VIRAL HEPATITIS

HEPATITIS - inflammation of the liver tissue

ACUTE HEPATITI S– symptoms persist up to 6 months
CHRONIC HEPATITIS – hepatic inflammation > 6 months

ANICTERIC HEPATITIS - mild form of hepatitis in which there is no jaundice

CIRRHOSIS - progressive scarring of the liver (loss of liver function)

HEPATOCELLULAR CARCINOMA (**HCC**) is the most common type of primary liver cancer in adults, and is the most common cause of death in people with cirrhosis .

acute hepatitis

⇩

chronic hepatitis*

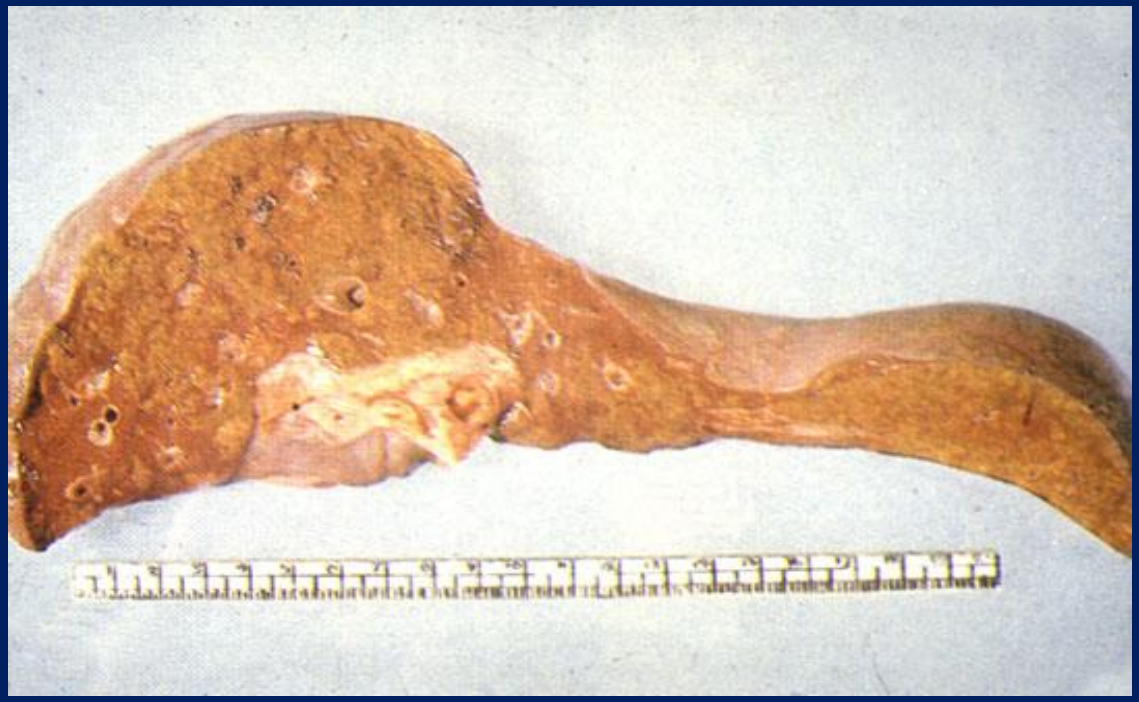
⇩

liver cirrhosis

⇩

hepatocellular carcinoma (HCC)

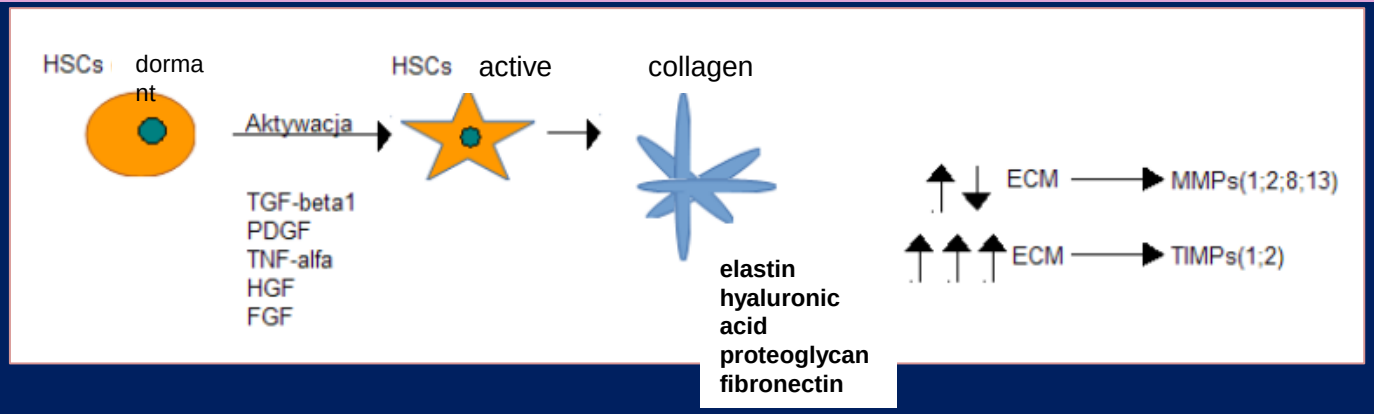
ALF /FHF
acute liver failure) /ang. fulminant hepatic failure



a) no previous history of liver disease
b) encephalopathy (any degree) that appears within 8 weeks of jaundice (serum bilirubin concentration > 50 μmol/L)
c) coagulopathy (INR ≥ 1.5)

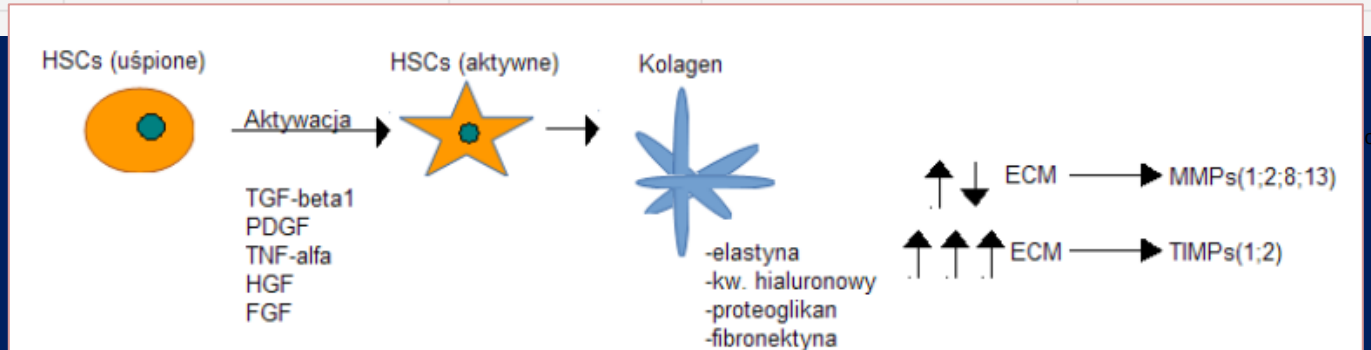
Fulminant fatal acute viral hepaptitis:
The liver is soft, flabby, friable, yellowish-green, collapsed, shrunken

HSCs (Hepatic stellate cells) = lipocytes = fat-storing cells = *Ito cells*, are liver-resident pericytes that reside within the space of Disse



Causal treatment, which involves removing the damaging factor

Leczenie włóknienia wątroby				
Substancje działające ochronnie na komórki wątrobowe	**Hamowanie aktywacji komórek gwiaździstych**	**Neutralizacja cytokin prozapalnych**	**Hamowanie syntezy macierzy zewnątrzkomórkowej**	**Przyśpieszanie degradacji macierzy zewnątrzkomórkowej**
▪ Prostaglandyny ▪ Sylimaryna ▪ Fosfatydylocholina ▪ Witamina E ▪ S-adenozylmetioniny ▪ Cynk ▪ Kwas ursodezoksycholowy ▪ Malotylat	▪ Glikokortykosteroidy ▪ Inferferony ▪ Retinoidy ▪ Estrogeny ▪ Antyoksydanty (N-acetylocysteina, Resweratrol) ▪ Halofuginon ▪ Inhibitory enzymu konwertującego przemianę angiotensyny I w II. ▪ Transformujący czynnik wzrostu beta (ang. Transforming Growth Factor beta- TGF-β)	▪ Pentoxyfilina ▪ Przeciwciała anty-PDGF i anty-TGF-β1	▪ Inhibitory hydroksylazy prolilowej (ang. Propyl-4-hydroxylase) ▪ Kolchicyna	▪ Glikokortykosteroidy ▪ Interferony ▪ Fosfatydylocholina* ▪ Prostaglandyny ▪ (Metalo)proteinazy ▪ Kolchicyna



All forms of acute viral hepatitis have similar presentation:

fatigue
loss of appetite
nausea
diarrhea
fever
dark urine
clay-colored stools
abdominal pain
jaundice
Relapse with cholestasis

