

## **Module "Fundamentals of diagnostics, treatment and prevention of major diseases of the digestive system"**

### **Practical training: "Chronic pancreatitis (CP)"**

#### **Topicality**

The incidence of chronic pancreatitis is 4.8 new cases per 100 000 of population per year. Prevalence is 25 to 30 cases per 100 000 of population. Total number of patients with CP increased in the world by 2 times for the last 30 years. In Ukraine, the prevalence of diseases of the pancreas (CP) increased by 10.3%, and the incidence increased by 5.9%.

True prevalence rate of CP is difficult to establish, because diagnosis is difficult, especially in initial stages. The average time of CP diagnosis ranges from 30 to 60 months depending on the etiology of the disease.

#### **Learning objectives:**

- to teach students to recognize the main symptoms and syndromes of CP;
- to familiarize students with physical examination methods of CP;
- to familiarize students with study methods used for the diagnosis of CP, the determination of incretory and excretory pancreatic insufficiency, indications and contraindications for their use, methods of their execution, the diagnostic value of each of them;
- to teach students to interpret the results of conducted study;
- to teach students how to recognize and diagnose complications of CP;
- to teach students how to prescribe treatment for CP.

#### **What should a student know?**

- Frequency of CP;
- Etiological factors of CP;
- Pathogenesis of CP;
- Main clinical syndromes of CP, CP classification;
- General and alarm symptoms of CP;
- Physical symptoms of CP;
- Methods of physical examination of patients with CP;
- CP diagnostics, assessment to disorders of endocrine and exocrine pancreatic function;
- Diagnostic capabilities of esophagogastroduodenoscopy, excretory retrograde cholangiopancreatography, abdominal ultrasonography, computed tomography, plain radiography of the abdomen in patients with CP, indications, contraindications;
- Method of duodenal intubation to determine the exocrine pancreatic function, clinical evaluation of its results;
- H.pylori diagnostic methods;
- Methods of functional tests for the diagnostics of exocrine pancreatic insufficiency;
- Complications of CP;
- CP treatment (lifestyle modification, nutrition, drug therapy, surgery).

#### **What students should be able to do?**

- To define the main clinical and physical syndromes in CP;
- To interpret the results of clinical, biochemical and immune-enzyme assays;
- To interpret the data of esophagogastroduodenoscopy, excretory retrograde cholangiopancreatography, ultrasonography of the abdomen, CT, plain radiography of the abdomen;
- To interpret the data of duodenal contents analysis in order to determine the exocrine pancreatic function, and to provide clinical evaluation of results;
- To evaluate the functional tests for the diagnostics of exocrine pancreatic insufficiency;

- To be able to identify the types of exocrine pancreatic insufficiency;
- To prescribe treatment for patients with CP.

**List of practical skills that students should possess:**

- Inspection of skin and mucosa
- determination of presence of malabsorption syndrome;
- examination of the abdomen;
- Inspection of the abdomen;
- Superficial palpation of the abdomen;
- Methodological deep sliding palpation of the abdomen after the method of Obratzov-Strazhesko;
- Determination of pain points and zones that are typical for CP;

**Topic content**

**Chronic pancreatitis (CP)**

**Definition:**

**Chronic pancreatitis** is a lingering progressive disease, with such classic symptoms as recurrent pain in the upper abdomen (80-95%), steatorrhea and weight loss (80%), diarrhea (50%), nausea and vomiting.

During the course of the disease the formation of pseudocysts, the development of diabetes and, in rare cases, pleural effusion and ascites may be observed.

**Clinical symptoms of pronounced CP are characterized by:**

- Pain (85%)
- Dyspeptic syndrome
- Malabsorption syndrome,
- Weight loss,
- Endocrine deficiency syndrome (impaired glucose tolerance or diabetes).

In 20-25% of cases latent disease course is observed.

Depending on the etiology of CP various syndromes prevail in the clinical picture. Thus, in case of alcoholic CP pancreatic calcification (58%), exocrine insufficiency (42%) is more common.

*Pain syndrome* in case of CP can occur as:

- Typical pain of circular character;
- Ulcer-like pains;
- Pain by type of left-sided renal colic;
- Pain in right upper quadrant, which is accompanied by jaundice in 30-40% of cases;
- Can have dysmotoric character;
- Might be widespread, with no clear localization.

