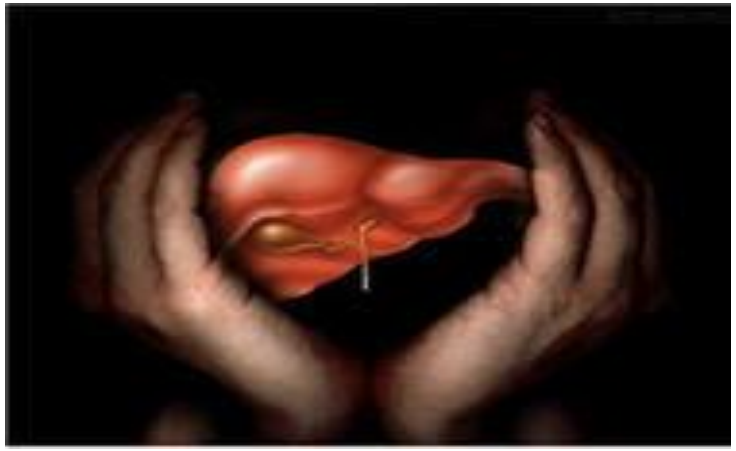


# Chronic hepatitis in children

# Chronic hepatitis

- **Poly-etiological diffuse inflammatory process in the liver**
- Is conditioned by primary damage of liver cells lasting more than 6 months
- Evolving or non-evolving in liver cirrhosis

# Etiology

- Chronic hepatitis is often caused by viruses
- Nowadays there are **7 types of viruses** are detected which have hepato-tropity : **A, B, C, D, E, G, F**
- The formation of chronic hepatitis occurs in case of infection by hepatitis viruses that transmittng by parenteral way – **B, C, D, G, F.**
- Viruses **B** and **C** can be transmitted not only by parenteral way and also by sexual and contact ways

After infection by viruses of hepatitis **B** – during immune response process anti-bodies against antigens (of virus) appear in blood.
First appearing anti-bodies are against to HBcAg – HbcAb (HBc Antibody), in 2 – 3 weeks after HBsAg appearing .
Great part of antibodies is represented by IgM (HbcAbIgM) class which can kept in blood serum of the patients during 6 – 9 months.
Presence of HbcAbIgM may give evidence about acute or chronic hepatitis with lasting replication (spread) of hepatitis B virus.
Later in blood HbcAb appears of IgG class which can be determined during several years in blood.

# Etio-pathogenesis

- Antibodies against to HBe Ag - HBe Ab – appear approximately in 2 weeks from the beginning of acute hepatitis B and acc to decrease of the concentration HBe Ag may stay in blood from 1 up to 5 years old and even more.
- Appearance of HBe Ab gives evidence about recovery of the patient or transfer of acute viral hepatitis into chronic type, thus, replication of viral hepatitis B stops or significantly decreases, integration of viral hepatitis B genome to hepatocyte's genome occurs that is accompanied by decreasing of activity of that inflammatory process.

# Etio-pathogenesis

- Antibodies against HBsAg – HbsAb – are detected in 3 – 5 months after the beginning of acute hepatitis B.
- They can be determined in blood of the patient during 5 – 10 years.
- Appearance of these antibodies means immune resolution of the infection, but in this case existence of B virus in hepatocytes is not excepted

# Etio-pathogenesis

- Viral DNA may integrate not only in hepatocytes and also, in cells of pancreas, salivary glands , leucocytes, spermatozoa, and kidney.
- Presence of DNA virus in other organs promotes the preservation of virus in the organism during long time at the absence of immune reaction of that organism
- At the decrease of immunity virus may activate and promote the damage not only in liver but also in various organs

# Etio-pathogenesis

- At the chronic viral hepatitis B auto-immune reactions development is important , starting mechanism of which is deficiency of T-suppressory function.
- As a result the stimulation of T-lymphocytes occurs by damaged hepatocytes, activation of B-lymphocytes also occurs that react on superficial antigens of hepatocytes and lipoprotein which represents normal component of membranes of hepatic cells.
- Synthesis of auto-antibodies occurs to this lipoprotein.

