Methodical recommendations
for 2nd level (a master's degree) specialist’s independent work
during practical class preparing

<table>
<thead>
<tr>
<th>Classroom discipline</th>
<th>Pathomorphology</th>
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<tbody>
<tr>
<td>Module 2</td>
<td>Systemic pathological anatomy</td>
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<tr>
<td>Theme</td>
<td>Diseases of the liver and pancreas: hepatitis, hepatosis, pancreatitis.</td>
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<tr>
<td>Course</td>
<td>3</td>
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<tr>
<td>Department</td>
<td>Foreign student’s training department Dentistry</td>
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Poltava 2020
1. **Relevance of the topic:** Liver diseases are common. Due to the widespread prevalence of hepatosis and hepatitis, knowledge of the pathomorphology of these diseases is important for dentists. Knowledge of the pathomorphology of these diseases, together with clinical signs, allows a more differentiated approach to the diagnosis of the disease, to be determined in treatment tactics and to anticipate complications and consequences.

2. **Specific goals:**
   - Define the concept of "hepatosis", "hepatitis".
   - Classification of hepatosis.
   - Know the name and etiology of acute hepatosis.
   - Describe the macroscopic signs of acute hepatosis at different stages.
   - Describe the macroscopic changes in the liver in acute hepatosis at different stages.
   - Describe the macroscopic changes in the liver in acute hepatosis at different stages.
   - Know the consequences of acute hepatosis.
   - Know the etiological factors of chronic hepatosis.
   - Know the macro- and microscopic manifestations of fatty liver.
   - Determine the consequences of chronic hepatosis.
   - Give a definition of the concept of "hepatitis".
   - Etiology of hepatitis.
   - Know the features of the pathomorphology of viral hepatitis A.
   - Know the features of the pathomorphology of viral hepatitis B.
   - Know the complications and consequences of hepatitis.
   - Know the definition, etiology, pathogenesis, classification, morphology of pancreatitis

3. **Basic knowledge’s and skills you need to learn the topic** (interdisciplinary integration)

<table>
<thead>
<tr>
<th>Name of previous discipline</th>
<th>Received knowledge’s</th>
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</table>
| Normal anatomy              | 1. To describe normal morphological structure of a liver.  
                              | 2. Be able to use knowledge’s about liver circulation.  
                              | 2. To draw normal liver structure. |
| Histology, cytology and embryology | 1. Be able to use knowledge’s about histological structure of liver acinus. |
| Physiology and pathophysiology | 1. Be able to use knowledge’s about both toxic and virus injury of hepatocytes.  
                              | 2. To use knowledge’s about the injury outcomes. |

4. **Tasks for self-studying during practical class prepare.**

4.1. **List of basic terms, characteristics, which a student mast take over at practical class:**

<table>
<thead>
<tr>
<th>Term</th>
<th>Determination</th>
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<tbody>
<tr>
<td>Massive necrosis (toxic degeneration of the liver)</td>
<td>is acute (rarely chronic) diseases characterized by massive necrosis of the hepatocytes with development of the hepatic failure.</td>
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<tr>
<td>Steatosis</td>
<td>is a chronic disease which characterized by increase of fat amount in the cytoplasm of the hepatocytes.</td>
</tr>
<tr>
<td>Viral hepatitis</td>
<td>is infection of the liver caused by hepatotropic viruses.</td>
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<tr>
<td>Chronic hepatitis</td>
<td>is a chronic inflammatory hepatic disease continuing for more than six months.</td>
</tr>
<tr>
<td>Chronic persistent hepatitis</td>
<td>is a benign, selflimiting condition in which recovery from an attack of acute viral hepatitis is delayed beyond six months.</td>
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<tr>
<td>Chronic active</td>
<td>is defined as a progressive form of chronic necrotising and</td>
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</table>
(aggressive) hepatitis  fibrosing disease involving portal tracts as well as hepatic parenchyma.
Mallory bodies  scattered hepatocytes accumulate tangled skeins of cytokeratin intermediate filaments and other proteins, visible as eosinophilic cytoplasmic inclusions.

4.2 Theoretical questions for the practical class:
1. Definition of hepatosis. Etiology, pathogenesis of fat steatosis, morphology, complications and outcomes.
2. Toxic dystrophy (massive necrosis) of liver. Causes, morphological features in different stages of this processes, complications and outcomes.
5. Pathogenesis, morphological peculiarities of viral hepatitis B, its complications, causes of death
6. Viral hepatitis C, D, E: present classification, their peculiarities. Which forms of these hepatitis can develop cirrhosis in time?