The mechanisms of pain syndrome development in CP is the following: acute inflammation of pancreas, increased intraductal pressure due to obstruction and dilation of the pancreatic and bile ducts, the pressure of enlarged and inflamed pancreas on neural plexus, pancreatic tissue ischemia, formation of pseudocysts, stenosis and dyskinesia of descending part of duodenum, the presence and exacerbation of comorbidities, and drug addiction.

*Dyspeptic syndrome* manifests with nausea, eructation, multiple vomiting.

*Malabsorption syndrome* is characterized by bloating, bone pain, diarrhea 3-10 times per day with polyfecalia, steatorrhea and creatorrhea.

*Data from physical examination of the patient:*

- Bright red spots on the skin of the abdomen and chest - the symptom of the "red droplets";

- Grott's symptom - atrophy of subcutaneous adipose tissue in the area of projection of the pancreas;
- jaundice or pale skin;
- Reduction of skin moisture and turgor;
- Dry tongue, smoothed lingual papillae;
- Abdomen enlarged in case of flatulence;
- tenderness in Chauffard's zone, Huberhryts-Skulsky's zone, Desjardin's point, Mayo-Robson's point;
- The presence of skin hyperalgesia areas by Zaharyin-Geda.

### **CP complications:**

Diabetes mellitus, obstructive jaundice, subhepatic portal hypertension, pancreatic calcification, fatty liver, pancreatic retention cysts and pseudocysts, erosive and ulcerative lesions of duodenum, enzymatic cholecystitis, stenosis of the splenic angle of the colon, splenic vein thrombosis with gastrointestinal bleeding and splenomegaly, thrombophlebitis and arteriopathies of lower extremities, ischemic heart disease, retroperitoneal fibrosis with following duodenostasis, effusions in the peritoneal, pleural and pericardial cavity, anemia, encephalopathy, pancreatic cancer.

### **Diagnosis**

#### **Study plan in case of CP consists of:**

#### **Laboratory diagnostics:**

- Complete blood count;
- Proteinogram;
- Aminotransferases;
- Alpha-amylase in serum and urine (sensitivity is 30% in case of CP);
- Blood trypsin (enzyme is pancreatospecific, however biochemical methods for determination of enzyme are unreliable; the radioimmune-enzyme assay is much more informative and is being performed to identify and assess the severity of the phenomenon of "enzyme deviation" in the blood);
- Elastase-1 in serum (test sensitivity is 100% in the first 48 hours of exacerbation) and feces ("gold standard" for the diagnosis of pancreatic exocrine insufficiency);
- Interleukin-6 levels (rises 1 day after the beginning of the CP attack, interleukin-8 (increases after 48 hours);
- Coprogram: steatorrhea, creatorrhea, amilorrhea, lientorrhea - these symptoms appear only in case of severe exocrine insufficiency when not more than 10% of acinar cells are functioning;
- D-xylose test;
- Study of bicarbonates, pancreatic enzymes and lactoferrins in duodenal contents (increased in pancreatic juice of patients with CP, but not in patients with cancer): probe studies (direct tests - secretin-pancreozymin test – is considered to be a "gold standard" in the diagnostics of pancreas pathology, secretin-caerulein, aminophylline-calcic tests etc. - direct stimulation of acinar and ductal cells; indirect tests – Lund's test (standard breakfast - a mixture of 18 g olive oil, 15 g of milk powder, 40 g of glucose, 15 g of strawberry syrup, 30 ml of warm water) - is informative only in case of severe exocrine insufficiency; hydrochloride-oil test - stimulation of secretin and pankreozymin production: hydrochloric acid stimulates S-12 cells of duodenal mucosa that produce secretin, which enters the bloodstream and then it stimulates ductal cells to produce bicarbonate and liquid part of pancreatic juice, olive oil stimulates I-cells of duodenal mucosa, which produces cholecystikinin-pankreozymin, and these substances, in turn, stimulate the acinar cells of pancreas to produce enzymes). The following types of pancreatic external secretion disorders can be defined:
  1. Hyposecretory type - decreased production of enzymes, normal volume of bicarbonate secretion (typical for pancreatic fibrosis, hypoenzymatic pancreatitis).

