Ministry of Healthcare of Ukraine

Poltava State Medical University

Approved
at the meeting of Internal Medicine №1
Department "____"_____
Protocol № ____ from _____
The Head of the Department
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_____

Methodical guidelines
for students' self-studying to prepare
for practical (seminar) classes and on the lessons

Academic discipline	Internal medicine
Module №	1
Topic of the lesson	**Modern examination methods in gastroenterology**
Course	IV
Faculty	of foreign students training

1. **Relevance of the topic**:

In recent decades, the instrumental base for the diagnosis diseases of the digestive system has been actively developed and improved. This, first of all, concerned highly informative studies used in gastroenterology. Currently, the final verification of the diagnoses of almost all diseases of the digestive system is associated with instrumental studies. Instrumental diagnostics is an important section of a comprehensive study of patients. It includes endoscopic, ultrasound, radiological, radioisotope, electrometric and other examination methods. Depending on the nature of the disease, the doctor prescribes a particular study that has the most information in this particular case. The fact that the volume of instrumental diagnostics is determined by the capabilities of the clinic, hospital or medical center is undoubted. Each of the instrumental research methods allows you to identify specific features of the body or its function.

2. Certain aims:

- Define the concept of "methods in gastroenterology."
- Conduct physical examination of patients with pathology of the gastrointestinal tract (GIT).
- To analyze the need for various examination methods in gastroenterology.
- Make a plan for the examination of patients with gastrointestinal pathology.
- Interpret the results of the main invasive and non-invasive diagnostic methods and determine the indications and contraindications for their implementation, possible complications.
- Suggest examination methods that are used for the differential diagnosis of various gastrointestinal diseases.
- Explain management tactics (recommendations regarding the regimen, diet, treatment, rehabilitation measures) of a patient with gastrointestinal tract pathology.
- Diagnose and assist with emergency conditions (esophageal and gastrointestinal bleeding).
- Determine the need for primary and secondary prevention of gastrointestinal diseases.

3. **Basic knowledge, abilities, skills required to study the topic (interdisciplinary integration).**

Names of previous disciplines	Obtained skills
1. Anatomy 2. Histology 3. Physiology 4. Pathology 5. Radiology 6. Propaedeutic internal medicine 7. Pharmacology	To describe the structure of the gastrointestinal tract, blood supply and innervation; to use additional methods of examination and interpret their data to make diagnosis; to identify markers of gastrointestinal tract function and to know their normal values; to draw a scheme of patient's follow-up; to demonstrate practical skills during physical examination of the patient, analyzing the clinical and laboratory results.

4. Tasks for self-studying to prepare for the lesson and on the lesson.

4.1. List of main terms, parameters, characteristics that should be learnt by student during preparation for the classes:

Term	Definition
Serological investigation	The method consists in the detection of specific immunoglobulins in the blood
Fibroesophagogastroduodenoscopy (FEGDS)	investigation of the mucosa of the esophagus, stomach and duodenum using an endoscope, which is administered to the patient from anesthesia throat.
Colonoscopy	allows investigaty the colon mucosa almost throughout, to biopsy and photography
Endoscopic retrograde cholangiopancreatography (ERCPG)	method is important in the diagnosis of diseases of pancreatic and biliary zone, filling the bile and pancreatic ducts with X-ray contrast substance
Rectoscopy	investigation of the mucous rectum and sigmoid intestines using rectoscope (35 cm)

4.2. Theoretical questions for the lesson:

1. Give the definitions of non-specific colitis, Crohn's disease.
2. Specify the risk factors of non-specific colitis, Crohn's disease.
3. Name the pathophysiological mechanisms of non-specific colitis, Crohn's disease.
4. Name the diagnostic criteria of non-specific colitis, Crohn's disease.
5. What are the endoscopic characteristics of non-specific colitis, Crohn's disease?
6. Modern classification of non-specific colitis, Crohn's disease.
7. Specify the principles and features of non-specific colitis, Crohn's disease pharmacotherapy according to modern recommendations.
8. What lifestyle modifications should be recommended for patients with non-specific colitis, Crohn's disease?

4.3. Practical work (tasks), performed on the lesson:

1. Interpret changes in general blood and biochemical blood tests in case of non-specific colitis, Crohn's disease.
2. Perform survey and physical examination of the patient and make preliminary diagnosis in case of non-specific colitis, Crohn's disease.
3. Manage the patient with suspected of non-specific colitis, Crohn's disease prescribe relevant laboratory and instrumental investigations and further treatment.
4. Interpret data of lower endoscopy with biopsy the intestines.
5. Analyze the radiological picture of the abdominal cavity.

Topic Content:

The gastrointestinal (GI) tract is composed of organs and tissues that have diverse forms and functions. It includes the esophagus, stomach, small intestine, large intestine, colon, rectum, biliary tract, gallbladder, liver, and pancreas. Despite the rapid proliferation of technology for the diagnosis of digestive diseases, the patient history and physical examination still hold central roles. When combined with a thorough patient history and physical examination, diagnostic

procedures are essential in the evaluation of GI disorders. This review describes the most commonly used tools available in clinical practice to evaluate patients with GI diseases.

A comprehensive patient history is the cornerstone in the evaluation of a patient with digestive complaints. A clear, detailed, chronologic account of the patient's problems should be ascertained. This account should include the onset of the problem, the setting in which it developed, and its manifestations. The onset of the problem often provides important information that helps to confirm diagnosis. For example, biliary pain, such as that encountered with symptomatic gallstone disease, typically evolves over minutes and lasts for hours, but pain caused by pancreatitis evolves over hours and lasts for days. The setting is always relevant as it provides clues to the possible origin of the disorder. For example, is the patient an alcoholic (liver disease, esophageal varices, or pancreatitis)? Does the patient have severe atherosclerosis (mesenteric ischemia)? Is the patient immunosuppressed (opportunistic infection)? Also aiding in the differential diagnosis is identification of factors that alleviate or exacerbate the principal symptom. For instance, ingesting a meal often relieves the pain of duodenal ulcer, but worsens that of gastric ulcer. The health care professional should ask questions that address the potential etiologic possibilities, including motility disorders, structural diseases, malignancies, infections, psychosocial factors, dietary factors, and travel associated diseases. Questions concerning past medical and family history detailing illnesses, surgeries, injuries, and habits are extremely valuable. Because many drugs have been reported to cause GI injury, a patient's medication history is also vital.

Physical Examination. Because the organ systems of the body interact and may provide important data needed for diagnosis, it is necessary to perform a thorough physical examination.3 A global evaluation of the patient should be performed with notable attention to appearances and vital signs because they may suggest clues to the patient's overall condition and stability. Careful examination of the abdomen is also an essential part of the work-up. Examination of the abdomen is classically approached by inspection, auscultation, percussion, and palpation. Inspection of the abdomen may reveal scars, hernias, bulges, or peristalsis. Auscultation is mainly focused on analysis of bowel sounds and identification of bruits. Percussion of the abdomen allows for detection of tympany, measurement of visceral organs, and detection of ascites. Palpation may allow the clinician to identify tenderness, rigidity, masses, and hernias. A digital rectal examination is used to detect masses, tenderness, and assess muscle tone. Stool on the examiner's glove obtained during rectal examination is often subjected to hemoccult testing for the indirect detection of occult blood [3].