# Etio-pathogenesis

- D virus (D-virus, delta-virus) consists of external cover (lipids and HBsAg) and internal parts.
- Delta-virus is defect one as in its replication presence of B virus is necessary , it has common point with virus in superficial antigen.
- Penetrating into the organism, D-virus gets to the nucleus of hepatocytes , it becomes full-grown and replicates only in HBsAg environment.
- D-virus different from virus of hepatitis B has cytotoxic action on hepatocytes.
- In the pathogenesis of viral hepatitis D cytopathic action of virus and auto-immune mechanisms are important

# Etio-pathogenesis

- At delta-superinfection – suppression of B virus replication is important as its antigen is applied by defected delta-virus for its own replication.
- Clinically delta-superinfection is frequently manifested by double-phased hepatitis, when the first peak of disease activity corresponds to hepatitis B, and second – lamination of delta-infection.
- At the co-infection, when 2 viruses (B and D) get to the organism at the same time, cytopathogenic effect is predominant but auto-immune component is not clear

# Etio-pathogenesis

- Association of B and D viruses lead to the potentiation of their pathogenetic effect, risk of transfer to chronic one increases.
- Chronic delta-infection proceeds with frequent, clear exacerbations accompanied by intoxication , growth of jaundice and increase of liver in size, also spleen, and deep biochemical manifestations of hepato-cellular failure.
- For delta-infection is characteristic – more acute current of the disease in comparison with classic chronic hepatitis B.

# Etio-pathogenesis

- Virus of C hepatitis is isolated recently but not from A and B groups.
- Virus of C hepatitis is the most dangerous one giving risk to the development of liver cancer.
- Transfer of acute viral hepatitis C to the chronic one can be observed in 50 - 80% .

# Etio-pathogenesis

- Virus C possesses cytotoxic (cytopathic) action giving immune-mediated damage to the liver.
- Distinctive feature of acute viral hepatitis C is soft or light, torpid, latent or less-symptomatic current. Current of HCV-infection lasts during many years, clinically clear chronic hepatitis is developed, in average, after 14 years, and cirrhosis – after 18 years, hepatocarcinoma – after 23 – 18 years.

# Etio-pathogenesis

- At the penetration of viruses to hepatocytes T-lymphocytes react onthem and give information to B-lymphocytes, as a result activation with the formation of antibodies occurs which destroys infected hepatocytes
- In case of insufficient production of antibodies hepatocytes are destroyed but infection of healthy hepatocytes by that viruses can not be prevented
- Antibodies start to react on unaffected lipoprotein - cover of uninfected hepatocytes and auto-immune process is joined
- Auto-antibodies reaching the liver link with surface of periportal hepatocytes. From this moment synthesis and release of damaging auto-antibodies starts which can not be controlled by depressing T-lymphocytes cells , that means by suppressory cells.

# Pathogenesis of auto-immune chronic hepatitis

- Auto-immune reactions can be primary cause of chronic hepatitis if it is impossible to establish any other causes.
- In the pathogenesis of auto-immune hepatitis there is immunological mechanisms of unknown etiology , serologic signs (markers) of viral hepatitis are absent.
- As a rule, there is congenital deficiency of T-suppressor function of lymphocytes.
- In the pathogenesis of auto-immune hepatitis - it is very important the formation place of auto-antibodies to the component of hepatocytes, hepato-specific lipoprotein, antinucleus antibodies and antibodies to smooth muscles

# Classification of chronic hepatitis

| Etiology | Level of activity (is established acc to clearness level of manifestations) | Stage of chronization (is established acc to fibrosis clearness |
|---|---|---|
| Viral<br>Autoimmune<br>Medicational<br>(reactive)<br>Cryptogenous | Minimal<br>Weakly clear<br>Moderate<br>Clear | No fibrosis<br>Weakly clear periportal fibrosis<br>Moderate fibrosis with portal septum<br>Clear fibrosis with portoceptal septum<br>Liver cirrhosis – severity of which is determined by clearness of portal hypertension and hepatic failure |

- Activity level of the process is determined by biochemical changes in blood, especially acc to content of ALT enzyme.
- At the increased level of ALT in 3 times – minimal activity, in 5 times – weakly clear activity, in 10 times – moderately clear activity, more than 10 times – clear activity of the process

