Ministry of Healthcare of Ukraine

Poltava State Medical University

«Approved»
at the meeting of the
Chair of Internal medicine №1
Head of the Chair
_____ G.S. Maslova
(signature) (PhD, MD., Assoc.Prof.)

Methodical instruction for the students self-training during preparing for practical classes (seminars)

Subject	**Internal medicine**
Module №1	**FUNDAMENTALS OF INTERNAL MEDICINE**
Topic	**Liver cirrhosis**
Course	**IV**
Faculty	**Medical**

***<u>The subject of the lesson</u>*: Liver cirrhosis**

Professional orientation of students: Liver cirrhosis is a diffuse process characterized by fibrosis and conversion of normal architecture to structurally abnormal nodules. These "regenerative" nodules lack normal lobular organization and are surrounded by fibrous tissue. The process involves the whole liver and is essentially irreversible. According to the World Health Organization, about 800,000 people die of cirrhosis annually. Because chronic liver disease affects people in their most productive years of life, it has a significant impact on the economy as a result of premature death, illness, and disability. The natural history of cirrhosis is characterized by an initial phase, termed compensated cirrhosis, followed by a rapidly progressive phase marked by the development of complications of portal hypertension or liver dysfunction (or both), termed decompensated cirrhosis.

The main goal: To be able to assess the typical clinical picture of liver cirrhosis, to determine tactics of treatment and prophylaxis.

Specific goals:

- To select the information indicating the presence of liver cirrhosis in a patient from the data history;
- To create a scheme of diagnostic search;
- To identify the signs of liver cirrhosis in an objective study of the patient (general examination, palpation, percussion, auscultation);
- To analyze and interpret the changes in the results of the laboratory and instrumental methods of investigation, depending on the course of the disease;
- To formulate and justify a preliminary diagnosis of liver cirrhosis according to classification;
- To conduct differential diagnostics of diseases with the similar clinical picture;
- To develop a strategy of treatment depending on the disease and the existing complications;
- To provide medical care;
- To assess the patient's prognosis and to propose a plan of preventive actions;
- To apply deontological communication skills with patients.

The student must know:

Basic knowledge, abilities, skills (interdisciplinary integration)

Discipline	To know	To be able to
Anatomy	The structure of the gastrointestinal tract, liver, blood supply, innervation	
Histology	The structure of liver in health and disease	To interpret results of liver biopsy
Regional anatomy	Interposition of the gastrointestinal organs	
Physiology	Indicators of gastrointestinal tract	To determine the function of

	function, its value	gastrointestinal organs
Morbid anatomy	Changes in the structure of liver in chronic hepatitis	
Propaedeutic therapy	Symptomatology of chronic hepatitis and complications	Conduct an objective examination of the patient, analyze the clinical and laboratory results
Pharmacology	The mechanism of action, indications and contraindications for the hepatoprotective drugs, antiviral drugs, diuretics, β-blockers, corticosteroids, statins, vitamins	Prescribe the drugs of these groups