4.3 Practical work students do at class:
Students must be able to learn macro- and micropreparations by use their diagnostic algorithms

<table>
<thead>
<tr>
<th>Test algorithm for macropreparation diagnosis</th>
<th>Test algorithm for micropreparation diagnosis</th>
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<tbody>
<tr>
<td>1. To indicate Latin name of a preparation.</td>
<td>1. To indicate used staining method for the organ tissue.</td>
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<tr>
<td>2. To describe macroscopic features of an organ (size, color, consistence)</td>
<td>2. To name both tissue and organ</td>
</tr>
<tr>
<td>3. To indicate pathological process</td>
<td>3. To indicate changes in the tissue of the organ</td>
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<tr>
<td>4. To indicate possible outcomes of the pathological process</td>
<td>4. To name the pathological process</td>
</tr>
<tr>
<td>5. What disease does the pathological process correspond to</td>
<td>5. To indicate the pathological process outcomes</td>
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Macropreparations:
1. “Massive necrosis of the Liver”. Pay attention to the size of the organ, condition of the capsule and consistence of the liver, appearance of the surface on section.
2. “Toxic degeneration of the Liver”. Pay attention to the size of the organ, condition of the capsule and consistence of the liver, appearance of the surface on section.
3. “Fatty degeneration of the Liver”. Pay attention to the organ size, flabby texture, and yellowish-ochre color of the parenchyma on the cut. Such liver is called “Goose Liver”.
4. “Fatty degeneration of the Liver ("False Nutmeg Liver")”. Pay attention to the organ’s size, flabby texture. The liver looks lumpy coloration with appearance of yellowish-gray spots on the brown background.

Macropreparations:
Slide 1. Liver in Acute Viral Hepatitis (ought to be drawn) We can see hepatic cell injury. Such injury includes “ballooning degeneration” marked by swelling and enlargement of the cytoplasm, which appears pale, and acidophilic bodies’ formation (Councilman’s body), a form of single cell death marked by loss of the nucleus and a prominently eosinophilic cytoplasm. These bodies are situated in perisinusoidal spaces. The inflammatory infiltrates are more prominent in the portal tracts. Most of the cells in the infiltrate are lymphocytes and macrophages.
Slide 2. **Massive hepatic Necrosis**
This pathological process is histologically characterized with widespread of hepatic cells necrosis. The necrotic hepatic cells disappear, leaving behind only the reticular connective tissue framework of the sinusoids and the Kupffer's cells. The space between the terminal veins and portal tracts is collapsed and contains connective tissue and blood. Regeneration following cellular necrosis is characterized by bile ductal proliferation and proliferation of fibroblasts.

Slide 3. **Chronic alcoholic hepatic steatosis** (ought to be drawn) Hepatocytes are enlarged. Lipid accumulations are seen as large clear macrovesicular spaces, compressing and displacing the nuclei to the periphery of the hepatocytes. Little fibrous tissue develops around the central veins and extends into the adjacent sinusoids (first sign of following cirrhosis).

Slide 4. **Chronic viral persistent hepatitis** (ought to be drawn) A structure of hepatic lobules is kept. Portal areas are infiltrated by lymphocytes, plasma cells, histiocytes. Hydropic and fatty changes of hepatocytes are showed poorly.

**Topic content:**

There are various diseases of the liver. According to the origin they are classified into inherited and acquired, primary or secondary (as a result other diseases).

According to the morphological changes there are several groups of these diseases:

a) hepatosis (when degeneration and necrosis in the hepatocytes prevail),

b) hepatitis (when inflammation in the liver prevail),

c) cirrhosis (when disregeneration is observed),

d) hepatic tumors.

**HEPATOSIS**

The term hepatosis is used to describe degeneration and necrosis in the liver caused by microbiologic, toxic, circulatory or traumatic agents.

Hepatosis may be inherited and acquired. Inherited hepatosis develops in accumulation diseases or enzymopathy. Acquired hepatosis may be acute and chronic.

The massive necrosis is the most common acute hepatosis. The steatosis (fat hepatosis) is the most common chronic one.

**Massive necrosis** (toxic degeneration of the liver) is acute (rarely chronic) diseases characterized by massive necrosis of the hepatocytes with development of the hepatic failure.

*Etiology.* It is most commonly caused by viral hepatitis, drug or mushroom toxicity.

*Pathology.* There are 2 stages in this hepatosis.