# Clinics of chronic hepatitis

- Asteno-vegetative syndrome
- Dyspepsic syndrome
- Pain  syndrome
- Hepato- and  splenomegaly and others.
- Clearness  of clinical  syndromes  depend on  the level of activity of the pathological process  on the liver level
- In case of long current  of the disease  some symptoms appear  that  indicating  clear  changes  from liver side  and indicating  the system of that damage

# Dyspeptic syndrome at chronic hepatitis

- Characterized by the following symptoms:
- Nausea during food intake and medications,
- Bad tolerance of fat, vegetables, cabbage and etc

# Dyspeptic syndrome at chronic hepatitis

- Feeling of overfilling, swelling of abdomen after food intake
- Bad passage of flatus (gas)
- Acid taste and dryness on mouth
- Decrease of appetite  up to anorexia
- Diarrhea and  constipations

# Pain syndrome

- Is a leading point of chronic hepatitis in its clinics, is observed in 60 – 70% of patients.
- Pain is prolonged or periodic, felt on the right subcostal area dependently on food intake.
- Pain intensifies after physical load.

# Pain syndrome

- Pain is conditioned by capsule tension because of hepatomegaly, perihepatitis, adhesive process, damage of extra-hepatic bile ducts.
- In some patients at the combination of perihepatitis with hepatomegaly - symptom of «Ванька-встанька» is observed, when patient prefers standing position as during stand pain which is on the right subcostal area decreases

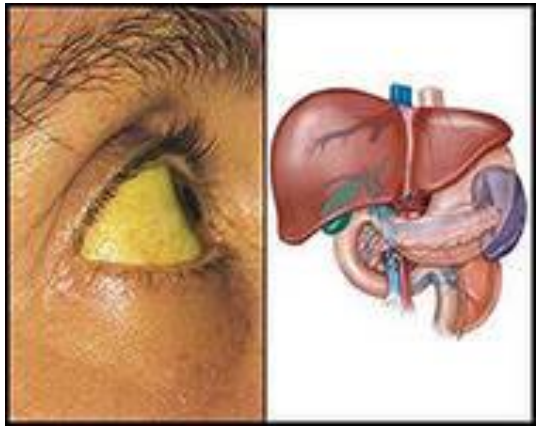
# Hepatomegaly

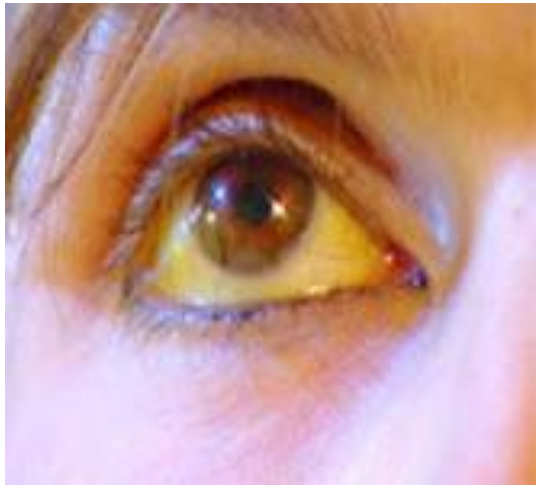
- Increase of the liver (hepatomegaly) is one of the most frequent sign of chronic hepatitis (at 85 – 90% of patients), occurs because of inflammatory edema and cellular infiltration
- Liver is dense, painful, smooth, margin is sharp (bordered). At the development of cirrhosis liver decreases in size, its surface becomes uneven.

# Splenomegaly

- Increase of spleen (splenomegaly) reflects generalized reaction of reticulo-endothelial system
- Splenomegaly also occurs in case of portal hypertension

