Viral hepatitises (VH)

Group of clinical similar viral diseases of the man with the peroral or parenteral modes of infection described by a preferred damage of hepatocytes and by toxic manifestations

Nowadays the following the agents of VH are known :

- **Hepatitis A virus (HAV) – cause of viral hepatitis A (VHA)**
- **Hepatitis E virus (HEV) - cause of viral hepatitis E (VHE)**
- **Hepatitis B virus (HBV) - cause of viral hepatitis B (VHB)**
- **Hepatitis C virus (HCV) - cause of viral hepatitis C (VHC)**
- **Hepatitis D virus (HDV) - cause of viral hepatitis D (VHD)**

There are in a stage of stading are following hepatitises:

- **Hepatitis F virus (HFV) - cause of viral hepatitis F (VHF)**
- **Hepatitis G virus (HGV) - cause of viral hepatitis G (VHG)**
- **Hepatitis TT virus (TTV) - cause of viral hepatitis TT (VHTT)**
- **Hepatitis SEN virus (SENV) –cause of viral hepatitis SEN**

All viral hepatitises are divided into 2 groups on the modes of transmission

1-st group - with peroral infection - (A, E)

2-nd group-with parenteral infection (B, C, D, F, G, TTV, SEN)

PATHOGENY:

at all viral hepatitises is observed virusemia with the subsequent damage of hepatocytes and development of the following syndromes:

- 1. Syndrome of an intoxication (exogenic and endogenic)
  2. Cytolitic syndrome
- 3. Syndrome of a cholestasia:
- 4. Syndrome hepato-cellular of unsufficiency:
- 5. Syndrome of an inflammation:

1. Syndrome of an intoxication (exogenic and endogenic)

The exogenous intoxication – it is caused of viremia and appears by the following variants:

- influenza-similar variant: - fever, cephalic and muscular pain by duration 5 - 7 days, but without catarrh and hypersecretion mucous of respiratory tract

- **arthralgia variant: - ostealgia or arthralgia often in evening time without limitation then function , sometimes with the phenomena of reactive arthritis**

- **dyspeptic variant: - nausea, vomiting, anorexia, perverted taste**

- **astheno-vegetative variant - weaknees, hypotonia, tachycardia, mental depression**

- **mixed variant (most often) - combined of the several variants is simultaneously !**

The endogenic intoxication - occurs as a result of violation of the desintoxication liver function with intensifying in accordance with weighting a state person

2 Cytolitic syndrome - signs of lesion hepatocytes, what are accompanied by rise activity of the following enzymes:

Indicator enzymes:

- **ALT (alanine-aminotransferase)- increase from tenfold to fifteenfold time.**
- **AST (aspartine-aminotransferase)**
- **LDG (lactat-dehydrogenase and its isoenzymes)**

Specific hepatic enzymes:

- **fructose-1-phosphataldolase**
- **Sorbitum - dehydrogenase**
- **Ornithine - carbamiltrasferase and other aldolases**

Organello-specific enzymes: (in mitochondrions of hepatocytes):

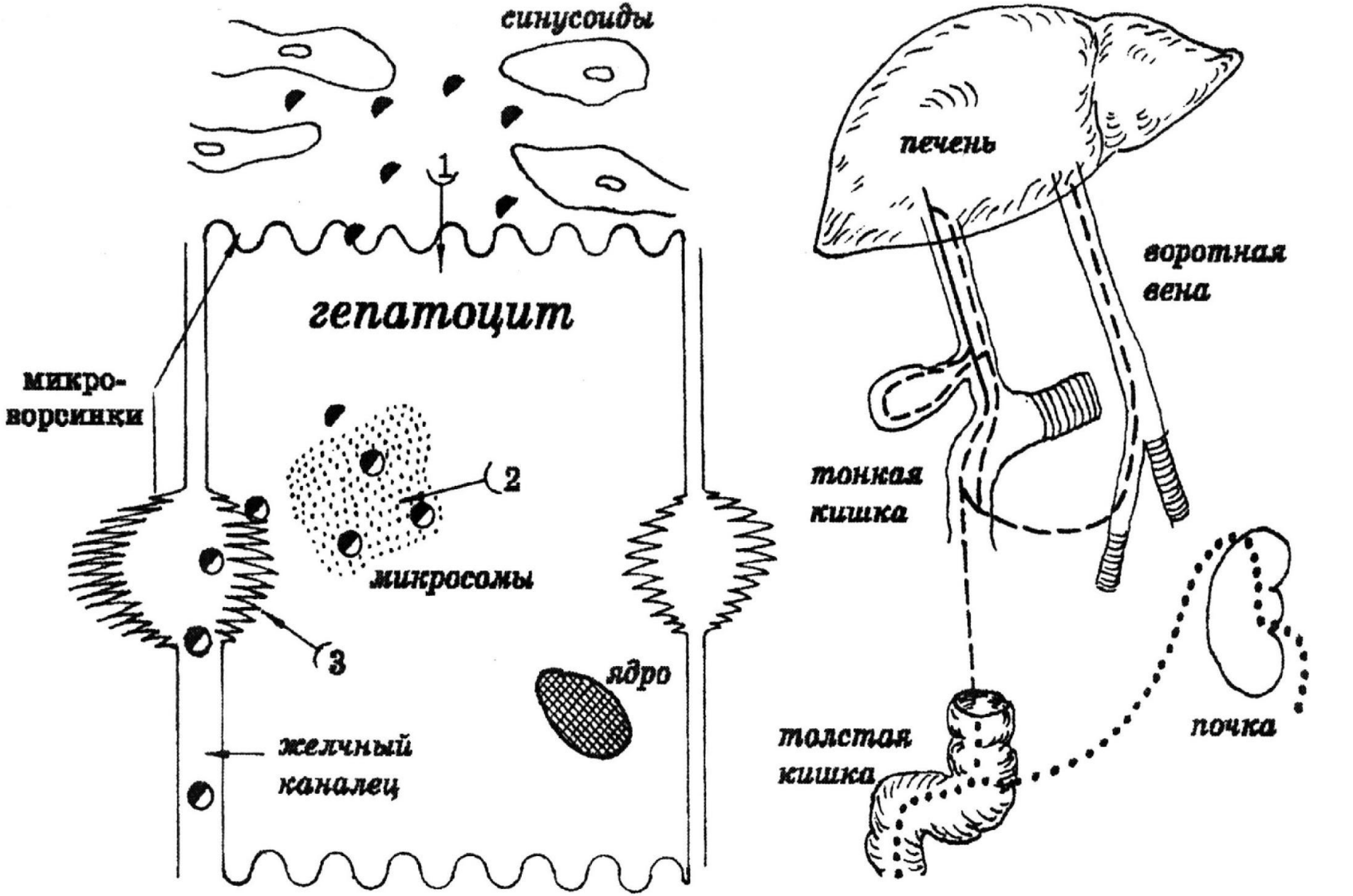
- **glutamat-dehydrogenase**
- **succinat-dehydrogenase**
- **hyperbilirubinemia**
- **increase of concentration in a blood of cyancobalamine**

3. Syndrome of a cholestasia:

- increase excretory of enzymes (alkaline phospha-tases, leucyn-aminopeptidase, 5 – nucleo-peptidase, gamma –glutamiltranspeptidase)
- increase of phospholipids
- increase in a blood of cholic acids

4. Syndrome hepato-cellular of unsufficiency:

- lowering activity of a cholinesterase
- lowering a thrombinogen
- the decrease of proteins (especial of albuminum)
- lowering 2,5,7 factors of coagulating blood
- lowering a cholesterin of blood
- increase in blood indirect bilirubin



Билирубин свободный ◤ , связанный ◐ . Уробилиногены ---- . Стеркобилиноген •••• .
Фазы: захвата (1), конъюгации (2), экскреции (3).

