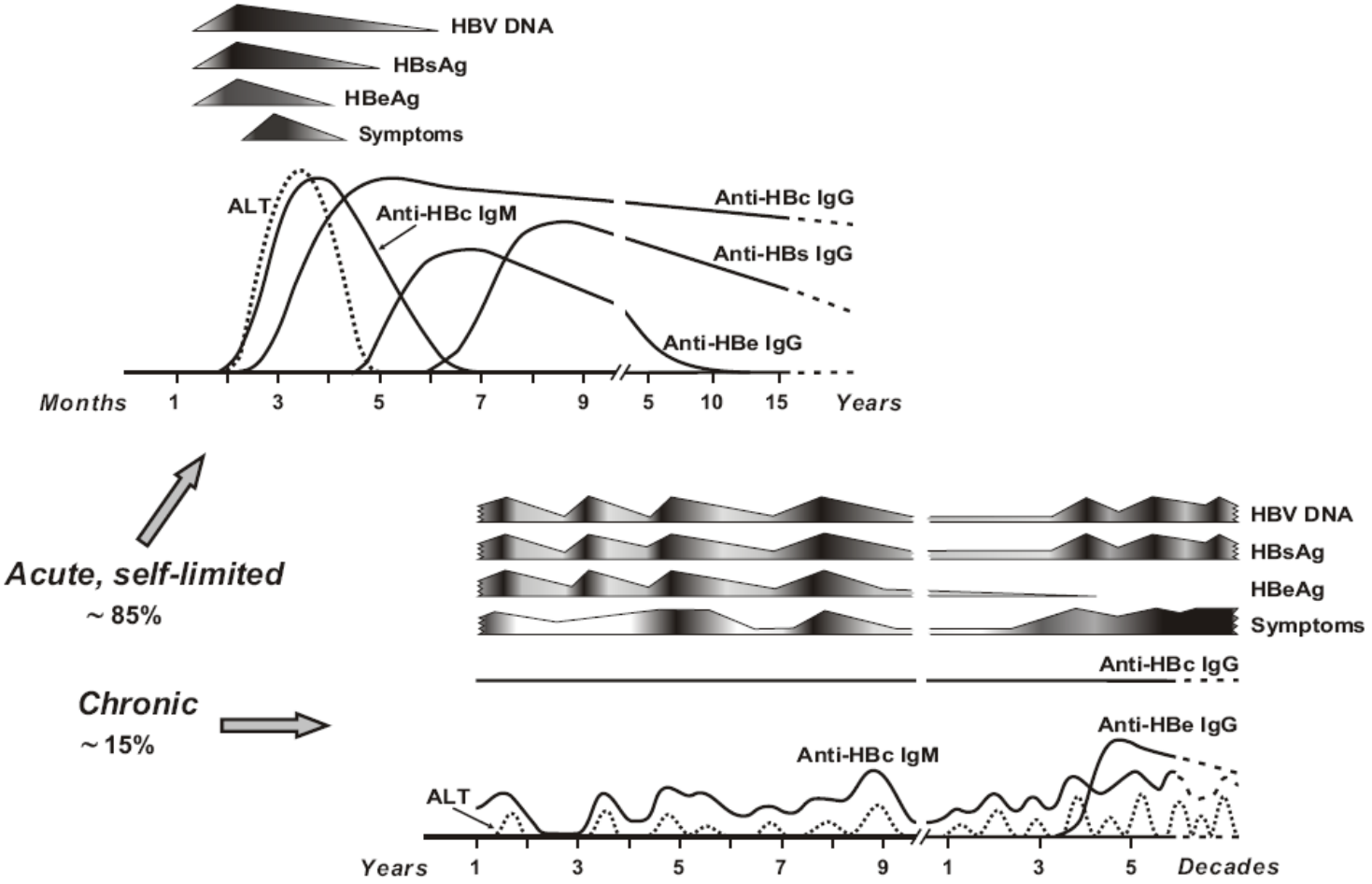
	Acute hepatitis B	Hepatitis B carrier	Hepatitis B carrier	Past hepatitis B virus infection[b]	Hepatitis B vaccine response
HBsAg[a]	+	+	+	–	–
HB core antibody (total)	+	+	+	+	–
HB core IgM	+	–	–	–	–
HBe antibody	–	+	–	+	–
HBe antigen	+	–	+	–	–
HB surface antibody	–	–	–	+	+

[a]Always confirm by neutralization if positive.
[b]Or passively acquired antibody having received blood products from someone with a history of past HBV infection.

HBV - Diagnosis

	HBs-Ag	HBe-Ag	HBV-DNA	HBc-IgM	HBc-IgG	HBs-Ab	HBe-Ab
Acute hepatitis	+	+	+	+	-/+	-	-
Chronic hepatitis	+	-/+	+	-/+	+	-	+
Resolution	-	-	-	-	+	+	+
Past infection	-	-	-	-	+	+	-/+
Remote infection	-	-	-	-	+	-	-
Vaccination	-	-	-	-	-	+	-
Occult hepatitis	-	-	+	-	-/+	-	-

HBV - Diagnosis



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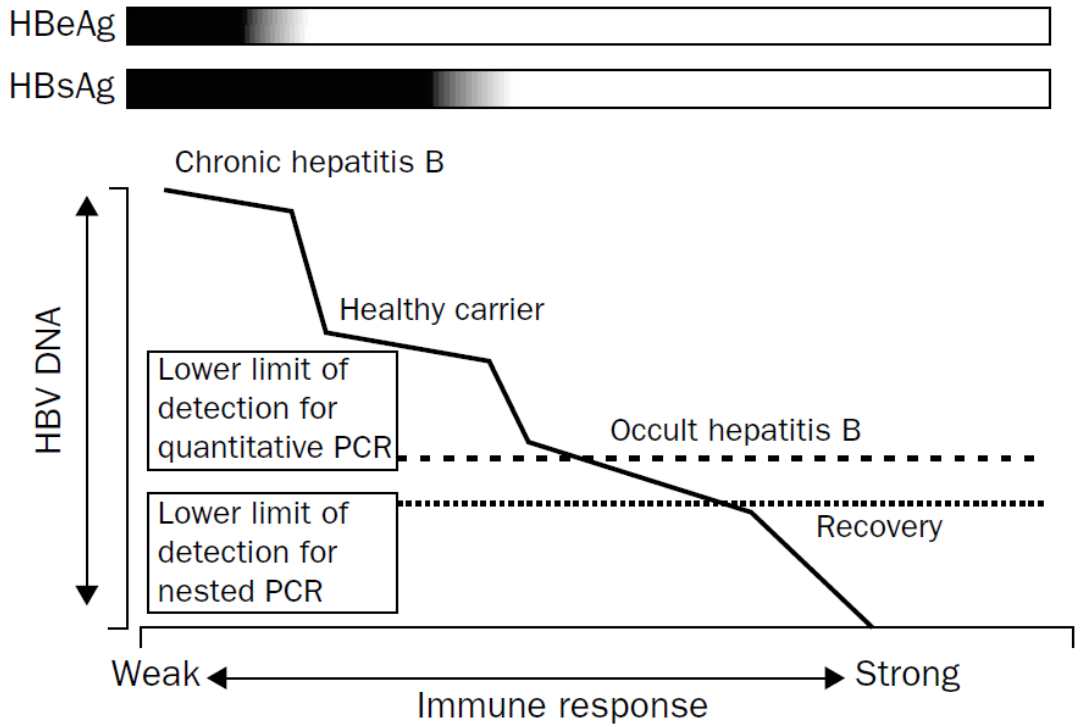
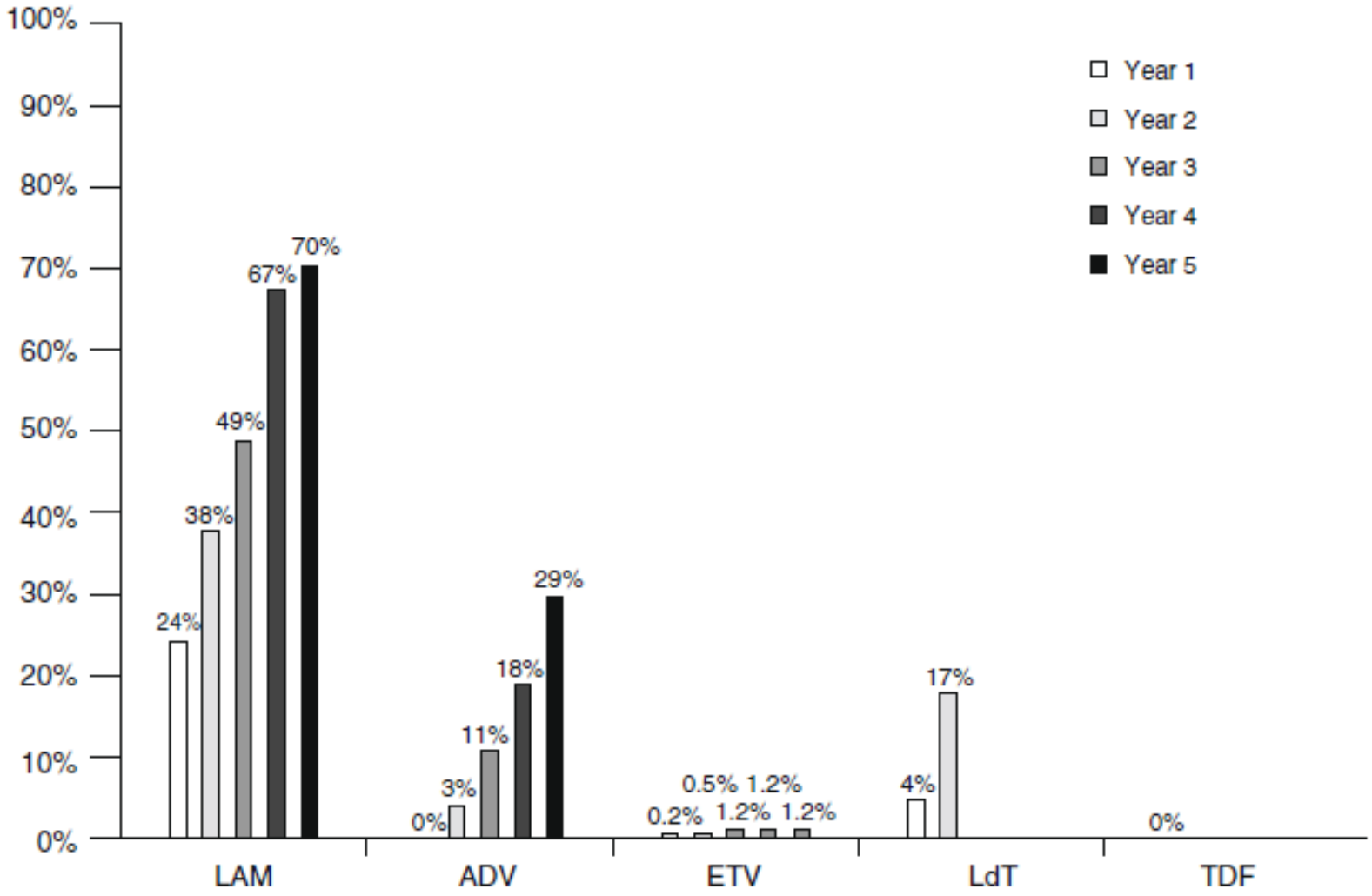