# **Jaundice** at chronic hepatitis



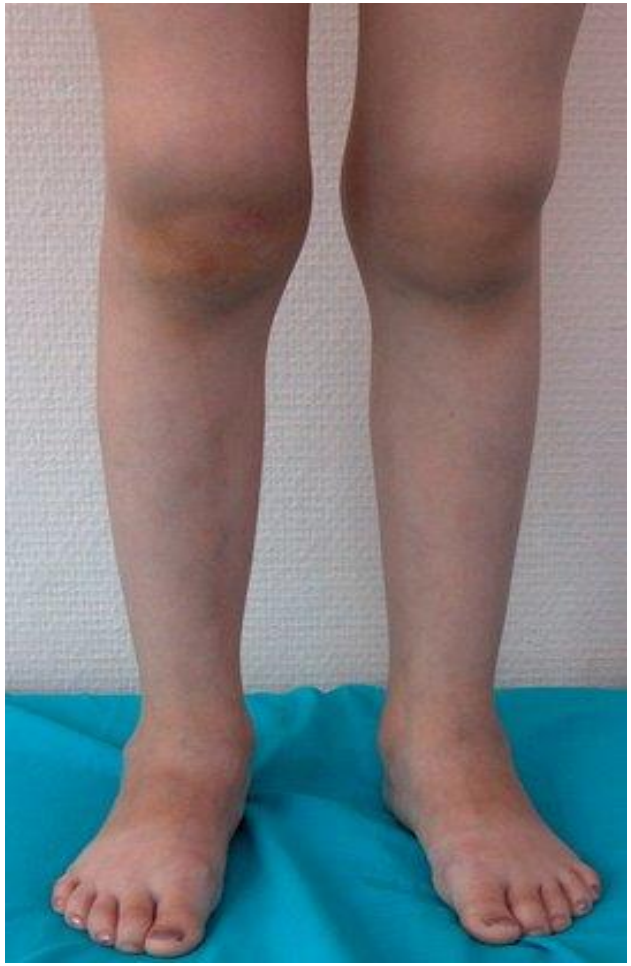


- Observed periodically, conditioned by disorder of excretory function of the liver and intrahepatic cholestasis.
- Rarely, in case of autoimmune reactions jaundice is conditioned by hemolytic anemia

# Clinics

- **Hemorrhagic syndrome** is developed because of synthesis disorder of coagulation factors on the level of liver, thrombocytepenia, indicating active process
- **Lymphadenopathy** – generalized increase of lymph nodes indicating active process with the development of damage

# Clinics

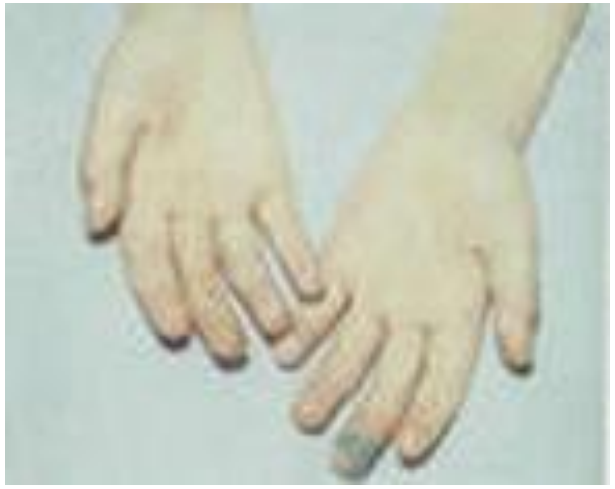


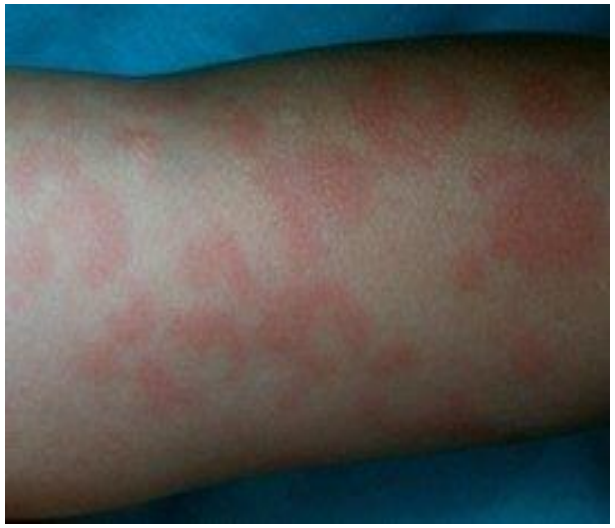
- Joint syndrome is characterized by damage of large joints, rarely by small joints and changes look like rheumatoid arthritis.
- Joint manifestations , in spite of their duration and clearness, disappear or decrease after treatment or independently.