Рис. 1. Основные этапы обмена билирубина

5 . Syndrome of an inflammation:

- increase in plasma Ig G, M, A

- change of albumino-sedimental tests (increase thymol test)

- the appearance in a blood of antibodies to DNA, smooth-muscular to fibers, mitochondrions and microsomas

- change of a leukopenia on neutrophia

The expressiveness of these syndromes is individual and depends both on sort of a virus, and from protective responses of an organism:

Viral hepatitis may proceed as:

Acute cyclic form of disease arise at sufficient **xenogenic** of **virus** and at expressed **the interferon answer** of an organism

Carriage or chronic hepatitis form at **low** paphogenic and antigenic **xenogenic of a virus**, inefficiency cellular and humoral immunity, **defective** of the system **interferon** of an organism (**low interferon the answer)**

Fulminant forms of hepatitises arise at **sufficient xenogenic** of a virus, **low interferon the answer** on a background **generically determine hypersesitivity** response of an organism

PATHOMORPHOLOGY

- at all hepatitises to change in liver, practically, identical and at research hepatobiopsy (percutaneus hepatic aspiration or at autopsy) reveal the following changes:

- dilatation of portal pathes and inflammatory infiltrates in them consisting from lymphocytes, macrophages, plasma cells, eosinophiles and neutrophils

- damage of an internal boundary slice

- proliferation of an epithelium cholic ducts, at causing to a stasis bile in them

- fatty a dystrophia of hepatocytes and their destruction. Sometimes it so considerable, that in a lesion zone preserves only reticular frame of a liver

- is simultaneously observed regeneration as mitosises, both particular cell and whole groups

- also the centers of a fibrosis is revealed

The morphology of a liver after clinical recovery is normalized not earlier than 3 months - histological changes of a liver in this period are conformed for clinic of a chronic hepatitis

CLASSIFICATION of VIRAL HEPATITIS

1. On an etiology (A,B,C Д, E, TT, SEN, G, F etc.)

2.On duration of current:
- Acute - about 3 of months
- Lingering - up to 6 of months
- Chronic - more 6 of months

3. On an expressiveness of clinical manifestations:
- Asymptomatic (carriage of virus and subclinical of the forms of disease)
- Demonstrative - (icteric and anicteric)

4. On current:
- Cyclic
- Acyclic (with peakings and relapses)

5. On a dominating syndrome:

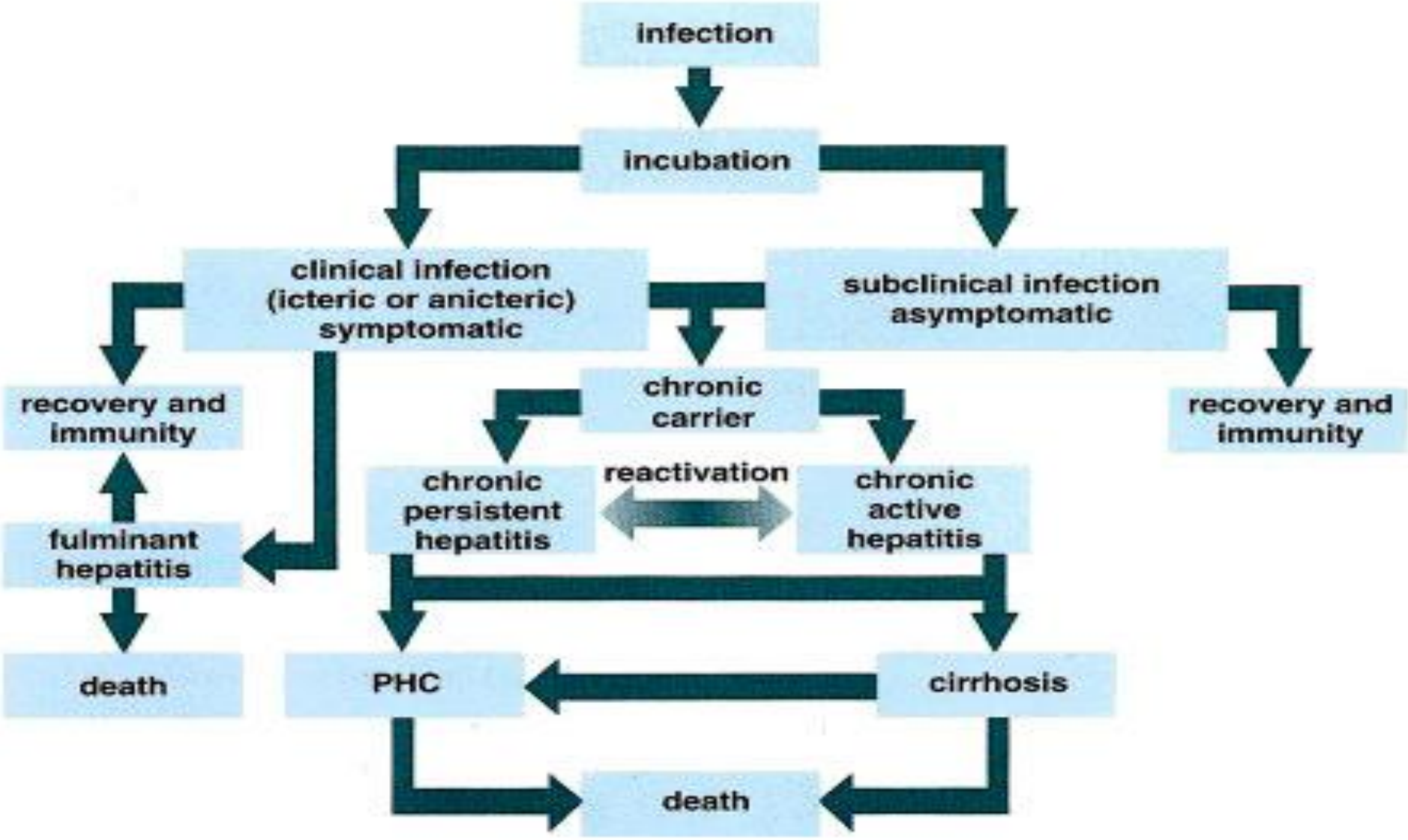
- cytolitic the forms
- cholestatic the forms (30 %)
- cholestatic the forms (1 %)

6. On a degree of clinical gravity and hyperbilirubinemia:

- mild (up to 80 - 100 mCml/l)
- moderate (up to 160 - 200 mCml/l)
- severe (more than 160 - 200 mCml/l)
- fulminant form - (early and late)

The example of the diagnosis: an acute viral hepatitis A, anti-HAV Ig M (+), mild icteric form - (common bilirubin is 65 mCml/l) cyclic current with predominance a cytolysis (ALT - 7 mMm/h/l)

Common pathogeny of viral hepatitis



Possible outcomes of HBV infection

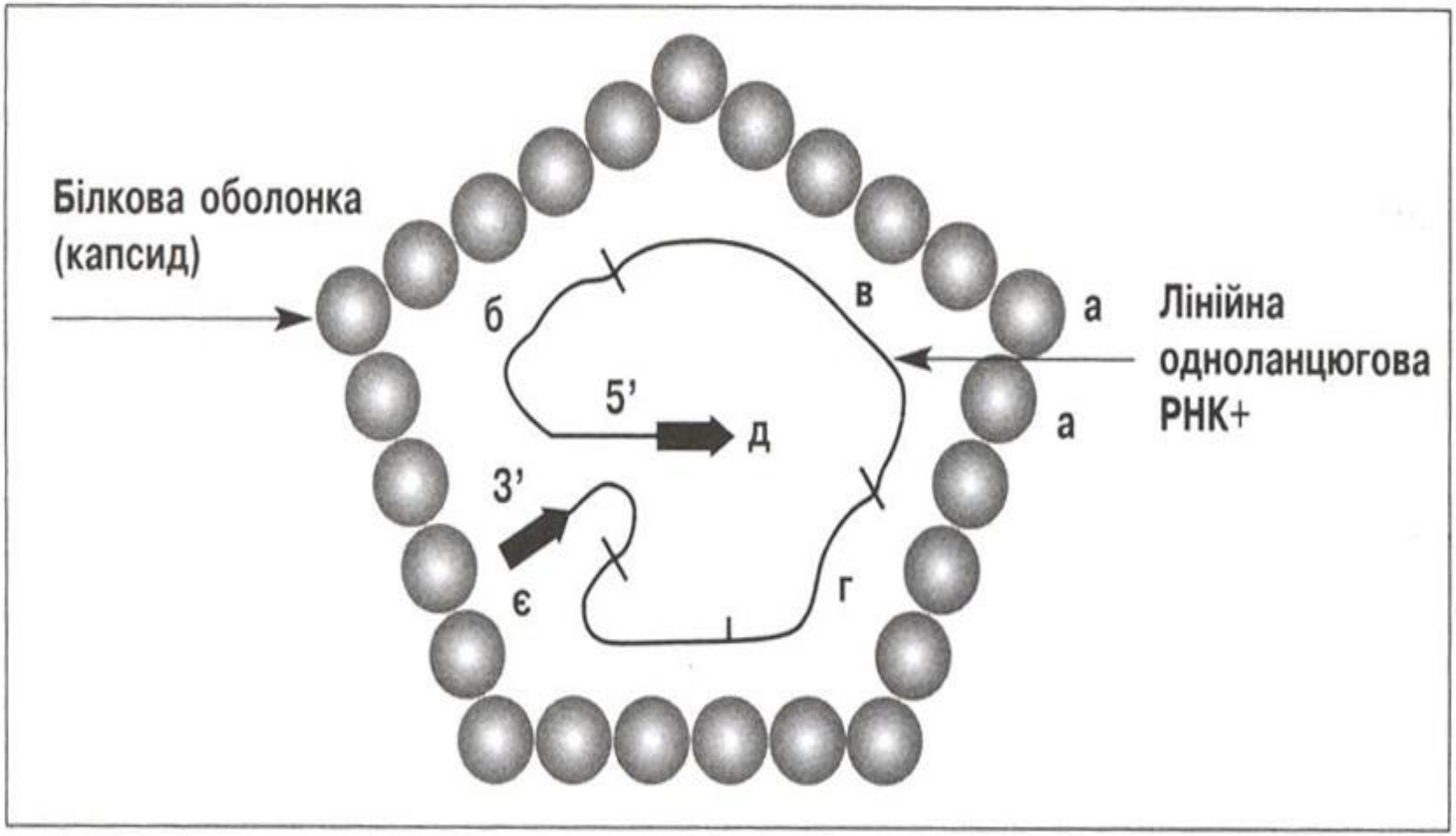
VIRAL HEPATITIS A (VHA)