Incubation periods of the disease

HAV 10-50 d

HEV 15-65 d

HBV 28-160 d

HDV 21-140 d

HCV 15-160 d

impaired mental functions
bleeding - > FHF

extrahepatic changes

HBV: glomerulonephritis, polyarteritis nodosa

HCV: mixed cryoglobulinemia, glomerulonephritis, autoimmune hepatitis

Laboratory and imaging findings

increased :
- liver enzymes (ALT, AST)
- bilirubin
- prothrombin time

decreased:
- albumin
- blood leukocytes

radiographic:
- hepatomegaly
- gall bladder and bile duct usually normal

POLYETIOLOGY OF HEPATITIS

primary hepatotropic viruses

hepatitis viruses A, B, C, D and E

secondarily hepatotropic viruses

CMV, EBV, HSV-1, HSV-2, VZV

Adenovirus

Yellow fever virus

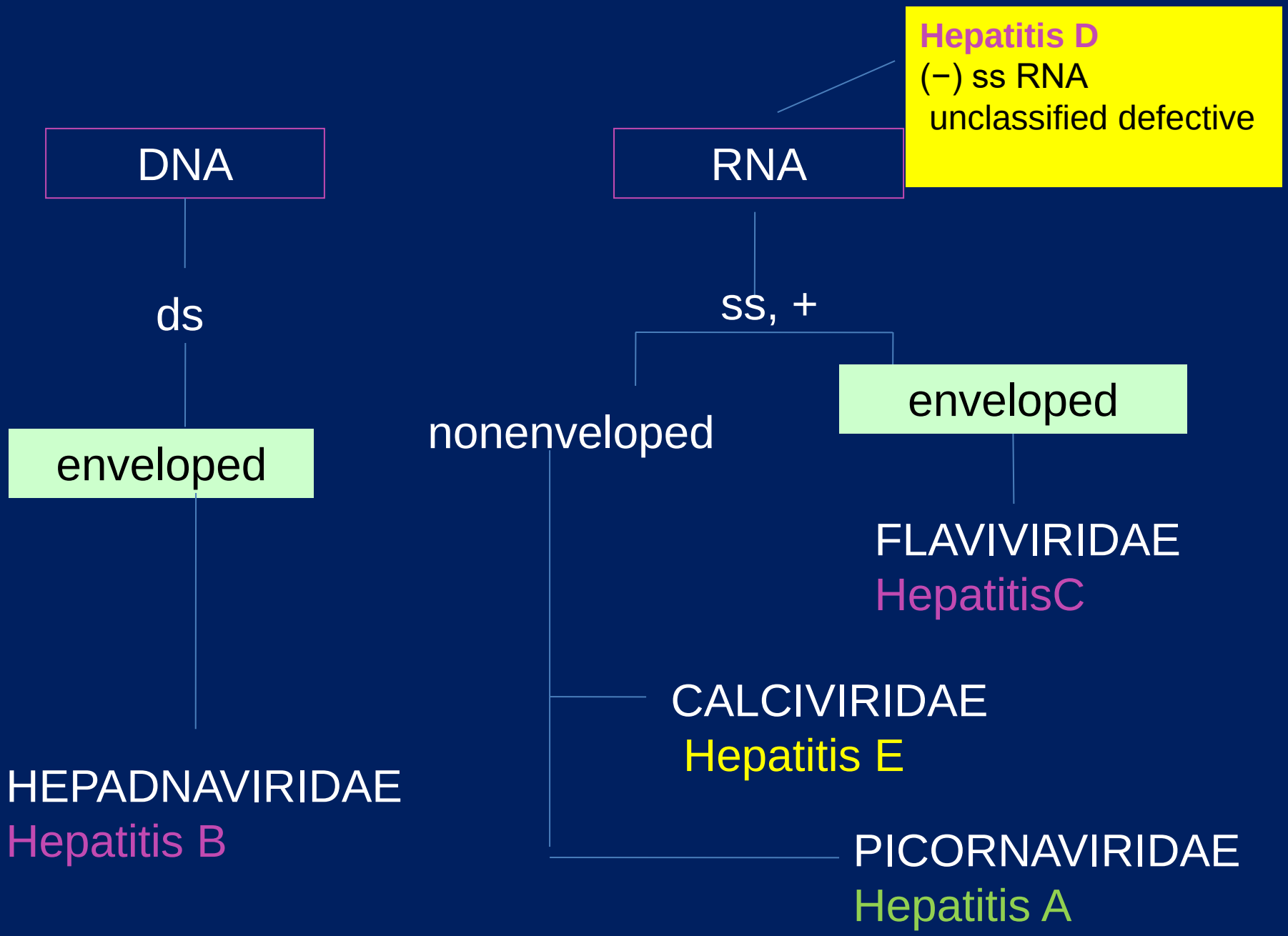
All forms of acute viral hepatitis have similar presentation:

fatigue
loss of appetite
nausea
diarrhea
fever
dark urine
clay-colored stools
abdominal pain
jaundice
Relapse with cholestasis

Incubation periods of the disease

- HAV 10-50 d
- HEV 15-65 d
- HBV 28-160 d
- HDV 21-140 d
- HCV 15-160 d

impaired mental functions, bleeding - > ALF/FHF

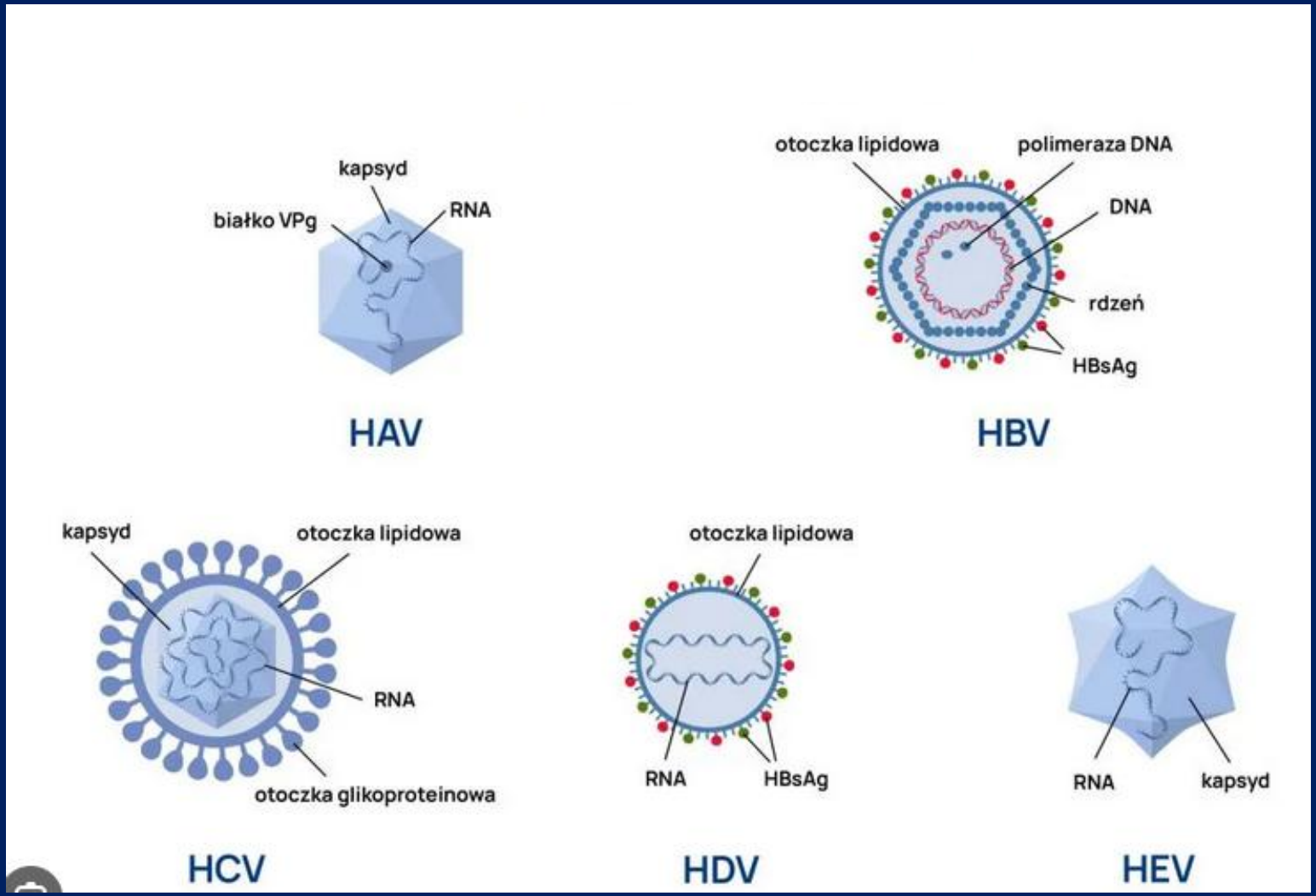

Hepatitis D
(−) ss RNA
unclassified defective
DNA
RNA
ds
ss, +
enveloped
nonenveloped
enveloped
FLAVIVIRIDAE
HepatitisC
CALCIVIRIDAE
Hepatitis E
HEPADNAVIRIDAE
Hepatitis B
PICORNAVIRIDAE
Hepatitis A

Treatment	Enveloped	Non-enveloped	Points to consider
Pasteurization	+	+/-	HBV is relatively heat stable
Terminal dry heat	+	+/-	At least 80 °C usually required for elimination of hepatitis viruses
Vapour heat	+	+/-	
Solvent/detergent	+++	-	
Acidic pH	+	-	Limited efficacy against non-enveloped viruses
precipitation	+	+	
chromatography	+	+	
nanofiltration	+	+/-	

+/- = some

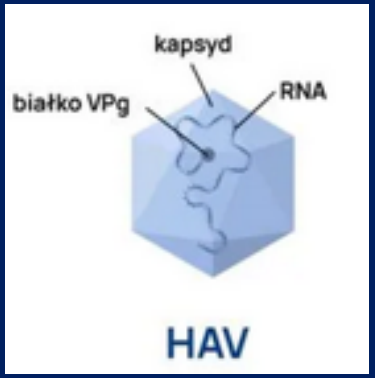
According to: World Health Organization
WHO Technical Report, Series No. 924, 2004

primary hepatotropic viruses



https://sklep.alablaboratoria.pl/centrum-wiedzy/wirusowe-zapalenie-watroby/

Hepatitis A



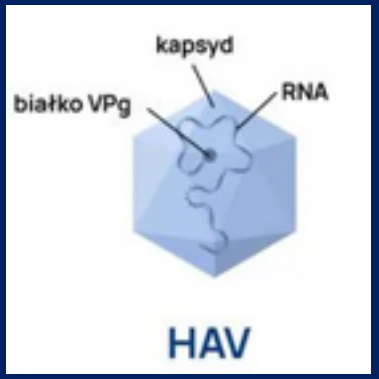
- „short incubation hepatitis” – 10-50 days (mean 25 days)
- abrupt onset
- disease common under condition of crowding and poor higiene

- self-limiting disease (99%)

- There is no chronic infection (no chronic carrier state)

- HAV infection induces lifelong immunity

HAV



- HAV infection ranges from asymptomatic infection (children) to fulminant hepatic failure (liver transplantation)

- risk of fulminant hepatic failure is very low (0.01–0.1%), but increases with age and in those with preexisting liver disease.

In patients over the age of 40, there is a 1% mortality rate

HAV mode of transmission

FECAL – ORAL (main)

SEXUAL (rarely): combined practices of anal and oral sex
PARENTERAL (rarely) :exist a brief window of viremia

Disease tends to be associated with heavy rainfall season

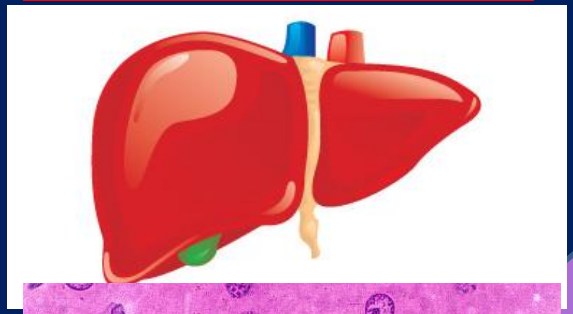
more frequent in children than in adults