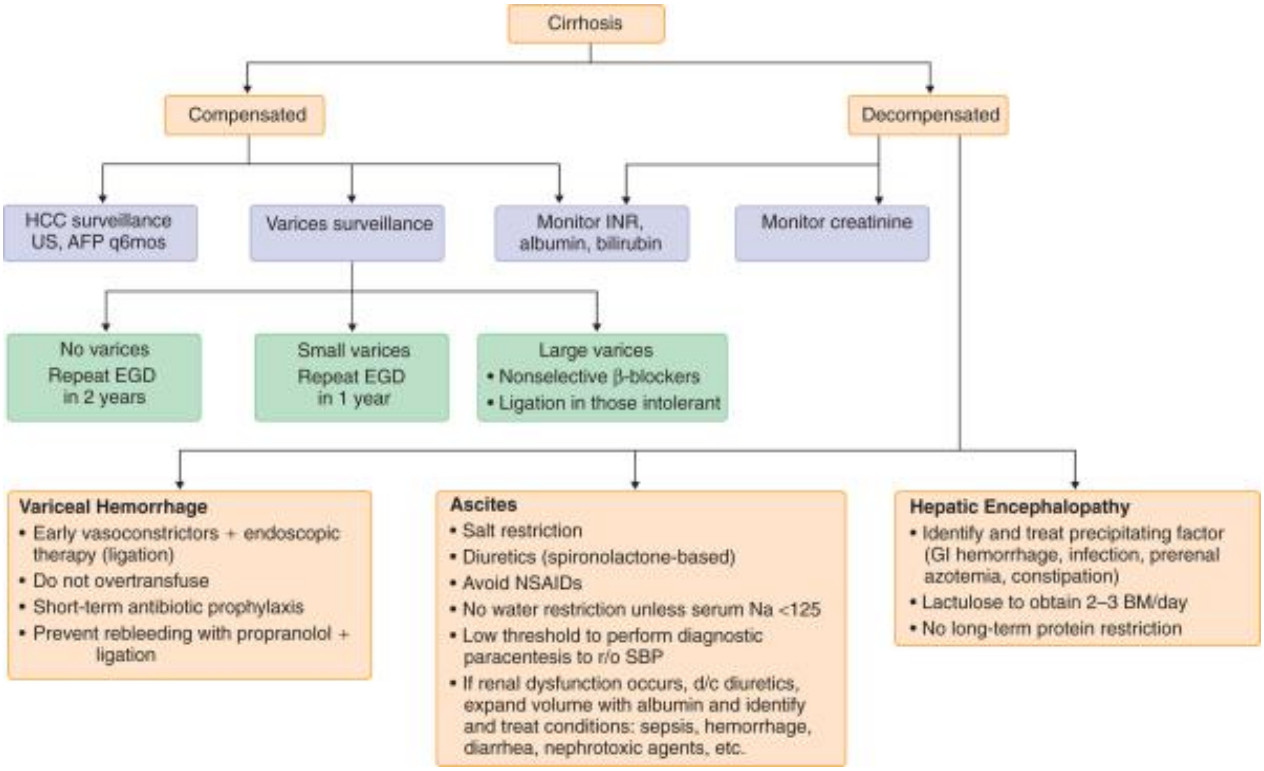
The list of key terms, parameters, characteristics:

Term	Definition
Liver cirrhosis	is a diffuse process characterized by fibrosis and conversion of normal architecture to structurally abnormal nodules.
Syndrome of cytolysis	complex of symptoms that includes clinical signs and elevated liver intracellular enzymes (AST, ALT, GDG, LDG) in blood that indicates on necrosis.
Cryptogenic cirrhosis	is a cirrhosis of unknown etiology when all the causes have been investigated and excluded.
Ascites	is an accumulation of fluid in the abdominal cavity.
Hepatic encephalopathy	is a spectrum of neuropsychiatric abnormalities in patients with liver dysfunction, after exclusion of brain disease that is characterized by personality changes, intellectual impairment, and a depressed level of consciousness.

Theoretical questions for the lesson:

1. Give the definitions of liver cirrhosis.
2. Specify the etiological and risk factors for liver cirrhosis.
3. The pathophysiological mechanisms of liver cirrhosis.
4. Diagnostic criteria of liver cirrhosis.
5. What are the laboratory characteristics of liver cirrhosis and its stages?
6. Modern classification of liver cirrhosis.
7. Specify the principles and features of liver cirrhosis pharmacotherapy according to etiology and modern recommendations.
8. What lifestyle modifications should be recommended for patients with liver cirrhosis?

Contents of the training materials



Definition. Liver cirrhosis is a diffuse process characterized by fibrosis and conversion of normal architecture to structurally abnormal nodules. These "regenerative" nodules lack normal lobular organization and are surrounded by fibrous tissue. The process involves the whole liver and is essentially irreversible.

Classification. Liver cirrhosis can be classified according to etiology (see etiological factors below).

Although cirrhosis is histologically an "all or nothing" diagnosis, clinically it can be classified by its status as compensated or decompensated. Decompensated cirrhosis is defined by the presence of ascites, variceal bleeding, encephalopathy, or jaundice, which are complications that result from the main consequences of cirrhosis: portal hypertension and liver insufficiency.

When all the causes have been investigated and excluded, cirrhosis is considered "cryptogenic".