ETIOLOGY: Shallow inenvelope a virus by a size 27 - 30 nm. S. Picornaviridae, R.Hepatovirus contains one-filamentous RNA (+)

Virus is opened in 1973 year. Virus has 1 serotype and 7 genotypes.

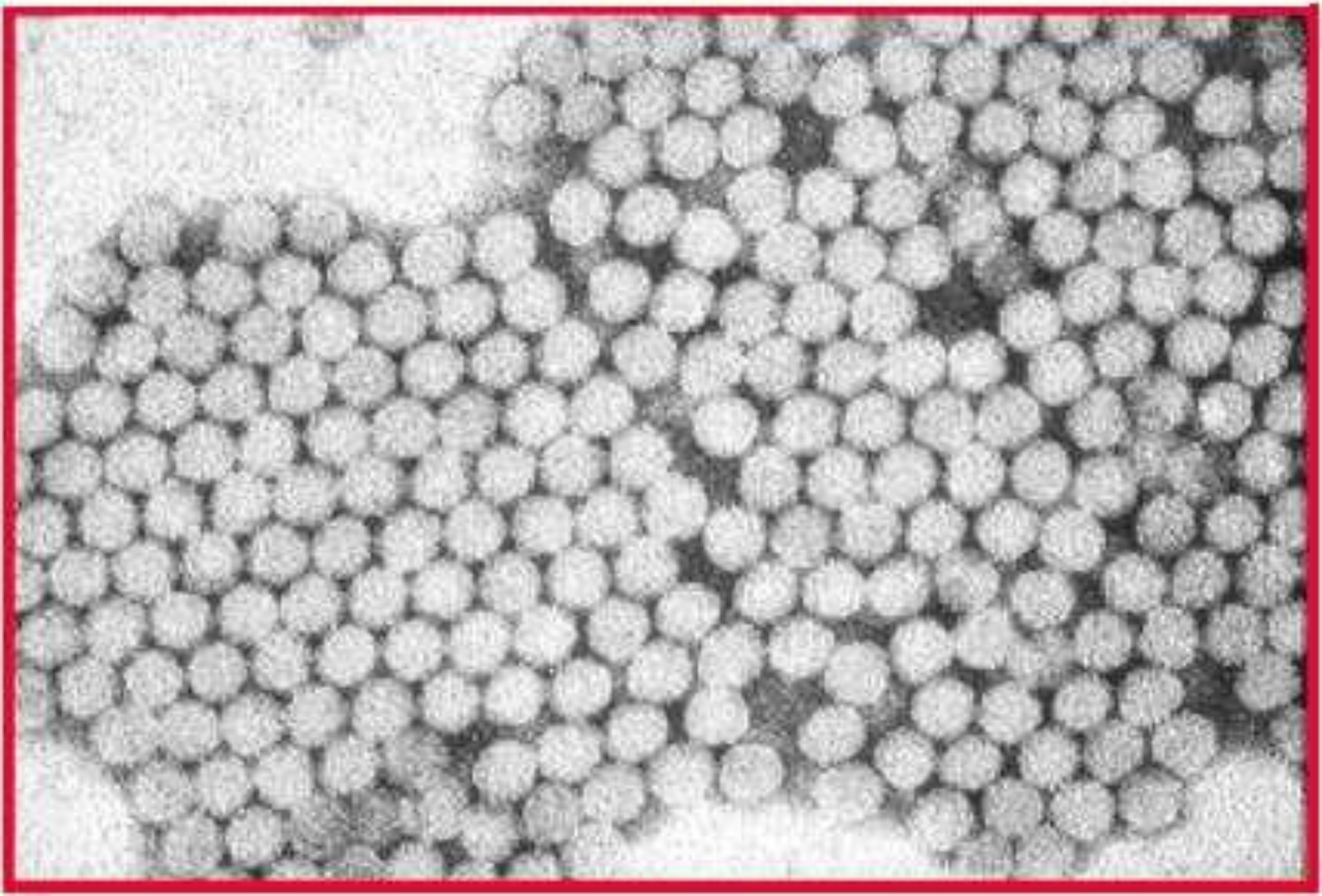
Virus is well survives in the environment:

- at 20 гр.С - 1 month
- at 4 гр.С - some years
- pH of a stomach from 3 up to 10 not influence a survival virus!!!
- at pH is lower 3 - survives till 4 hours
- at 60dg. C - maintains 12 hours
- at 100 гр.С - perishes instantly
- desinfectants inactivate its for 15 minutes
- is steady to alcohol



Малюнок 2. Схематичне зображення HAV.

Hepatitis A Virus



EPIDEMIOLOGY- it is antroponosis

The sourse - the patient with any form Illnesses (obvious or erased)

