Ministry of Healthcare of Ukraine

Poltava State Medical University

«Approved»
at the meeting of the
Chair of Internal medicine №1
Head of the Chair
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Methodical instruction for the students self-training during preparing for practical classes (seminars)

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

***The subject of the lesson*: Chronic pancreatitis**

Chronic pancreatitis is a complex process that implies the presence of irreversible and permanent fibrosis, often with chronic mononuclear cell inflammation, damage to nerves, and loss of ducts, acini, and islets. Thus, the condition is defined by the presence of histologic abnormalities, including chronic inflammation, fibrosis, and progressive destruction of both exocrine and eventually endocrine tissue (atrophy). The prevalence of symptomatic chronic pancreatitis in Western countries is about 25 to 30 per 100,000 people, with an estimated incidence of 3 to 9 cases per 100,000.

Educational goal: To be able to assess the typical clinical picture of chronic pancreatitis, to determine tactics of treatment and prophylaxis.

Specific goals:

- to select the information indicating the presence of chronic pancreatitis in a patient from the data history;
- to create a scheme of diagnostic search;
- to identify the signs of chronic pancreatitis 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 chronic pancreatitis 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.

Basic knowledge, abilities, skills (interdisciplinary integration)

Discipline	To know	To be able to
Anatomy	The structure of the gastrointestinal tract, pancreas, blood supply, innervation	
Histology	The structure of the intestines, pancreas and its ducts in health and disease	To interpret results of upper endoscopy with biopsy
Regional anatomy	Interposition of the gastrointestinal organs	
Physiology	Indicators of pancreatic function, its value	To determine the function of pancreas, to interpret results of tests
Morbid anatomy	Changes in the structure of the pancreas in chronic pancreatitis	
Radiology	Radiological changes at chronic pancreatitis	Analyze the radiological picture of the abdominal cavity
Propaedeutic therapy	Symptomatology of chronic pancreatitis and its complications	Conduct an objective examination of the patient, analyze the clinical and laboratory results

Pharmacology	The mechanism of action, indications and contraindications for the IPP, H2-blockers, prokinetics, antibiotics, ferments, pain-relievers	Prescribe the drugs of these groups

The list of key terms, parameters, characteristics:

Term	Definition
Chronic pancreatitis	is a disease process characterized by irreversible damage to the pancreas as distinct from the reversible changes noted in acute pancreatitis, which leads to condition that is defined by the presence of histologic abnormalities, including chronic inflammation, fibrosis, and progressive destruction of both exocrine and eventually endocrine tissue (atrophy).
ERCP	endoscopic retrograde cholangiopancreatography uses a sideviewing endoscope that accesses the second part of the duodenum, where a small catheter is introduced into the bile or pancreatic duct to inject radiographic contrast medium under fluoroscopic monitoring.
Steatorrhea	is the presence of excess fat in feces.
Amylorrhea	the presence of an abnormal amount of starch in the feces.
Creatorrhea	is the abnormal excretion of muscle fibre in feces.
Malabsorption	is inadequate assimilation of dietary substances due to defects in digestion, absorption, or transport.
Maldigestion	is incomplete breakdown of nutrients in the gastrointestinal tract, usually due to lack of digestive enzymes.

Theoretical questions for the lesson:

1. Give the definition of chronic pancreatitis.
2. Specify the risk factors for chronic pancreatitis.
3. The pathophysiological mechanisms of chronic pancreatitis.
4. Diagnostic criteria of chronic pancreatitis.
5. What are the endoscopic and ultrasound characteristics of chronic pancreatitis?
6. Modern classification of chronic pancreatitis.
7. Specify the principles and features of chronic pancreatitis pharmacotherapy according to modern recommendations.
8. What lifestyle modifications should be recommended for patients with chronic pancreatitis?

Contents of the training materials

Chronic pancreatitis. Classification.

- <u>according to etiology:</u> primary, secondary, idiopathic.

- Toxic-metabolic (Alcoholic, Tobacco smoking, Hypercalcemia, Hyperlipidemia, Chronic renal failure, Medications—phenacetin abuse, Toxins—organotin compounds (e.g., dibutylin dichloride, DBTC));
- Idiopathic (Early onset, Late onset, Tropical);

- Genetic (Cationic trypsinogen (PRSS1), Cystic fibrosis transmembrane conductance regulator gene (CFTR), Calcium-sensing receptor (CASR), Chymotrypsin C gene (CTRC), Pancreatic secretory trypsin inhibitor gene (SPINK1));
- Autoimmune (Type 1 autoimmune chronic pancreatitis, IgG4 systemic, Type 2 autoimmune chronic pancreatitis);
- Recurrent and severe acute pancreatitis (Postnecrotic (severe acute pancreatitis), Recurrent acute pancreatitis, Vascular diseases/ischemia, Radiation induced);
- Obstructive (Pancreas divisum, Duct obstruction (e.g., tumor), Preampullary duodenal wall cysts, Posttraumatic pancreatic duct scars).