Figure 2. A model of occult hepatitis B highlighting the potential role of the immune system. Other factors such as HBV mutations and co-infection with HCV also appear to have a role.



Cumulative incidence of HBV resistance to lamivudine (LAM), adefovir (ADV), entecavir (ETV), telbivudine (LdT) and tenofovir (TDF) in published pivotal trials in NUC-naive patients. For method of calculation, see [61]. These trials included different populations, used different exclusion criteria and different follow-up endpoints

Main features of all antiviral vaccines commercially available (2)

Virus	Type of vaccine	Route of administration	Protocols for administration	Effectiveness	Duration of protection	Possible adverse events
JEV	inactivated	intramuscular	3 doses given on days 0, 7 , 30 before travel to endemic areas	80% after 2 doses 99% after 3 doses	(?)	Fever, headache, nausea, abdominal pain, myalgia, dizziness, neurological complications, skin rashes
VZV	attenuated	subcutaneous	1 dose in children up to 12 years old, 2 doses in older individuals	>90%	(?)	Local: redness, swelling, tenderness General: fever with skin rash
Smallpox	attenuated	subcutaneous	single administration	>95%	3-5 years	Fever, hypersensitivity, cutaneous manifestations, cardiac abnormalities and abnormalities of CNS
HBV	recombinant	intramuscular	3 dosi in the 1st year of life (3-5-12 months)	50-99%	3-5 years	Local:pain General: headache
Rabies virus	inactivated	intramuscular	Pre-exposure: 3 doses given on days 0-7-21 or 28 Post-exposure: 5 doses given on days 0-3-7-14-28 with hyperimmune globulins	100%	>2 years	Headache, dizziness, myalgia, abdominal pain, hypersensitivity, rare neurological complications

Legend: MMR:measles-mumps-rubella; HAV: hepatitis A virus; JEV: Japanese encephalitis virus; VZV: varicella-zoster virus; HBV: hepatitis B virus; HPV: human papilloma virus; LAIV: live attenuated influenza vaccine.

G. Antonelli, M. Clementi, G. Pozzi, G.M. Rossolini
Principi di Microbiologia Medica, II edizione. Copyright 2017 C.E.A. Casa Editrice Ambrosiana

DELTAHEPATITIS - HEPATITIS D VIRUS

World Health Organization

Hepatitis D

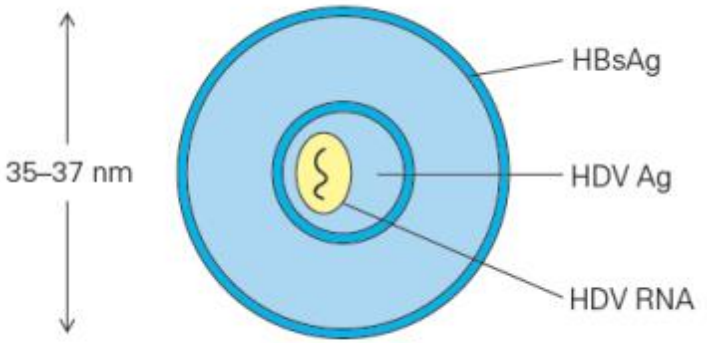
24 June 2022

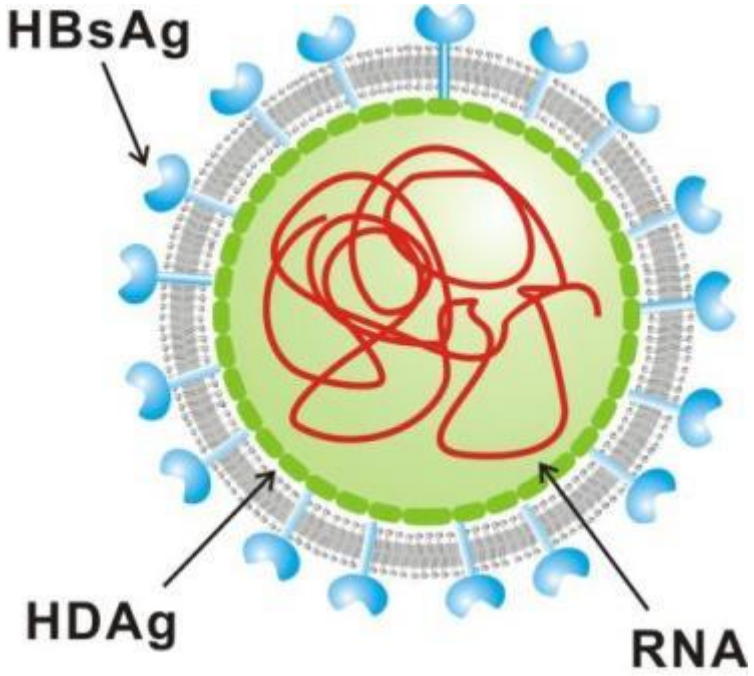
Key facts

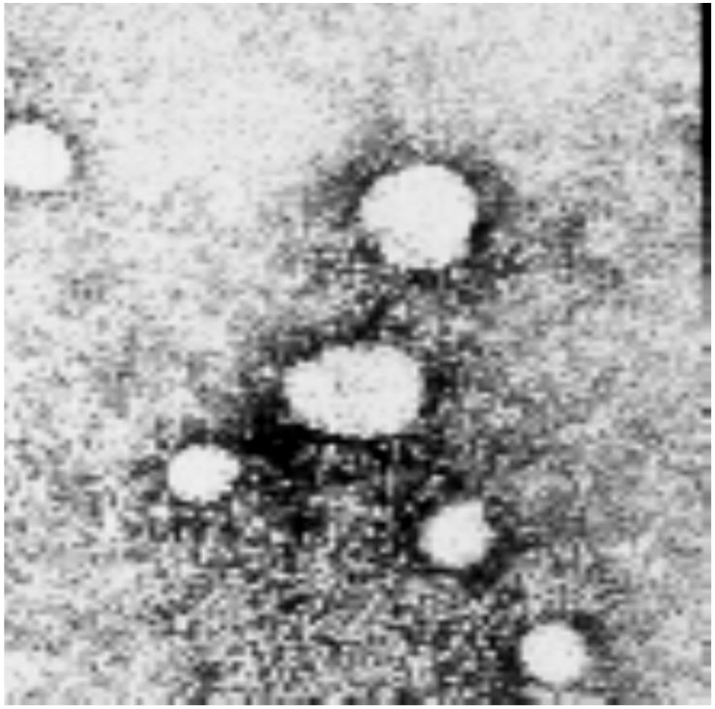
- Hepatitis D virus (HDV) is a virus that requires hepatitis B virus (HBV) for its replication.
- Hepatitis D virus (HDV) affects globally nearly 5% of people who have a chronic infection with hepatitis B virus (HBV).
- HDV infection occurs when people become infected with both hepatitis B and D simultaneously (co-infection) or get hepatitis D after first being infected with hepatitis B (super-infection).
- Populations that are more likely to have HBV and HDV co-infection include indigenous populations, recipients of haemodialysis and people who inject drugs.
- Worldwide, the number of HDV infections has decreased since the 1980s, due mainly to a successful global HBV vaccination programme.
- The combination of HDV and HBV infection is considered the most severe form of chronic viral hepatitis due to more rapid progression towards liver-related death and hepatocellular carcinoma.
- Hepatitis D infection can be prevented by hepatitis B immunization, but treatment success rates are low.