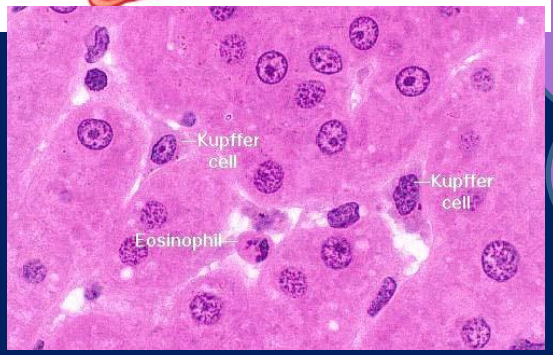
HEPATITIS A

Replicates initially in the enteric mucossa

Viremia with spread to the liver

replication in the liver

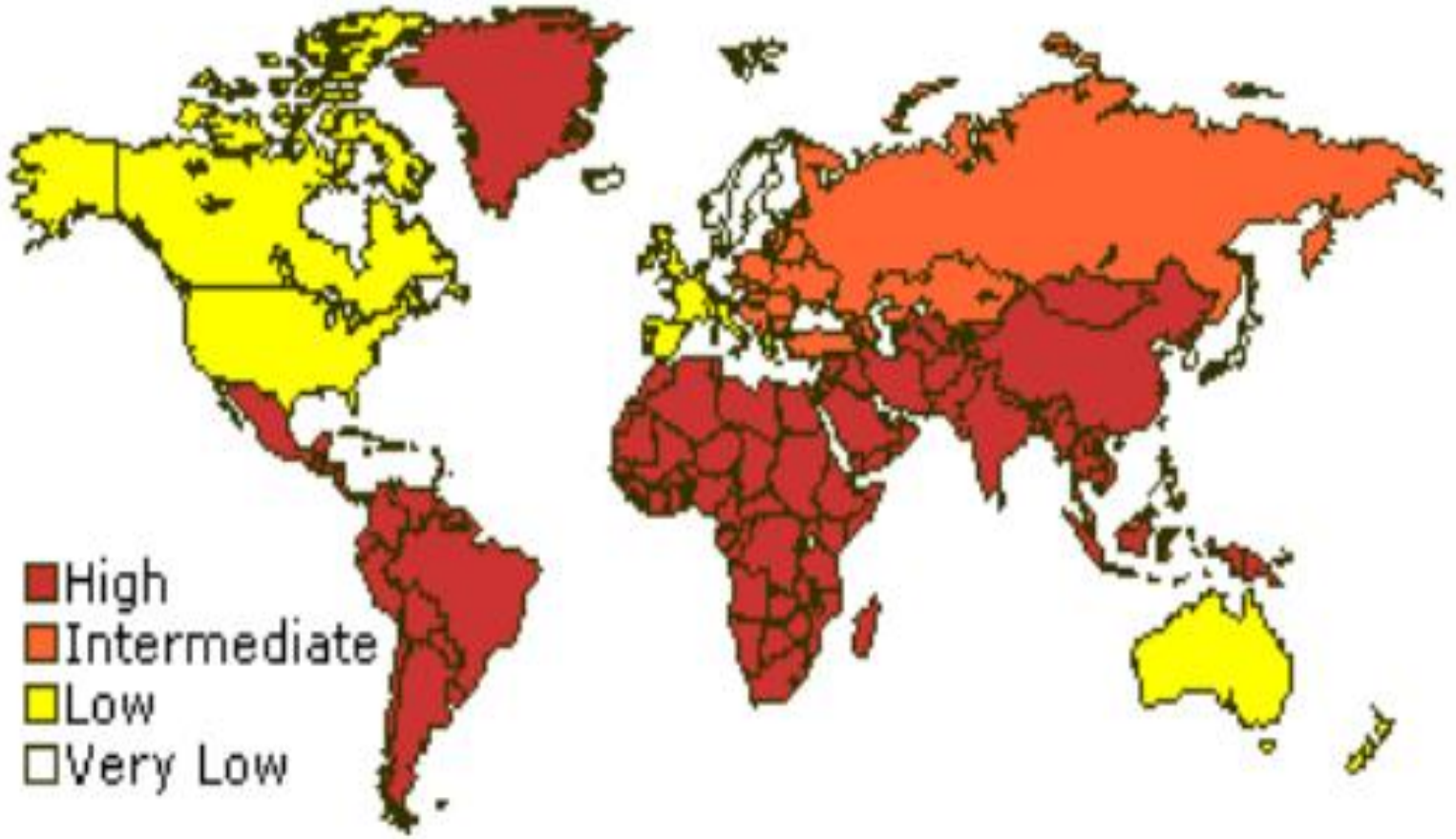




<u>response to viral replication:</u>

- lymphoid cell infiltration
- necrosis of liver parenchymal cells
- proliferation of Kupffer cells

Fig. 2 Prevalence of hepatitis A



http://www.worldgastroenterology.org/guidelines/global-guidelines/management-of-acute-viral-hepatitis/acute-viral-hepatitis-english

Management of acute hepatitis HAV

- no effective treatment, other than supportive measures, is available
- Hygiene !!!
- Contacts should be vaccinated
- Oral contraceptive treatment and hormone replacement therapy should be stopped to avoid cholestasis.
  Alcohol consumption is not advised

HAV - Prevention

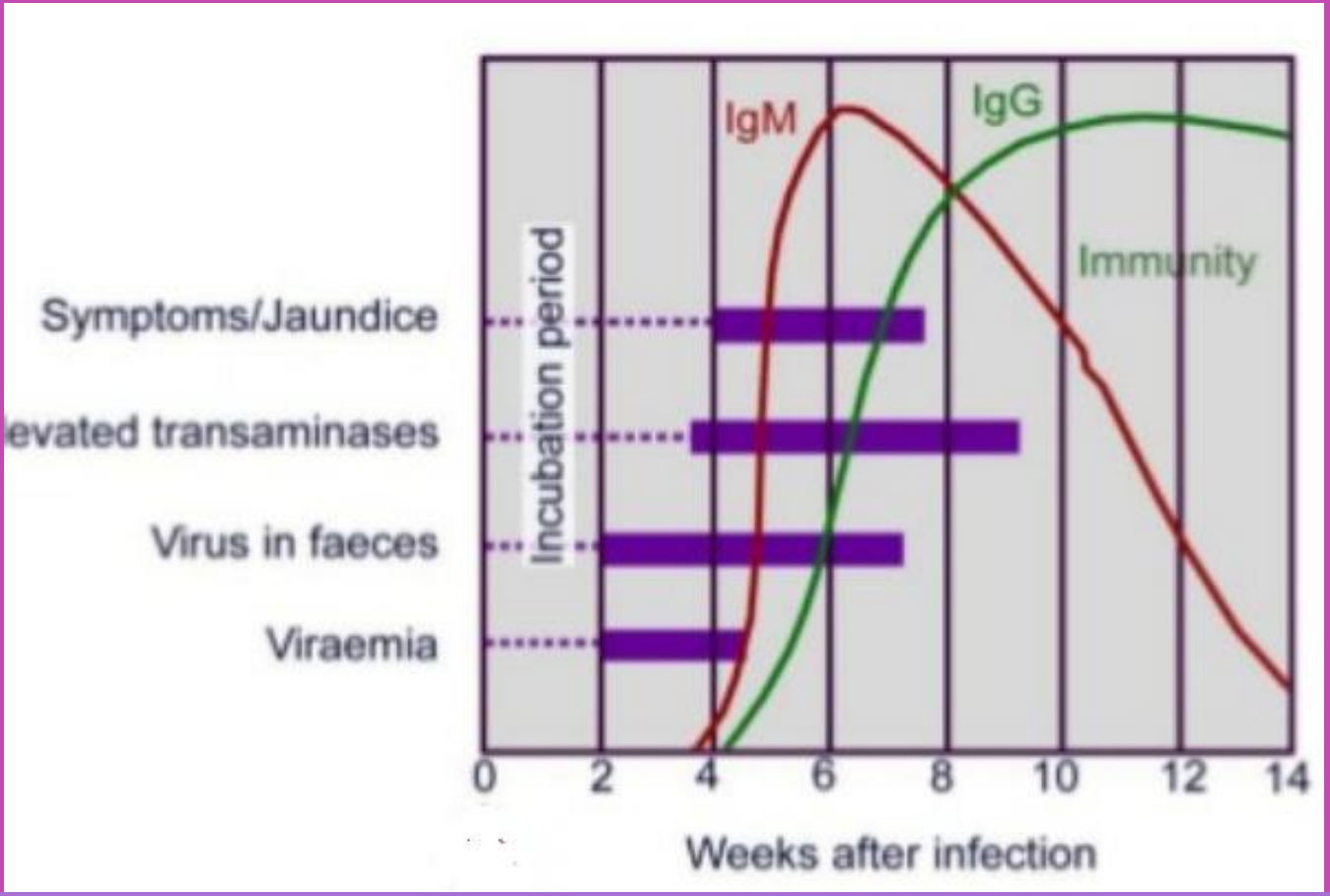
- Pre-exposure prophylaxis (IG, immune globulin)

IG is recommended for all susceptible travelers to developing countries
(0.06 ml/kg should be given every 5 months)

- inactivated vaccines

postexposure Prophylaxis (also IG) should be given as early as possible

HAV – course of infection

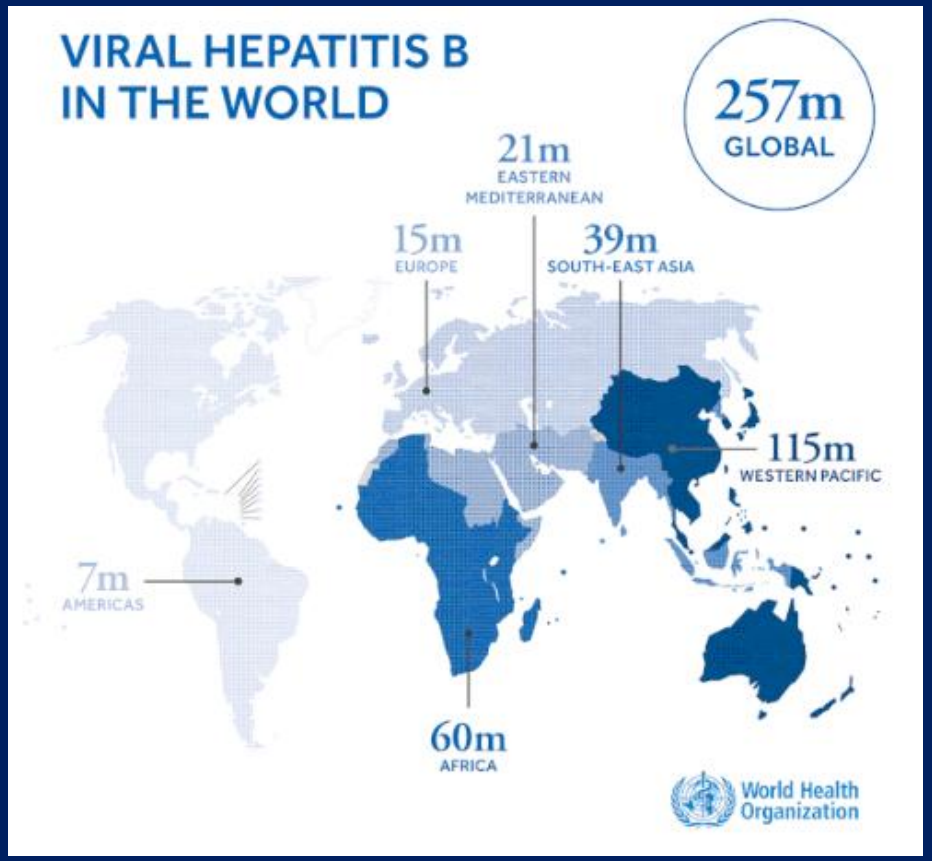


The diagnosis of acute hepatitis A is made by detecting IgM anti-HAV in the serum.