# Clinics

- Arthralgia is usually multiple having  migrating character, sometimes accompanied by constraint.
- Muscular syndrome as myalgia and myopathy is observed not in all patients

# Skin syndrome at chronic hepatitis





- Characterized by various symptoms:
- Vascular stars
- Palmar erythema
- Nidal disorders of pigmentation
- Nodular erythema
- Erythematous spots
- Nettle rash
- Residiving purpur and etc.

# Clinics of chronic hepatitis

- **Fever** frequently has residive character
- Because of immune changes and reactions that are responsible for necrosis of hepatic cells
- **Intestinal endotoxemia** because of disbacteriosis and decrease of phagocytar function of the liver
- Gives **subfebrile rises of temperature**

# Clinics

- **Endocrine disorders** occurs as a result of change of hormones metabolism in damaged liver, manifested as acne, stria, hirsutism, obesity and moon-shaped face, amenorrhea and dismenorrhea, gynecomastia and escutcheon.
- **Reino syndrome** occurs because of vaso-motor disorders as vasospastic crisis, accompanied by fading and (or) cyanosis and numbness of fingers and toes occurring due to cold.
- Possible - disorders in other organs and systems : kidneys, heart, lungs and etc., as manifestation of immune-complex and immune-cellular genesis

# Chronic autoimmune hepatitis

- Occurs in girls in pubertate period and young women, rarely in women in their menopause period .
- Disease starts with astenization, pain on the right subcostal area, with insignificant but stable jaundice of hepatocellular type
- Often disease starts suddenly:
- Symptomocomplex of acute damage of the liver with jaundice is developed
- Suddenly increased activity of aminotransferase in blood
- Rapid development of signs of chronic damage of the liver

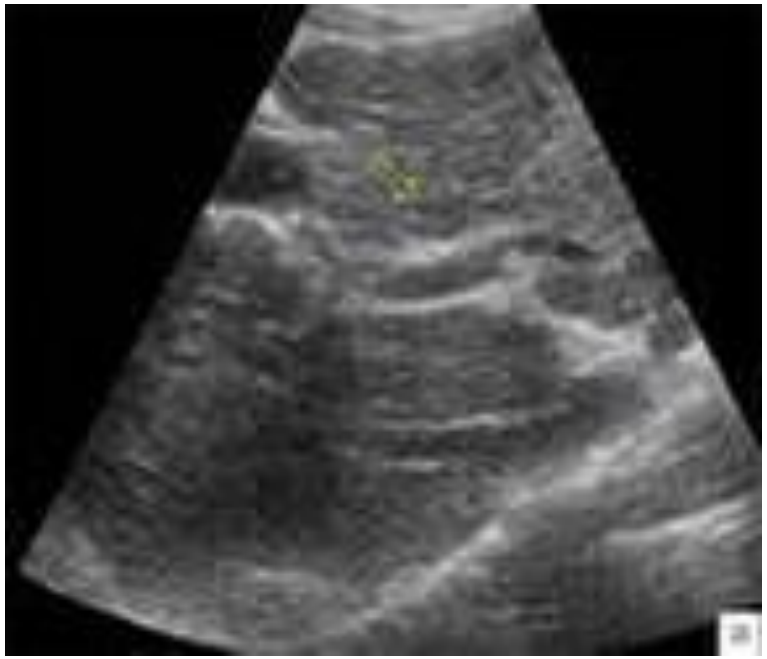
## Diagnostics of chronic hepatitis

- GAB: moderate anemia, lymphopenia, SSE incrases.
- GAU – without any change, but in case of high stage of activity - proteinuria, cylinderuria, microhematuria, as a manifestation of glomerulonephritis. Possible - bilirubin in urine

## Diagnostics of chronic hepatitis

- Biochemistry of blood: protein and protein fraction, bilirubin and its fractions, content of enzymes (aminotransferase, lactatdehydrogenase), alkaline phosphatase, organo-specific enzymes of the liver, prothrombin, cholesterol, proaccelerine, serumal iron, glucose, blood serum, electrolytes, urea, creatinin and etc.