Chronic hepatitis represents a series of liver disorders of varying causes and severity in which hepatic inflammation and necrosis continue for at least 6 months. Milder forms are nonprogressive or only slowly progressive, while more severe forms may be associated with scarring and architectural reorganization, which, when advanced, lead ultimately to cirrhosis. Finally, clinical and laboratory features of chronic hepatitis are observed occasionally in patients with such hereditary/metabolic disorders as Wilson's disease (copper overload), α1 antitrypsin deficiency, and nonalcoholic fatty liver disease and even occasionally in patients with alcoholic liver injury. Although all types of chronic hepatitis share certain clinical, laboratory, and histopathologic features, chronic viral and chronic autoimmune hepatitis are sufficiently distinct to merit separate discussions.

Classification. Chronic hepatitis includes chronic viral hepatitis, drug-induced chronic hepatitis, and autoimmune chronic hepatitis. In many cases, clinical and laboratory features are

insufficient to allow assignment into one of these three categories; these “idiopathic” cases are also believed to represent autoimmune chronic hepatitis.

Common to all forms of chronic hepatitis are histopathologic distinctions based on localization and extent of liver injury. These vary from the milder forms, labeled chronic persistent hepatitis and chronic lobular hepatitis, to the more severe form, formerly called chronic active hepatitis. When first defined, these designations were believed to have prognostic implications, which were not corroborated by subsequent observations. Categorization of chronic hepatitis based primarily on histopathologic features has been replaced by a more informative classification based on a combination of clinical, serologic, and histologic variables. Classification of chronic hepatitis is based on its cause; its histologic activity, or grade; and its degree of progression, or stage. Thus, neither clinical features alone nor histologic features—requiring liver biopsy—alone are sufficient to characterize and distinguish among the several categories of chronic hepatitis.

By cause:

- viral hepatitis (hepatitis B, hepatitis B plus D, or hepatitis C);
- autoimmune hepatitis, including several subcategories, I and II and III, based on serologic distinctions;
- drug-associated chronic hepatitis;
- toxic (including alcohol);
- metabolic;
- unknown cause, or cryptogenic chronic hepatitis.

Non-alcoholic liver disease is also known as “non-alcocholic steatohepatitis” can be related to chronic hepatitis.

By grade. Grade, a histologic assessment of necroinflammatory activity, is based on examination of the liver biopsy. An assessment of important histologic features includes the degree of periportal necrosis and the disruption of the limiting plate of periportal hepatocytes by inflammatory cells (so-called piecemeal necrosis or interface hepatitis); the degree of confluent necrosis that links or forms bridges between vascular structures— between portal tract and portal tract or even more important bridges between portal tract and central vein—referred to as bridging necrosis; the degree of hepatocyte degeneration and focal necrosis within the lobule; and the degree of portal inflammation.

Several scoring systems that take these histologic features into account have been devised, and the most popular are the histologic activity index (HAI), used commonly in the United States, and the METAVIR score, used in Europe.

Based on the presence and degree of these features of histologic activity, chronic hepatitis can be graded as mild, moderate, or severe.

By stage. The stage of chronic hepatitis, which reflects the level of progression of the disease, is based on the degree of hepatic fibrosis. When fibrosis is so extensive that fibrous septa surround parenchymal nodules and alter the normal architecture of the liver lobule, the histologic lesion is defined as cirrhosis. Staging is based on the degree of fibrosis as categorized on a numerical scale from 0−6 (HAI) or 0−4 (METAVIR). Several noninvasive approaches have been introduced to provide approximations of hepatic histologic stage, including serum biomarkers of fibrosis (e.g. Fibro-test, Acti-test, Steato-test, Nash-test) and imaging determinations of liver elasticity.

Epidemiology. Chronic infection by hepatitis viruses is by far the main cause of chronic hepatitis worldwide, with more than 500 million individuals chronically infected with hepatitis B

virus (HBV) or hepatitis C virus (HCV). Chronic viral hepatitis B and C are the leading cause of cirrhosis and hepatocellular carcinoma worldwide and account for more than 1 million deaths per year. Chronic HBV infection can be associated with infection by hepatitis D virus (HDV). Hepatitis A virus does not cause chronic hepatitis. Hepatitis E virus (HEV) does not cause chronic hepatitis, except rarely in patients who undergo liver transplantation. More than 350 million individuals, or 8.5% of the world's population, are chronic HBV carriers. HCV, which is present on all continents, is estimated to cause chronic infection in approximately 170 million individuals, or 3% of the world's population. Acute HCV infection evolves into chronic infection in 50 to 80% of cases. HDV infection occurs only in HBsAg carriers. Only approximately 2% of patients acutely coinfected with HDV and HBV develop chronic hepatitis D. Autoimmune hepatitis typically presents between the ages of 15 and 25 years or between the ages of 45 and 60 years, and it is more common in women. Along with primary biliary cirrhosis and primary sclerosing cholangitis, autoimmune hepatitis is one of the three major autoimmune liver diseases. NAFLD has a prevalence ranging from 15 to 30% in the United States. The true prevalence of alcoholic liver disease is not known, but nearly 1% of North American adults are believed to have alcoholic liver disease. NAFLD is one of the most common causes of elevated liver enzymes and chronic liver disease in the Western world. Its incidence in adults and children is rising rapidly owing to the ongoing epidemics of obesity, type 2 diabetes mellitus, and metabolic syndrome. Its prevalence is quite high in certain patient populations; for example, nearly 80% of type 2 diabetic patients and 90% of morbidly obese individuals have imaging evidence of NAFLD.

Etiology and pathogenesis. *HBV* is not a cytopathic virus. Rather, liver injury in chronic hepatitis B is a consequence of the local immune response at the immune elimination phase. In particular, liver injury is related to cytotoxic T cells that recognize and kill infected hepatocytes that express HBV antigens at their surface and to the local production of cytokines. Chronic inflammation triggers fibrogenesis through the activation of hepatic stellate cells. The hepatitis B X protein may also directly activate fibrogenesis. As a result, many patients with chronic hepatitis B have progressive fibrosis, which may evolve into cirrhosis.

Chronic HCV infection is responsible for necroinflammatory lesions of varying severity, sometimes associated with steatosis, which is the accumulation of triglycerides in hepatocytes. HCV is not a cytopathic virus. Liver injury in chronic hepatitis C is related to the action of immune effectors that recognize and kill infected hepatocytes that express HCV antigens at their surface. Chronic inflammation triggers fibrogenesis through the activation of hepatic stellate cells. Fibrosis progresses at nonlinear rates that are generally faster in older patients, in males, and in the presence of chronic alcohol intake, viral coinfections, or immunosuppression. The severity of chronic hepatitis is independent of the HCV RNA level and of the HCV genotype. This chronic inflammation and progression of fibrosis predispose patients to cirrhosis and hepatocellular carcinoma.

Chronic hepatitis D is generally severe, with more than 80% of patients developing cirrhosis.