HEPATITIS D (Delta) VIRUS

Hepatitis D virus can multiply only in a cell infected with HBV







Hepatitis D - Clinical Features

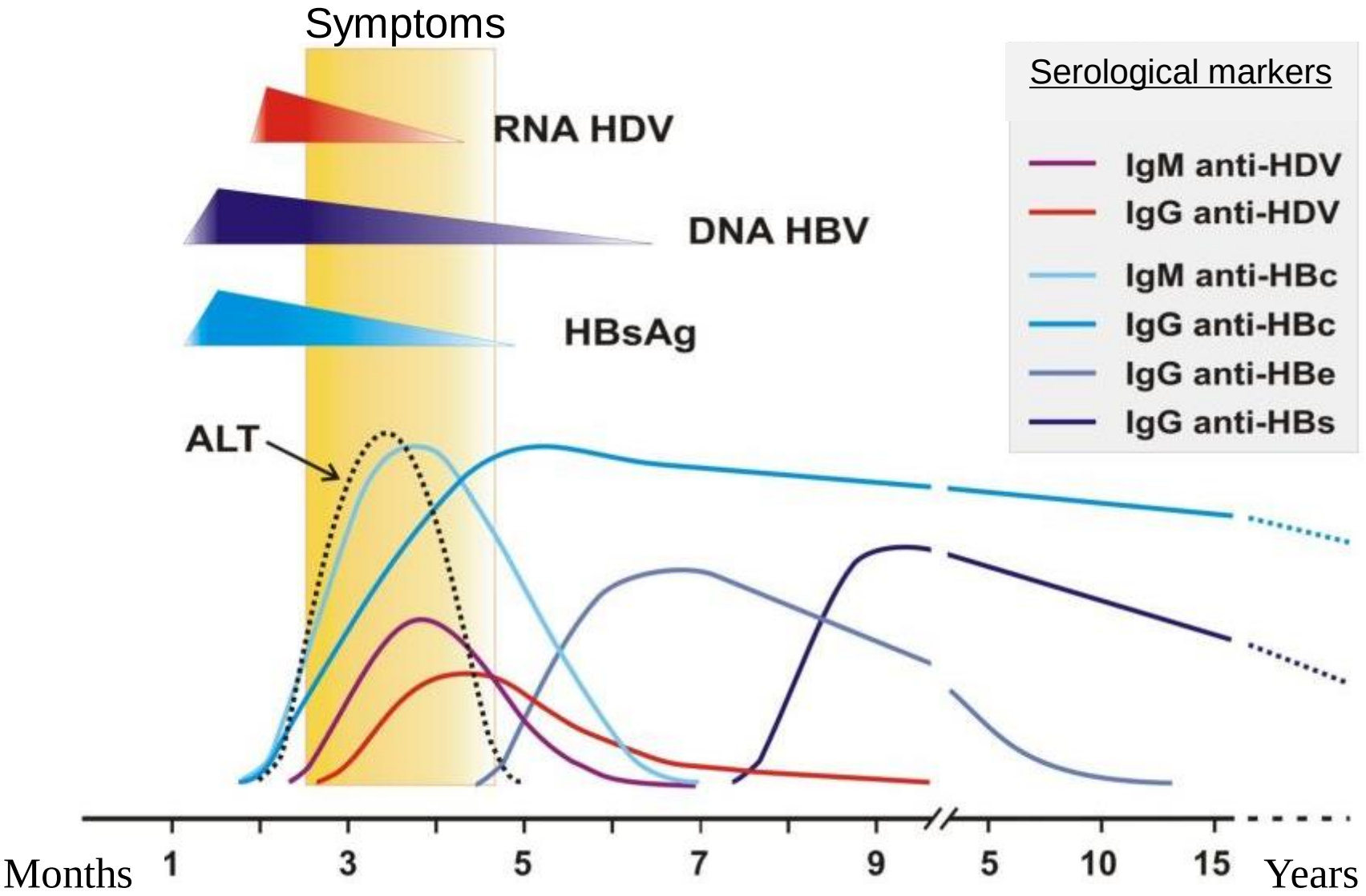
Coinfection

- severe acute disease
- low risk of chronic infection

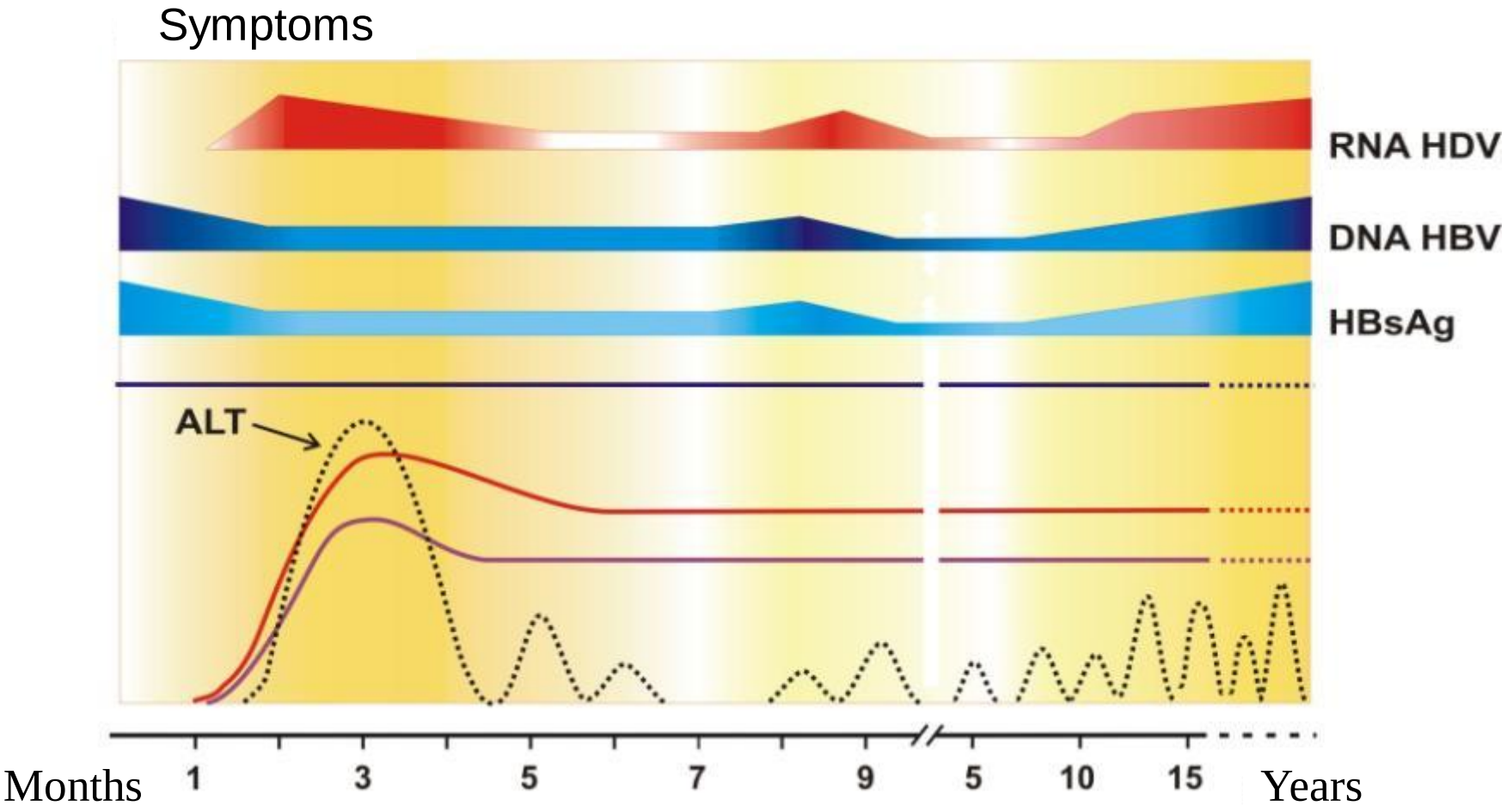
Superinfection

- usually develop chronic HDV infection
- high risk of severe chronic liver disease

Coinfection



Superinfection



HEPATITIS C VIRUS

Hepatitis C

24 June 2022

Key facts

- Hepatitis C is an inflammation of the liver caused by the hepatitis C virus.
- The virus can cause both acute and chronic hepatitis, ranging in severity from a mild illness to a serious, lifelong illness including liver cirrhosis and cancer.
- The hepatitis C virus is a bloodborne virus and most infection occur through exposure to blood from unsafe injection practices, unsafe health care, unscreened blood transfusions, injection drug use and sexual practices that lead to exposure to blood.
- Globally, an estimated 58 million people have chronic hepatitis C virus infection, with about 1.5 million new infections occurring per year. There are an estimated 3.2 million adolescents and children with chronic hepatitis C infection.
- WHO estimated that in 2019, approximately 290 000 people died from hepatitis C, mostly from cirrhosis and hepatocellular carcinoma (primary liver cancer).
- Antiviral medicines can cure more than 95% of persons with hepatitis C infection, but access to diagnosis and treatment is low.
- There is currently no effective vaccine against hepatitis C.

Table 1.*Flaviviridae*. Characteristics of the family *Flaviviridae*.

Characteristic	Description
Typical member	yellow fever virus-17D (X03700), species *Yellow fever virus*, genus *Flavivirus*
Virion	Enveloped, 40–60 nm virions with a single core protein (except for genus *Pegivirus*) and 2 or 3 envelope glycoproteins
Genome	9.0–13 kb of positive-sense, non-segmented RNA
Replication	Cytoplasmic, in membrane vesicles derived from the endoplasmic reticulum (ER); assembled virions bud into the lumen of the ER and are secreted through the vesicle transport pathway
Translation	Directly from genomic RNA containing a type I cap (genus *Flavivirus*) or an internal ribosome entry site (other genera)
Host range	Mammals (all genera); most members of genus *Flavivirus* are arthropod-borne
Taxonomy	Four genera containing 89 species