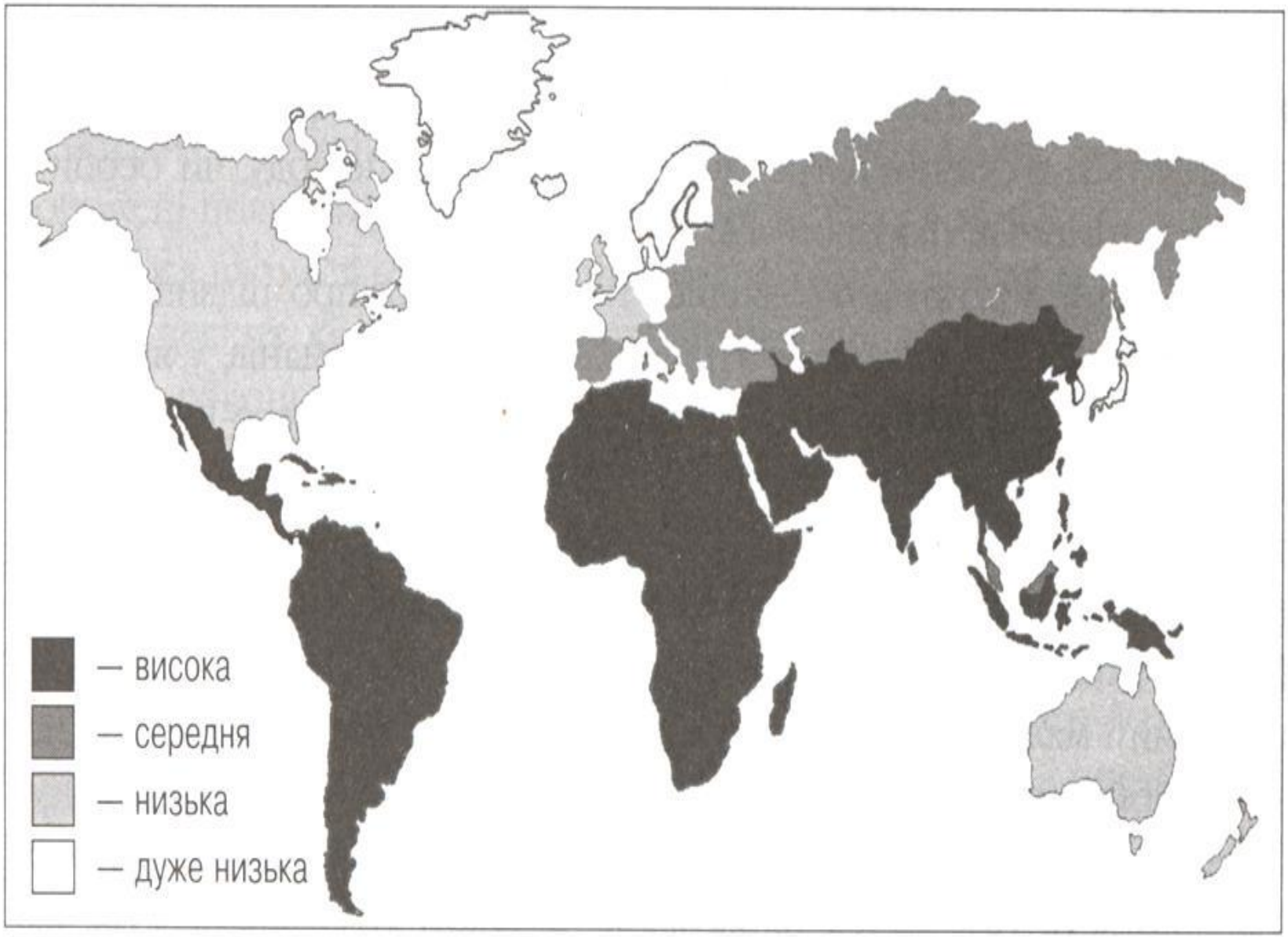
The mode of transmission - faeco-oral

The factors of transmission:

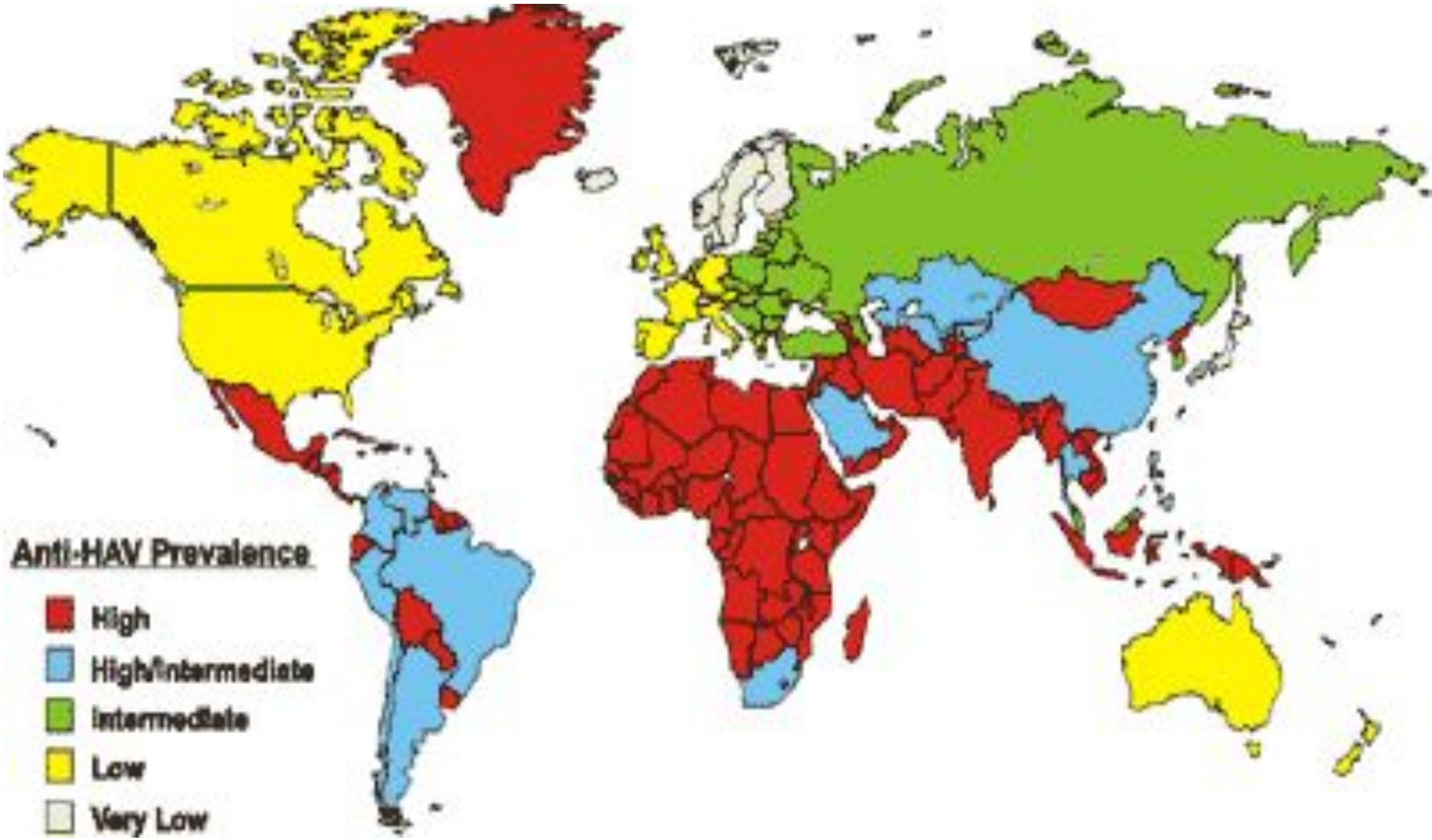
- **personal contact to the patient or polluted him by subjects (do not have seasonal prevalence!!!)**
- **polluted nutrition and water (as flashouts)**
- **is possible percutaneus (seldom)**

Susceptibility general!! More often children are sick after 1 year of life.

By 40 years up to 80 -90 % of the people transfer a hepatitis A (In their blood is taped anti-HAV Ig G)



Розповсюдження ГА у світі


Anti-HAV Prevalence
High
High/Intermediate
Intermediate
Low
Very Low

CLINIC:

- **Incubation** 15 - 50 days (30 days)
- **Prodromal stage** - 1 - 2 weeks
- **Appearance of an icterus** for 70 - 80 % **hospitalized** of the patients