- according to integral index of severity M-ANNHEIM: A, B, C, D.
- according to severity: mild, moderate, severe.
- according to deficiency of gland: with/without exocrine/endocrine deficiency.
- according to faze: exacerbation, remission.
- according to clinical picture: painful, pseudotumor, painless forms.
- according to Cambridge classification: it divides chronic pancreatitis to five severity groups according to morphologic changes of the main pancreatic duct and its side branches. It was defined in 1983 in the Cambridge symposium.

Score	**Cambridge Class**	**Severity**	**ERCP findings**	**Ultrasound or CT findings**
Score 1	**0**	**none**	no abnormal signs	no abnormal signs
Score 2	**0**	**equivocal**	<3 abnormal branches	one abnormal sign: main pancreatic duct 2 – 4 mm in diameter enlarged gland 1 to 2 times the normal
Score 3	**I**	**mild**	3 or more abnormal branches	≥ 2 abnormal signs: cavities <10mm duct irregularity focal acute necrosis panrenchymal heterogeneity increased echogenicity of duct wall contour irregularity of head or body
Score 4	**II**	**moderate**	>3 abnormal side branches and abnormal main duct	as score 3
Score 5	**III**	**severe**	all above and 1 or more of: • large cavity >10mm • intraductal filling defects • duct obstruction (stricture) • duct dilatation or irregularity	all above and 1 or more of: large cavity >10mm intraductal filling defects duct obstruction (stricture) duct dilatation or irregularity calculi and/or pancreatic calcification contiguous organ invasion

A modified, clearer version of Cambridge classification:

Severity	ERCP findings	Ultrasound or CT findings
none	no abnormal LSB	normal gland size and shape, homogeneous parenchyma
equivocal	MPD normal	one of the following: <3 abnormal LSB MPD 2-4mm gland enlarged over 2 times the normal size heterogeneous parenchyma
mild	MPD normal	two or more of the following: >3 abnormal LSB MPD 2-4mm slight gland enlargement heterogeneous parenchyma
moderate	MPD changes LSB changes	small cysts <10mm MPD irregularity focal acute pancreatitis (<1/3 of the gland) increased enhancement or echogenicity of MPD walls gland contour irregularity
severe	Any of the above changes plus one or more of the following: cavity >10mm in diameter intraductal filling defects calculi MPD obstruction or stricture severe MPD irregularity contiguous organ invasion	

Epidemiology. The prevalence of symptomatic chronic pancreatitis in Western countries is about 25 to 30 per 100,000 population, with an estimated incidence of 3 to 9 cases per 100,000. Interestingly, the prevalence of histologic evidence of chronic pancreatitis in autopsy studies approaches 5%, indicating that many people apparently develop chronic pancreatic damage as a consequence of normal aging, other diseases, or exposure to toxins, such as consumption of alcohol, but do not develop any symptoms or signs of chronic pancreatitis during life.

Etiological factors and risk factors. In Western countries, alcohol and tobacco abuse are the dominant causes of chronic pancreatitis. Alcohol causes about 70 to 80% of all cases of chronic pancreatitis in the United States and other major industrial countries. Substantial and prolonged ingestion of alcohol is usually required, on the order of 5 to 8 drinks daily over more than 5 years. Most people who consume this much alcohol do not develop chronic pancreatitis, pointing to important cofactors such as genetic background and cigarette smoking. There is evidence that tobacco alone can cause chronic pancreatitis, and the combination of alcohol and tobacco may be synergistic.

Other factors are hereditary (this pancreatitis is an autosomal dominant disease characterized by early onset of acute and chronic pancreatitis, the development of exocrine and endocrine pancreatic insufficiency, and a high risk of pancreatic adenocarcinoma) and autoimmune lesions.

Risk factors also include nutritive factors (e.g., excessed fat consumption with meal, etc.) and less common metabolic processes (hypercalcemia, chronic renal failure, etc.)