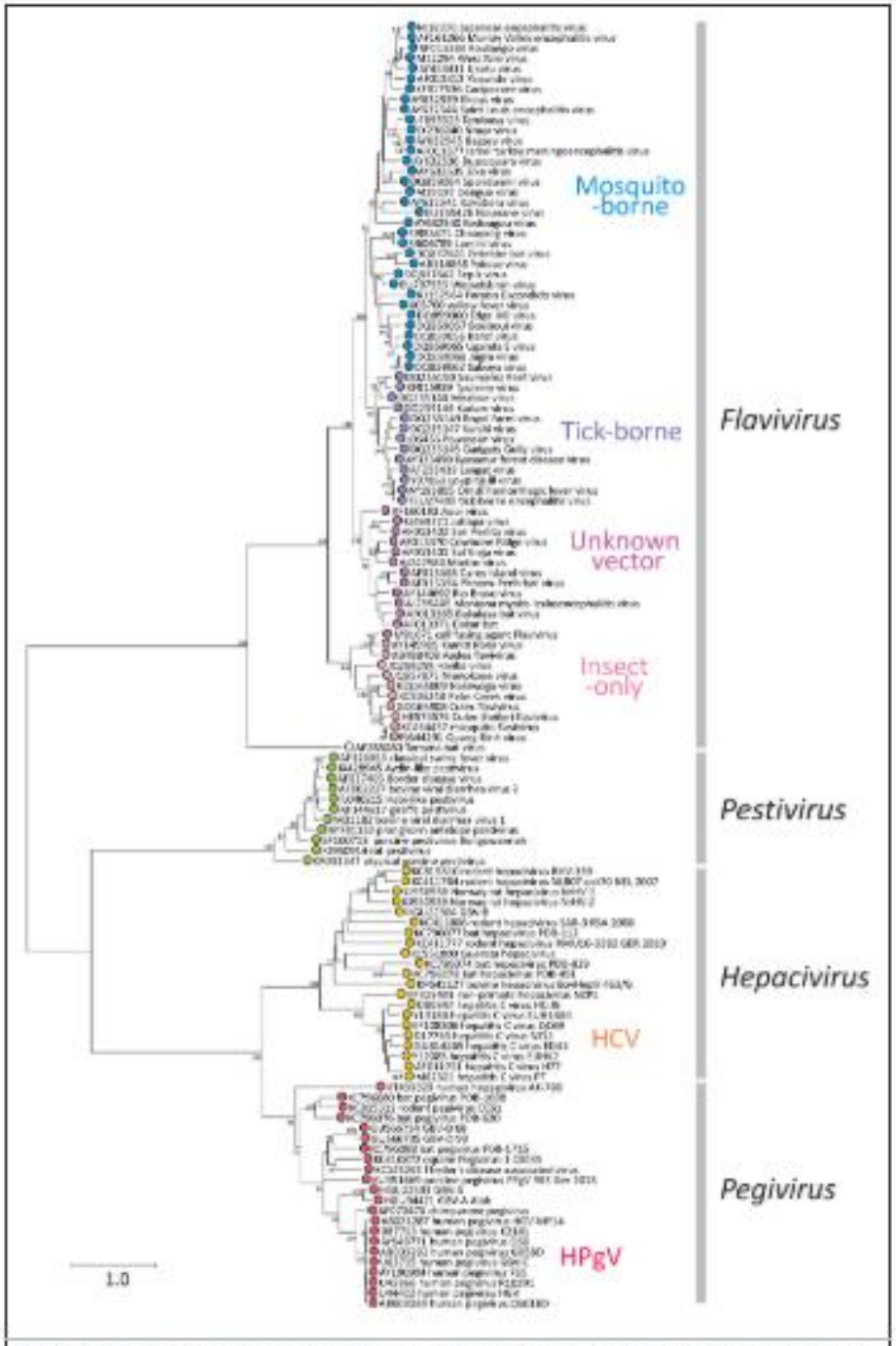
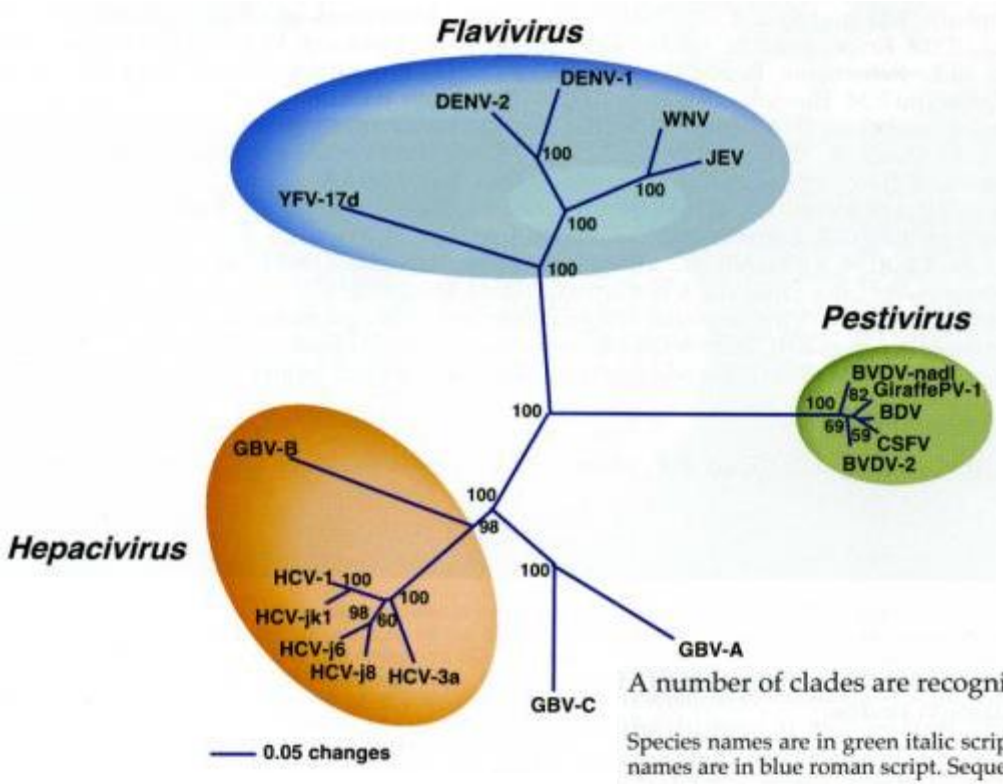


Figure 1. ***Flaviviridae***. Phylogeny of conserved amino acid sequences in the RdRP (NS5 or NS5B)



A number of clades are recognized for *Hepatitis C virus*. Examples are listed below.

Species names are in green italic script; strain names and synonyms are in black roman script; tentative species names are in blue roman script. Sequence accession numbers, and assigned abbreviations ( ) are also listed.

SPECIES IN THE GENUS

Hepatitis C virus

HCV clade 1		
HCV genotype 1a	[M62321]	(HCV-1)
HCV genotype 1b	[D90208]	(HCV-J)
HCV clade 2		
HCV genotype 2a	[D00944]	(HCV-J6)
HCV genotype 2b	[D01221]	(HCV-J8)
HCV clade 3		
HCV genotype 3a	[D17763]	(HCV-NZL1)
HCV genotype 10	[D63821]	(HCV-JK049)
HCV clade 4		
HCV genotype 4a	[Y11604]	(HCV-ED43)
HCV clade 5		
HCV genotype 5a	[Y13184]	(HCV-EVH1480)
HCV clade 6		
HCV genotype 6a	[Y12083]	(HCV-EUHK2)
HCV genotype 11	[D63822]	(HCV-JK046)