Autoimmune hepatitis is believed to be caused by autoimmune reactions against normal hepatocytes in genetically predisposed persons or persons exposed to unidentified triggers of an autoimmune process against liver antigens. Associations are seen with the human leukocyte antigen (HLA) class I B8 and class II DR3 and DR52a loci. In Asians, autoimmune hepatitis is associated with HLA DR4.

Toxic hepatitis. The liver is central to the metabolism of exogenous substances. Most drugs and xenobiotics cross the intestinal brush border because they are lipophilic. Biotransformation is the process by which lipophilic therapeutic agents are rendered more hydrophilic by the liver, resulting in drug excretion in urine or bile. In most instances, biotransformation changes a nonpolar to a polar compound through several steps. Foremost are oxidative pathways (e.g., hydroxylation) mediated by the cytochromes (CYPs) P-450. The next step is typically esterification to form sulfates and glucuronides, a process that results in the addition of highly polar groups to the hydroxyl group. These two enzymatic steps are referred to as phase I (CYP oxidation) and phase II (esterification). Other important metabolic pathways involve glutathione-S-transferase, acetylating enzymes, and alcohol dehydrogenase, but the principal metabolic pathways for most pharmacologic agents involve CYPs and subsequent esterification. The exact details of the pathogenesis of liver injury are unclear for most drugs. Although most liver injury involves direct hepatocyte necrosis or apoptosis (hepatocellular injury), some drugs injure primarily the bile ducts or canaliculi and cause cholestasis without significant damage to hepatocytes. Other drugs affect sinusoidal cells or present a particular pattern of liver injury affecting multiple cell types (mixed type). Another approach to drug reactions emphasizes the histologic changes involved and the cell type.

REACTION TYPE	IMPLICATED DRUGS OR TOXINS
Autoimmune (attack on cell surface markers)	Lovastatin, methyldopa, nitrofurantoin
Cholestatic (attack on bile ducts)	Anabolic steroids, carbamazepine, chlorpromazine, estrogen, erythromycin
Fibrosis (activation of stellate cells leads to fibrosis)	Methotrexate, vitamin A excess
Granulomatous (macrophage stimulation)	Allopurinol, diltiazem, nitrofurantoin, quinidine, sulfa drugs
Hepatocellular (damage to smooth endoplasmic reticulum and immune cell surface)	Acetaminophen, Amanita poisoning, diclofenac, isoniazid, lovastatin, nefazodone, trazodone, venlafaxine
Immunoallergic (cytotoxic cell attack on surface determinants)	Halothane, phenytoin, sulfamethoxazole
Mixed (see above)	Amoxicillin-clavulanate, carbamazepine, cyclosporine, herbs, methimazole
Oncogenic (hepatic adenoma formation)	Oral contraceptives, androgenic agents
Steatohepatitis (mitochondrial dysfunction: β-oxidation and respiratory chain)	Amiodarone, perhexiline maleate, tamoxifen
Vascular collapse (ischemic damage)	Cocaine, ecstasy, nicotinic acid
Veno-occlusive disease (endotheliitis of sinusoidal endothelial cells)	Busulfan, cytoxan

Steatosis in the liver can be present in a microvesicular or macrovesicular pattern. Macrovesicular steatosis, the most common form, is characterized histologically by a single vacuole of fat filling up the hepatocyte and displacing the nucleus to the cell's periphery. Macrovesicular steatosis is typically caused by alcohol, diabetes, or obesity. Sometimes drugs such as corticosteroids or methotrexate may cause these hepatic changes. Amiodarone has been associated with a picture resembling alcoholic hepatitis, occasionally with progression to cirrhosis. The pathophysiology involves accumulation of phospholipids in the liver, eyes,

thyroid, and skin. Treatment is primarily withdrawal of the drug and observation, although the half-life of amiodarone is prolonged.

In microvesicular steatosis, hepatocytes contain numerous small fat vesicles that do not displace the nucleus. These lesions are associated with disruption of mitochondrial DNA, resulting in anaerobic metabolism that leads to lactic acidosis in the most severe cases. Macrovesicular and microvesicular lesions may be observed concomitantly in some patients, and microvesicular lesions are more often associated with a poor prognosis. Hepatocellular necrosis may also be present. Acute fatty liver of pregnancy and Reye's syndrome are two examples of severe liver diseases caused by microvesicular steatosis.

Nonalcoholic fatty liver disease NAFLD is seen most commonly in obese, diabetic, and hyperlipidemic nonalcoholic patients. Not all obese patients have fatty liver disease, but NASH occurs in about 3 to 5% of the overweight and obese population, and liver fibrosis is increased in up to 40% of these individuals. Most patients with hepatic steatosis have stable, nonprogressive disease, but NASH can progress to cirrhosis. Many patients who were previously described as having cryptogenic cirrhosis are now thought to have NASH, especially because catabolic cirrhosis reduces macrovesicular steatosis, so late biopsy may show just a bland cirrhosis. Histologically, NAFLD resembles alcoholic liver disease, but it occurs in individuals without significant alcohol consumption. Average alcohol consumption greater than two drinks per day in men and greater than one drink per day in women generally is not consistent with a diagnosis of NAFLD. In addition, the definition of NAFLD excludes patients with a history of exposure to steatogenic medications such as amiodarone, methotrexate, and tamoxifen. NAFLD encompasses a spectrum of abnormal liver histology, ranging from simple steatosis to nonalcoholic steatohepatitis (NASH) and cirrhosis. In simple steatosis, liver histology reveals macrovesicular steatosis without ballooning degeneration of hepatocytes or liver fibrosis. NASH, which is a more advanced form of NAFLD, is histologically characterized by macrovesicular steatosis, ballooning degeneration of the hepatocytes, and sinusoidal fibrosis.

The major risk factors for NAFLD include obesity, type 2 diabetes mellitus, metabolic syndrome, and dyslipidemia. Other comorbidities associated with NAFLD include polycystic ovary syndrome, hypothyroidism, hypopituitarism, and sleep apnea. Two fundamental defects in NAFLD are insulin resistance/hyperinsulinemia and excessive levels of nonesterified fatty liver within the hepatocytes. An excessive influx of nonesterified fatty acids into the hepatocytes results in macrovesicular steatosis, which is predominantly centrilobular in location. Additionally, patients with NAFLD have increased de novo intrahepatic lipogenesis. Although patients with NAFLD robustly esterify free fatty acids in neutral triglycerides, free fatty acids within the hepatocytes are considered the primary mediators of cell injury (lipotoxicity). In the background of hepatic steatosis, factors that promote cell injury, inflammation, and fibrosis include oxidative stress, endoplasmic reticulum stress, apoptosis, adipocytokines, and stellate cell activation. The sources of oxidative stress include mitochondria and microsomes. Adipocytokines that play an important role in the pathogenesis of NAFLD include adiponectin and TNF-α. It is unclear why some patients with NAFLD exhibit NASH, whereas other patients with a comparable risk factor profile have only simple steatosis. There is a consistent and significant relationship of PNPLA3 genetic polymorphisms with the severity of steatosis and other histologic features of NAFLD. However, the genetic factors that play a role in NASH and NAFLD have not been fully elucidated.