- **The asymptomatic forms** - 10 - 25 % of the adults

- **Complications:**

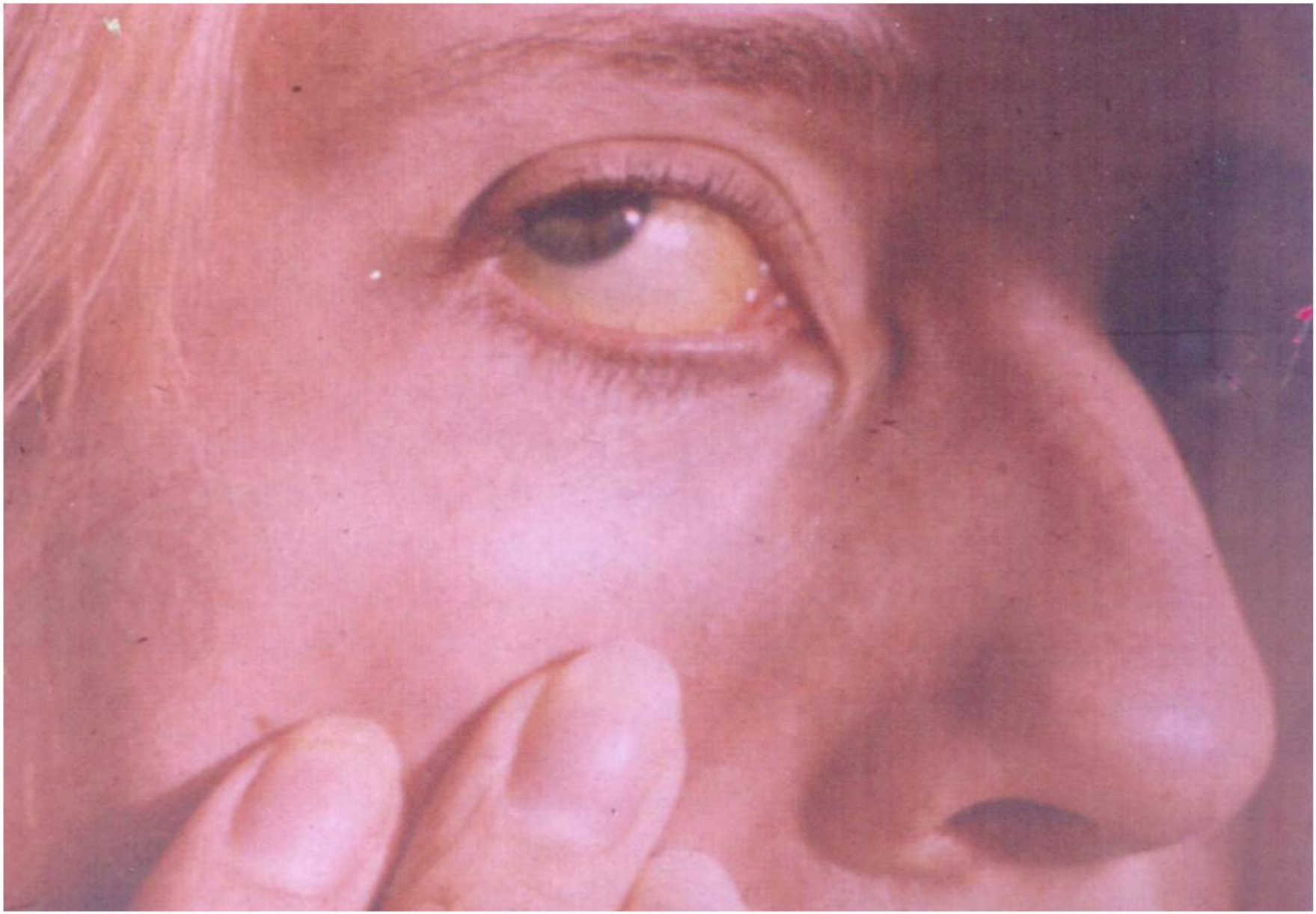
- fulminant current - 0,04 - 0,4 %
- lingering current (2 - 3 months) - less than 10 %
- relapses - 6 - 10 %

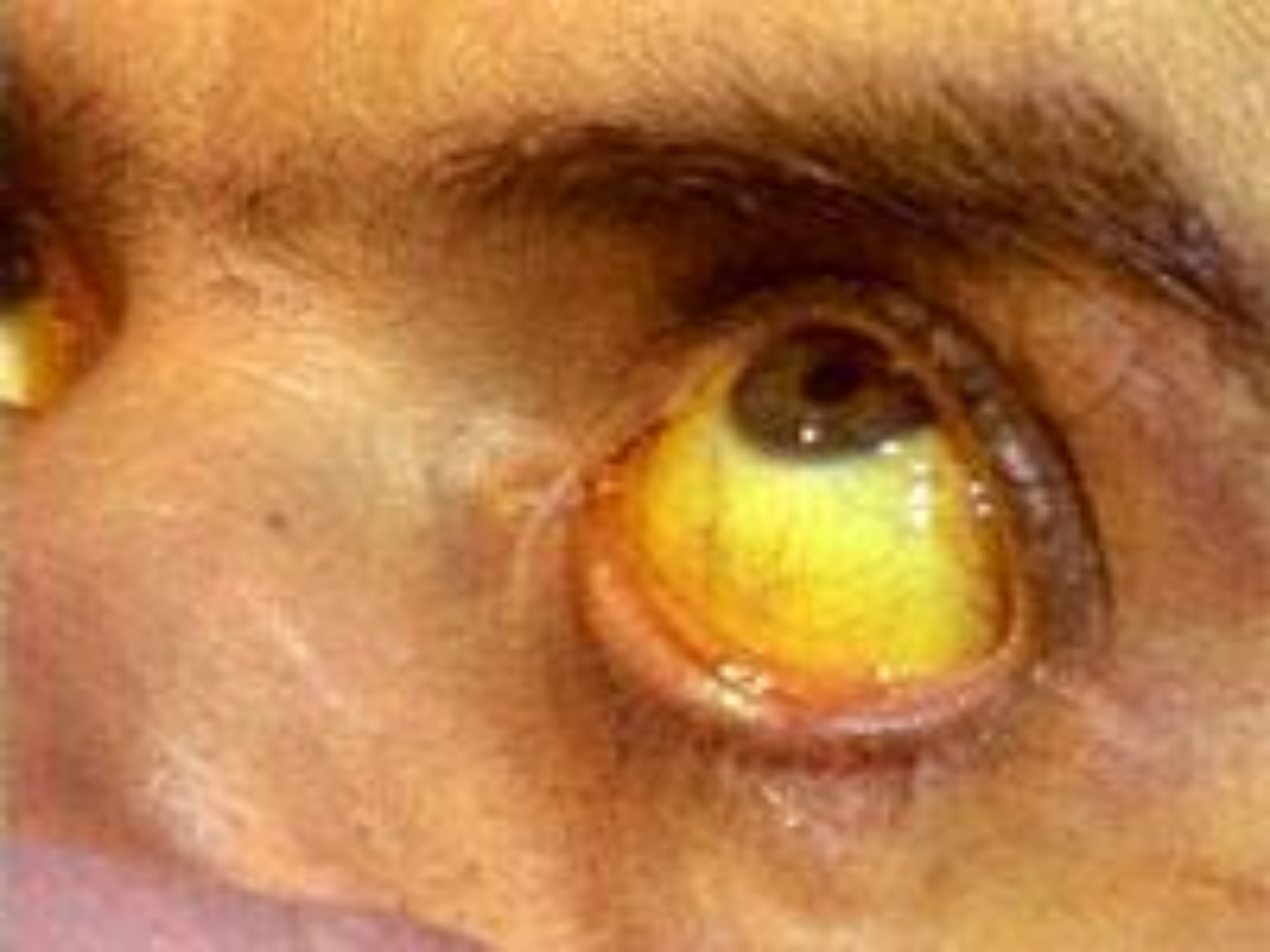
The chronic current - **is not described!!!**