Pathogenesis. Multiple episodes of acute inflammation, whether clinical or subclinical, eventually change the inflammatory milieu of the pancreas, with a shift to chronic inflammation, the activation of pancreatic stellate cells, and the production of fibrosis. This process is self-sustaining and produces the characteristic histologic damage noted previously. Genetic mutations predispose to chronic pancreatitis, but the genetic predisposition is superimposed on exposure to various toxins, which precipitate acute pancreatitis, with cellular necrosis or apoptosis, that progresses in some individuals, particularly those with multiple episodes, to a chronic and fibrotic process. One important contributor to the pain in chronic pancreatitis is damage to pancreatic nociceptive nerves and the complex neuroimmune interaction driven by the chronic inflammatory state. Chronic pain produces visceral, spinal cord, and central hyperalgesia, and the pain may become selfperpetuating even if therapy on the pancreas is successful. In addition to this neural mechanism, increased pressure within the gland, associated ischemia, obstruction of the pancreatic duct, and a pseudocyst can cause pain.

Mutations in the trypsinogen (PRSS1) gene in these families appear to cause a gain in function in which the mutant trypsinogen, once activated to trypsin, is difficult to inactivate. This trypsin, if present in an amount that overwhelms normal protective mechanisms, can activate other pancreatic enzymes and lead to pancreatic damage and eventually to chronic pancreatitis. One of the protective mechanisms is a trypsin inhibitor called SPINK1. Loss of function mutations in SPINK1 may predispose to chronic pancreatitis, but unlike PRSS1 mutations, are not sufficient to cause chronic pancreatitis. Major mutations in CFTR lead to cystic fibrosis, which is associated with chronic pancreatitis and pancreatic atrophy. Milder mutations in CFTR, which predispose to chronic pancreatitis without causing the sinopulmonary features of cystic fibrosis, are encountered in patients with idiopathic chronic pancreatitis.

Autoimmune pancreatitis is a disease that most often presents as a masslike lesion with obstructive jaundice, mimicking cancer, but it also may present as chronic pancreatitis and rarely as acute pancreatitis. Characteristic features of the disease include a diffuse swelling of the pancreas, elevations in serum immunoglobulin G4 (IgG4), and involvement of other organs, especially biliary strictures, salivary gland inflammation, retroperitoneal fibrosis, and renal lesions. Histologically, these organs are infiltrated by chronic inflammatory cells, especially plasma cells bearing IgG4 on their surface. Tropical pancreatitis is seen primarily in southern India. Characteristic features include childhood onset, exocrine insufficiency, diffuse pancreatic calcifications, and inevitable diabetes. There may be a genetic component (SPINK1), but cofactors such as malnutrition and dietary toxins have been suggested. In southern India, this disease is becoming uncommon and is being replaced by alcohol as the most common cause of idiopathic chronic pancreatitis.

Clinical features. Patients with chronic pancreatitis seek medical attention predominantly because of two symptoms: abdominal pain or maldigestion and weight loss. The abdominal pain may be quite variable in location, severity, and frequency. The pain can be constant or intermittent with frequent pain-free intervals, and it is generally felt in the epigastrium with radiation to the back. If pain is episodic, the patient may be labeled as

having acute pancreatitis or an acute flare of chronic pancreatitis. When pain is severe, nausea and vomiting may occur. Pain may worsen, improve, or remain stable over time. Eating may exacerbate the pain, leading to a fear of eating with consequent weight loss. The spectrum of abdominal pain ranges from mild to quite severe, with narcotic dependence as a frequent consequence.

Maldigestion is manifested as chronic diarrhea, steatorrhea, weight loss, and fatigue. Patients with chronic abdominal pain may or may not progress to maldigestion, and ~20% of patients will present with symptoms of maldigestion without a history of abdominal pain. Despite steatorrhea, clinically apparent deficiencies of fat-soluble vitamins are surprisingly uncommon.

Up to 5% of patients do not have pain and instead present with exocrine (steatorrhea, weight loss) or endocrine (diabetes) pancreatic insufficiency. The disease tends to be progressive over time, even if the original cause (e.g., alcohol) is removed.

Diagnosis. The diagnosis may be suspected based on the clinical features but should be confirmed by tests that identify structural damage to the pancreas or derangements in pancreatic function.