Alcoholic fatty liver disease will develop in nearly 90% of individuals who consume alcohol heavily (on average, >6 drinks per day), and some individuals develop the more severe

conditions of alcoholic hepatitis and alcoholic cirrhosis. The mechanisms underlying alcoholic liver injury can be broadly categorized into those caused by the effects of alcohol directly on hepatocytes and those caused by the effects mediated by Kupffer cells. The hepatocyte mechanisms include the altered redox state induced by alcohol and aldehyde dehydrogenase reactions, the oxidative stress and lipid peroxidation caused by the induction of CYP2E1 enzymes and the mitochondrial electron transfer system, and the effects of alcohol on the nuclear transcription factors (AMP kinase and SREBP-1c), protein adduct formation, and altered methionine and folate metabolism with resulting endoplasmic reticulum stress. Chronic alcohol consumption increases gut permeability, and the resulting portal endotoxemia activates Kupffer cells. Activated Kupffer cells release a number of proinflammatory mediators, including tumor necrosis factor-α (TNF-α), transforming growth factor-β1 (TGF-β1), interleukins 1, 6, 8, and 10, and platelet-derived growth factor (PDGF). TNF-α has plethora of biologic effects and causes hepatocyte apoptosis, whereas TGF-β1 and PDGF play important roles in stellate cell activation, collagen production, and hepatic fibrosis. Among the known risk factors for developing alcoholic liver disease, the amount of alcohol consumed is the single most important. For unclear reasons, only 30 to 35% of individuals with heavy and long-term drinking develop alcoholic hepatitis, and less than 20% develop cirrhosis. Women are at higher risk; for example, the risk of alcoholic cirrhosis increases after 10 years of alcohol consumption at quantities of more than 60 to 80 g/ day in men, whereas in women, it can develop at quantities of only more than 20 g/day. Moreover, the peak incidence of alcoholic liver disease in women is approximately a decade earlier than in men. The type of alcoholic beverage consumed may not be as critical, but “spirits” and beer may be more hepatotoxic than wine. African-American and Hispanic ethnic groups may be predisposed to more significant alcoholic liver injury. Both obesity and protein-calorie malnutrition, in which micronutrients and antioxidant capacity are diminished, also are important predispositions. Polymorphisms in genes associated with alcohol metabolism (alcohol and aldehyde dehydrogenases and cytochrome P-450 enzymes) and dysregulated cytokine production (e.g., TNF-α) may also influence genetic susceptibility. In patients with other forms of chronic liver disease (e.g., viral hepatitis B or C), concomitant alcohol consumption significantly aggravates liver injury.

Clinical features and diagnosis. The clinical symptoms of *chronic viral and autoimmune hepatitis* are typically nonspecific, and many patients have no symptoms. Fatigue, sleep disorders, and right upper quadrant pain may be present. Often the diagnosis is made when liver test abnormalities are identified by blood testing during a routine health evaluation or assessment for an unrelated problem or at the time of voluntary blood donation. More advanced symptoms include poor appetite, nausea, weight loss, muscle weakness, itching, dark urine, and jaundice. Patients can progress to full-blown cirrhosis, with its typical clinical manifestations. If cirrhosis is present, weakness, weight loss, abdominal swelling, edema, bruisability, gastrointestinal bleeding, and hepatic encephalopathy with mental confusion may arise. Other findings may include spider angiomas, palmar erythema, ascites, edema, and skin excoriations.

Levels of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) are usually two to five times the upper limit of normal. The ALT level is generally higher than the AST level, but both can be normal in mild or inactive disease or 10 to 25 times the upper limit of normal during acute exacerbations. Biologic tests can establish the specific diagnosis. Alkaline phosphatase and γ-glutamyl transpeptidase levels are usually minimally elevated unless cirrhosis is present. Serum bilirubin and albumin levels and the prothrombin time are normal unless the disease is severe or advanced. Serum immunoglobulin levels are mildly elevated or normal in

chronic viral hepatitis but may be very elevated in autoimmune hepatitis. Results that suggest the presence of advanced fibrosis are a platelet count below 160,000, AST levels higher than ALT levels, elevation in serum bilirubin, decrease in serum albumin, prolongation of the prothrombin time, elevation in α-fetoprotein levels, and presence of rheumatoid factor or high globulin levels.

Serologic markers used to diagnose chronic hepatitis B include HBsAg, anti-HBs antibodies, total anti–hepatitis B core (HBc) antibodies and anti-HBc immunoglobulin M (IgM), HBeAg, and anti-HBe antibodies. Molecular markers include HBV DNA and HBV resistance substitutions; real-time polymerase chain reaction (PCR)–based assays are the best way to detect and quantify HBV DNA. Chronic HBV infection is defined by the persistence of HBsAg in the serum for more than 6 months after the acute episode.

Chronic HCV infection is defined by the persistence of HCV RNA for more than 6 months. In patients with clinical and/or biologic signs of chronic liver disease, chronic hepatitis C is diagnosed by the simultaneous presence of anti-HCV antibodies and HCV RNA. Detectable HCV replication in the absence of anti-HCV antibodies is observed almost exclusively in patients who are profoundly immunosuppressed, on hemodialysis, or agammaglobulinemic. The HCV genotype, which has important therapeutic implications, should be determined. Anti-HCV IgM, which is found in about 50% of patients with chronic hepatitis, is of no significance.

Markers of HDV infection should be sought at least once in every chronic HBsAg carrier. Both total anti-HD antibodies and anti-HD IgM remain at high levels in chronic HDV infection, and HDV RNA is present.

Autoimmune type 1 (classic) hepatitis is characterized by the presence of titers of 1 : 80 or higher of antinuclear (ANA), anti–smooth muscle (SMA), antiactin, and anti-asialoglycoprotein receptor antibodies. Type 2 autoimmune hepatitis is characterized by similar elevations of anti– liver-kidney microsomal 1 antibodies and anti–liver cytosol 1 antibodies (anti-LKM1) without antinuclear or anti–smooth muscle antibodies. Type 3 is characterized by elevation of anti-SLA (auto-antibodies against soluble liver and pancreas antigen) without ANA, SMA and LKM-1. Liver biopsy shows features that are typical of all chronic types of hepatitis, except plasma cell infiltrates.

Hepatic ultrasound can determine the texture and size of the liver and spleen, exclude hepatic masses, and assess the gallbladder, intrahepatic bile ducts, and portal venous flow. Computed tomography and magnetic resonance imaging of the liver are helpful if a mass or other abnormality is found by ultrasound. Hepatic elastography can assess liver stiffness as a marker of fibrosis.

Liver biopsy is usually critical for diagnosis and to determine the severity of disease. Hepatocellular necrosis is typically eosinophilic degeneration or ballooning degeneration throughout the parenchyma, greater in the periportal area, spotty, or piecemeal. Fibrosis also typically begins in the periportal regions and can link adjacent portal areas or portal and central areas (bridging fibrosis), distort the hepatic architecture, and lead to cirrhosis and portal hypertension. The histologic grade of chronic hepatitis can be determined by combining scores for periportal necrosis and inflammation, lobular necrosis and inflammation, and portal inflammation.