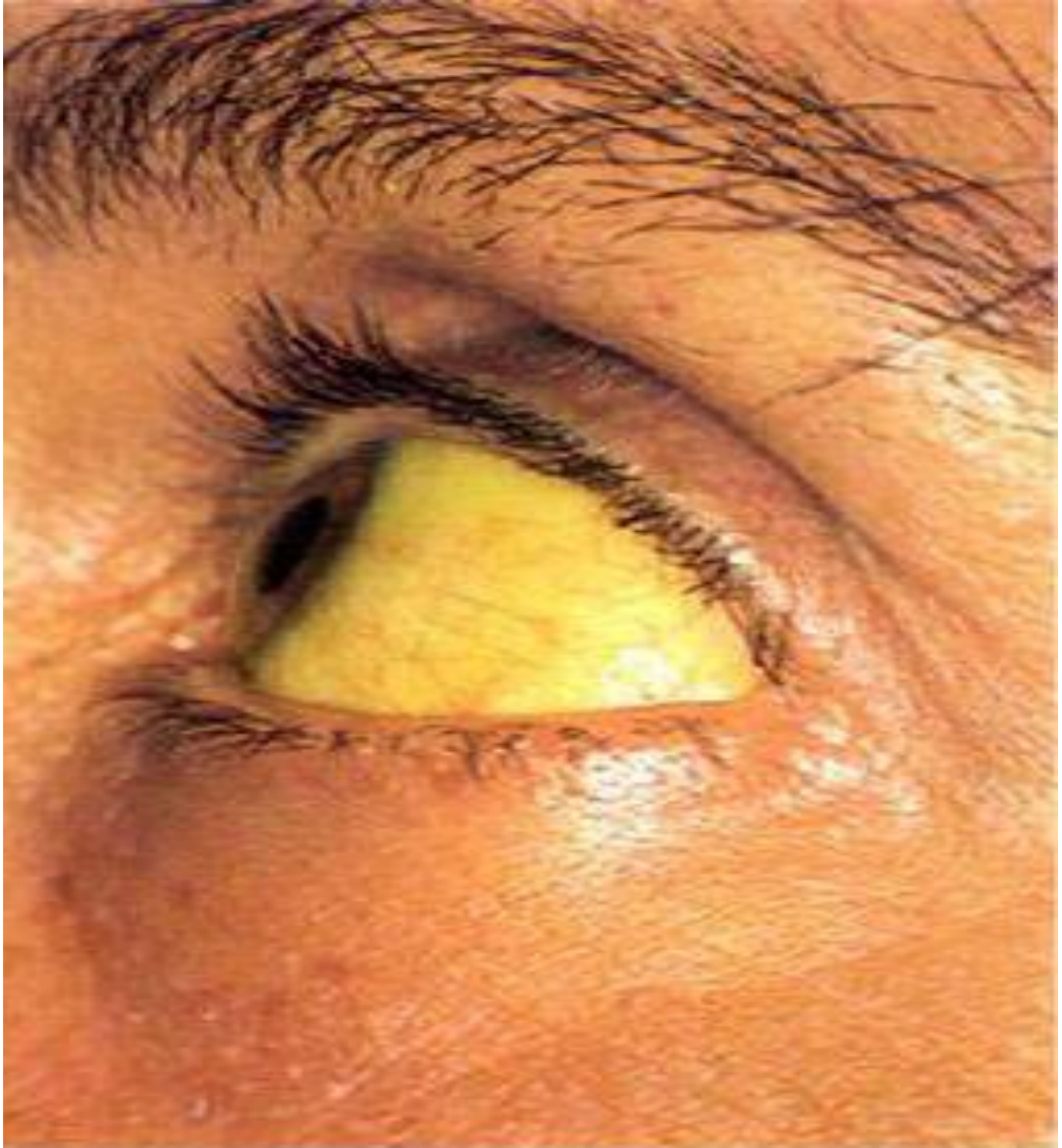
Lethality - 0,02 - 1,5 %

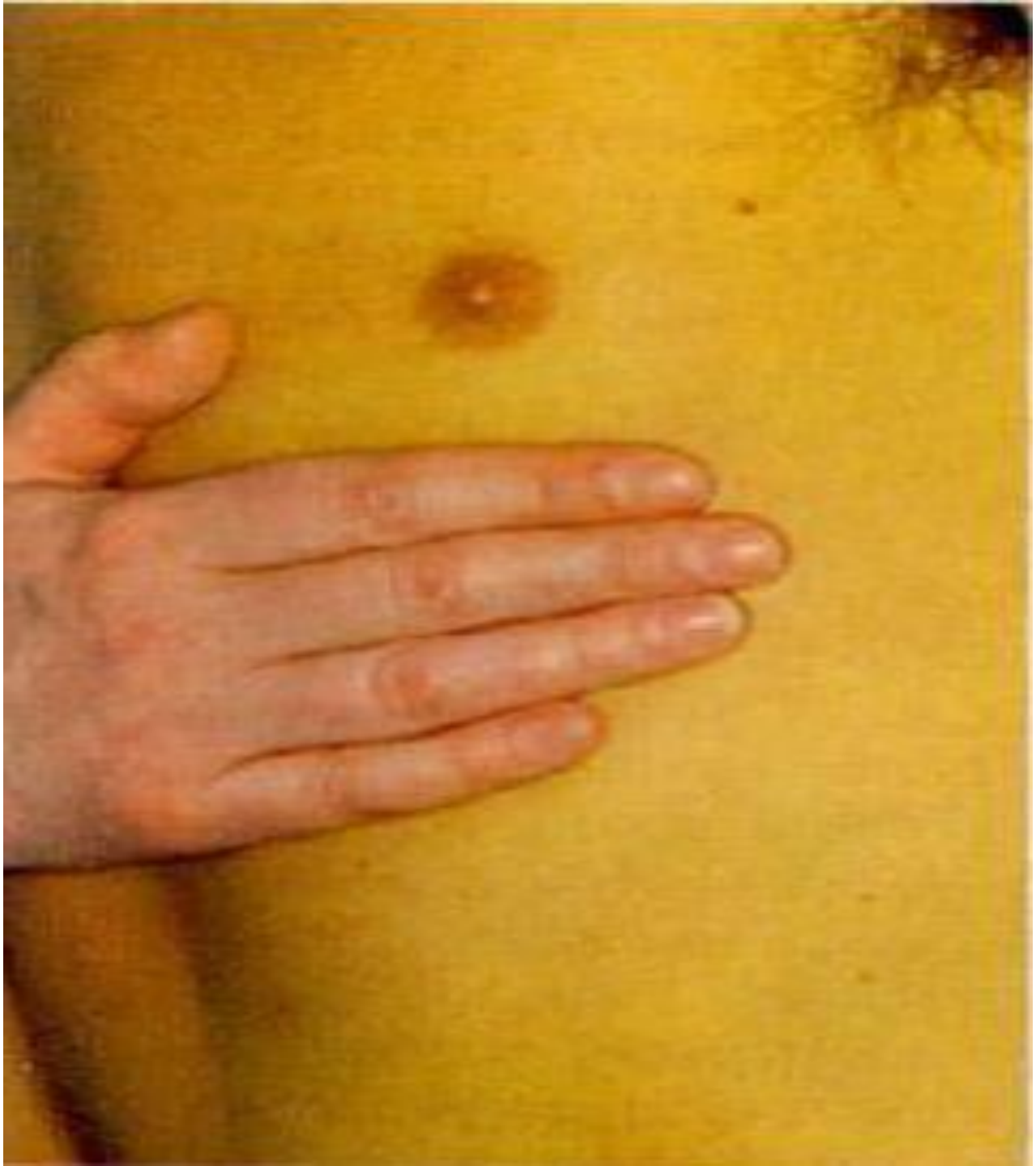
FREQUENCY of SIGNS VHA in %:

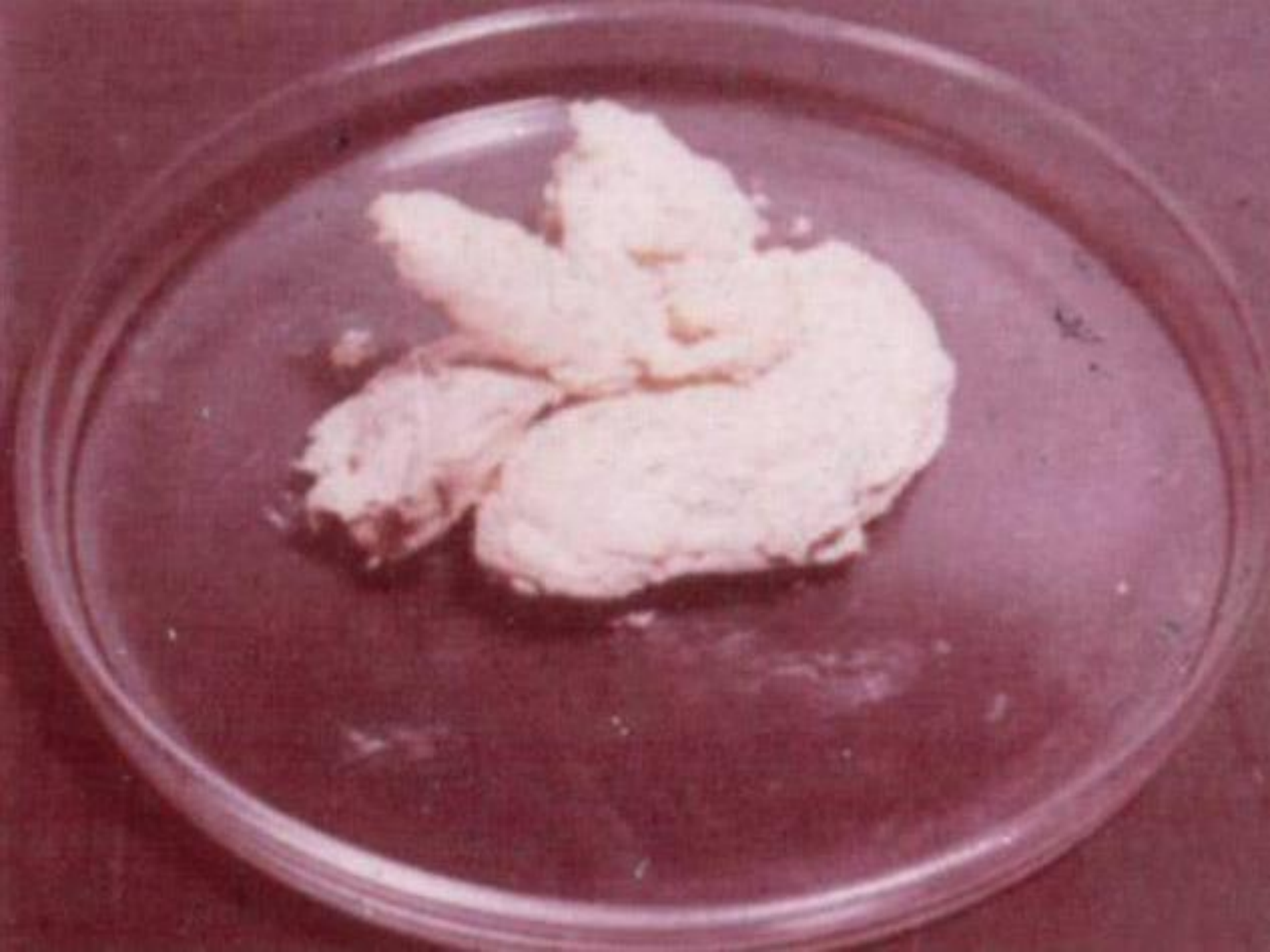
	Children	adults
• Nausea, vomiting	65	26
• Yellowness of white of the eyes	65	88
• Yellowness of a skin	65	88
• Diarrhea	58	18
• Dark urine	58	68
• Decolorized feces	58	58
• Pain in epigastriums	48	37
• Weakness	48	63
• Fever, chill	41	32
• Anorexia	41	42
• Pain in muscles, joints	6	30
• Headache	-	17
• Pharyngitis	6	-









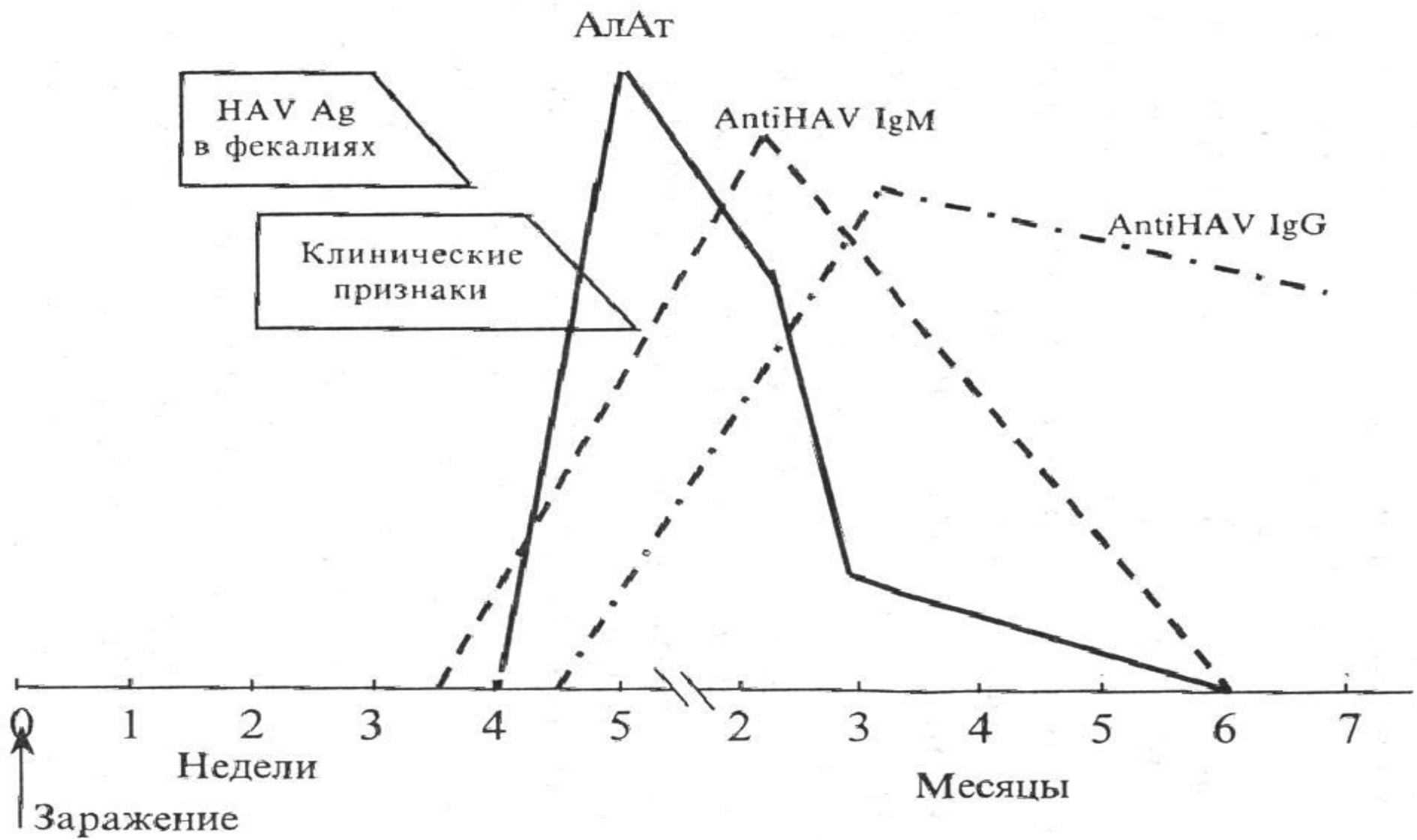


Diagnosis marks of VHA (ELISA and PCR)

1 anti -HAV Ig M – sign of acute infection
2 anti - HAV Ig G – sign forming of a immunity or vaccination
3 HAV Ag – sign of presense HAV in feces or blood (seldom)
4 RNA – HAV - sign of presense HAV in feces or blood and it replication

Therapy - pathogenetic and symptomatic:
- bed rest,
- diet N5,
- hepatoprotections,
- vitamin therapy,
- desintoxication PO or IV (seldom),
- antioxidants
- antiviral therapy does not used

Диагноз подтверждается методом ELISA and PCR



Маркеры ИФА острого вирусного гепатита А /4/

A 53-year-old male presented with jaundice, fatigue,and hepatomegaly. These symptomes developed 3 days after onset of dark urine, fever, and chill. He denid alcohol abuse and exposure to rick factors for viral hepatitis. However, 6 weeks disease onset he visited North Africa. Laboratory investigations: Bilirubin 248 mmol/L (1.7 – 17.1 mmol/l), ALT 640 U/L (5 – 40 U/L) , AST –200 U/L (5 – 40 U/L), Prothrombin time 16 seconds, Platelet count 240 x10 in 9dg /L

HBs Ag absent, Anti- HCV absent, IgM anti HAV present.

The diagnosis (Acute infection with hepatitis A virus) rest on detection of serum IgM antibody to hepatitis A virus. IgM antibody is almost invariably found at onset of symptoms or 1 week later, and may persist for months. The clinical picture of hepatitis A differs according to the patient's age. Jaundice is unusual in infants, whereas symptomatic, icteric hepatitis is common in adults. Fulminant hepatitis A occurs in 1% patients above the age of 50.