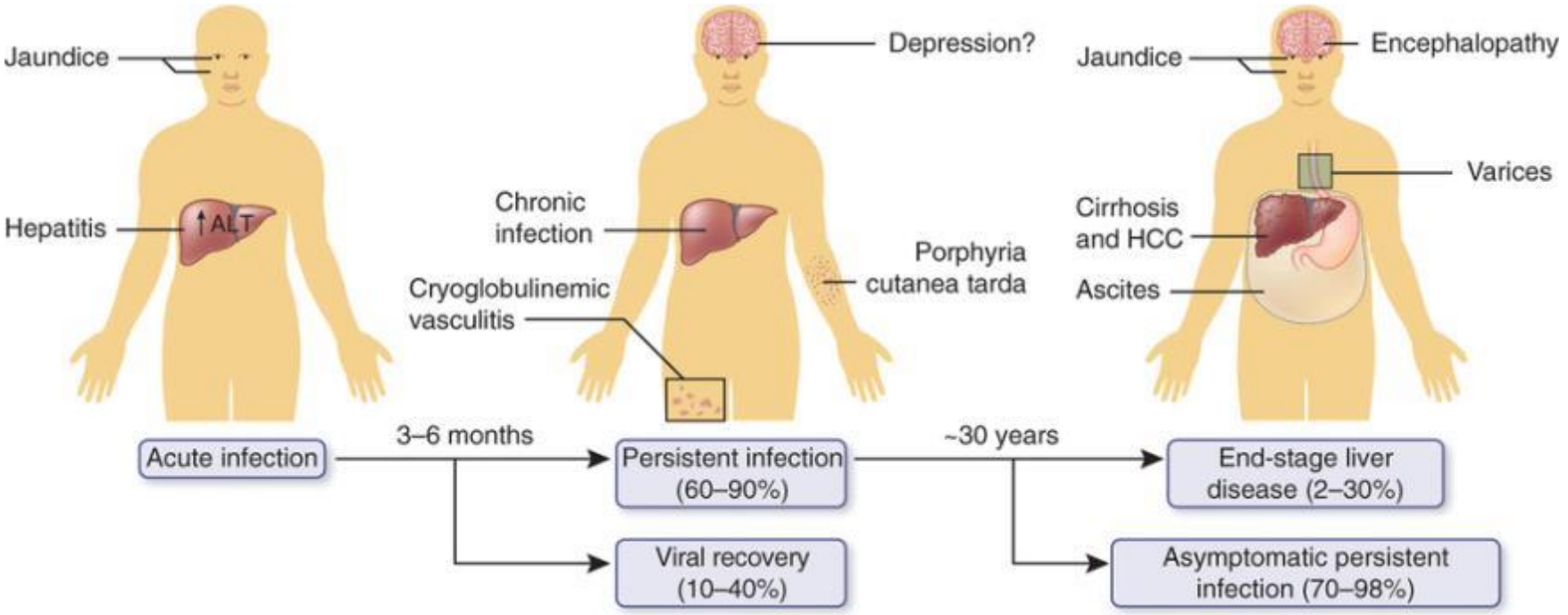
TENTATIVE SPECIES IN THE GENUS

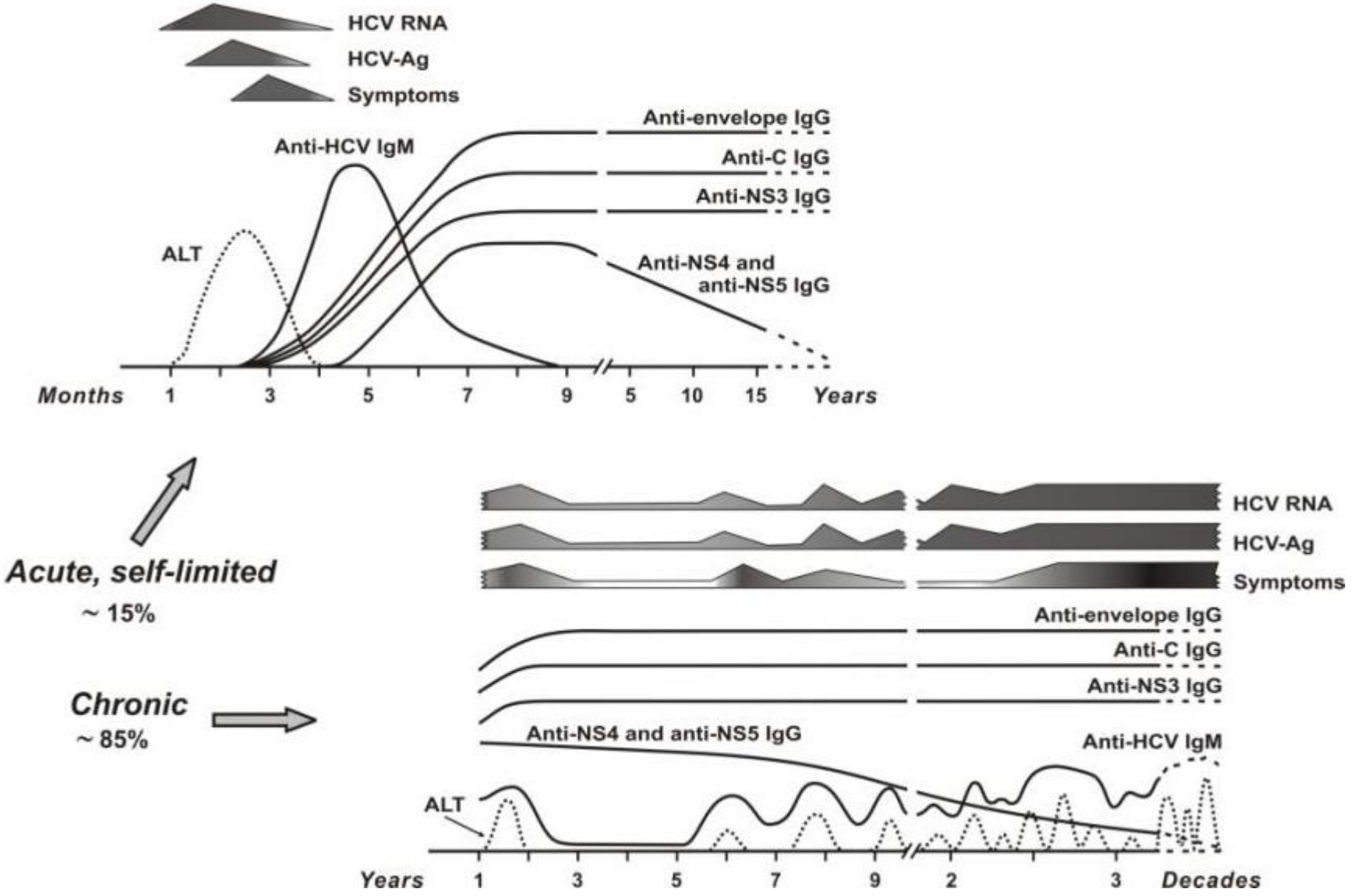
GB virus B	[U22304; AF179612]	(GBV-B)

Features of HCV Infection

Incubation period	Average 6-7 weeks Range 2-26 weeks
Acute illness (jaundice)	Mild ($\leq$20%)
Case fatality rate	Low
Chronic infection	60%-85%
Chronic hepatitis	10%-70% (most asx)
Cirrhosis	<5%-20%
Mortality from CLD	1%-5%

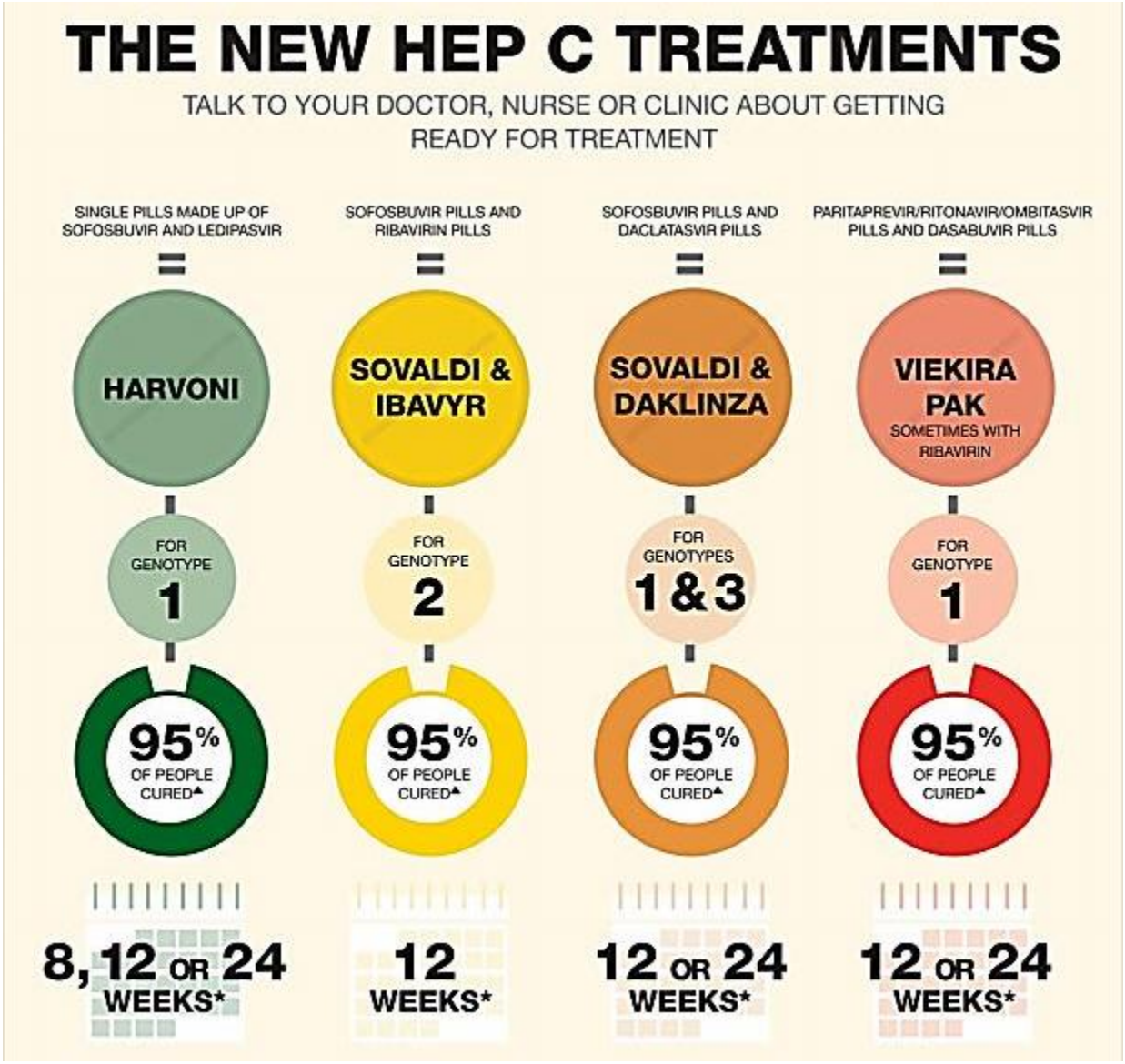
Outcome and exitus of HCV infection





Bendinelli, Pistello *et al.*, **Manual of Clinical Laboratory Immunology**, Rose et al. eds, American Society for Microbiology, VIIth ed., *in press*.