Markers of viral hepatits:

	Antigen(s)	**Antibodies**	**Remarks**
HCV	C100-3 C33c C22-3	Anti-HCV	Bloodborne agent, formerly labeled non-A, non-B

	NS5		hepatitis Acute diagnosis: anti-HCV (C33c, C22-3, NS5), HCV RNA Chronic diagnosis: anti-HCV (C100-3, C33c, C223, NS5) and HCV RNA; cytoplasmic location in hepatocytes
HBV	HBsAg HBcAg HBeAg HBcAg HBeAg HBsAg	Anti-HBs Anti-HBc Anti-HBe Anti-HBc Anti-HBe Anti-HBs	Bloodborne virus; carrier state Acute diagnosis: HBsAg, IgM anti-HBc Chronic diagnosis: IgG anti-HBc, HBsAg Markers of replication: HBeAg, HBV DNA Liver, lymphocytes, other organs Nucleocapsid contains DNA and DNA polymerase; present in hepatocyte nucleus; HBcAg does not circulate; HBeAg (soluble, nonparticulate) and HBV DNA circulate—correlate with infectivity and complete virions HBsAg detectable in >95% of patients with acute hepatitis B; found in serum, body fluids, hepatocyte cytoplasm; anti-HBs appears following infection—protective antibody
HDV	HBsAg HDAg	Anti-HBs Anti-HDV	Defective RNA virus, requires helper function of HBV (hepadnaviruses); HDV antigen (HDAg) present in

			hepatocyte nucleus Diagnosis: anti-HDV, HDV RNA; HBV/HDV co-infection—IgM anti-HBc and anti-HDV; HDV superinfection—IgG anti-HBc and anti-HDV

Evaluation of a patient with a suspected drug reaction is directed toward establishing the timeline for all drugs or herbs the patient may have taken. Responsible drugs have usually been started between 5 and 90 days before the onset of symptoms. Evidence of viral hepatitis, gallstones, alcoholic liver disease, pregnancy, severe right heart failure, or a period of hypotension points to these specific causes. Less commonly, cytomegalovirus, Epstein-Barr virus, or herpesviruses can cause hepatic injury, primarily in immunosuppressed individuals. If all these causes can be excluded, the temporal relationship fits, and the patient begins to improve after withdrawal of the drug, the diagnosis is more secure. Liver biopsy is of limited value because the histologic picture in most cases of drug-induced liver injury is no different from that of viral hepatitis. Nevertheless, an occasional liver biopsy specimen in an enigmatic case might reveal eosinophils or granulomas, consistent with a drug reaction.

Critical to the diagnosis of NAFLD is a careful history to be sure that alcohol ingestion is less than 20 g/day. Routine laboratory testing for other common liver diseases (e.g., hepatitis B and C, hemochromatosis), as well as less common ones (e.g., Wilson disease, α1-antitrypsin deficiency, autoimmune liver diseases), should be performed. Imaging studies can confirm characteristic features of a fatty liver (e.g., bright liver on ultrasound). These findings are nonspecific, however, and the ultimate diagnosis of NAFLD or NASH requires liver biopsy. The principal treatments are dietary changes and weight loss, but some medications can also be helpful in selected patients.

Patients with alcoholic liver disease may have signs and symptoms from underlying alcoholism as well as those caused by liver disease. Stigmata of chronic alcoholism include palmar erythema, spider nevi, bilateral gynecomastia, testicular atrophy, bilateral parotid enlargement, and Dupuytren's contractures. The clinical features of liver disease will depend on the stage of alcoholic liver disease, that is, whether a patient has alcoholic fatty liver or more advanced liver disease such as alcoholic hepatitis and cirrhosis. Patients with alcoholic fatty liver disease are generally asymptomatic, but some patients may have anorexia, fatigue, right upper quadrant discomfort, and tender hepatomegaly. These patients may also have biochemical evidence of alcoholism and alcoholic liver disease with macrocytosis as well as elevated levels of aspartate aminotransferase (AST) and γ-glutamyl transpeptidase (GGT). Patients with alcoholic fatty liver typically do not have jaundice, ascites, or splenomegaly. Patients with alcoholic hepatitis may have a more dramatic presentation with severe malaise, fatigue, anorexia, fever, evidence of protein-calorie malnutrition, and features of decompensated liver disease, including jaundice, coagulopathy, ascites, and encephalopathy. Physical examination invariably shows at least some features of chronic alcoholism, and jaundice, ascites, and splenomegaly are common. The laboratory examination is typically abnormal. Common hematologic abnormalities include leukocytosis with neutrophil predominance, macrocytic anemia, thrombocytopenia, and a prolonged prothrombin time. Liver biochemistries are abnormal with an elevated AST and

ratio of AST to alanine transferase (ALT), alkaline phosphatase, GGT, and total bilirubin, but decreased levels of serum albumin. The AST rarely exceeds 300 IU/L. Serum electrolyte abnormalities including hypokalemia, hypomagnesemia, hypocalcemia, and hypophosphatemia are frequent. The diagnosis of alcoholic liver disease strongly depends on the history of excessive alcohol consumption and the presence of liver disease. Although laboratory abnormalities are not specific for alcoholic liver disease, they can be quite suggestive in the context of excessive alcohol consumption. An AST/ALT ratio of more than 2 is typical in alcoholic liver disease, and ALT values greater than 150 to 200 IU/L are very rare in alcoholic liver disease. Serology testing for co-existing chronic viral hepatitis is critical. Diagnostic dilemmas arise when a patient denies excessive alcohol consumption in the face of clinical features that are suggestive of alcoholic liver disease. Interviewing family members regarding specific alcohol consumption may be helpful in the accurate ascertainment of alcohol consumption. Elevated blood levels of carbohydrate-deficient transferrin, which is a form of transferrin with fewer than the four sialic acid chains present in normal transferrin, can identify recent heavy alcohol consumption. Hepatic imaging by ultrasound, computed tomography (CT), or magnetic resonance imaging (MRI) will show changes consistent with hepatic steatosis or more advanced forms of liver disease, such as alcoholic hepatitis and cirrhosis. Imaging is also important to exclude other forms of liver disease, including malignancy and biliary obstruction. Imaging findings specific for alcoholic liver disease include an enlarged caudate lobe, greater visualization of the right posterior hepatic notch, and focal fat sparing or geographic fat distribution. Because specific treatment for alcoholic hepatitis may be harmful in patients with other liver diseases, it is very important to exclude other predominant or coexisting liver diseases, including chronic viral hepatitis and drug-induced liver injury, especially from acetaminophen, by history, blood tests, and biopsy if needed. Hyperferritinemia generally reflects an acute phase reactant, rather than an iron overload disorder, so it usually will return to normal when the acute liver injury resolves. Liver biopsy is the key to precisely characterizing the nature of alcoholic liver disease and determining whether a patient has fatty liver or more advanced alcoholic hepatitis. Histologic features of alcoholic fatty liver include macrovesicular steatosis that is predominantly zone 3 in nature. In alcoholic hepatitis, the biopsy is more striking and reveals macrovesicular steatosis, lobular neutrophilic infiltration, Mallory’s hyaline, balloon degeneration of the hepatocytes, and perivenular fibrosis. In general, patients with alcoholic hepatitis also have histologic evidence of chronic liver injury in the form of more advanced fibrosis (periportal or bridging fibrosis, or cirrhosis).