Physical findings in these patients are usually unimpressive, so that there is a disparity between the severity of abdominal pain and the physical signs that usually consist of some mild tenderness. The diagnosis of early or mild chronic pancreatitis can be challenging because there is no biomarker for the disease. In contrast to acute pancreatitis, the serum amylase and lipase levels are usually not strikingly elevated in chronic pancreatitis. Elevation of serum bilirubin and alkaline phosphatase may indicate cholestasis secondary to common bile duct stricture caused by chronic inflammation. Many patients have impaired glucose tolerance with elevated fasting blood glucose levels. The fecal elastase-1 and small-bowel biopsy are useful in the evaluation of patients with suspected pancreatic steatorrhea. The fecal elastase level will be abnormal and small-bowel histology will be normal in such patients. A decrease of fecal elastase level to <100 μg per gram of stool strongly suggests severe pancreatic exocrine insufficiency.

Chronic pancreatitis is a slowly progressive disease in which visible damage to the gland (e.g., on a CT scan) and functional failure (e.g., steatorrhea or diabetes) may not be apparent for years. All diagnostic tests are most accurate when the disease is far advanced, and all are far less accurate in the early stages of disease.

Tests of Pancreatic Structure. Plain abdominal radiographs may demonstrate diffuse or focal pancreatic calcification in patients with advanced chronic pancreatitis. Although specific for chronic pancreatitis, these findings are quite insensitive. Abdominal ultrasound is of limited utility because overlying gas often limits the ability to visualize the pancreas. An abnormal pancreatic duct, pancreatic calcifications, gland atrophy, or changes in echotexture are seen in about 60% of patients. CT is the most widely used diagnostic test for chronic pancreatitis, and high-quality images can be obtained of the pancreas and pancreatic duct. Characteristic findings include a dilated pancreatic duct, ductal or parenchymal calcifications, and atrophy. These structural changes take years to develop, so CT is not as accurate in early or less advanced disease. Like CT, MRI allows detailed images of the pancreas, and the addition of MRCP allows even better assessment of pancreatic duct morphology. At some centers, secretin is administered at the time of MRCP to allow better visualization of the pancreatic duct. ERCP provides the most detailed

images of the pancreatic duct. Changes in the duct, including dilation, irregularity, ductal stones, and strictures, can be appreciated. These findings are not completely specific for chronic pancreatitis and can be seen in other situations, including with pancreatic cancer and in very elderly individuals. ERCP carries risk but has the advantage of providing both diagnostic and therapeutic impact. EUS allows very detailed images of pancreatic parenchyma and duct. A normal EUS essentially excludes chronic pancreatitis, whereas a very abnormal EUS is highly consistent with chronic pancreatitis.

Tests of Pancreatic Function. Serum trypsinogen (also called trypsin) is abnormally low in patients with far advanced chronic pancreatitis but is often normal in patients with less advanced disease. Levels lower than 20 ng/mL are seen in patients with chronic pancreatitis that is sufficient to cause functional failure (e.g., steatorrhea). Serum levels of amylase or lipase are not useful for chronic pancreatitis. Serum glucose levels will be elevated in those with endocrine insufficiency. Quantification of fat in stool during a 72-hour collection while on a highfat diet can be used to document steatorrhea but is rarely performed. Qualitative analysis of fat with Sudan staining of a stool specimen has poor sensitivity and specificity. Fecal levels of pancreatic elastase are diminished to less than 100 μg/g in patients with advanced chronic pancreatitis and steatorrhea. The test can be performed while patients are taking pancreatic enzyme therapy. For a pancreatic function test, a tube is passed into the duodenum, where pancreatic secretions are collected over the course of 1 hour in 15-minute aliquots and analyzed for bicarbonate concentration after a supraphysiologic dose of secretin is administered. A normal study is defined by at least one of the samples having a bicarbonate concentration of more than 80 mEq/L.

As the disease advances over years, structural and functional damage accumulate to the point that essentially all diagnostic tests are positive. In most patients, the diagnosis is established by routine tests such as CT or MRI; EUS and ERCP are rarely needed for diagnostic purposes in patients with longstanding chronic pancreatitis. The diagnostic challenge lies with patients who present with a severe pain syndrome suggestive of chronic pancreatitis but who have a normal CT or MRI. In these patients, EUS is the best choice unless the physician has access to a secretin-based pancreatic function test. ERCP should not be used for purely diagnostic purposes because patients with a normal-appearing pancreas are particularly prone to complications, especially post-ERCP pancreatitis.