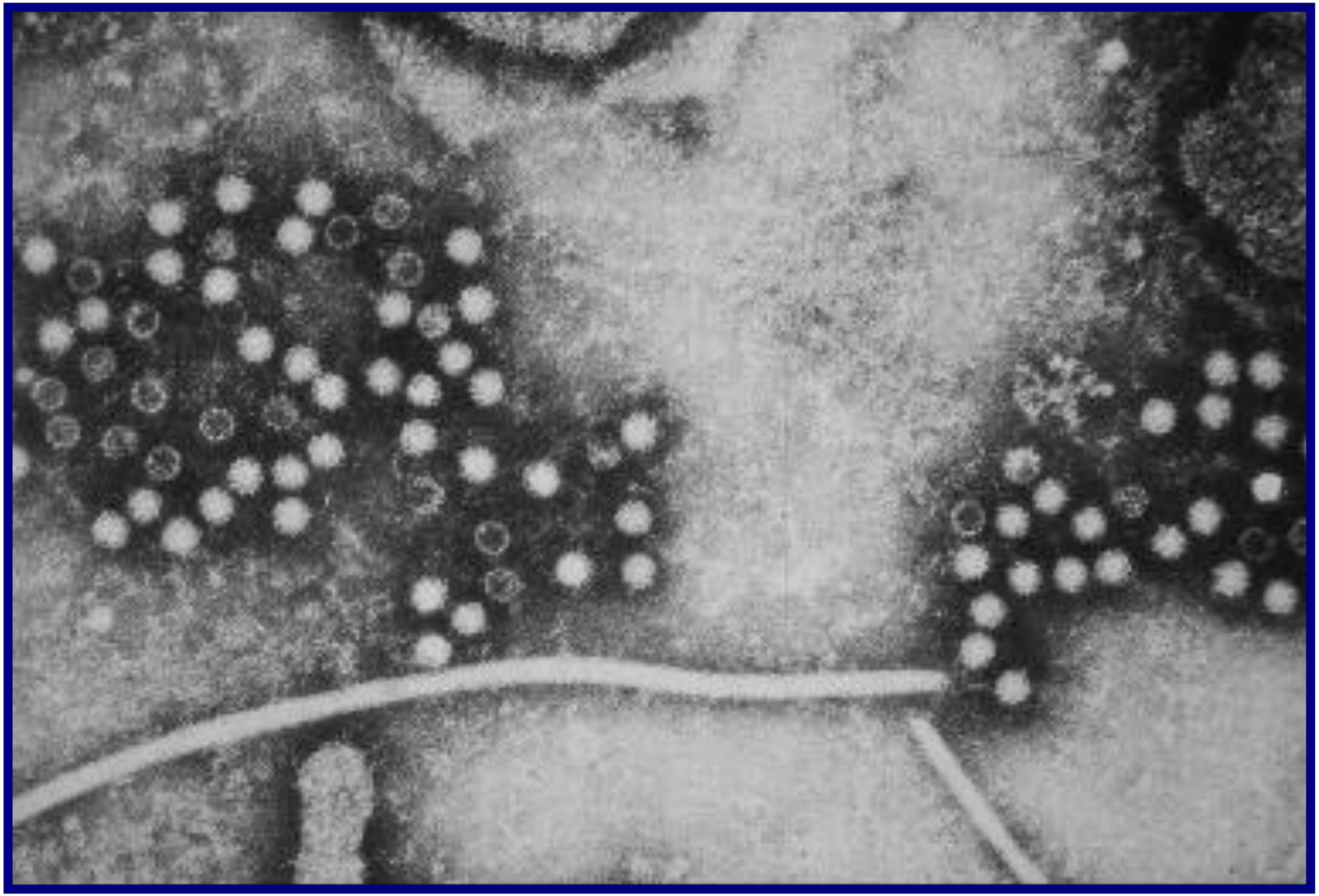
Current targets of HCV therapy / 3



Brand Name	Manufacturer	Approximate Cost for 12-Week Therapy
Sovaldi	Gilead Sciences	$84,000
Harvoni	Gilead Sciences	$94,500
Olysio	Janssen Therapeutics	$66,360
Viekira Pak	AbbVie	$83,319
Technivie	AbbVie	$76,653
Daklinza	Bristol-Meyers Squibb	$63,000

May 2016

HEPATITIS E VIRUS



World Health Organization

Hepatitis E

24 June 2022

Key facts

- Hepatitis E is an inflammation of the liver caused by infection with the hepatitis E virus (HEV).
- Every year there are an estimated 20 million HEV infections worldwide, leading to an estimated 3.3 million symptomatic cases of hepatitis E.
- WHO estimates that hepatitis E caused approximately 44 000 deaths in 2015 (accounting for 3.3% of the mortality due to viral hepatitis).
- The virus is transmitted via the fecal-oral route, principally via contaminated water.
- Hepatitis E is found worldwide, but the disease is most common in East and South Asia.
- A vaccine to prevent hepatitis E virus infection has been developed and is licensed in China, but is not yet available elsewhere.

Hepatitis E virus (HEV) infection is being increasingly recognized in medical research as HEV infection has reached industrialized countries.
Although HEV was discovered in 1983 and subsequent experimental analyses were initiated since 1990/1991 on HEV isolates , there exists a considerable lack of understanding and knowledge of transmission routes, life-cycle, pathogenesis, genome variability and viral evolution.