# US of liver at chronic hepatitis



# Clinico –laboratory  syndromes at chronic hepatitis

- **Cytolytic yndrome (hepatocytolysis)** – increase of ALT, AST, lactatdehydrogenase, ferritine, serum of ferrum.
- Level of activity is determined by activity of ALT enzymes.

# Clinico –laboratory  syndromes at chronic hepatitis

- **Syndrome of immune inflammation (mesenchymal –inflammatory syndrome, syndrome of poly-clonal gammapathy):**
- Hypergammaglobulinemia, hyper- and  disimmunoglobulinemia
- Increase of thymol test
- Increase of SSE
- Products of  connective tissue degradation -  SRB, seromucoid
- Shift to cellular and humoral immune reactions.
- Determination of rheumatoid factor
- Antibodies onto subcellular fractions of hepatocytes (DNA, hepatic lipoprotein)
- Anti-nuclear antibodies
- Change of  number and functional activity of  T- and B-lymphocytes.

# Clinico –laboratory syndromes at chronic hepatitis

- **Cholestasis syndrome**
- Disorder of excretory function of the liver:
- Increase of conjugating fraction of bilirubin, alkaline phosphatase, β-lipoproteids, bile acids, phospholipids
- decrease or disappear of urobilin in urine
- Decrease of bromsulfalen secretion

# Clinico –laboratory syndromes at chronic hepatitis

- **Syndrome of hepato-cellular failure:**
- Hyperbilirubinemia at the expense of unconjugated fraction of bilirubin
- Decrease of albumin, prothrombin, transferin, ethers of cholesterol, proconvertin, estherase.

# Treatment of chronic hepatitis

- **Major principles of the therapy**:
- Diet and regimen
- Suppression of virus replication in case of chronic viral hepatitis
- Correction of immune reaction of the organism
- Recovery of disordered metabolism of hepatic cells, elimination of cholestasis and etc.
- Symptomatic therapy

# Диета

- Стол 5 печеночный, с исключением тугоплавких животных жиров, ограничение грибов, консервированных продуктов, копченостей и вяленых продуктов, жареных блюд, изделий из шоколада, крема и сдобного теста.

# Противовирусная терапия

- Проводится с целью элиминации или прекращения репликации вируса, купирования или уменьшения степени активности воспаления, предупреждения прогрессирования хронического гепатита с развитием цирроза и гепатоцеллюлярной карциномы.
- В лечении хронических вирусных гепатитов B, C, D, а также острого гепатита С эффективными являются ИНФ-α, как в качестве монотерапии, так и в комбинации с другими средствами (синтетическими нуклеозидами, урзодезоксихолевой кислотой, антиоксидантами и др.).

# Противовирусная терапия

- ИНФ-α ингибирует синтез специфических макромолекул, участвующих в репликации компонентов вируса и в сборе полного вируса.
- Кроме того, оказывает иммунумодулирующее действие: повышает цитотоксическийэффект Т-киллеров, активность нуклеарных клеток и макрофагов, влияет на гуморальные факторы иммунитета.

# При аутоиммунном гепатите

- Проводится иммуносупрессивная терапия:
- Глюкокортикоиды из расчета 1 – 1,5 мг/кг/сутки преднизолона.
- Эту дозу дают 2 – 3 месяца до достижения клинико-лабораторной ремиссии.
- Постепенно переходят на поддерживающую дозу, которую дают 2 года.
- В отдельных случаях назначают азатиоприн 1 – 2мг/кг/сутки.

# Симптоматическая терапия

- Для улучшения метаболических процессов в печени назначают гепатопротекторы: карсил, гептрал, эсссенциале, тиотриазолин, легалон, силимарин, галстена, гепабене, гепатофальк, рибоксин, лецитин, кокарбоксилаза, витамины группы В и др. при явлениях холестаза показаны урсосан, холестерамин, онданстерон, фенобарбитал и др.

# Симптоматическая терапия

- Спазмолитики,
- Желчегонные средства,
- Энтеросорбенты и т.д.
- Учитывая диспепсические явления, связанные с нарушением биоценоза кишечника, назначают пробиотики, пребиотики, дюфалак.