Hepatitis B

- the average annual incidence of acute hepatitis B in Europe is 20 per 100,000 population

- The number of HBV related deaths due to liver cirrhosis and/or hepatocellular carcinoma (HCC) increased between 1990 and 2013 by 33%, relating to 686,000 cases in 2013 worldwide



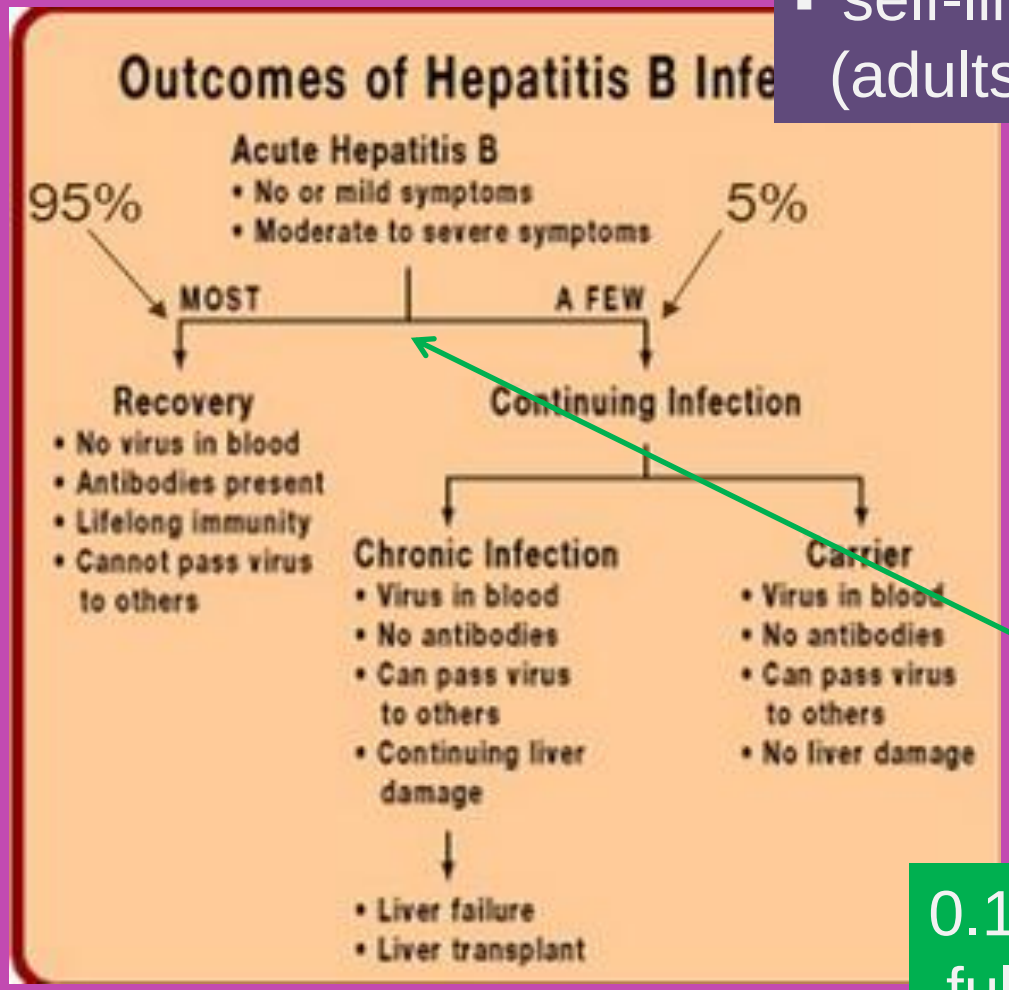
2022r POLAND chronic infections	2023r POLAND chronic infections
WZW B – 2 471	WZW B – 3 115
WZW C - 2 503	WZW C– 3 269

Hepatitis B

- Incubation period 45 -160 days (mean 10 weeks)
- gradual onset of symptoms (+ joints/rash)
- anicteric disease and asymptomatic infection may occour

Hepatitis B

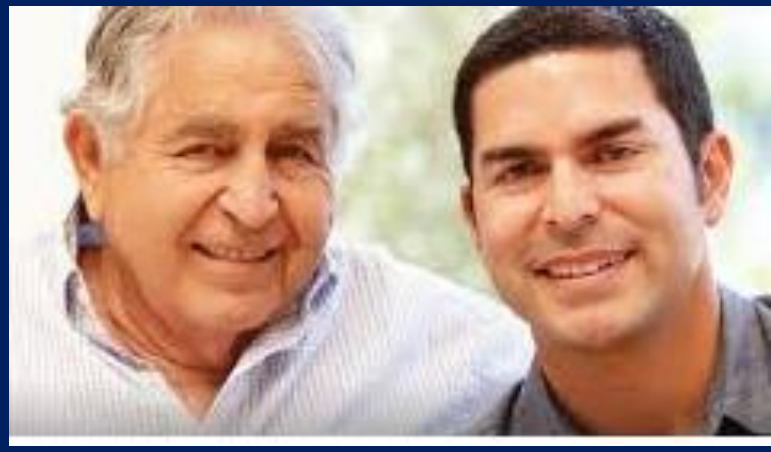
- self-limiting in 95% of cases (adults only)



0.1–0.5% of patients develop fulminant hepatitis

infants under 1 year of age,
chronic infection
in 80–90% of cases

children between the ages of 1 and 5,
30–50%
will go on to develop chronic infection

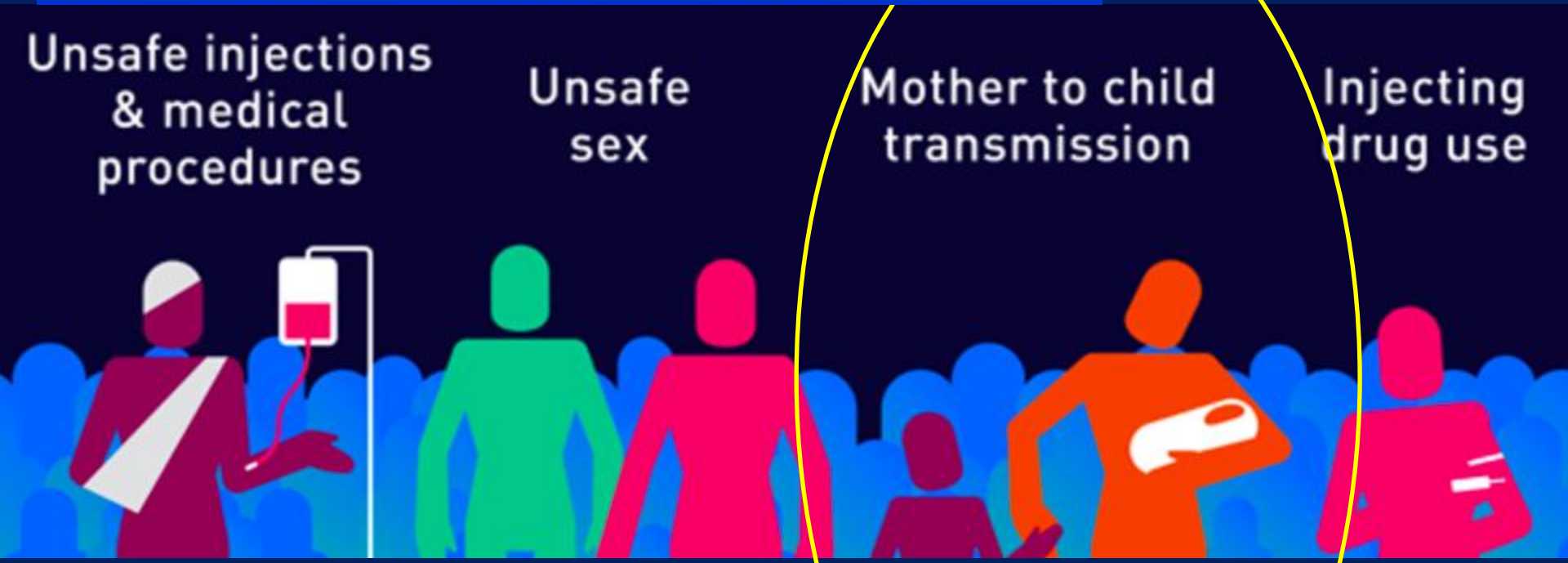


adults only 2–6% develop chronic infection

Hepatitis B - the age is matter…

Concentration of HBV in various body fluids

- **High**: Blood, serum, wound exudates
- **Medium**: saliva, semen, and vaginal secretions
- **Low/not detectable**: urine, feces, sweat, tears, breastmilk



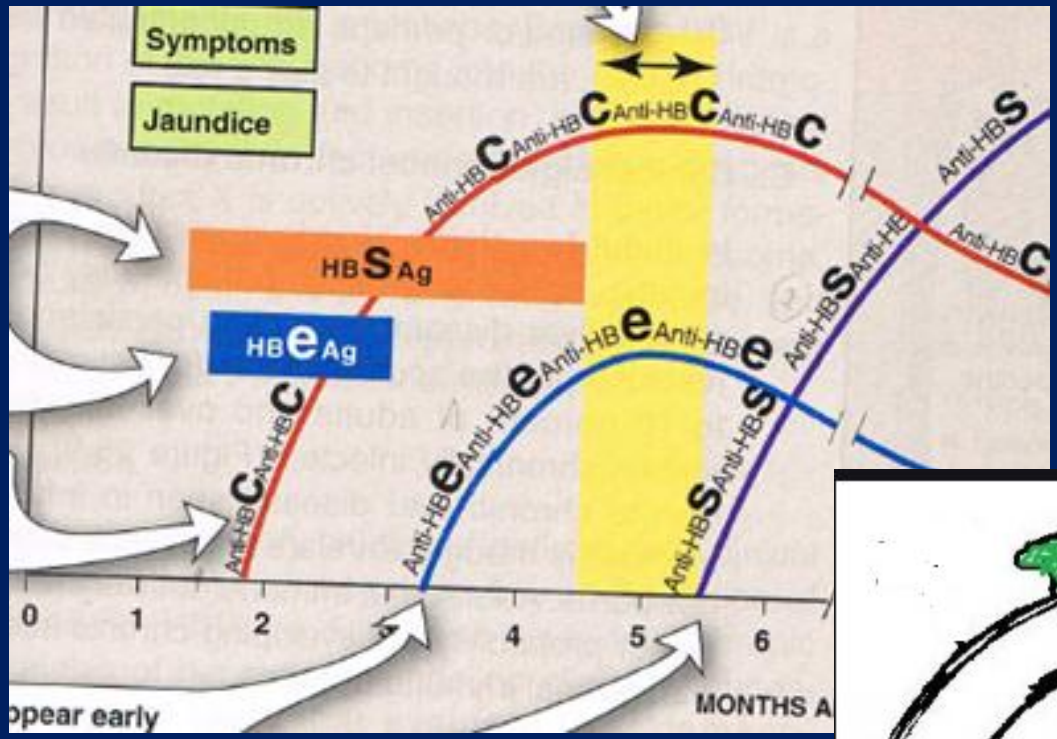
self-limiting in 95% of cases (adults only),

BUT NOT in children under the age of 5

HBV is highly infectious, can be transmitted in the absence of visible blood and remains infectious on environmental surfaces for at least 7 days

possible routes for transmission of HBV from an infected mother to infant:

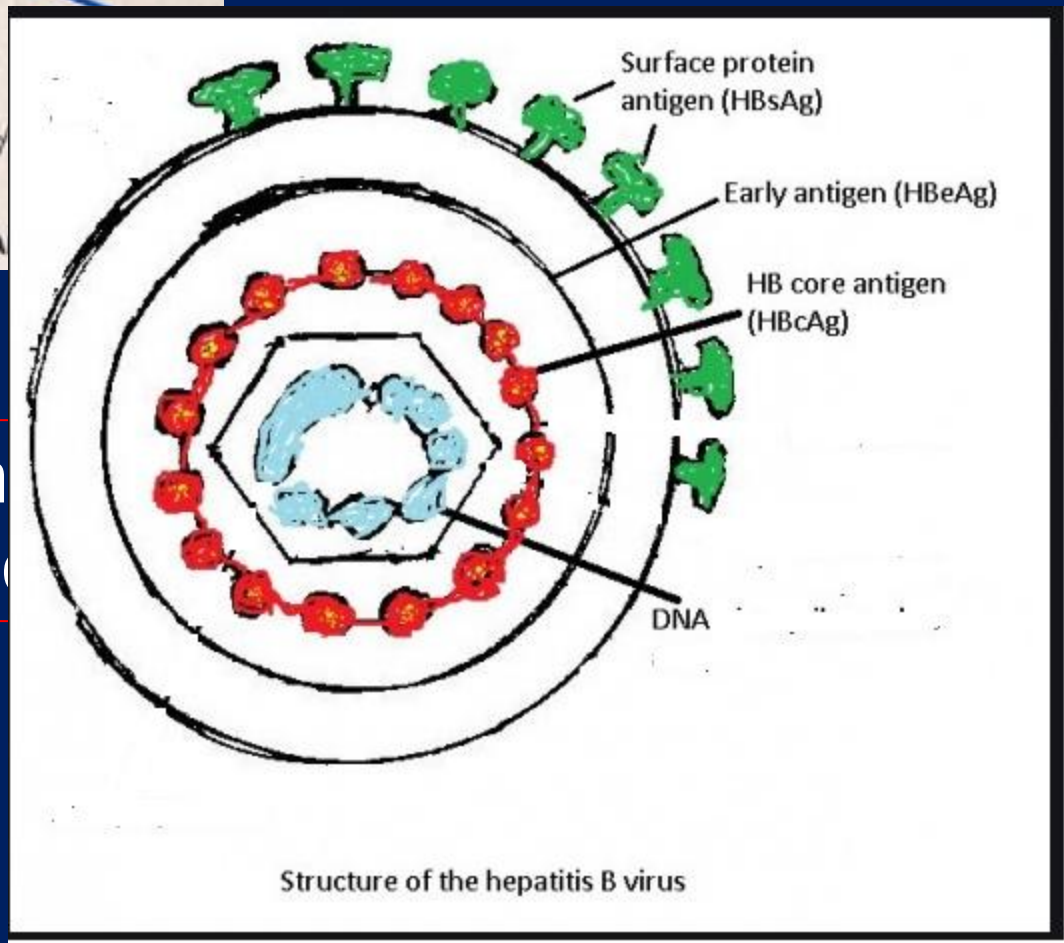
- transplacental transmission of HBV in utero
- natal transmission during delivery
- postnatal transmission during care or through breast milk



Acute infection

Incubation time 6-23 weeks

Chron
infecti



Structure of the hepatitis B virus

Perinetal transmission rates of HBV

CLINICAL STATUS	TRANSMISSION RATE
HBsAg + HBeAg -	10 – 20%
HBsAg + HBeAg +	90 %
Acute hepatitis B first trimester	10%
Acute hepatitis B third trimester	80 – 90%

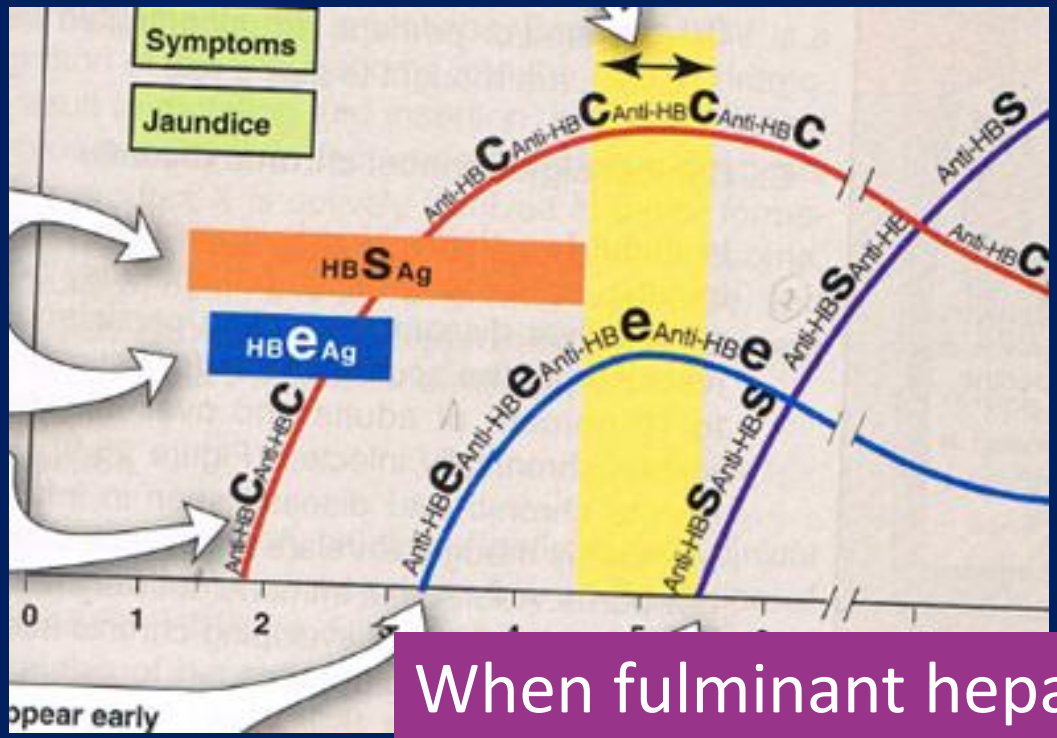
in the absence of post-exposure immunoprophylaxis

For perinatal exposure to a mother
HBsAg +and HBeAg+
a regimen combining HBIG and initiation of the HepB vaccine series at birth is 85%–95% effective in preventing HBV infection

HBIG - Hepatitis B immunoglobulin

Situations potentially subject to passive prophylaxis:

- Occupational exposure of medical staff
- Newborn from HBV carrier mothers
- Unknown serological status of patient undergoing invasive procedure (current HbsAg level)



When fulminant hepatitis occurs, the immune response to infected hepatocytes is overwhelming and there is often no evidence of viral replication.

<u>Testing for HBsAg may be negative;</u>

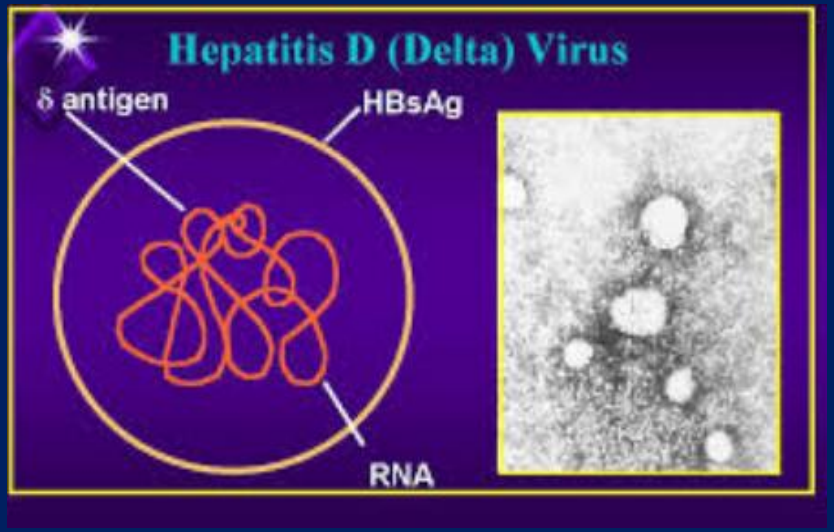
there is therefore a need for further anti-HBc (IgM) testing.

COINFECTIONs

HBV/HIV
HBV/HCV
HBV/Tuberculosis
&
HBV/HDV

Hepatitis D

- Hepatitis D is unclassified defective RNA virus (−) ssRNA
- Genome codes for 1 protein (delta antigen)
- is replicated and transcribed in the nucleus by cellular enzymes



- Presence of HDV results usually in more extensive and severe damage
- Higher risk to fatal fulminant hepatitis by the presence of HDV

Hepatitis D

2 major types of infection

co-infection - virus is acquired with HBV

5% of HBV-infected are also infected with HDV

superinfection -HDV infects only those persons who already have HBV infection

Prevention of HBV infection through vaccination also prevents HDV infection.

self-limiting if HBV is self-limiting HDV

Hepatitis C

- NANB = non-A, non-B hepatitis - the old name
- 6 genotypes, 2 of which have subtypes (1a and b; 2a and b)
- Incubation period: 6 -12 weeks
- Does not cause acute hepatic cellular necrosis

HCV does **not have reverse transcriptase** so unlike HBV, it is not able to integrate into the genome of hepatocytes

Poland – 200 tys.
Genotype 1 – 79%
Genotype 3 – 14%
Genotype 4 – 5%
Other genotypes - sporadic