HEV is a small RNA, non-enveloped virus, 32–34nmin diameter and belonging to the genus Orthohepevirus of the Hepeviridae family
The HEV genome is a positive-sense single-stranded RNA molecule of 7.2 kb containing three open reading frames (ORF1, ORF2, and ORF3), 5′- and 3′-untranslated regions (UTRs), and a polyA-tract at the 3′-end

Classification of the hepatitis E viruses

The most accepted classification of hepatitis E viruses has involved their categorization into four major genotypes, with genotype 1 (Pakistan Sar55 strain—M80581) and genotype 2 (Mexican strain—M74506) only infecting humans, while genotype 3 (US strains—AF082843) and genotype 4 (Chinese T1 strain—AJ272108) are zoonotic[22,47–49]. Genotypes 1 and 2 are relatively conserved because they only infect humans, but genotypes 3 and 4 are much more diverse since they have a broader host spectrum[50]. The identification of more HEV isolates from different species, such as trout, deer, rabbit, chicken, mongoose, rats, bats, ferrets, and camels has demonstrated the need for a new taxonomic system of the Hepeviridae family[51–53].

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and ORF3), 5′- and 3′-untranslated regions (UTRs), and a polyA-tract
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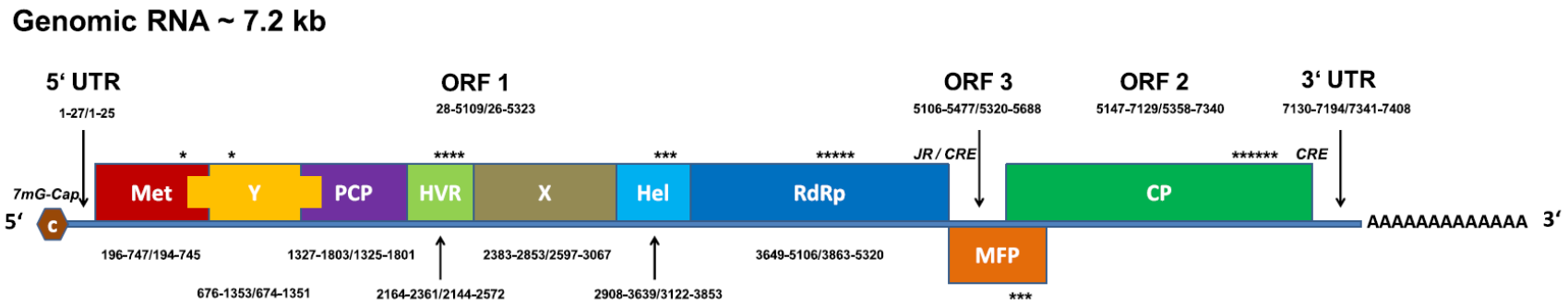
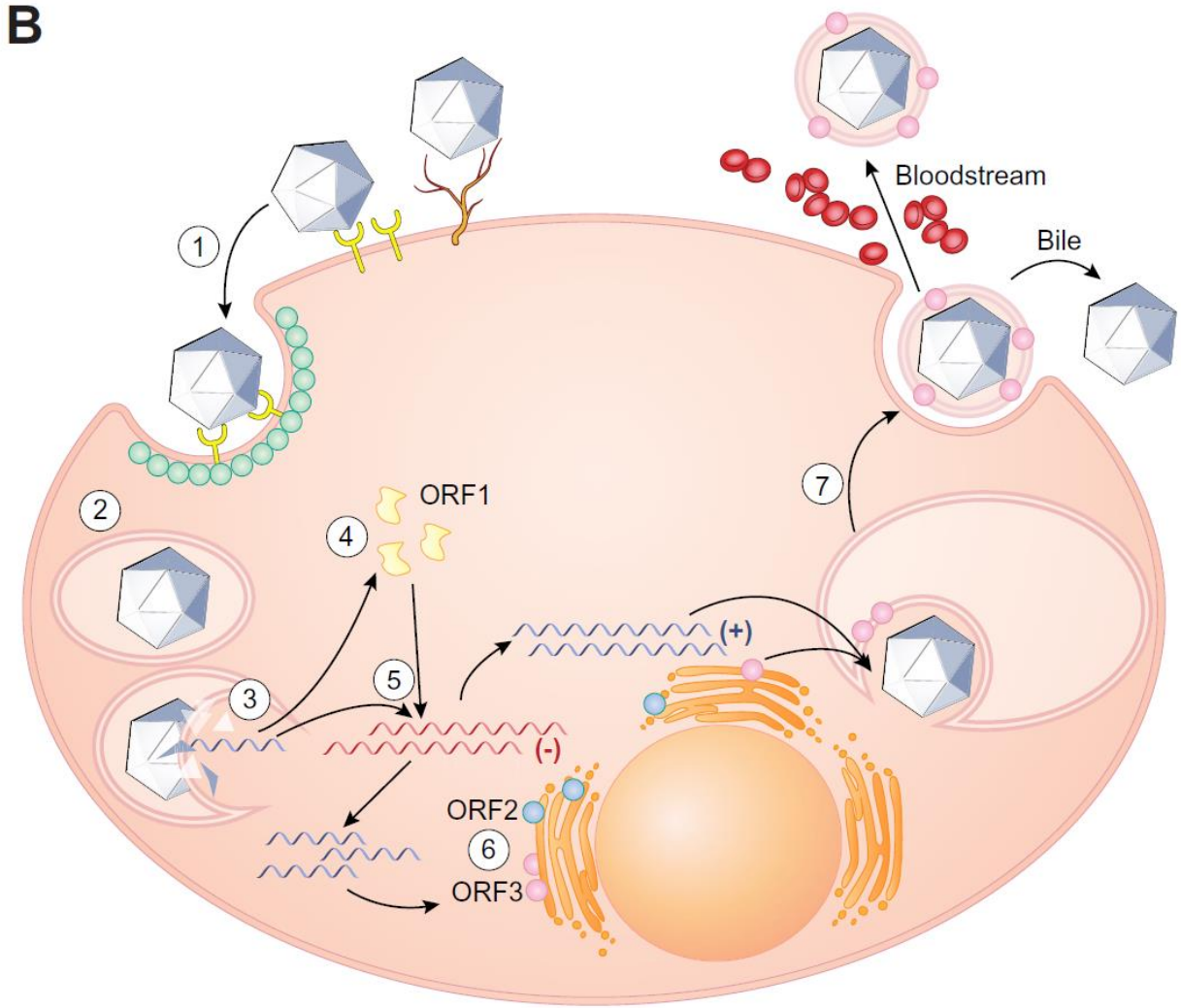
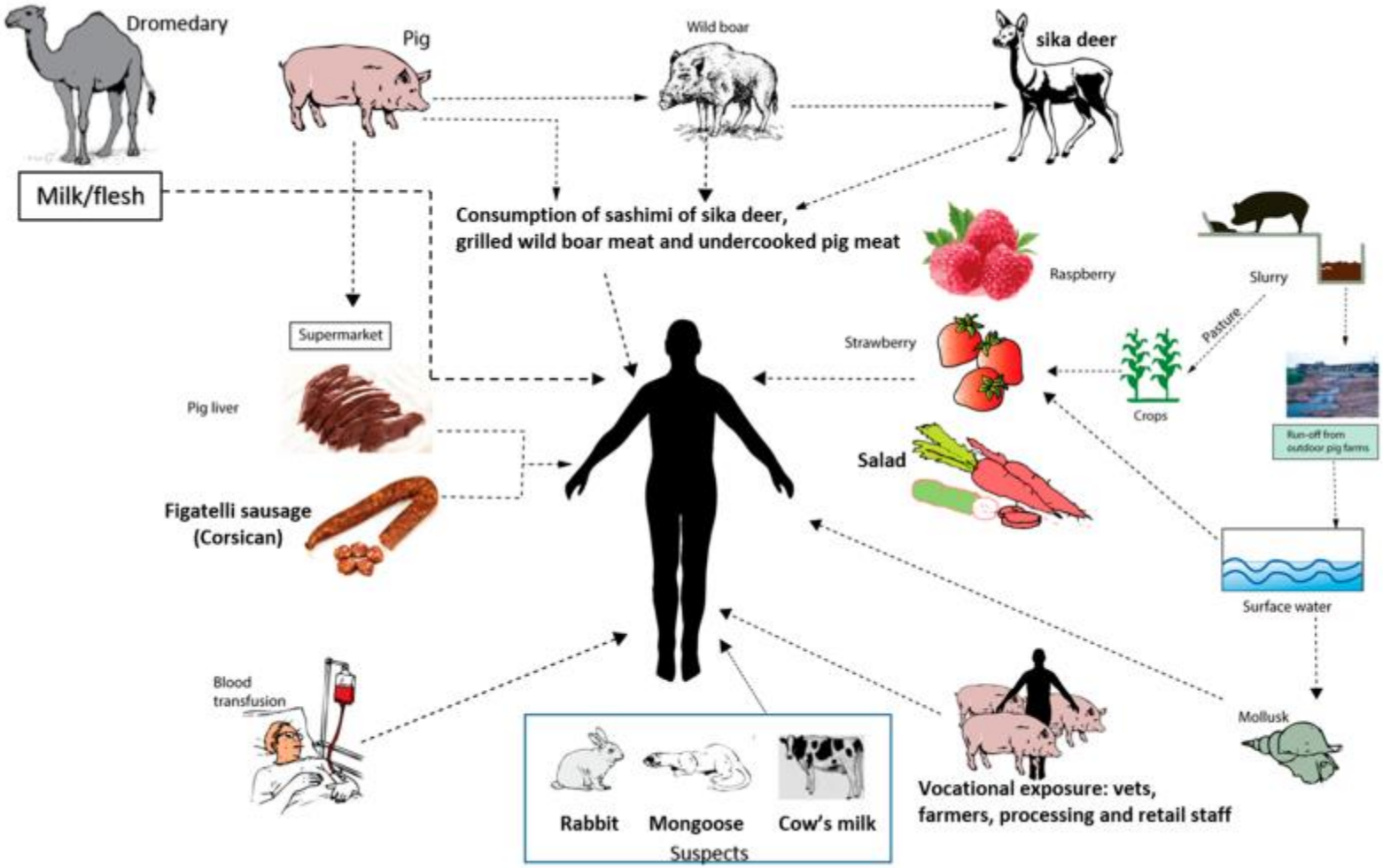