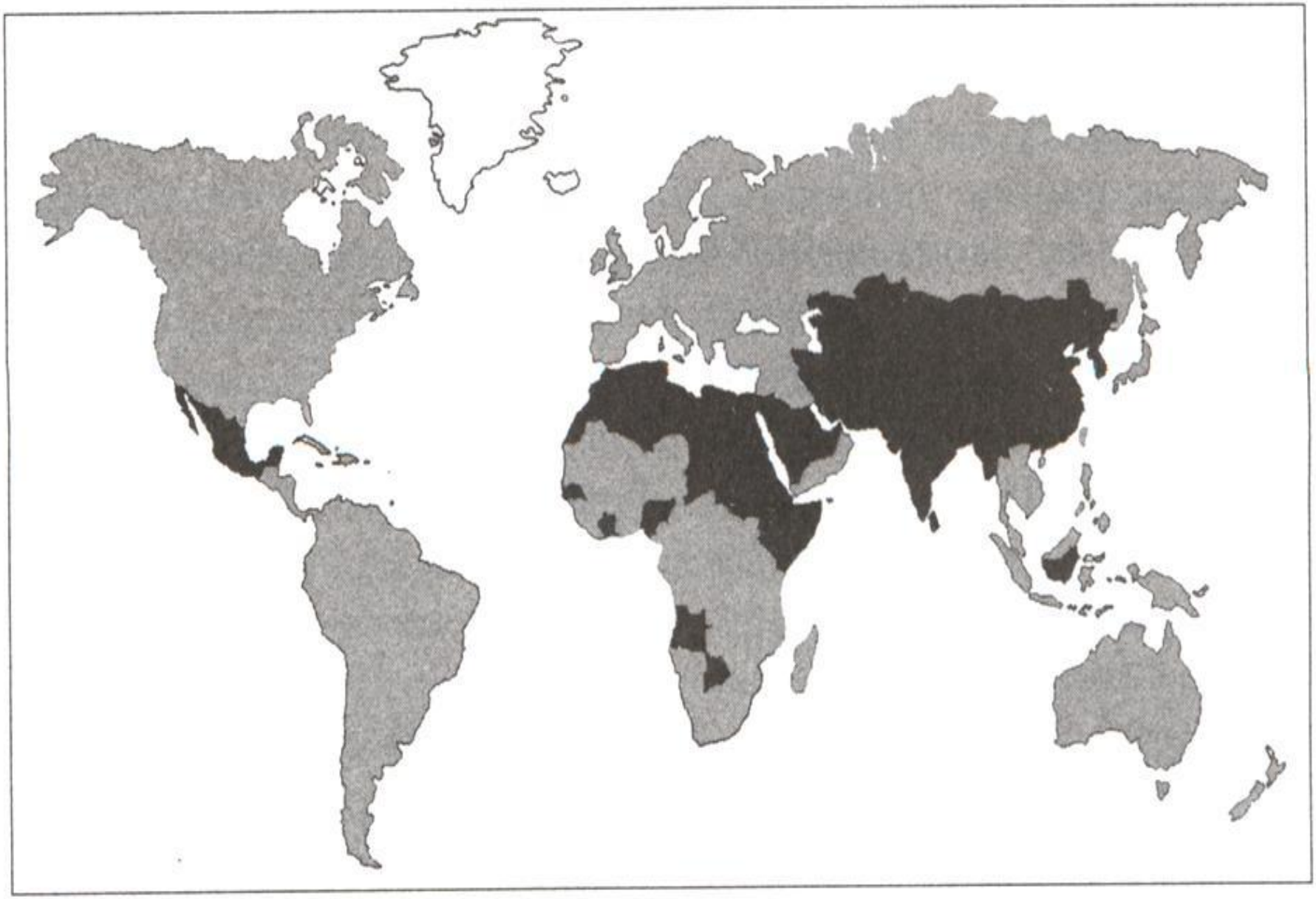
VIRAL HEPATITIS E (VHE)

The agent - shallow spherical Calicinoviruses 27 - 34 nm, containing one chain RNA, well sevives at temperature (-) 20 гр.С, but at temperature is higher 0 гр.С are fast inactivated. Are very sensitive to desinfectants

Teratogenic of operation does not render, with milk of the mother do not secrete. Are sensitive to its- monkeis and pigs, on cellular cultures does not grow.

FEATURES of a VIRUS HEPATITIS E:

- the age is more often than 15-40 years (man more often in 2 times)
- is more often as aqueous explosive character of the flashouts
- low family case rate (contrast to VHA)



Географічне розповсюдження гепатиту Е.

- The seasonal prevalence - is more often in period monsoon of rains
- Irregular distribution on territory
- To othen in locales with scanty water supply
- The mode of transmission - faeco-oral
- The carrying on factor of transmission - potable water

- High lethality among the pregnant woman in 3rd trimester (to 25 %) and children in neonatal period (Up to 77 %)
- Incubation interval from 2 about 8 weeks (36 days)

- The expressed pain syndrome in the right hypochondrium and epigastriums for 70 % of the patients

- In preicteric period frequently arthralgias and diarrhea

- fever – sign is nonconstant
- with appearance of an icterus aggravation of symptoms with by increase of intoxication (contrast to VHA)!
- is accompanied micro and macrohematuria
- typical two-phase rise cytolitical of enzymes (on 6-12 and 14 - 26 days of illness)
- normal or slightly increase thymol test (contrast to VHA)
- the test antibody VHE Ig M it raises!!!)
- can has lingering current, but chronic the forms are not registered
- relation icteric and anictericof the forms 1:5
- duration of icteric period 1 - 2 weeks

- Lethality no more than 0,4 %
- The pregnant women in 3td trimester- interuption of pregnency (40%) and perish from DIC – syndrome (disseminated intravascular coagulopathy) and acute hepatic insuffiency (5,6% - 17,6%).

Differential diagnosis VHA and VHE - hard in preicteric period and more often is registered as ARVD. With appearance of an icterus it is necessary to eliminate all superhepatic, hepatic and subhepatic of its reason

Diagnosis marks of VHE (ELISA and PCR)

1 anti - HEV Ig M – sign of acute infection

2 anti - HEV Ig G – sign forming of a immunity

3 HEV Ag – sign of presense HEV in feces or blood

4 RNA – HEV - sign of presense HEV in feces or blood and it replication

A 39-year-old Chinese businessman travelling to Italy presents fatigue, anorexia, jaundice, and elevated ALT. He denies risk factors for viral hepatitis or heavy alcohol consuption. On admission, the liver is tender with a 14 cm span. The spleen is palpable.

Laboratory investigation:

ALT –740 U/L, ASI –680 U/L, Bilirubin – 188 mmol/L, ALP -178 U/L, HBsAg- abcent , anti- HBs Ag – present, anti- HBc Ag – present, Total anti-HAV - present, anti-HAV IgM- abcent, anti-HEV IgM – present

1. What is the diagnosis? The diagnosis (Acute infection with hepatitis E) rest on detection of serum IgM antibody to hepatitis E virus.

- A 27-year-old water engineer returns from working in West Africa and 3 weeks later develops: low grade fever, malaise and jaundice.

- Laboratory investigation are shown:

- Hemoglobin – 134 g/L, WBC count – 4.0 x 10 in 9 dg./L with lymphocytosis on a differential count, Albumin – 42 g/L, ALP – 280 U/L, Prothrobin time – 13 seconds.

- ALT –538 U/L, AST – 220 U/L, Bilirubin – 80 mmol/L,
- ALP -178 U/L, HBsAg- abcent , Total anti-HAV - present, anti-HAV IgM- abcent, anti-HEV IgM – present

- What is the diagnosis?

- The diagnosis (Acute infection with hepatitis E) rest on detection of serum IgM antibody to hepatitis E virus.

Therapy - pathogenetic and symptomatic: bed rest, diet N5, hepatoprotections, vitamin therapy, PO desintoxication, antioxidants

Prophylaxis:

- improvement of quality of water and nutrition
- the isolation contact (brings small effect)
- passive (VHA, VHE) and active immunization (VHA)

Appearance encephalopathy with an oppression of consciousness, degree expressivenesses which is estimated in marks on Glasgow scale :

1 Opening of an eyes	spontaneous	4
	in reply to the verbal order	3
	In reply to pain stimulation	2
	absence	1
2. Active move-ments	spontaneus and reply in the order	6
	single-minded on pain	5
	unsingle-minded on pain	3
	pathological tonical flexion to pain	3
	pathological tonical extension to pain	2
	absence of a motion to pain stimulation	1

3. Verbal is oriented

Fast answers	- 5
The answers the confused speech	- 4
The inadequate answers	- 3
Inarticulate sound	- 2
Absence of speech	- 1

15 numbers - norm,

13 - 14 numbers - somnolencea

9-12 numbers - sopor,

4-8 numbers - coma,

4 numbers and less - out-of-limit coma.