According to morphological features: micronodular (nodules 1-3 mm), macronodular (nodules >3mm), mixed, septal.

There are two most commonly used scoring systems in cirrhosis: Child-Pugh (range, 5-15) and model of end-stage liver disease (MELD) score (range, 6-40).

MELD score: [0.957 × LN (creatinine in mg/dL) + 0.378 × LN (bilirubin in mg/dL) + 1.12 × LN (INR) + 0.643] × 10. Where LN is natural logarithm.

Child-Pugh classification: Child A - score of 5-6; Child B - score of 7-9; Child C - score of 10-15 (table 1).

TABLE 1.

	Points Ascribed		
Parameters	**1**	**2**	**3**
Ascites	None	Grade 1-2 (or easy to treat)	Grade 3-4 (or refractory)
Hepatic encephalopathy	None	Grade 1-2 (or induced by a precipitant)	Grade 3-4 (or spontaneous)
Bilirubin (mg/dL) (μmol/L)	<2 <34	2-3 34–51	>3 >51
Albumin (g/dL) (g/L)	>3.5 >35	2.8-3.5 30–35	<2.8 <30
Prothrombin time (seconds> control) or INR (international normalized ratio)	<4 <1.7	4-6 1.7-2.3	>6 >2.3

The two main consequences of cirrhosis are portal hypertension, with the accompanying hyperdynamic circulatory state, and liver insufficiency.

The development of varices and ascites is a direct consequence of portal hypertension and the hyperdynamic circulatory state, whereas jaundice occurs as a result of an inability of the liver to excrete bilirubin (i.e., liver insufficiency).

Encephalopathy is the result of both portal hypertension and liver insufficiency.

Ascites, in turn, can become complicated by infection, which is called spontaneous bacterial peritonitis, and by functional renal failure, which is called hepatorenal syndrome.

Portal Hypertension and the Hyperdynamic Circulatory State. In cirrhosis, portal hypertension results from both an increase in resistance to portal flow and an increase in portal venous inflow. The initial mechanism is increased sinusoidal vascular resistance secondary to deposition of fibrous tissue and subsequent compression by regenerative nodules (fixed component) and active vasoconstriction (functional component), which is amenable to the action of vasodilators such as nitroprusside and is caused by a deficiency in intrahepatic nitric oxide (NO), as well as enhanced activity of vasoconstrictors. Early in the portal hypertensive process, the spleen grows and sequesters platelets and other formed blood cells, thereby leading to hypersplenism.

As collaterals develop, an increase in portal blood inflow maintains the portal hypertensive state as a result of splanchnic vasodilation, which in turn is secondary to increased production of NO. Thus, the paradox in portal hypertension is that a deficiency of NO in the intrahepatic vasculature leads to vasoconstriction and increased resistance, whereas overproduction of NO in the extrahepatic circulation leads to vasodilation and increased flow.

Varices and Variceal Hemorrhage. The complication of cirrhosis that results most directly from portal hypertension is the development of portal-systemic collaterals, the most relevant of which are those that form through dilation of the coronary and gastric veins and constitute gastroesophageal varices. The initial formation of esophageal collaterals depends on a threshold portal pressure, clinically established by a hepatic venous pressure gradient of 10 to 12 mm Hg, below which varices do not

develop. Development of a hyperdynamic circulatory state leads to further dilation and growth of varices and eventually to their rupture and variceal hemorrhage, one of the most dreaded complications of portal hypertension.

Ascites and Hepatorenal Syndrome. Ascites in cirrhosis is secondary to sinusoidal hypertension and retention of sodium. Cirrhosis leads to sinusoidal hypertension by blocking hepatic venous outflow both anatomically by fibrosis and regenerative nodules and functionally by increased postsinusoidal vascular tone. Similar to the formation of esophageal varices, a threshold hepatic venous pressure gradient of 12 mm Hg is needed for the formation of ascites. In addition, retention of sodium replenishes the intravascular volume and allows the continuous formation of ascites.