NAFLD is often asymptomatic but may rarely also cause fatigue and right upper quadrant pain. Physical examination may reveal hepatomegaly, palmar erythema, and spider nevi. If liver disease is advanced, the features of liver failure, such as ascites, encephalopathy, and abdominal collateral vessels, are present. Simple steatosis is benign with a minimal risk of cirrhosis, whereas NASH is progressive and can lead to cirrhosis and liver failure. In up to 20% of patients with NASH, liver histology will worsen and cirrhosis will develop over a 10- to 15-year period. Disease progression during the early phase can be identified only with a repeat liver biopsy, but in later stages, the signs and symptoms of portal hypertension (e.g., abdominal collateral vessels and low platelet count) indicate the development of cirrhosis.

NAFLD is generally suspected when aminotransferase levels are asymptomatically elevated in an individual with metabolic risk factors (obesity and diabetes) or when liver imaging (ultrasound, CT, or MRI) obtained for another reason shows fatty infiltration. The diagnosis of NAFLD requires that there is no history of previous or ongoing significant alcohol consumption,

no exposure to steatogenic medications, and no evidence of other causes of liver disease, such as viral hepatitis B or C. Elevated levels of aminotransferases, although common, are not required for the diagnosis of NAFLD. In contrast to alcoholic liver disease, ALT levels are higher than AST levels, but they rarely exceed 250 IU/L. In general, AST and ALT levels do not have diagnostic or prognostic significance.

Mild hyperferritinemia is common and should not be confused with hereditary hemochromatosis. Similarly, low-grade autoantibody (antinuclear antibody, anti–smooth muscle antibody) positivity is not uncommon and should not be confused with autoimmune liver disease. Because steatosis is common in patients with Wilson's disease, serum ceruloplasmin should be obtained as part of the diagnostic evaluation. Fatty liver on ultrasonogram has a positive predictive value of only 77% and a negative predictive value of only 67% when compared with liver biopsy. Abdominal MRI is more accurate, but its high cost limits its usefulness in routine practice. Because none of these three tests can differentiate simple steatosis from NASH nor identify cirrhosis until hepatic fibrosis has caused overt portal hypertension, liver biopsy is required to establish the presence of NASH or cirrhosis. Common indications for a percutaneous liver biopsy in patients with NAFLD include persistently high aminotransferase levels, inability to exclude a competing or a coexisting cause (e.g., iron overload or autoimmune liver disease), or clinical suspicion of severe liver disease. In patients with NASH, liver histology shows steatosis, inflammation, ballooning, and fibrosis.

Differential diagnosis. Patients with suspected chronic viral or autoimmune hepatitis should be evaluated carefully for fatty liver, alcohol- or drug-induced liver disease, and metabolic liver diseases, each of which can coexist with hepatitis. Liver biopsy can exclude other diagnoses that mimic chronic hepatitis, including fatty liver, alcoholic liver disease, steatohepatitis, drug-induced liver disease, sclerosing cholangitis, iron overload, and veno-occlusive disease.

Liver test patterns in hepatobiliary disorders.

Type of Disorder	Bilirubin	Aminotransferases	Alkaline Phosphatase	Albumin	Prothrombin Time
Hemolysis/Gilbert's syndrome	Normal to 86 μmol/L (5 mg/dL) 85% due to indirect fractions No bilirubinuria	Normal	Normal	Normal	Normal
Acute hepatocellular necrosis (viral and drug hepatitis, hepatotoxins, acute heart failure)	Both fractions may be elevated Peak usually follows aminotransferases Bilirubinu	Elevated, often >500 IU, ALT > AST	Normal to <3× normal elevation	Normal	Usually normal. If >5× above control and not corrected by parenteral vitamin K, suggests poor prognosis

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Chronic hepatocellular disorders	Both fractions may be elevated Bilirubinuria	Elevated, but usually <300 IU	Normal to <3× normal elevation	Often decreased	Often prolonged Fails to correct with parenteral vitamin K
Alcoholic hepatitis, cirrhosis	Both fractions may be elevated Bilirubinuria	AST:ALT >2 suggests alcoholic hepatitis or cirrhosis	Normal to <3× normal elevation	Often decreased	Often prolonged Fails to correct with parenteral vitamin K
Intra- and extrahepatic cholestasis	Both fractions may be elevated	Normal to moderate elevation	Elevated, often >4× normal elevation	Normal, unless chronic	Normal If prolonged, will correct with parenteral vitamin K
(Obstructive jaundice)	Bilirubinuria	Rarely >500 IU		Normal	Normal
Infiltrative diseases (tumor, granulomata); partial bile duct obstruction	Usually normal	Normal to slight elevation	Elevated, often >4× normal elevation Fractionate, or confirm liver origin with 5'-nucleotidase or γ glutamyl transpeptidase		

Differences in diagnostic and therapy of viral hepatitis.

Type of Hepatitis	Diagnostic Test(s)	Autoantibodies	Therapy
Chronic hepatitis B	HBsAg, IgG anti-HBc, HBeAg, HBV DNA	Uncommon	IFN-α, PEG IFN-α Oral agents: First-line: entecavir, tenofovir Second-line: lamivudine, adefovir, telbivudine
Chronic hepatitis C	Anti-HCV, HCV RNA	Anti-LKM1a	PEG IFN-α plus ribavirin Telaprevirb Boceprevirb
Chronic hepatitis D	Anti-HDV, HDV	Anti-LKM3	IFN-α, PEG IFN-αc

	RNA, HBsAg, IgG anti-HBc		
Autoimmune hepatitis	ANAd (homogeneous), anti-LKM1 (±) Hyperglobulinemia	ANA, anti-LKM1 anti-SLAe	Prednisone, azathioprine
Drugassociated —	-	Uncommon	Withdraw drug
Cryptogenic	All negative	None	Prednisone (?), azathioprine (?)

Treatment. Chronic HBV infection is not curable, but it can usually be controlled by appropriate antiviral drugs. HCV infection is curable, but less than 50% of patients who have access to therapy are cured (look table above).

Autoimmune hepatitis responds to immunosuppression with corticosteroids and azathioprine. The clinical symptoms and liver test abnormalities of autoimmune hepatitis generally respond promptly to prednisone, usually at a dose of 20 to 30 mg/ day, with a decrease in serum aminotransferase levels to the normal or nearnormal range within 1 to 3 months; higher doses may be required in patients with more severe disease. Lack of a biochemical or clinical response should lead to reevaluation of the diagnosis. Azathioprine 50 to 100 mg can be combined with prednisone or added later to reduce long-term steroid side effects.

Prompt discontinuation of a suspected drug in toxic hepatitis is mandatory. Available antidotes should be used for acetaminophen (N-acetylcysteine) and Amanita poisoning (penicillin 300,000 to 1 million U/kg/day intravenously and thioctic acid 5 to 100 mg every 6 hours intravenously have been recommended, but there are no controlled trials). General supportive therapy ranges from intravenous fluid replacement to intensive monitoring and treatment of patients with hepatic encephalopathy secondary to acute liver failure. Liver transplantation is performed in more than 50% of patients with idiosyncratic drug-induced acute liver failure because the survival rate in this setting without transplantation is less than 20%.