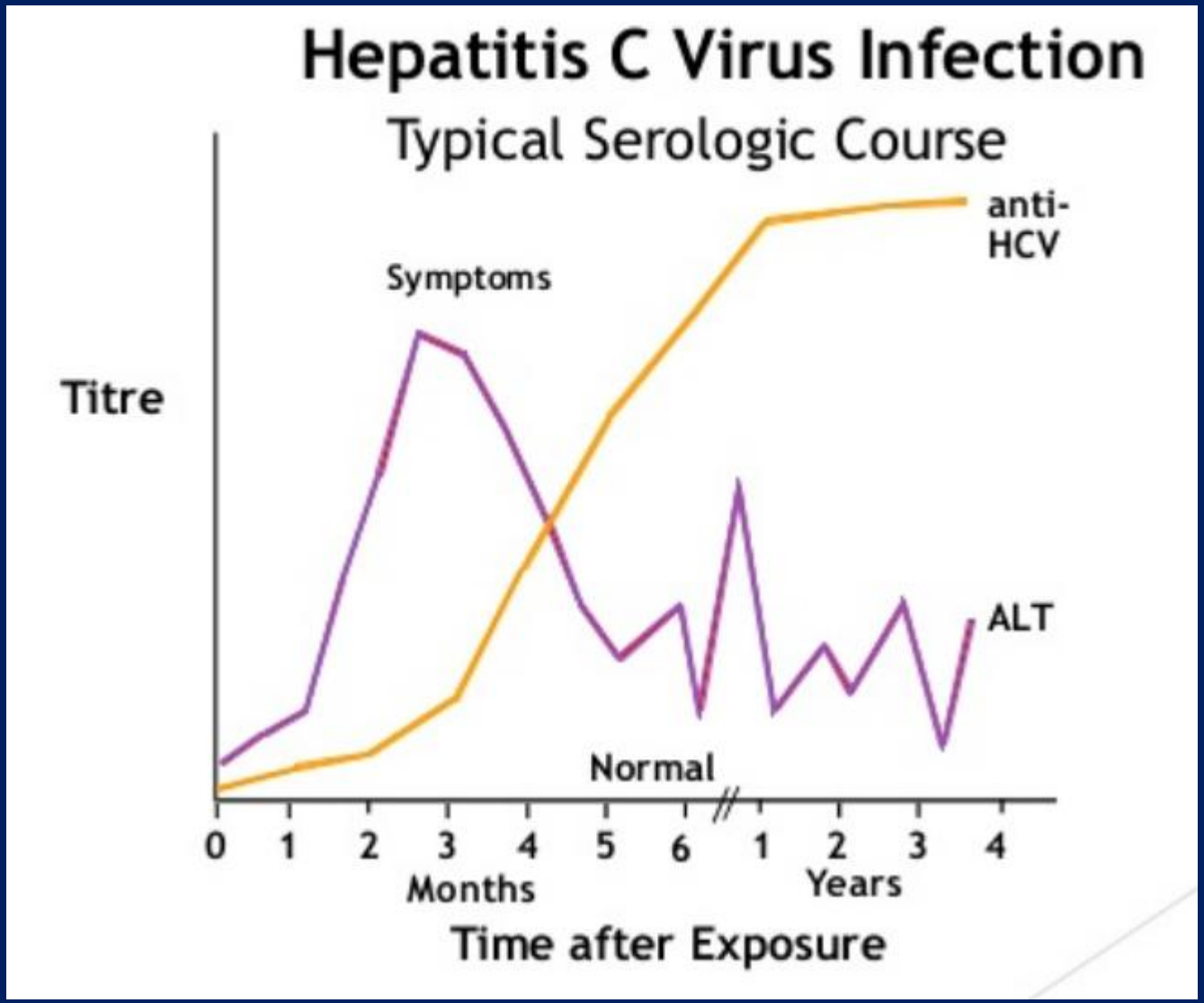
Due to the highly error prone RNA polymerase

HCV
displays remarkable
genetic diversity

propensity for
selection
of immune evasion

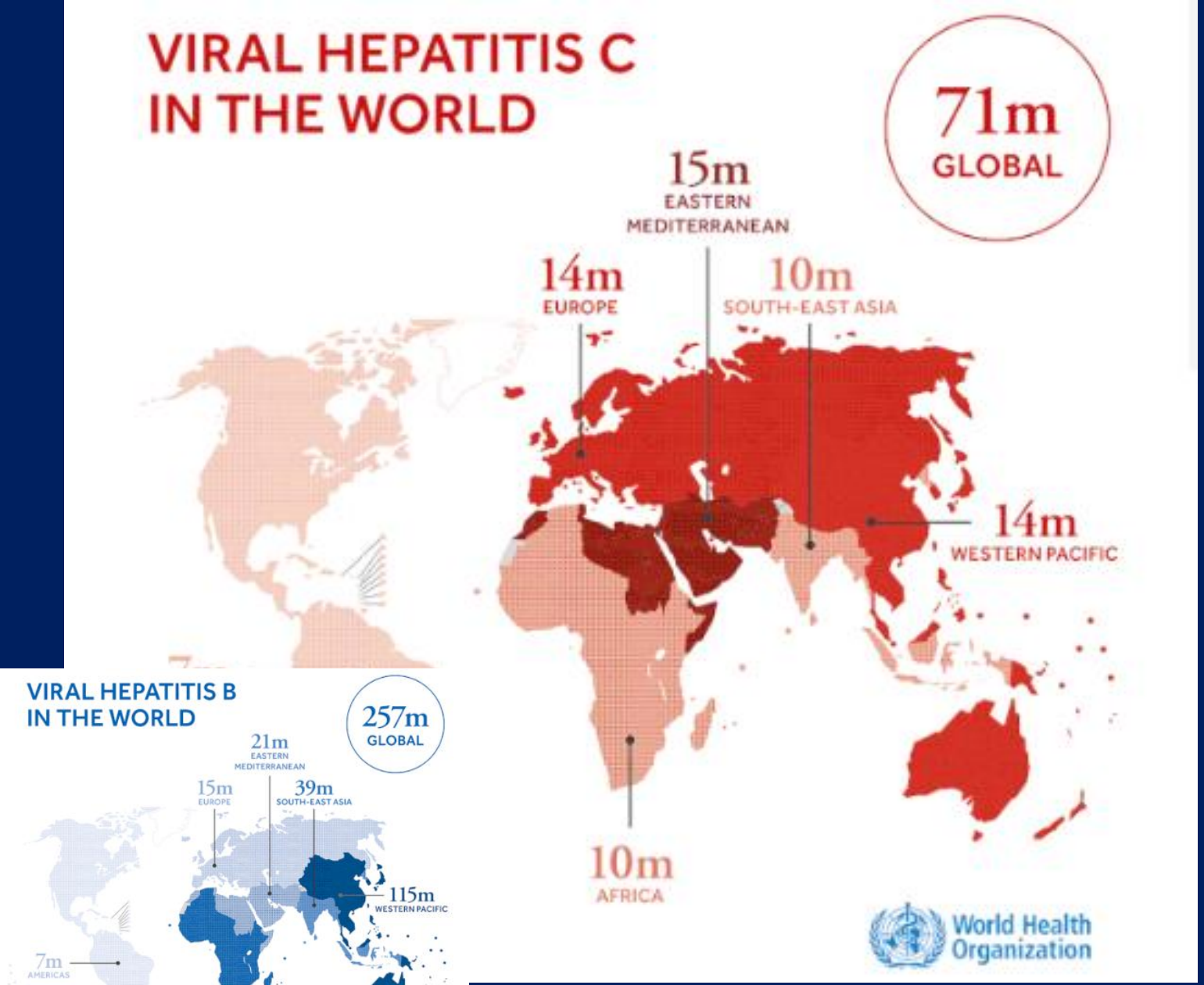
drug resistance
mutations

no prophylactic
vaccine



newe generations of antibody tests start be+approximately 4-8 weeks after the onset of infection

HCV RNA can be detected within 10-14 days after infection



data based on the presence of anti-HCV antibodies rather than HCV RNA

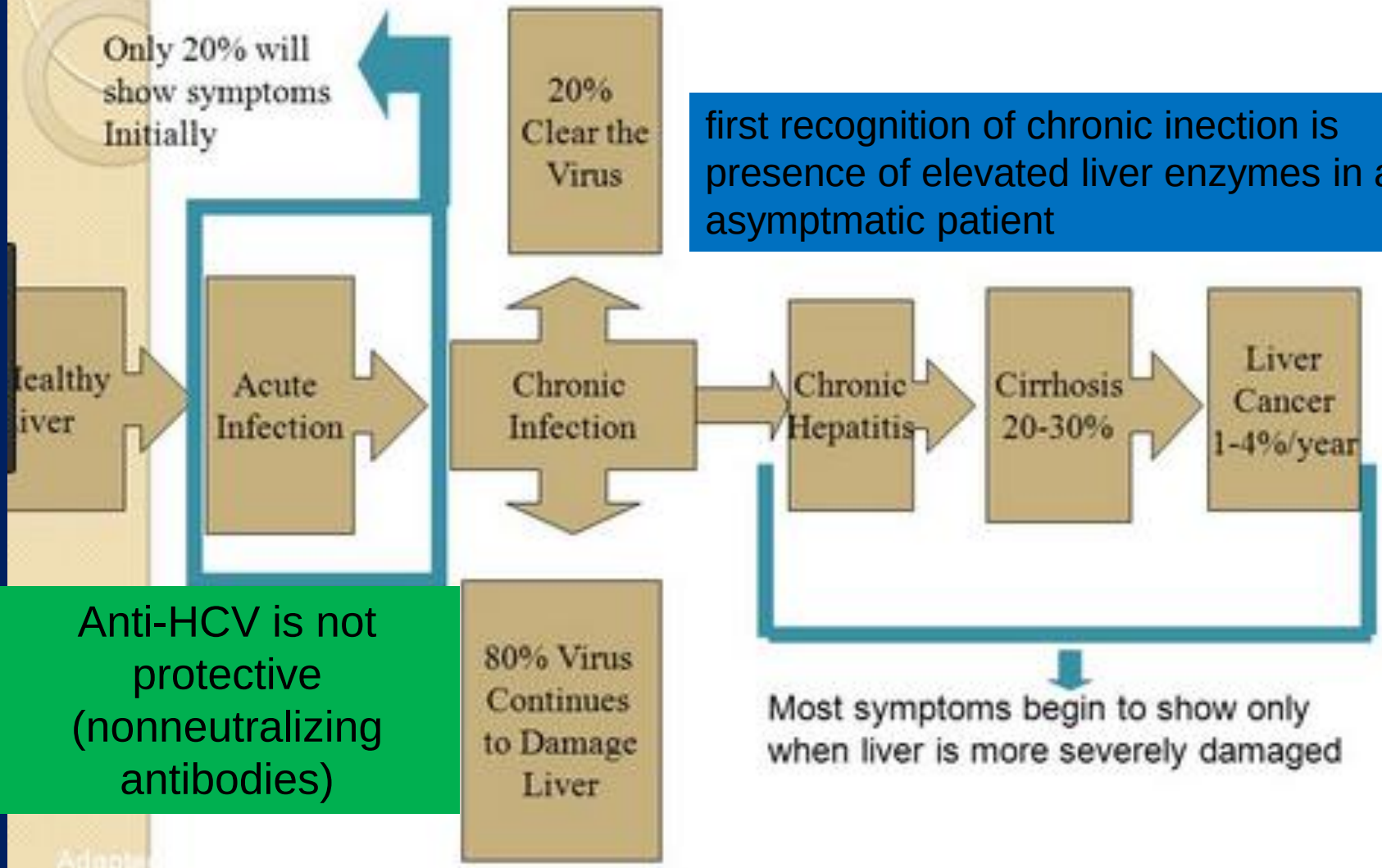
Table 1 Risks of hepatitis C virus

Persons	Risk of infection	Testing recommended?
• Drug users injecting with nonsterile or used needles	High	Yes
• Recipients of clotting factors made before 1987 (before heat inactivation)	High	Yes
• Hemodialysis patients	Intermediate	Yes
• Recipients of blood and/or solid organs before 1992	Intermediate	Yes
• People with undiagnosed liver problems	Intermediate	Yes
• Infants born to infected mothers	Intermediate	After age 12–18 months
• Health-care/public safety workers	Low/intermediate	Only after known exposure
• People having sex with multiple partners	Low	No
• People having sex with an infected steady partner	Even lower	No

According to CDC

HEPATITIS C has a worse diagnosis than HBV, since a high proportion of cases develo p cirrhosis (<33%)

Natural History of Hep C



first recognition of chronic inection is presence of elevated liver enzymes in an asymptmatic patient

Anti-HCV is not protective (nonneutralizing antibodies)