Spontaneous Bacterial Peritonitis. Spontaneous bacterial peritonitis, an infection of ascitic fluid, occurs in the absence of perforation of a hollow viscus or an intra-abdominal inflammatory focus such as an abscess, acute pancreatitis, or cholecystitis. Bacterial translocation, or the migration of bacteria from the intestinal lumen to mesenteric lymph nodes and other extraintestinal sites, is the main mechanism implicated in spontaneous bacterial peritonitis. Impaired local and systemic immune defenses are a major element in promoting bacterial translocation and, together with shunting of blood away from the hepatic Kupffer cells through portosystemic collaterals, allow a transient bacteremia to become more prolonged, thereby colonizing ascitic fluid. Spontaneous bacterial peritonitis occurs in patients with reduced ascites defense mechanisms, such as a low complement level in ascitic fluid. Another factor that promotes bacterial translocation in cirrhosis is bacterial overgrowth attributed to a decrease in small bowel motility and intestinal transit time.

Jaundice. Jaundice in cirrhosis is a reflection of the inability of the liver to excrete bilirubin and is therefore the result of liver insufficiency. However, in cholestatic diseases leading to cirrhosis (e.g., primary biliary cirrhosis, primary sclerosing cholangitis, vanishing bile duct syndrome), jaundice is more likely due to biliary damage than liver insufficiency. Other indicators of liver insufficiency, such as the prothrombin time or the presence of encephalopathy, help determine the most likely contributor to hyperbilirubinemia.

Encephalopathy. Ammonia, a toxin normally removed by the liver, plays a key role in the pathogenesis of hepatic encephalopathy. In cirrhosis, ammonia accumulates in the systemic circulation because of shunting of blood through portosystemic collaterals and decreased liver metabolism (i.e., liver insufficiency).

Treatment. Treatment of cirrhosis should ideally be aimed at interrupting or reversing fibrosis. However, antifibrotic drugs have not been shown to reverse fibrosis consistently or improve outcomes in cirrhotic patients. Treatment of compensated cirrhosis is currently directed at preventing the development of decompensation by treating the underlying liver disease (e.g., antiviral therapy for hepatitis C or B) to reduce fibrosis and prevent decompensation; avoiding factors that could worsen liver disease, such as alcohol and hepatotoxic drugs (Nonsteroidal anti-inflammatory drugs, Isoniazid, Valproic acid, Erythromycin, Amoxicillin-clavulanate, Ketoconazole, Chlorpromazine, Ezetimibe etc.); and screening for varices (to prevent variceal hemorrhage) and for hepatocellular carcinoma (to treat at an early stage).

- Prednisone and azathioprine - For autoimmune hepatitis;

- Interferon and other antiviral agents - For hepatitis B and C;
- Phlebotomy - For hemochromatosis;
- Ursodeoxycholic acid - For primary biliary cirrhosis;
- Trientine and zinc - For Wilson disease.

Treatment of decompensated cirrhosis focuses on specific decompensating events and the option of liver transplantation.

- Hepatorenal syndrome - patients with early hepatorenal syndrome may be salvaged by aggressive expansion of intravascular volume with albumin and fresh frozen plasma and by avoidance of diuretics.
- Hepatic encephalopathy - pharmacologic treatment includes the administration of lactulose and antibiotics.

The main treatment for encephalopathy is **lactulose syrup**. This nonabsorbable disaccharide stimulates the passage of ammonia from tissues into the gut lumen and inhibits intestinal ammonia production. Initial lactulose dosing is 30 mL orally once or twice daily. Dosing is increased until the patient has 2-4 loose stools per day. Dosing should be reduced if the patient complains of diarrhea, abdominal cramping, or bloating. Higher doses of lactulose may be administered via either a nasogastric or rectal tube to hospitalized patients with severe encephalopathy.

Antibiotics serve as second-line agents. They work by decreasing the colonic concentration of ammoniagenic bacteria. Neomycin dosing is 250-1000 mg orally 2-4 times daily. Treatment with neomycin may be complicated by ototoxicity and nephrotoxicity. Rifaximin (Xifaxan) is a nonabsorbable antibiotic that received FDA approval in 2004 for the treatment of travelers' diarrhea and was given approval in 2010 for the reduction of recurrent hepatic encephalopathy. This drug was also approved in May 2015 for the treatment of diarrhea-predominant irritable bowel syndrome (IBS-D). Data from Europe suggest that rifaximin can decrease colonic levels of ammoniagenic bacteria, with resulting improvement in the symptoms of hepatic encephalopathy.