2. Hypersecretory type - normal or increased volume of secretion and bicarbonate discharge and increased enzyme activity (typical for the initial inflammatory processes in pancreas without any signs of atrophy).
3. Obstructive type is divided into two subtypes:
  - Lower block – reduction of secretion volume with normal concentration of bicarbonates and enzymes, leading to a decrease in their discharge (obstructive pancreatitis - papillitis, plugging with stone etc.);
  - Upper block - reduction of secretion volume, increased enzyme concentration (but their discharge is reduced), normal contents of bicarbonates (swelling of the pancreas, which is typical for hypoenzyme pancreatitis).
4. Ductular type - reduction of secretion volume, normal production of enzymes, an abrupt increase in bicarbonate concentration (inflammation of the ducts with impaired reabsorption of bicarbonate).

It is especially important to determine the content of lipase in duodenal contents as the reduction of this enzyme is primarily responsible for maldigestion and pancreatic exocrine insufficiency in general.

- Fasting plasma glucose
- Determination of immunoglobulin G and M by ELISA method,
- H. pylori determination.

The highest diagnostic value in case of pancreatic diseases belongs to serum elastase-1 determination (test sensibility - 100%) that can detect the presence or absence of acute pancreatitis or CP exacerbation

The study of elastase-1 in stool allows to determine pancreatic insufficiency of mild degree in 80-85% of cases, moderate and severe cases - in 95-100%.

These tests allow to determine or to rule out pancreatic exocrine insufficiency and its degree.

#### **Instrumental methods:**

- Ultrasonography of the abdomen;
- Excretory retrograde cholangiopancreatography;
- Computed tomography;
- Plain radiography of the abdomen.

#### **Respiratory pancreatic tests:**

*<sup>13</sup>C-triglyceride breath test* - determines pancreatic lipase activity in the lumen of the intestine and can differentiate pancreatic steatorrhea from enteric steatorrhea.

*Protein breath test with <sup>13</sup>C-marked egg white* - reduced in case of CP - lack of trypsin.

*Amylase (<sup>13</sup>C-corn-starch) breath test* – allows to detect deficiency of pancreatic amylase in duodenum (normal – in the end of 4th hour - 10-30%).

#### **In order to evaluate pancreatic endocrine insufficiency the following tests are used:**

1. *Static tests* - blood glucose, insulin, C-peptide, pancreatic polypeptide, glucagon levels.

2. *Dynamic tests* - determination of blood glucose and pancreatic hormones before the load with glucose, arginine, secretin, etc., and after it in dynamics.

*Arginine test is the most specific for CP* - determination of glucagon levels in blood after infusion of arginine - changes are present only in case of pancreatic diabetes, but not in primary diabetes.

Thus, in order to determine the activity of pancreatic enzymes in blood it is necessary to detect the "deviation" of enzymes in the blood - for the diagnosis of CP attacks, but not to assess pancreatic exocrine insufficiency.

Functional tests (intubation) are indicated for the diagnostics of pancreatic exocrine insufficiency.

## **Classification of CP**

ICD-10

C 86.0 Alcoholic CP

C. 86.1 Other forms of CP

    Infectious

    Continuously recurrent

    Reverse (recurrent)

C 86.2 Pancreatic cyst

C 86.3 Pancreatic pseudocyst

C. 86.8 Other unspecified pancreatic diseases

    Atrophy

    Lithiasis

    Fibrosis

    Cirrhosis

    Pancreatic infantilism

    Necrosis: aseptic

        Fatty necrosis

C 90.1 Pancreatic steatorrhea

## **Clinical classification of CP**

(Summarised Data of the 1st International Symposium of Pancreatology, 1963; Cambridge Conference, 1983; 2nd Marseille Symposium, 1984; International Rome Conference, 1988)

CP is classified into 3 categories:

1. Chronic calcifying pancreatitis:

    A. Alcoholic

    B. Nutritional (tropical)

    B. Hereditary

2. Chronic idiopathic pancreatitis

    A. Juvenile (under 35 years)

    B. Senile (after 65 years)

3. Chronic obstructive pancreatitis

The course of the disease may be mild, moderate and severe:

- Mild course - characterized by rare and short-term exacerbations (not more than 1-2 times a year), which are quickly and easily stopped, no signs of functional pancreatic insufficiency, body weight is not reduced, the patient's general condition is satisfactory;
- Moderate severity - exacerbations occur 3-4 times a year, pain is more intense and long-lasting; pronounced phenomenon of enzymes "deviation" in blood; disorders of exocrine function; derangements of endocrine function are moderate and reversible; weight loss during the disease attack, which is usually restored after relief;
- Severe course - frequent and prolonged exacerbations (or continuously relapsing course) with persistent and severe pain and dyspeptic syndrome, with symptoms of maldigestion and malabsorption; typical "pancreatic" stool with steatorrhea; pancreatic diabetes; progressive emaciation of the patient.