STRUCTURAL TESTS	FUNCTIONAL TESTS
Biopsy	Hormonal (secretin) test
Endoscopic ultrasound	Fecal elastase
Endoscopic retrograde cholangiopancreatography	Serum trypsin
Magnetic resonance imaging with magnetic resonance cholangiopancreatography	Fecal fat
Computed tomography	Blood glucose
Ultrasonography	
Plain x-ray	

Complications. Exocrine or endocrine insufficiency, pancreatic pseudocyst, malignancy, chronic abdominal pain, jaundice, diabetes mellitus/impaired glucose tolerance, gastroparesis, malabsorption/maldigestion, biliary stricture and/or biliary

cirrhosis, portal hypertension, bacterial (abccess, parapancreatitis), systemic (renal failure, liver failure, DIC).

Treatment. Medical therapy starts with vigorous attempts to assist patients in stopping alcohol and tobacco.

- Abdominal pain: Most patients will require analgesics and adjunctive agents. If there is mild to moderate pain, acetaminophen and/or non-steroidal anti-inflammatory drugs (NSAIDS) may bring relief. Ibuprofen, Naproxen are examples of NSAIDS. If these medications do not control the pain opioids such as Hydrocodone, Codeine, Methadone, Fentanyl, Oxycodone, Hydromorphone or Morphine can be prescribed. If they don't bring relieve, Tramadol, 50 mg, one to three times daily can be used. It may be helpful to use selective serotonin reuptake inhibitors (citalopram, fluoxetine, sertraline, paroxetine, and others), gabapentin (starting at 100 mg at night), or pregabalin (starting at 50 mg three times daily). Finally, pancreatic enzyme therapy may have some beneficial effect on pain. Autoimmune pancreatitis responds promptly to steroid therapy (usually 40mg of prednisone daily for 4 weeks, with a taper of 5 mg/week over the next 7 weeks), but relapse may occur, particularly in the biliary tree.
- Exocrine insufficiency: the treatment of steatorrhea with pancreatic enzymes is straightforward even though complete correction of steatorrhea is unusual. Enzyme therapy usually brings diarrhea under control and restores absorption of fat to an acceptable level and affects weight gain. Thus, pancreatic enzyme replacement has been the cornerstone of therapy. Recent data suggest that dosages up to 80,000–100,000 units of lipase taken during the meal may be necessary to normalize nutritional parameters in malnourished chronic pancreatitis patients, and some may require acid suppression with proton pump inhibitors. Recommended dose of lipase per one meal is 25000-40000 IU.
- Endocrine insufficiency: like exocrine insufficiency, diabetes mellitus is a very late complication of chronic pancreatitis, occurring years or decades after disease onset. Unlike type 1 diabetes mellitus, there is destruction of the entire islet, which reduces secretion of both insulin and glucagon.
- Surgical therapy: patients with a dilated pancreatic duct (generally >5 mm) are candidates for endoscopic and surgical therapy, which involves decompression of the dilated duct. Endoscopic ultrasound–guided celiac plexus block or neurolysis can help to relieve the pain. Thoracoscopic splanchnicectomy, endoscopic therapy (stent, stone removal, lithotripsy), such surgical therapy as pancreaticojejunostomy (modified Puestow operation), partial pancreatic resection (Whipple operation, duodenum preserving pancreatic head resection, others), total pancreatectomy with islet cell autotransplantation can be performed in treatment according to present indications in patient.

Test evaluation and situational tasks.

Situation tasks:

1. 32 years old woman complains of pain in the left subcostum, which appears in 2 hours after meal, nausea, abdominal bloating, tendency to diarrhea. Objectively: subicteric colour of scleras. Abdomen is painful upon the palpation in the point of Gubergric-Sculsky. Liver is near the edge of costal arc. In blood: amylase - 256, general bilirubin - 20. What is the most probable diagnosis? What additional obligatory test is necessary?

2. Patient has symptoms of digestive disorder, such as fatty diarrhea in 4 hours after meal, abdominal pain, especially in upper left part. Diarrhea can be changed by constipation for 3-5 days. Moderate pain found in the choledochpancreatic area. The level of amylase in blood is normal. Survey sciagraphy: calcinates, located highly to newel. What is the probable diagnosis? What groups of preparations for treatment can be prescribed?

Tests:

1. Patient suffers from chronic recurrent pancreatitis with failed exocrine secretion. After rich, spicy meals and alcohol "fat" feces appears. Declined production of what factor is the most reliable reason of fatty diarrhea?

A. Alkaline phosphatase
B. Trypsin
C. Acidity of gastric juice
D. Amylase
E. Lipase

2. 48 years old man complains of permanent pain in the upper half of abdomen, more on the left, which increases after meal; diarrhea, weight loss. Patient abuses an alcohol. From the anamnesis: acute pancreatitis 2 years ago. Blood amylase is 4. Coprogram showed fatty diarrhea, creatorrhea. Sugar of blood is 6,0 mmol/l. What treatment the patient needs?