1. Stage of yellow degeneration, when liver becomes enlarged, dense and yellow. Then it size increases, it consistency becomes flabby, capsule is shrunken. The cut surface is grey. Microscopically fat degeneration, necrosis and autolysis of hepatocytes are observed.

2. Stage of red degeneration is characterized by progressive reduction of liver size and mass. Macroscopically the liver is red due to necrosis and autolysis of hepatocytes with appearance of plethoric blood vessels. Jaundice, hyperplasia of lymph nodes and spleen, numerous hemorrhages in the skin and mucous, necrosis of the renal epithelium, degenerative and necrotic changes in pancreas, myocardial, CNS are observed in the patients with massive necrosis of the liver.

**Steatosis** is a chronic disease which characterized by increase of fat amount in the cytoplasm of the hepatocytes.

*Etiology* of steatosis is similar to massive necrosis of the liver. But in this case pathologic agent has less toxicity and as a rule human compensatory and adaptive processes are higher.

*Macroscopically* the liver is enlarged, flabby. Fat drops are seen on the incision. The colour is yellow. This is called «gooses's» liver.

*Microscopically*—dust-like, small and large drop in the liver cells are observed.
VIRAL HEPATITIS
Viral hepatitis is infection of the liver caused by hepatotropic viruses. There are 6 varieties of these viruses. Four of them are main ones causing distinct types of viral hepatitis:
1. Hepatitis A virus (HAV), causing a fecally-spread self-limiting disease.
2. Hepatitis B virus (HBV), causing aparenterally transmitted disease that may become chronic.
3. Hepatitis C virus (HCV), also termed non-A, non-B (NANB) hepatitis virus involved chiefly in transfusion-related hepatitis.
4. Hepatitis delta virus (HDV), which is sometimes associated as superinfection with hepatitis B infection.

Hepatitis A is responsible for 20—25% of clinical hepatitis in the developing countries of the world. The disease occurs in epidemic form as well as sporadically. The spread is related to close personal contact such as in overcrowding, poor hygiene and sanitation. An incubation period carries on 15—45 days.

Hepatitis B has a longer incubation period (30—180 days) and is transmitted parenterally such as in recipients of blood and blood products, intravenous drugs, etc.

Pathology. The typical pathologic changes of hepatitis A, B and C are similar. The various clinical patterns and pathologic consequences of different hepatotropic viruses can be considered under the following headings:

1) Carrier state.
2) Acute hepatitis.
3) Chronic hepatitis.
4) Fulminant hepatitis (Submassive to massive necrosis).

Acute hepatitis clinically is divided into 4 phases:

a) incubation period,
b) pre-icteric phase,
c) icteric phase
d) post-icteric phase.

Macroscopically the liver is slightly enlarged, soft and greenish.

Microscopically the changes are follows:
1. Hepatocellular injury:
a) ballooning degeneration,
b) appearance of the necrotic acidophilic mass,
c) bridging necrosis is characterized by bands of necrosis linking portal tracts to central hepatic veins, one central hepatic vein to another, or a portal tract to another tract.
2. Inflammatory infiltration by mononuclear cells in the portal tracts.
5. Regeneration — as a result of necrosis of hepatocytes, there is lobular disarray.

CHRONIC HEPATITIS
Chronic hepatitis is a chronic inflammatory hepatic disease continuing for more than six months.

It is divided into 2 types:

1) persistent hepatitis
2) active (aggressive) hepatitis.

Two important factors which determine the vulnerability of a patient of viral hepatitis to develop chronicity are:
1) the impaired immunity,
2) the extremes of age at which the infection is contracted.

**Chronic persistent hepatitis** is a benign, self-limiting condition in which recovery from an attack of acute viral hepatitis is delayed beyond six months.

*Pathology.* The diagnosis of chronic persistent hepatitis is confirmed by needle biopsy of the liver which is invaluable in distinguishing it from more serious form of chronic active hepatitis.

Microscopically:

1) there is portal triaditis characterized by expansion of the portal tract by mononuclear inflammatory cells,
2) the lobular architecture of hepatic parenchyma is usually preserved, 3) there is absence of piecemeal necrosis.

**Chronic active (aggressive) hepatitis** is defined as a progressive form of chronic necrotising and fibrosing disease involving portal tracts as well as hepatic parenchyma.