Total abstinence, which is the most important treatment measure, is mandatory for the improvement of the clinical and histologic features of alcoholic liver disease. Its benefits are unequivocal, even in patients with severe decompensation. However, long-term abstinence is difficult to achieve, so a multidisciplinary approach with counseling and medications that promote abstinence should be considered. Disulfiram is not commonly used owing to its poor tolerability and hepatotoxicity. Opioid antagonists, such as naltrexone (50 mg/day for up to 6 months or even longer), nalmefene (20 mg/day as maintenance), and acamprosate (333 mg tablets, 2 tablets three times each day for 1 year) can help promote abstinence when used as part of a multidisciplinary approach. If a patient's liver biopsy is consistent with alcoholic hepatitis and there is no evidence ofother inflammatory liver diseases, such as hepatitisC, corticosteroids and pentoxifylline (400 mg three times daily for 28 days) are of some benefit. Prednisolone (40 mg per day for 4 weeks) should be given to carefully selected patients who have a score of greater than 32 on Maddrey's discriminant function (4.6 × [patient's prothrombin time—control prothrombin time] + total bilirubin level) and encephalopathy, but do not have gastrointestinal bleeding or systemic infection. All patients with alcoholic hepatitis and alcoholic cirrhosis should be assessed and treated for protein-calorie malnutrition and micronutrient deficiency.

Lifestyle modification with dietary restriction and regular exercise is the first choice of treatment for NAFLD. It is generally recommended that patients with NAFLD lose 10% of their body weight in a gradual fashion, but this goal is difficult to achieve. If resources are available, a multidisciplinary approach with behavioral therapy, dietary advice, and monitoring by a professional nutritionist and an exercise expert is more successful than a prescriptive approach. Statins (e.g., atorvastatin 20 mg daily) with or without vitamins C and E can improve liver test results and reduce subsequent NAFLD. In a large trial, 800 IU of vitamin E administered daily for 2 years significantly improved liver histology. Thiazolidinedione insulin sensitizers (pioglitazone and rosiglitazone) improve steatosis, inflammation, and ballooning, but may not improve fibrosis. Unfortunately, the weight gain that is common with thiazolidinediones may offset the histologic benefits that they offer. In morbidly obese individuals with NASH and other significant metabolic comorbidities, foregut bariatric surgery can lead to significant improvement in hepatic histology, but the physician must exclude the presence of portal hypertension before offering this type of surgery. Patients with NAFLD often have dyslipidemia that puts them at excessive risk for coronary artery disease; their dyslipidemia should be treated aggressively with statins and other lipidlowering agents, which can be safely administered to patients with NAFLD and NASH. Carefully selected patients with decompensated cirrhosis owing to NASH can be treated with liver transplantation, but recurrence during the post-transplantation period is common.

Materials for self-control:

A. Tests and situational tasks for self-control:

1. A 24-year-old female patient complains of pain in the right hypochondrium that is getting worse after taking meals; nausea, fever up to37,7oC, icteric skin, pain in the large joints. These presentations have been observed for 8 months. Objectively: hepatosplenomegaly. Blood test results: ESR- 47 mm/h, total bilirubin - 86,1 mmol/l, direct bilirubin - 42,3 mmol/l. Total protein - 62 g/l, albumins - 40%, globulins - 60%, gamma globulins - 38%. Viral hepatitis markers were not detected. The antibodies to smooth muscle cells are present. On ultrasound the portal vein diameter was of 1 cm. What is the most likely diagnosis?

A. Primary biliary cirrhosis
B. Autoimmune hepatitis
C. Gilbert’s syndrome
D. Cholangiogenic hepatitis
E. Hemachromatosis

2. A 40 y. o. patient was admitted to the gasteroenterology department with skin itching, jaundice, discomfort in the right subcostal area, generalized weakness. On examination: skin is jaundice, traces of scratches, liver is +5 cm, spleen is 6x8 cm. In blood: alkaline phosphatase - 2,0 mmol/(hour*L), general bilirubin - 60 mkmol/L, cholesterol - 8,0 mmol/L. What is the leading syndrome in the patient?

A. Cytolytic
B. Cholestatic
C. Mesenchymal inflammatory
D. Asthenic
E. Liver-cells insufficiency

3. 23 years old patient has complaints on pain in the right subcostal area, periodic bitter belch, nausea, appetite loss. From the anamnesis: appendectomy had been conducted three years ago. In 2 months icterus appeared and patient was treated in infectious hospital. At the examination liver is enlarged on 2 cm. In blood: general bilirubin - 76 mkmol/l, direct bilirubin - 14,9 mkmol/, ALT - 1,35. What disease are you thinking of?

A. Cirrhosis of liver
B. Chronic cholangitis
C. Chronic cholecystitis
D. Benign Gilber`s icterus
E. Chronic hepatitis B

4. Patient K., 24 years old, complains of pain in the right subcostum and joints, icteric skin, weight loss - 10 kg for a year, temperature 38°C. A disease began after childbirth half a year ago. Objectively: icteric skin and scleras, there are xanthomas on eyelids. Liver +4 cm, dense, painful, edge is sharp. Spleen +2 cm. Blood tests: AST - 2,8, ALT - 3,4, general bilirubin - 97,6, free - 54,6, HbsAg was not determined. Name the basic mechanism of pathogenesis:

A. Viral infection
B. Toxic damage of hepatocytes
C. Fatty dystrophy of liver
D. Violation of bile outflow
E. Autoimmune

5. 20 years old patient was diagnosed chronic viral hepatitis in gastroenterologic unit. What group of preparations can be included to the base therapy?

A. Hepatoprotector
B. Antibacterial
C. Anabolic steroid hormones
D. Vitamins
E. Glucocorticoids and cytostatic

6. 36 years old patient complains of general weakness, excitability, heavy feeling in the right subcostum, subfebrile temperature. From the anamnesis: viral hepatitis 2 years ago. The condition worsened during last 3 months. Objectively: lower edge of liver 3 cm below right costal arc. Laboratory analysis: general bilirubin - 64,5 mkmol/l, direct - 22,7 mkmol/l, gamma - globulins - 31%, AST - 1,42, ALT - 1,96. The signs of active virus replication (HBeAg-positive reaction) are found. Choose one of preparations for ethiotropic treatment of the patient:

A. Alpha - interferon
B. Prednizolon
C. Essentiale - forte
D. Carsil
E. Levamizol

7. A man, 40 years old, suffers on autoimmune hepatitis. In blood: general bilirubin 42 mkmol/l, transaminases: ALT - 2,3, AST - 1,8. What is the most effective treatment?

A. Glucocorticoids, cytostatic preparations
B. Antibacterial preparations

C. Hepatoprotector preparations
D. Antiviral preparations
E. Hemosorbtion, vitaminotherapia

8. Patient, 28 years old, has been contacting with toxic chemicals for 6 years. His complaints are headache, incresed fatigue, heavy feeling in the right subcostum, decreased appetite, icterus. Objectively: skin and scleras are subicteric. Abdomen is bloated, liver +5 cm, surface is even. In blood: Hb - 110 g/l, L - 8,1x109/l, blood sedimentation - 30 mm/h, general bilirubin - 65 mkmol/l, sugar - 6,3 mmol/l. What diagnosis is the most credible?