A. Creon
B. Insulin
C. Gastrozepin
D. Contrykal
E. No-shpa

3. 60 years old woman complains of acute pain in the right subcostum. In the anamnesis acute pancreatitis. Temperature - 38,2°C. Objectively: yellowness of scleras. There are no symptoms of peritoneal irritation. Positive Ortner`s, Gubergric-Sculsky symptoms. Urine diastase - 256. What is the most credible diagnosis?

A. Chronic pancreatitis
B. Acute cholangitis
C. Chronic cholecystitis
D. Acute cholecystitis
E. Cancer

4. 42 years old patient complains of nausea, attacks of pain in abdomen before defecation, diarrhea, frequent meteorism. From the anamnesis: systematic abuse of alcohol. He is considered to be ill for 6 years. Objectively: body weight is reduced; pulse is 98/min., rhythmic. Tongue is coated with white fur. Abdomen is soft, sensible upon the palpation in paraumbilical area. Liver and spleen are not increased. In the analysis of feces there are fatty diarrhea, creatorrhea. In the analysis of urine: diastase activity - 128. What diagnosis is the most credible?

A. Chronic hepatitis
B. Chronic reccurent alcoholic pancreatitis
C. Chronic enterocolitis
D. Chronic cholecystitis
E. Helminthosis

5. A 24 y.o. male complains of abdominal spastic pain, which occurs after emotional stress, relieves with defecation, and is accompanied by abdominal winds, constipation and the feeling of incomplete evacuation. These symptoms have lasted for over 3 months. No changes in laboratory tests, GDS and colonoscopy. What is the most proper treatment of constipation?
A. Antidepressants
B. Antibiotics
C. Lactulose
D. Loperamide
E. Fluocsetine

6. A 56 y. o. man, who has taken alcoholic drinks regularly for 20 years, complains of intensive girdle pain in the abdomen. Profuse nonformed stool 2-3 - times a day has appeared for the last 2 years, loss of weight 8 kg for 2 years. Data of examination: abdomen is soft, painless. Blood amylase - 12g/L. Feces examination - neutral fat 15 g per day, starch grains. What is the most reasonable treatment of this condition?
A. Levomicytine
B. Contrykal
C. Aminocapron acid
D. Pancreatine
E. Imodium

7. A patient is 65 y. o. He has been a smoker for 40 years. He has lost 10 kg during the last 3 months. Complains of pain in the epigastric area after taking meals, diarrhea, jaundice. Physical examination revealed enlarged, painless gallbladder. Feces are light-coloured and clay-like. Blood analysis revealed increased level of general and direct bilirubin, alkaline phosphatase and glutaminepyruvate transferase. Clinical urine analysis showed positive bilirubin reaction and negative urobilinogene reaction. Where is the initial process that caused these changes?
A. In pancreas
B. In common bile duct
C. In liver
D. In duodenum
E. In gallbladder

8. A 75 years old man who has been suffering from diabetes for the last six months was found to be jaundiced. He was asymptomatic except the weight loss of 10 kg in 6 months. Physical examination revealed a hard, globular, right upper quadrant

mass that moves during respiration. ACT scan shows enlargement of the head of the pancreas, with no filling defects in the liver. The most likely diagnosis is:

A. Carcinoma of the head of the pancreas
B. Infectious hepatitis
C. Chronic pancreatitis
D. Malignant biliary stricture
E. Metastatic disease of liver

9. A 68 years old patient has been suffering from chronic pancreatitis for 35 years. During the last 5 years he has been observing because of pain syndrome, abdominal bloating, frequent defecations up to 3-4 times a day (feces are greyish, glossy, with admixtures of undigested food), progressing weight loss. The symptoms are caused by:

A. Exocrine pancreatic insufficiency
B. Endocrine pancreatic insufficiency
C. Syndrome of lactase deficiency
D. Irritable bowels syndrome
E. Chronic enterocolitis

10. A 40-year-old woman has been suffering from chronic pancreatitis for the last 8 years. Lately she has been noticing an increase in daily feces with foul smell, abdominal distention, gurgling. The patient complains of diarrhea, weakness, fatigability, loss of appetite, loss of weight. What syndrome can be suspected in this case?

A. Irritable colon
B. Malabsorption
C. Maldigestion
D. Exudative enteropathy
E. Endocrine gland failure

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:
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II. Additional literature:

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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.

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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).

Composed by **Lymanets T.V.**