## **The peculiarities of CP clinical course.**

Chronic calcifying pancreatitis - the most common form with predominantly alcoholic origin - is characterized by uneven distribution of foci of tissue destruction with intraductal plugs and stones, atrophy, stricture formation in pancreatic ducts.

Structural and functional changes progress even when the primary cause of the disease is eliminated. Etiologic factor is usually chronic alcohol abuse, diet with low protein content (kwashiorkor), low-or high lipid diet, hypercalcaemia. Also hereditary variants take place. Calcifying pancreatitis may develop when certain medications are taken - azathioprine, hydrochlorothiazide, sulfonamides, and others. The pathogenesis is mostly associated with lack of

litostatine secretion - pancreatic stone protein, PSP, which prevents precipitation of calcium salts. This form of the disease is prone to exacerbations and complications (pancreatic necrosis), which may threaten the life of the patient. The development of attacks is typical after alcoholic excesses.

Chronic obstructive pancreatitis – is the result of obstruction of the main pancreatic duct by tumors, strictures or papillary stenosis, occurs rarely; is characterized by lysis and partial obstruction of the gland, ductal epithelium is always preserved; pancreatic stones and calcifications are not observed.

Lesion develops evenly at the parts distal to the obstruction point. The typical features also include diffuse atrophy and fibrosis of exocrine pancreatic tissue and preserved ductal epithelium at the site of obstruction.

The main causes for obstructive CP - tumors that clog pancreatic ducts, ampullary stenosis, pseudocysts or scarring after acute pancreatitis, traumas that narrow the lumen of the pancreatic duct.

Inflammatory CP - characterized by atrophy of the pancreatic parenchyma that is replaced by areas of fibrosis infiltrated by mononuclear cells. In domestic literature inflammatory CP is often called infiltrative-fibrous.

Pancreatic fibrosis - diffuse pancreatic fibrosis (peri- and intralobular), accompanied by the loss of significant part of the parenchyma and is characterized by progressive exocrine and endocrine pancreatic insufficiency; is the result of other forms of CP. In domestic literature this type is often called fibrous or sclerosing indurative CP.

Morphological classification of pancreatitis (Cambridge, 1984)

Stage	Data of ERCPG	Data of US and CT
Normal	Absence of visual changes in entire pancreas	Absence of visual changes in entire pancreas
Ambiguous	Less than 3 changed ducts	Dilation of main duct
Mild	More than 3 changed ducts	Size of cavities less than 10 mm. Duct roughness Focal acute pancreatitis
	More than 2 signs of the following	Parenchyma heterogeneity Increased echogenicity of ductal wall
Moderate	Abnormality of main duct and its branches	Roughness of pancreas head and body contours
Pronounced	Abnormality of main duct and its branches More than 1 sign of the following	Size of cavities is over 10 mm. Increase of pancreas size more than 2 times; Intraductular defects or stones; Obstruction or strictures of ducts

## CP ETIOLOGY

Alcohol abuse (70 - 80%).

Pancreatic ducts obstruction (calcifications, odditis due to sphincter hypertrophy, papillitis).

Presence of cholelithiasis.

Acute Pancreatitis in anamnesis.

Affection by B, C, A hepatitis virus, parotitis virus, cytomegalovirus. Pancreatitis due to parasitic invasion. H. pylory infection.

Chemical substance effect (including medications). Hyperlipidemia.

Hypocalcaemia. Heredity. Nutritive factors: limitation of protein and fat. Deficit of antioxidants in food.

Pancreatic traumas (including surgery).

Combination of factors.

Among these etiologic factors the first place belongs to alcohol ingestion - 80%, idiopathic CP - 10%, cholelithiasis - 5%, hereditary and other factors - 5%.