Extrahepatic Manifestations of chronic HCV Infection

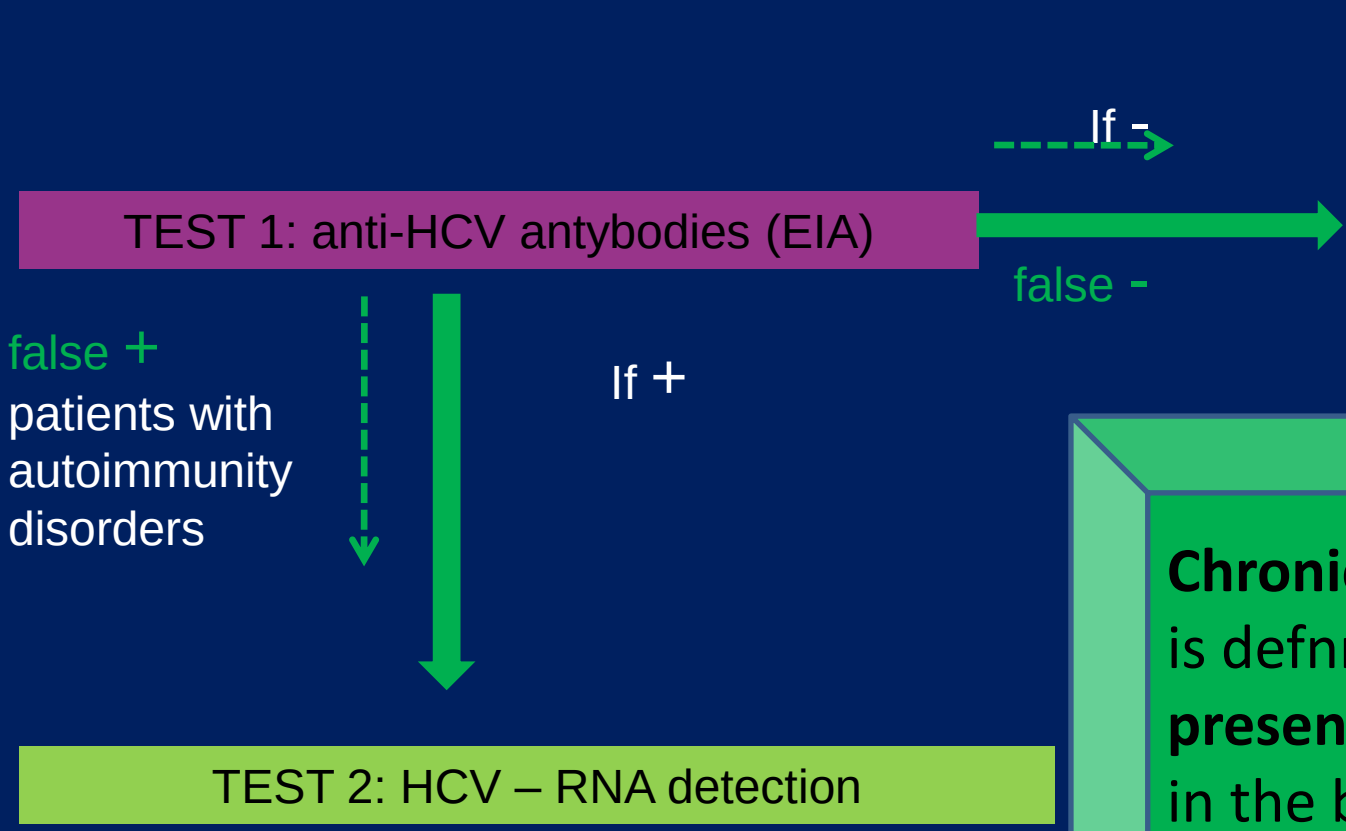
extrahepatic manifestations or syndromes considered to be of immunologic origin:

- rheumatoid symptoms
- keratoconjunctivitis sicca
- glomerulonephritis
- lymphoma
- cryoglobulinemia
- porphyria cutanea tarda

Psychological disorders including depression have been associated with HCV infection in up to 20 to 30 percent of cases.

HCV diagnosis

No antigenes in blood



Chronic HCV hepatitis is defnned as the **presence of HCV RNA** in the bloodstream for at least **6 months**

Since passive (transplacental) maternal antibody can persist for up to 18 months, the infants born to HCV-infected mothers should be screened by anti-HCV antibody at age 18 months postpartum

Chronic HCV hepatitis

- Assessment of the degree of liver damage (biopsy or non-invasive tests)

- Laboratory test to identyfy the genotype (different treatment)

- one person can be infected more than one genotype

HCV **Prevention**

There is no really effective passive or active immunization.

primary prevention interventions recommended by WHO:

- hand hygiene: including surgical hand preparation, hand washing and use of gloves;
- safe and appropriate use of health care injections;
- safe handling and disposal of sharps and waste;
- provision of comprehensive harm-reduction services to people who inject drugs including sterile injecting equipment;

testing of donated blood for hepatitis B and C (as well as HIV and syphilis);

- training of health personnel;
- promotion of correct and consistent use of condoms.

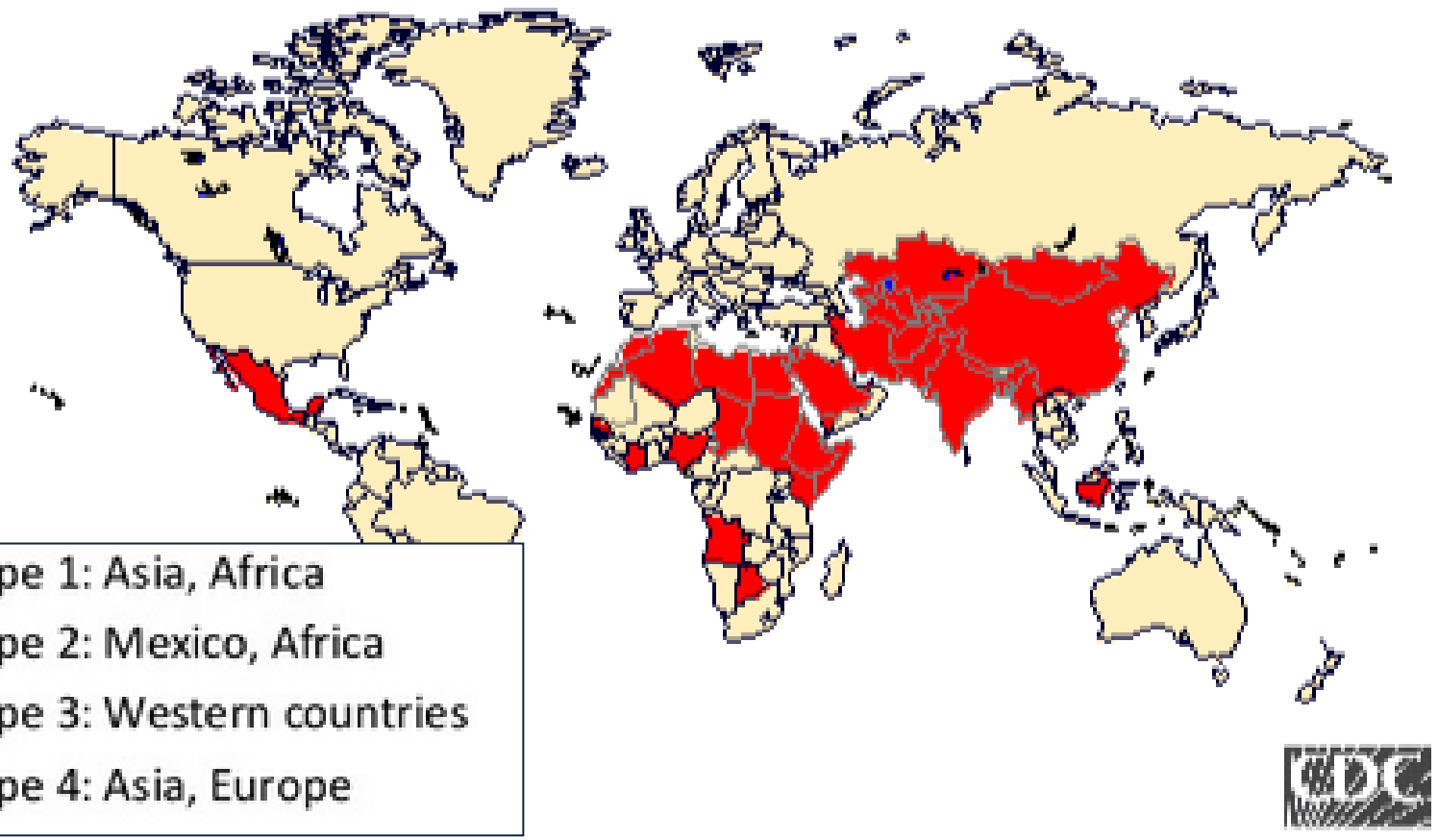
Hepatitis E

- self-limiting
- incubation period 15-60 days
- fecal-oral transmission; rarely by blood
- no chronicity
- at least 4 different genotypes :
  1 & 2 (only in humans),
  3 & 4 (zoonotic infections)

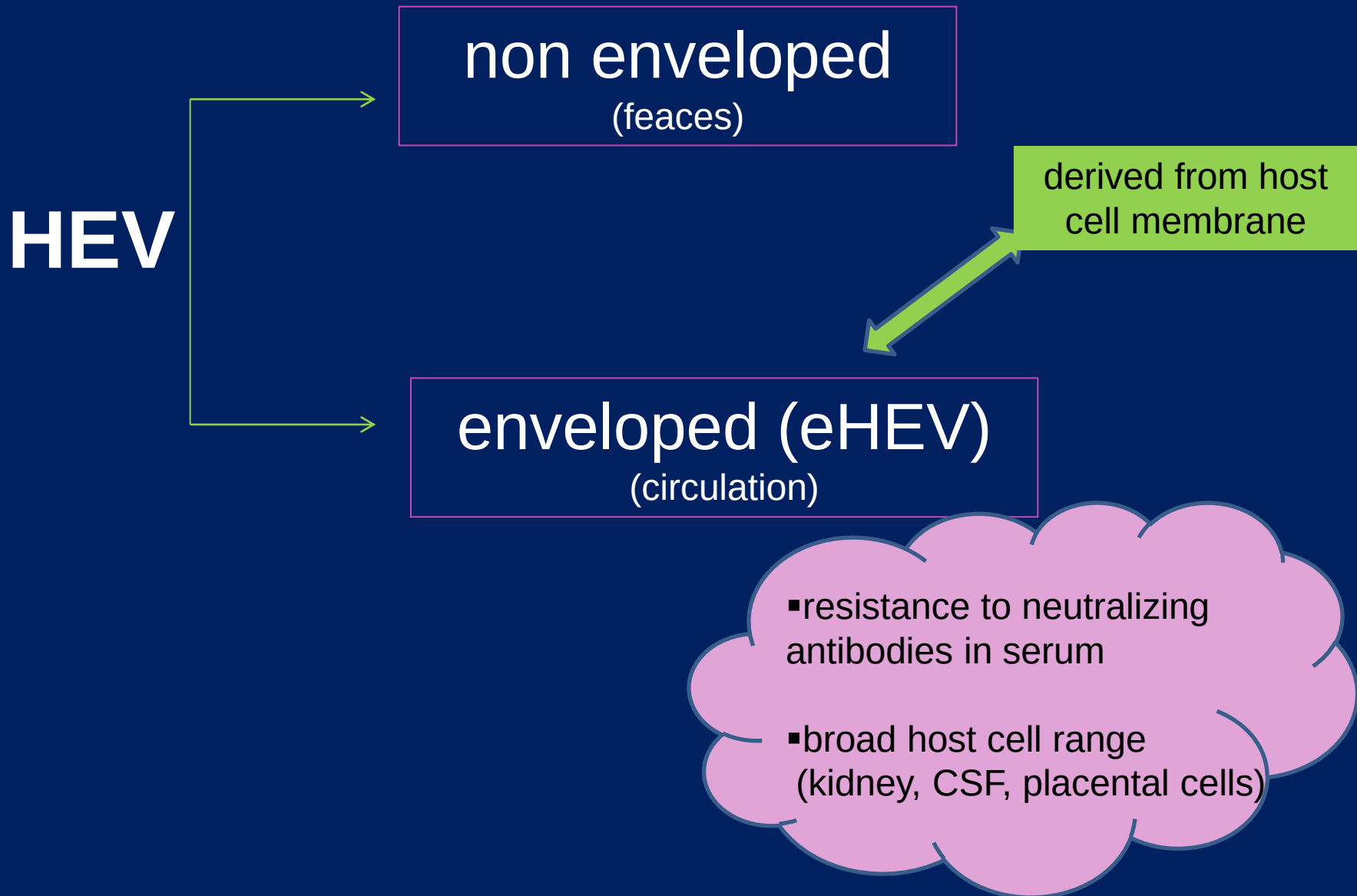
- The overall mortality rate is FHF is 1–3%;