Microscopically:

1) there is abundant mononuclear inflammatory cell infiltrate that is not confined to portal tracts, but the infiltrate spills out into the periportal hepatic parenchyma after eroding the limiting plate. There may be formation of lymphoid follicles,
2) two types of necrosis develop. They are piecemeal and bridging,
3) the collapsed reticulin framework left at the areas of bridging necrosis undergoes fibrous scarring, eventually progressing to cirrhosis.

The major **cases of death** are liver failure with hepatic encephalopathy, cirrhosis with hematemesis, and hepatocellular carcinoma.

**ALCOHOLIC HEPATITIS**

Alcoholic hepatitis exhibits the following. **Liver cell necrosis**, single or scattered foci of cells undergo swelling (*ballooning*) and necrosis, more frequently in the centrilobular regions of the lobule. **Mallory bodies**, scattered hepatocytes accumulate tangled skeins of cytokeratin intermediate filaments and other proteins, visible as eosinophilic cytoplasmic inclusions. These may also be seen in primary biliary cirrhosis, Wilson’s disease, chronic cholestatic syndromes, focal nodular hyperplasia, and hepatocellular carcinoma.

**Neutrophilic reaction**, neutrophils permeate the lobule and accumulate around degenerating liver cells, particularly those having Mallory bodies.

**Lymphocytes** and **macrophages** also enter portal tracts and spill into the lobule. Fibrosis-alcoholic hepatitis is almost always accompanied by a brisk sinusoidal and perivenular fibrosis; occasionally perportal fibrosis may predominate, particularly with repeated bouts of heavy alcohol intake. Fat may be present or entirely absent.

**Self-check materials:**

1. A microscopic examination of a biopsy from the liver of a male with clinical manifestations of hepatic insufficiency revealed a structural disorder of the lobules, hydropic and balloon dystrophy of hepatocytes, their necrosis on the periphery of the lobules. Besides, there was a diffuse lymphohistiocytic infiltration of scleroid portal tracts; it spread to the periphery of the lobules, surrounding and destroying the hepatocytes. Which of the diagnoses listed below was the most probable?
   A. Chronic active alcoholic hepatitis*
   B. Acute alcoholic hepatitis
   C. Acute cyclic form of viral hepatitis
   D. Cholestatic form of viral hepatitis
   E. Chronic persistent alcoholic hepatitis
2. An autopsy of a 48-year-old female, who died from intoxication, revealed icteric colouring of the skin and sclerae, the liver was characterized by a sharply reduced size, flaccid consistency and a contracted capsule. On section, the hepatic tissue was red and plethoric. Microscopically, the hepatocytes were necrotized in the centres of the lobules and in the state of fatty degeneration on the periphery; the reticular stroma of the organ was exposed, the sinusoids were dilated and sharply plethoric. Which of the diagnoses listed below was the most probable?
   A. Steatosis
   B. Toxic dystrophy of liver at the stage of red dystrophy*
   C. Acute productive hepatitis
   D. Chronic active hepatitis
   E. Toxic dystrophy of liver at the stage of yellow dystrophy

3. In biopsy of the liver of a 40-year-old man, who received injections of narcotics the pathologist has found out acidophilic Councilmen’s bodies, lymphocytes and macrophages surrounding portal tracts, "ground-glass” hepatocytes (an etiology of disease is virus B) Call this disease
   A. Tuberculosis
   B. Virus chirrosis
   C. Parasitogenic hepatitis
   D. Virus hepatitis B *
   E. Steatosis

4. A patient of infection department complained on weakness, absence of appetite, increased temperature (38 °C). On the day, he developed acute pain in the right hypochondrium and yellow skin. Microscopy of the biopsy material has demonstrated disturbances in the beam structure, hydropic and balloon dystrophy in the hepatocytes, necrosis, Councilmen’s bodies in some of them, increased amount of polynuclear hepatocytes on the periphery of the lobules. What form of viral hepatitis is the most probable?
   A. Carrier state
   B. Chronic hepatitis
   C. Fulminant hepatitis
   D. Acute hepatitis*
   E. Incubation period

5. A 22year-old patient was ill with a virus hepatitis B 2 years ago is hospitalized in clinic with the complaints to pain in the right hypochondrium, dyspepsia, loss of weight. In a biopsy of the liver tissue the pathologist found out: irreversible intracellular changes, which were characterized the transferred virus hepatitis B. Call this changes.
   A. Hydropic dystrophy of hepatocytes
   B. Mucoid swelling
   C. Intracellular obesity
   D. Councilmen bodies *
   E. Intracellular glycogen accumulation in hepatocytes

**Literature:**
Informational resources
1. Testing Center - database of licensed test tasks "Krok-1"