A. Hemochromatosis
B. Chronic toxic hepatitis
C. Chronic pancreatitis
D. Viral hepatitis
E. Benign hyperbilirubinemia

9. Woman, 37 years old, saw her doctor owing to the exacerbation of chronic hepatitis. Increased indirect bilirubin, AST, ALT levels and decreased protein and prothrombin levels were found in blood. What pathological process can stipulate these changes?

A. Cholestasis
B. Cytolysis
C. Portal hypertension
D. Hypersplenism
E. Violation of hemostasis

10. 39 years old patient complains of icterus, skin itching, nausea, pain in the right subcostum, especially after rich, fried food, increased body temperature in the evening, general weakness, hemorrhage of gums. He is ill for nearly two years. Skin and scleras are icteric, there are scratch tracks on the skin and xanthelasmas on eyelids. Liver is increased on 4 cm. In the analyses there are hyperbilirubinemia at the expense of conjugated bilirubin, hypercholesterinemia, increased activity of alkaline phosphatase. What is the most reliable diagnosis?

A. Chronic cholestatic hepatitis
B. Chronic cholecystitis
C. Hemolytic anemia
D. Cholecystolithiasis
E. Cancer of pancreas head

11.A 22 years old woman complained of right subcostal pain, nausea, and decreased appetite. She fell ill 2 months after appendectomy when jaundice appeared. She was treated in an infectious hospital. 1 year later mentioned symptoms recurrenced. Examination detected subicteric sclerae, enlarged firm liver. What is the preliminary diagnosis? What additional tests are necessary?

12. 32 years old patient suffers from chronic viral hepatitis. He complains of dull pain in the right subcostal area, nausea, dry feeling in mouth. Objectively: liver size is 13-21-11 cm (according to Kurlov), spleen is enlarged by 2 cm, aspartate aminotransferase is 3,2 micromole/l·h, alanine

aminotransferase - 4,8 millimole/l·h. Serological study revealed HBeAg, high concentration of DNA HBV. What is the diagnosis? What additional tests are necessary for the patient? What is the treatment?

The answers for the tests:

1-B, 2-B, 3-E, 4-E, 5-A, 6-A, 7-A, 8-B, 9-B, 10-A.

11. Chronic viral hepatitis. Biochemical blood analysis (liver tests), markers of hepatitis in serum, US of abdominal cavity, Fibro-test, Acti-test.

12. Chronic viral hepatitis B. US of abdominal cavity, Fibro-test, Acti-test. α-interferon.

Recommended literature

I. Main:

1. Internal Medicine: in 2 books. Book 1. Diseases of the Cardiovascular and Respiratory Systems: textbook / N.M. Seredyuk, I.P. Vakaliuk, R.I. Yatsyshyn et al. Київ, Медицина., 2019. - 664 + 48 кольор. вкл.).
2. Internal medicine: Part 1 (cardiology, rheumatology, haematology): textbook for English-speaking students of higher medical schools / edited by Professor M.A. Stanislavchuk and Professor V.A. Serkova. - Vinnytsia: Nova Knyha, 2019. - 392 p.
3. Медицина за Девідсоном: принципи і практика / Навчальний посібник: пер. 23-го англ. вид.: у3 т. Т.3 С. Ралстона, Я. Пенмана, М. Стрекена, Р. Гобсона; К.: ВСВ «Медицина», 2021. – 642 с.
4. CURRENT Medical Diagnosis and Treatment 2012, Fifty-First Edition (LANGE CURRENT Series) by Stephen McPhee, Maxine Papadakis and Michael W. Rabow (Paperback - Sep 12, 2011)/
5. Побічнадіяліків – SideEffectsofMedications: навчальнийпосібнику 2 т. / зазаг.ред. В.М. Бобирьова, М.М. Потяженка. – Вінниця:
6. Cardiovascular diseases. Classification, standards of diagnosis and treatment / Edited by Academician Kovalenko V.M., Prof. Lutaia M.I., Prof. Sirenko Yu.M., Prof. Sychova O.S. – Kyiv. – 2020.
7. Perederii V.H., Tkach S.M. Principles of internal medicine. – Vol.2 / Textbook for students of higher educational institutions. – Vinnytsia: Nova knyha. – 2018.
8. Internal diseases. The textbook based on the principles of evidentiary medicine, 2018.

II. Additional literature:

1. Recommendations of the Association of Cardiologists of Ukraine for the diagnosis and treatment of chronic heart failure / Voronkov L.H. – moderator, working group of the Ukrainian Association of Heart Failure Specialists. – 2017.
2. Respiratory diseases / Ghanei M. - In Tech, 2012. - 242 p.
3. Clinical respiratory medicine / Spiro S., Silvestri G., Agusti A. - Saunders, 2012. - 1000 p.
4. Principles and practice of interventional pulmonology / Ernst A., Herth F. -Springer, 2012. - 757 p.
5. Clinical respiratory medicine / Spiro S., Silvestri G., Agusti A. - Saunders, 2012. - 1000 p.
6. Petrov Y. The chief symptoms and syndromes in patients with cardiovascular pathology : The practical handbook fur medical students / Ye. Petrov, Yu. Goldenberg, N. Chekalina; UMSA. - Poltava : TexcepBic, 2010. - 143 .
7. Gastroenterology and Hepatology Board Review: Pearls of Wisdom, Third Edition (Pearls of Wisdom Medicine) by John K. DiBaise (May 11, 2012)

8. Clinical Pulmonology 2012 (The Clinical Medicine Series) by M.D., C. G. Weber (Oct 30, 2011) - Kindle eBook
9. Clinical Nephrology 2012 (The Clinical Medicine Series) by M.D., C. G. Weber (Sep 19, 2011) - Kindle eBook
10. Clinical Nephrology 2012 (The Clinical Medicine Series) by M.D., C. G. Weber (Sep 19, 2011) - Kindle eBook
11. Hematology: Clinical Principles and Applications, 4e by Bernadette F. Rodak MS MLS (Feb 18, 2017)
12. Rheumatology, 2-Volume Set: EXPERT CONSULT - ENHANCED ONLINE FEATURES AND PRINT, 5e by Marc C. Hochberg MD MPH, Alan J. Silman MD, Josef S. Smolen MD and Michael E. Weinblatt MD (Oct 19, 2019)
13. Endocrine Pathology: Differential Diagnosis and Molecular Advances by Ricardo V. Lloyd (Nov 5, 2018)
14. Clinical Endocrinology 2012 (The Clinical Medicine Series) by M.D., C. G. Weber (Sep 19, 2017) - Kindle eBook
15. Williams Textbook of Endocrinology: Expert Consult-Online and Print, 12e by Shlomo Melmed, Kenneth S. Polonsky MD, P. Reed MD Larsen and Henry M. Kronenberg MD (May 27, 2016)
16. Electrocardiography, 3e with Student CD (Booth, Electrocardiography for Health Care Personnel) by Kathryn A. Booth (Jan 27, 2017)
17. Echocardiography Review Guide: Companion to the Textbook of Clinical Echocardiography: Expert Consult: Online and Print, 2e (Expert Consult Title: Online + Print) by Catherine M. Otto (Mar 7, 2017).

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