BUT in pregnant women the rate is 15–25%

Hepatitis E



- Genotype 1: Asia, Africa
- Genotype 2: Mexico, Africa
- Genotype 3: Western countries
- Genotype 4: Asia, Europe


HEV
non enveloped
(feaces)
derived from host cell membrane
enveloped (eHEV)
(circulation)
▪resistance to neutralizing antibodies in serum
▪broad host cell range (kidney, CSF, placental cells)

HEV diagnosis

- IgM response to HEV infection is detectable at the onset of symptoms, followed shortly by anti-HEV IgG

- real-time RT-PCR assays to detect HEV RNA; however, the window of detectable viremia is narrow

- Treatment – no available

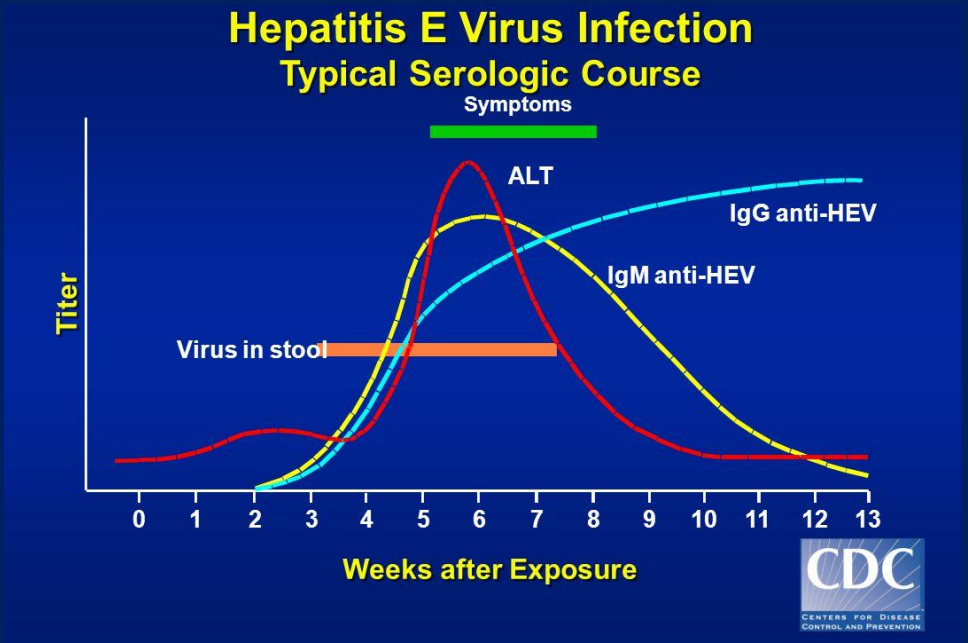
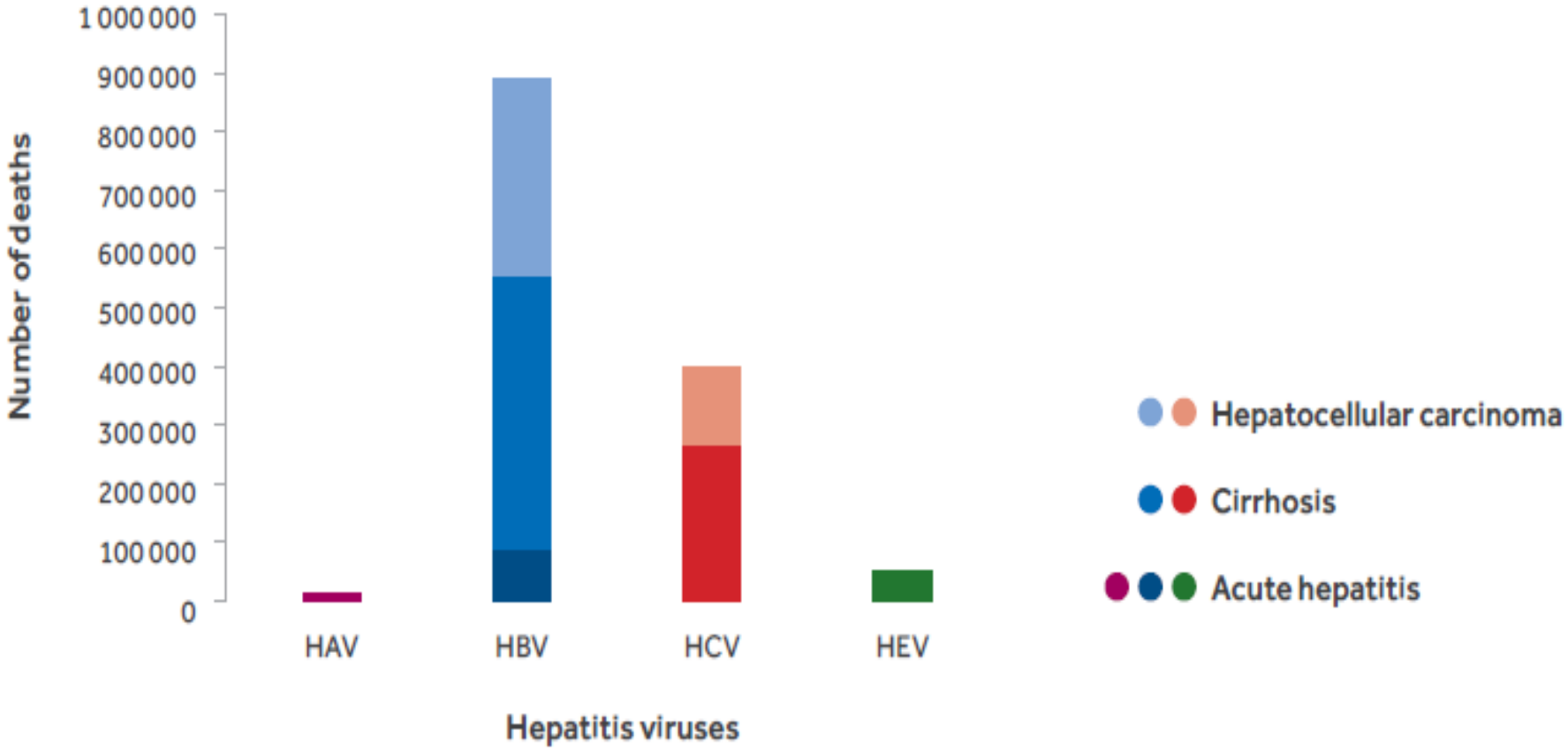
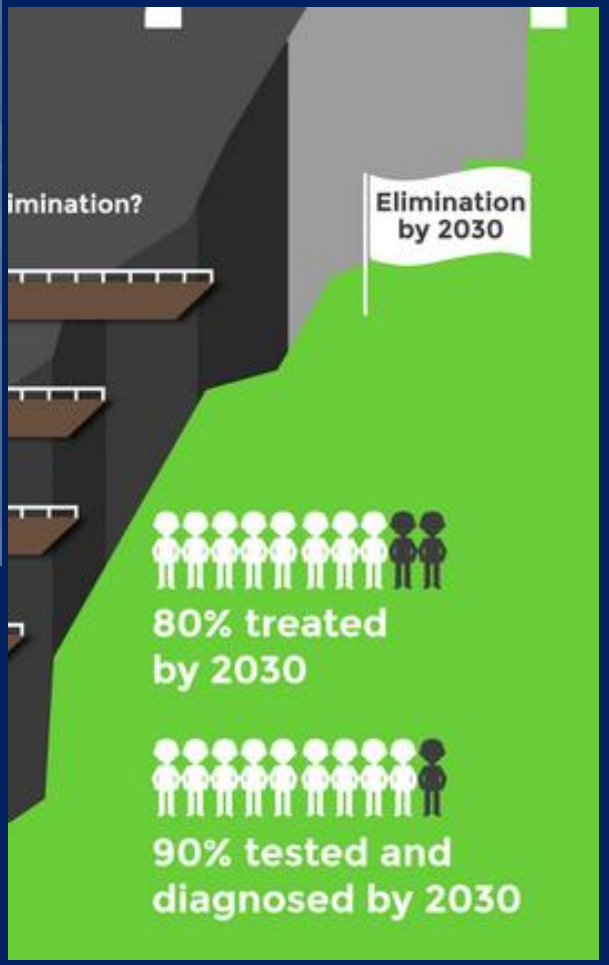


Fig. 1. Deaths from viral hepatitis, by virus and type of sequelae, 2015:
most viral hepatitis deaths are due to the late complications of HBV and HCV infection



viral hepatitis led to 1.34 million deaths


2030


imination?
Elimination by 2030
80% treated by 2030
90% tested and diagnosed by 2030

Answer questions

The risk for chronic HBV infection varies according to the age at infection and is greatest among……

Perinetal transmission rates of HBV is the highest in case of mathers with serum immunological status……

Hepatitis viruses that are transmitted primarily by the faecal-oral route are ..... and ..... They are both ……. (non/enveloped) ……. (DNA/RNA) viruses.

Knowledge of the hepatitis virus genotype is particularly important in the treatment of hepatitis type ……...

HDV hepatitis can be prevented by..... because.....

HEV infection can cause fulminant hepatitis failure, especially in pregnant women, with a mortality rate of up to …… Acute liver failure, also known as fulminant hepatic failure is ……..


Thank you!