- Ascites - treatment can include sodium restriction and the use of diuretics, large-volume paracentesis, and shunts (peritoneovenous, portosystemic, transjugular intrahepatic portosystemic).

Spironolactone (Aldactone) blocks the aldosterone receptor at the distal tubule. It is dosed at 50-300 mg once daily. Although the drug has a relatively short half-life, its blockade of the aldosterone receptor lasts for at least 24 hours. Adverse effects of spironolactone include hyperkalemia, gynecomastia, and lactation. Other potassium-sparing diuretics, including amiloride and triamterene, may be used as alternative agents, especially in patients complaining of gynecomastia.

Furosemide (Lasix) may be used as a solo agent or in combination with spironolactone. The drug blocks sodium reuptake in the loop of Henle. It is dosed at 40-240 mg daily in 1-2 divided doses. Patients infrequently need potassium repletion when furosemide is dosed in combination with spironolactone.

Vasopressin V2 receptor antagonists are a class of agents with the potential to increase free-water excretion, improve diuresis, and decrease the need for paracentesis.

• Vitamin K and a blood plasma can be given in emergencies to treat episodes of bleeding.

Nonselective beta-blockers (propranolol, nadolol) reduce portal pressures and are used in the primary and secondary prophylaxis of variceal hemorrhage. β-adrenergic blockers reduce portal pressure by producing splanchnic vasoconstriction and decreasing portal venous inflow. Propranolol is initiated at a dose of 20 mg orally twice a day, whereas nadolol is initiated at a dose of 20 mg orally every day. The dose should be titrated to produce a resting heart rate of about 50 to 55 beats per minute. In patients who have early cirrhosis without moderate-to-large varices, beta-blockers do not prevent the development of varices and also result in adverse effects. The clinical window opens when moderate-to-large esophageal varices develop, with or without variceal bleeding, and beta-blockers are indicated for primary and secondary prophylaxis of variceal bleeding. Increasingly, evidence suggests that the clinical window for beta-blockers closes and that they are no longer effective when refractory ascites, hypotension, the hepatorenal syndrome, spontaneous bacterial peritonitis, sepsis, or severe alcoholic hepatitis develops, owing to unfavorable hemodynamic effects in advanced cirrhosis.

Analgesic agents must be carefully selected in patients with cirrhosis. Because of the risk of acute renal failure and gastrointestinal bleeding, nonsteroidal antiinflammatory drugs are contraindicated, except for low-dose aspirin in patients in whom the severity of cardiovascular disease exceeds the severity of cirrhosis. Opiates should be used cautiously or avoided, because they may precipitate or aggravate hepatic encephalopathy. Tramadol is safe in low doses, and topical medications such as lidocaine patches are generally safe. Acetaminophen is effective and safe in patients with liver disease, provided that the patient does not drink alcohol.

Patients should be referred for consideration for liver transplantation after the first signs of hepatic decompensation.

Test evaluation and situational tasks.

Situation tasks:

1. A patient, 54 years old, complains of general weakness, absence of appetite, dull pain in the right subcostum, abdominal bloating, weight loss. Lately periodic vomiting with blood appeared. Examination: body weight is reduced, icterus of scleras, skin is dry, "vascular stars" on face and upper extremities, hyperemia of hands, gynecomastia. Tongue is of raspberry colour. Abdomen is enlarged, lower edge of liver is acute, dense, comes from the edge of costal arc on 4 cm. Spleen comes from a costal arc on 6-7 cm. Blood sedimentation is 14 mm/h, thymol test – 8. What is the preliminary diagnosis? What additional tests are necessary?

2. Patient was confirmed micronodular liver cirrhosis. During last 2 months he noticed the development of dyspnea, edemas of lower extremities, ascites. Patient was taking hepatoprotectors and glucocorticoids. What combination of medicines should be added to the treatment, which is already conducted?

3. A woman, 42 years old, is suffering from micronodular cryptogenic hepatic cirrhosis. During the last week state worsened: cramps and dizzinesses appeared, memory had worsened, icterus increased. What complication developed? What research can explain the reason of worsening?