B
Bloodstream
Bile
1
2
3
4
5
6
7
ORF1
(+)
(-)
ORF2
ORF3


Dromedary
Pig
Wild boar
sika deer
Milk/flesh
Consumption of sashimi of sika deer,
grilled wild boar meat and undercooked pig meat
Raspberry
Slurry
Supermarket
Strawberry
Pasture
Pig liver
Crops
Run-off from outdoor pig farms
Salad
Figatelli sausage (Corsican)
Surface water
Blood transfusion
Mollusk
Rabbit
Mongoose
Cow's milk
Suspects
Vocational exposure: vets, farmers, processing and retail staff

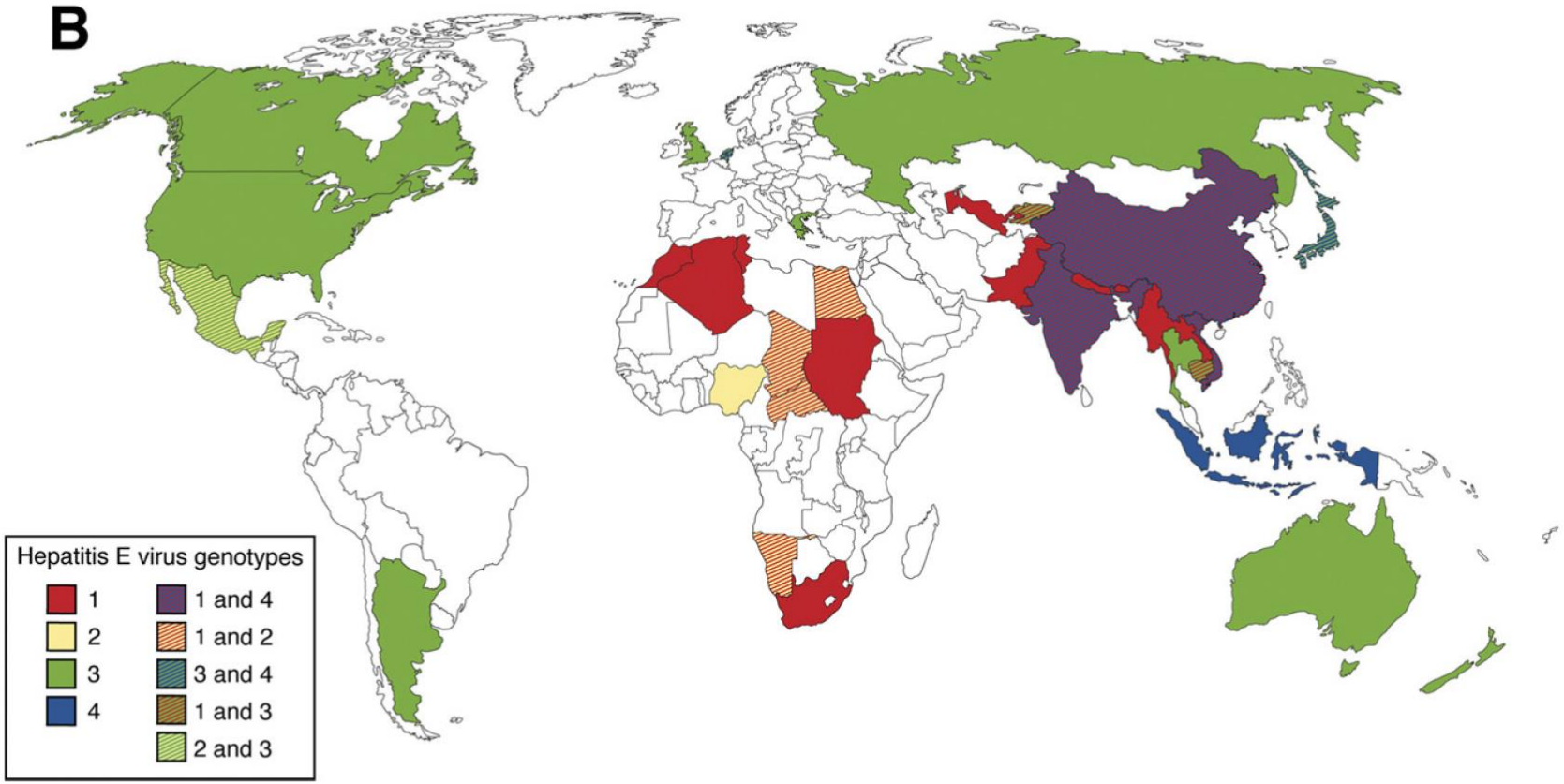


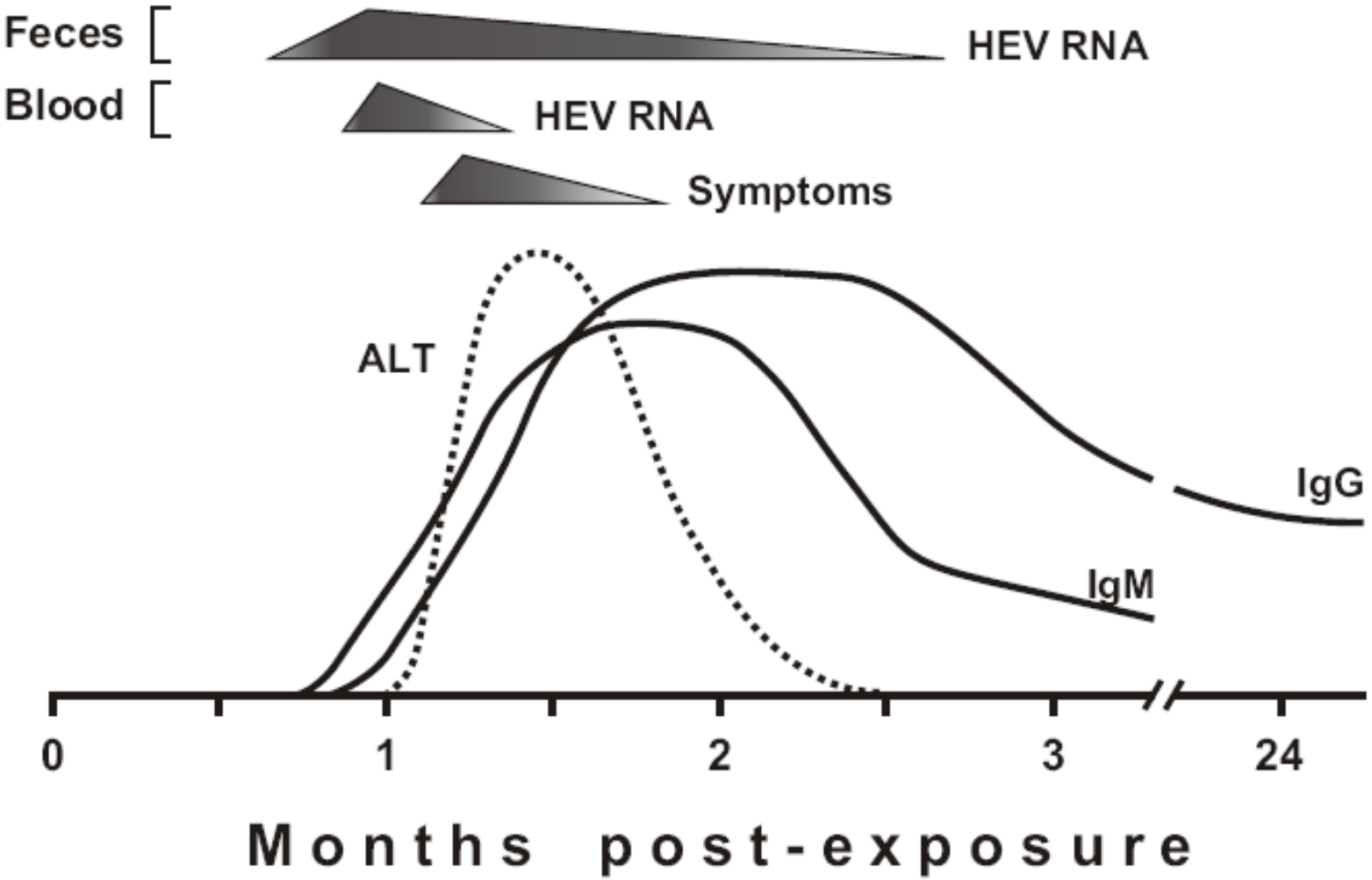
Figure 2. (*A*) Worldwide prevalence of HEV and (*B*) the geographic distribution of the different HEV genotypes.

Hepatitis E - Epidemiologic Features

- Most outbreaks associated with faecally contaminated drinking water.
- Several other large epidemics have occurred since in the Indian subcontinent and the USSR, China, Africa and Mexico.
- In the United States and other nonendemic areas, where outbreaks of hepatitis E have not been documented to occur, a low prevalence of anti-HEV (<2%) has been found in healthy populations. The source of infection for these persons is unknown.
- Minimal person-to-person transmission.

Hepatitis E - Clinical Features

Incubation period:	Average 40 days Range 15-60 days
Case-fatality rate:	Overall, 1%-3% Pregnant women, 15%-25%
Illness severity:	Increased with age
Chronic sequelae:	None identified



Bendinelli, Pistello *et al.*, **Manual of Clinical Laboratory Immunology**, Rose et al. eds, American Society for Microbiology, VIIth ed., *in press*.

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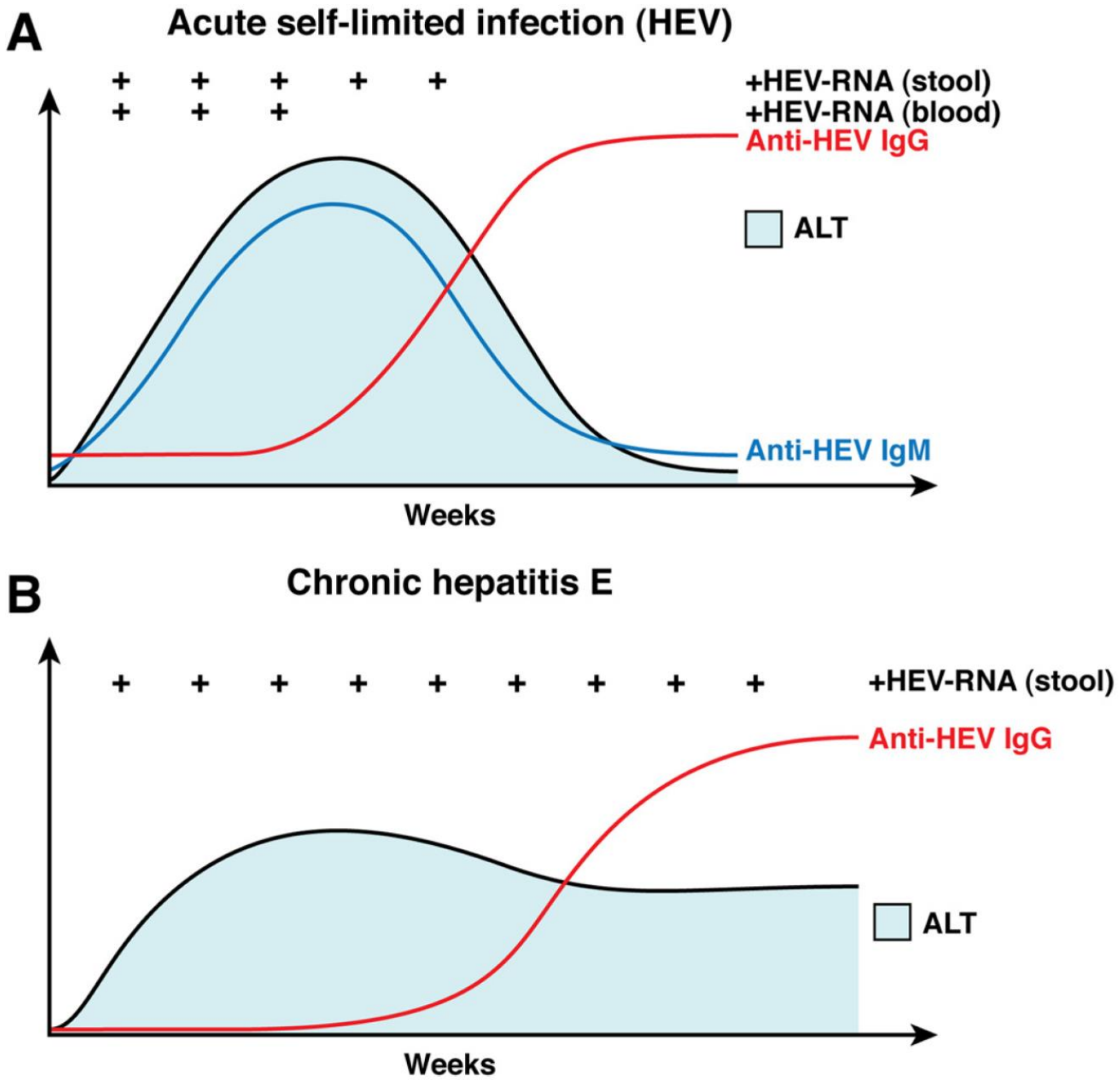
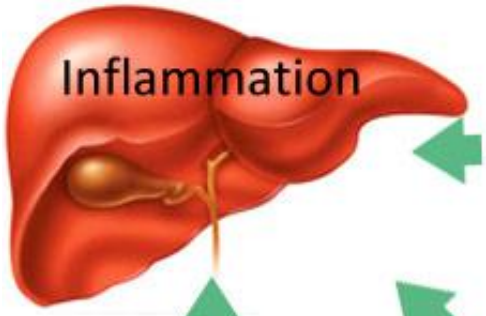

A
Acute self-limited infection (HEV)
+HEV-RNA (stool)
+HEV-RNA (blood)
Anti-HEV IgG
ALT
Anti-HEV IgM
Weeks
B
Chronic hepatitis E
+HEV-RNA (stool)
Anti-HEV IgG
ALT
Weeks

Table 3. Laboratory diagnosis of HEV infection.

Infection status	Positive markers
Current infection - acute	• HEV RNA • HEV RNA + anti-HEV IgM • HEV RNA + anti-HEV IgG* • HEV RNA + anti-HEV IgM + anti-HEV IgG • Anti-HEV IgM + anti-HEV IgG (rising) • HEV antigen
Current infection - chronic	• HEV RNA (± anti-HEV) ≥3 months • HEV antigen
Past infection	• Anti-HEV IgG

*Patients with re-infection are typically anti-HEV IgM negative, but IgG and PCR positive. HEV, hepatitis E virus.

HEPATITIS - inflammation of the liver tissue



Toxic Damage
Alcohol
Drugs
Poisons/Chemicals

Immunologic Damage

Infections
Viruses
Bacteria
Fung
Protozoa

- **Hepatitis A - HAV**
- **Hepatitis B - HBV**
- **Hepatitis C - HCV**
- **Hepatitis D - HDV**
- **Hepatitis E - HEV**

Differential Diagnosis of Acute Hepatitis	
Infectious	***Noninfectious***
Epstein-Barr virus Cytomegalovirus Herpes simplex virus Yellow fever Leptospirosis Q fever HIV Brucellosis Lyme disease Syphilis	