Tests:

1. A patient with hepatic cirrhosis drank some spirits that resulted in headache, vomiting, aversion to food, insomnia, jaundice, fetor hepaticus, abdominal swelling. What complication of hepatic cirrhosis is meant?

A. Hepatocellular insufficiency
B. Hemorrhage from varicosely dilatated veins of esophagus
C. Portal hypertension
D. Acute stomach ulcer
E. Thrombosis of mesenteric vessels

2. In which of the following disorders does the pathophysiology of portal hypertension involve presinusoidal intrahepatic obstruction?

A. Alcoholic cirrhosis
B. Congenital hepatic fibrosis
C. Hemochromatosis
D. Budd-Chiari syndrome
E. Cavernomatous transformation of the portal vein

3. A 42-year-old female patient suffers from micronodular cryptogenic cirrhosis. Over the last week her condition has deteriorated: she developed convulsions, mental confusion, progressing jaundice. What study may give reasons for such aggravation?

A. Determination of serum ammonia
B. Determination of cholesterol ethers
C. Determination of alpha-phetoprotein
D. Determination of ALAT and ASAT
E. Determination of alkaline phosphatase

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. A man, 40 years old, suffers from 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. Hepatoprotectors
D. Antiviral preparations
E. Hemosorbtion, vitamin therapy

6. Patient, 49 years old, complains of general weakness, increased ascites during 2 months. After the abdominal puncture 10l of pale yellow transparent liquid was got. Painless liver is palpated with acute even edge, it comes under a costal arc on 4 cm and spleen is 2 cm below an edge of costal arc. The syndrome of cytolysis is absent. Roentgenologically stomach and duodenum have no changes. What disease is it possible to think about?

A. Pick`s pseudocirrhosis
B. Cryptogenic micronodular hepatic cirrhosis
C. Chronic toxic hepatitis
D. Biliary hepatic cirrhosis
E. Phlebitis of hepatic vein (Budd – Chiari disease)

7. 49 years old man, invalid of the I group, treats concerning the hepatic cirrhosis during a few years. For the last months abdomen increased in size, weakness intensified. He took furosemide daily for 2 weeks. What blood changes of electrolytes do you expect to find out?

A. Hypokaliemia
B. Hypocalciemia
C. Hypernatriemia
D. Hypercalciemia
E. Hyperkaliemia

8. A man, 46 years old, complains of vomiting with bright red blood. In the anamnesis: micronodular hepatic cirrhosis of viral etiology for 5 years. During last half year increasing abdominal size due to ascites was observed. What preparation is it necessary to begin with?

A. Cordiamin - 2 ml intramuscular
B. Intravenous vasopressin - 20 units
C. Mesaton 1% - 2 ml intramuscular
D. Prednizolon - 20 mg intravenous
E. Swallowing of ice pieces

9. Patient I., 50 years old, was got to hospital in extremely hard condition. At the examination: common sense is absent, skin and scleras are icteric. Liver is enlarged, splenomegaly. Ascites is determined, acidic breathing, tachycardia, AP 90/40. There are subdermal hematomas, erythemas of hands. Metabolic hyperacidity: pH - 7,1, AST -

1,8, ALT - 2,1. General bilirubin of blood - 334,2 mkmol/l, sodium of blood serum - 122 mmol/l, potassium of blood serum - 5,9 mmol/l. Worsening of patient's condition is associated with:

A. Thrombosis of mesenterial vessels
B. Poisoning with alcohol substitutes
C. Heart failure, III stage
D. Violation of cerebral blood circulation
E. Hepatic coma

10. A patient, 44 years old, abuses alcohol for a long time. Objectively: thenar and hypothenar are red, vascular stars on the front surface of thorax, veins of anterior abdominal wall are dilated. Abdomen is bloated, free liquid is determined in abdominal cavity. Liver + 4 cm, smooth, unpainful. The edge of spleen is palpated. In blood: L - 8,7x109/l. What complication developed?

A. Subacute hepatic dystrophy
B. Portal hypertension
C. Coagulopathy
D. Thrombosis of mesenteries vessels
E. Hypersplenism

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).

1.

Composed by **Lymanets T.V.**