## **CP PATHOGENESIS**

Pancreatic parenchyma consists of endocrine and exocrine glandular tissue. Acinar cells that form exocrine glandular tissue produce digestive enzymes in inactive form (zymogens), which are expelled to ducts that contain sodium bicarbonate and further are moved to small intestine where they are getting activated. This process, if it takes place in pancreas, can cause marked gland destruction, that's why the exocrine part of the organ has strong protective system of zymogen activity regulation.

When protective system is damaged, digestive enzymes cause the direct damage of the organ parenchyma, which in combination with the immune response reveals as pancreatitis in future.

The state, which develops as the result of pancreatic damage with following immune response, favors the cytotoxic damage of acinar cells in patients with CP. Immune system activation is accompanied by anti-inflammatory response (production of interleukins and other substances) and the following stimulation of fibrotic process that proceed with the participation of activated pancreatic stellate cells.

### **Pathogenetic aspects of alcoholic CP**

Chronic alcohol ingestion causes direct injury of pancreas acinar cells and intraductal protein release with the following cell calcification. Secretion pressure increases and results in the duct widening. In the future a cell inflammation and fibrosis or even necrosis might develop. This causes the development of pseudocysts and exocrine and endocrine pancreatic insufficiency.

### **Pathogenetic aspects of biliary CP**

Cholelithiasis, miliary or duodenal hypertension, disorders in ductal and sphincter systems of miliary zone, biliary dyskinesia, inflammations and other injuries of major duodenal papilla cause regurgitation of bile and duodenal content to pancreatic ducts. This leads to the activation of pancreatic juice enzymes, damage of acinar cells and development of chronic inflammation in pancreas.

### **Pathogenetic aspects of hereditary CP**

As a part of intensive research a specific "susceptibility gene" was discovered - PRSS1 ("protease, serine, 1") that codes the structure of cationic trypsinogen, mutations of which are reliably observed in the families of patients with hereditary CP. As the result of such mutation the structure of autolytic site is created, which ensures quick molecule self-destruction in the environment with low calcium ions concentration. Low concentration of such ions prevents the activation of a specific peptide area of trypsinogen by trypsin. When the concentration is high, calcium binds with the remains of the asparaginic acid at the area of activation peptide (trypsinogen), as the result a quick trypsinogen activation by trypsin occurs.

The reduction of secretion and SPS-protein level due to external influences (alcohol, chemical substances) or genetic defects favor the increase of  $\text{Ca}^{+}$  concentration in pancreatic juice. Calcium stimulates microcrystallization and calcification in pancreatic ducts that leads to their blockade with the following dilation. The increase of intraductal pressure develops with the following diffuse atrophy of acinar structures and fibrosis development.

To determine the pathogenetic and functional CP variant it is necessary to consider the following. When acinar cells are damaged, the enzymes they contain come into the interstitial fluid, then to lymph, blood, and later appear in urine. Pancreatic enzymes also penetrate into

blood from secretory tracts and pancreatic ducts. In addition to that enzymes are absorbed in proximal parts of small intestine. Thus, the increase of the enzymes level in blood and urine can be associated with acinar cell destruction, intraductal pressure rise. Such diseases are called hyperenzymatic as they are accompanied by the phenomenon of enzymes "deviation" to blood ("deviate" from the usual path of excretion).

When the exocrine organ function is decompensated, it is depressed, the enzymes production and their content in blood and duodenal content reduces. Such diseases are called hypoenzymatic.

Depending on whether the CP is hypo- or hyperenzymatic the treatment policy is chosen.

### **CP treatment algorithm**

#### *Etiological treatment:*

1. Alcohol renunciation
2. Fatty food elimination
3. Removal of protein deficit in nutrition
4. Elimination of pancreotoxic medications
5. Antibiotic therapy
6. Treatment of diseases that cause CP
7. Antihelicobacter therapy
8. Interferon inducers use

#### *Pathogenetic treatment:*

Hyperenzymatic pancreatitis:

1. Correct nutrition
2. Functional rest
3. Sandostatin
4. Correction of Oddi's sphincter tone
5. Protease inhibitors
6. Correction of microcirculation disorders

Hypoenzymatic pancreatitis:

1. Correct nutrition
2. Correction of hypopancreatism
3. Correction of Oddi's sphincter tone
4. Correction of microcirculation disorders

### **Step-by-step regimen of pain syndrome management in case of CP (according to WHO data)**

#### *Stage 1*

1. Strict alcohol elimination
2. Ferment replacement therapy
3. Dietary measures (reduce of animal fat, frequent small portion meals)

#### *Stage 2*

1. Spasmolytics
2. Analgesics - salicylates
3. Analgesics - codeine phosphate + paracetamol
4. Derivatives of phenothiazide (trifluoperidol, promethazine) + tricyclic antidepressant (imipramine)



### Stage 3

1. Central action analgesics (pentazocine, buprenorphine)
2. Combination with psychoactive drugs

### **Exocrine pancreatic insufficiency treatment**

*Mild degree* - treated by diet therapy

*Medium-severe and severe degree* – prescription of enzymatic agents considering their formula and the individual level of pancreatic enzymes (due to the results of study of duodenal content and coprogram).

Enzymatic agents: Kirshner's pancreal, licrease, creon, pancreatine, digestal, mezim- forte, pangrol 10000, Panzytrat, solizymum, solmylase, festal H, etc.

*Demands to modern enzymatic agents:*

- nontoxicity
- resistance to hydrochloric acid and pepsin action
- well tolerated by patients
- optimal effect within pH range 5.0 - 7.0
- absence of significant side effects

*Mechanism of enzymatic agent action:*

- primary - nutritional substrate hydrolysis;
- secondary - reduction of abdominal pain syndrome and dyspepsia

*Side effects of enzymatic agents:*

- painfulness in mouth cavity;
- skin irritation in perianal area;
- discomfort in abdomen;
- nausea;
- hyperuricemia;
- fibrosing of terminal sections of ileum with obstruction - in case of long-term usage of large doses of a medication;
- allergic reactions.

### **Correction of Oddi's sphincter tone**

- M-cholinolytics- gastrozepin;
- Calcium antagonists;
- Myotropic spasmolytics: no-spa, papaverine;
- Xanthines - aminophylline;

In case of cicatricial stenosis - endoscopic papilosphincterotomy.

In case of reflux - blockers of dopamine receptors - sulpirine, eglonil, cerucal, motilium, cirapride.

### **Protease inhibitors (PI)**

Natural and synthetic PIs exist.

Natural: reduce kallikrein activity in blood that reduces bradykinin synthesis and results in decrease of pancreas edema and pain intensity.

Representatives: contrical, gordox, trasilol, salol, aprotinin, pantrypin, gabexate.

Synthetic: suppress tripsinogen conversion into tripsin. Representatives: E-aminocaproic acid, methyluracil, pentoxil.

### **Correction of microcirculation disorders**

Heparin, nootropil, curantyl, trental - medications that assist microcirculation normalization.

In addition to that reopoliglucin solutions (200 ml), reopoliglucin-complamin-trental mixture, platelet-activating factor antagonist - lexipafant (unregistered in Ukraine) - are used.

### **Treatment of CPs associated with viral infection**

Cycloferon, laferon (Ukraine); nitron A (USA); roferon A (Switzerland); realdiron (Lithuania); acyclovir (zovirax, herpevir).

### **Combined immunomodulatory therapy**

- Cycloferon + methyluracil
- Cycloferon + methyluracil + laferon
- Cycloferon + methyluracil + acyclovir

### **Symptomatic therapy**

*In case of hyperenzymatic CP:*

1. Correction of fluid-electrolyte disorders
2. Thrombohemorrhagic syndrome treatment
3. Endotoxemia treatment
4. Correction of immunologic disbalance
5. Use of adaptogenes and antioxidants

*In case of hypoenzymatic CP:*

1. Maldigestion and malabsorption syndrome treatment
2. Intestinal disbacteriosis treatment
3. Hypotrophy treatment
4. Correction of carbohydrate metabolism
5. Stimulation of reparative processes
6. Use of adaptogenes and antioxidants

### **Indications for surgery**

1. Strictures or stones that obturate pancreatic duct and their presence is proven by ERCP
2. Choledoch and duodenum narrowing
3. Pancreatic pseudocysts and abscesses
4. Persistent, recurrent CP course with stable pain syndrome, resistant to conservative therapy
5. Segmental portal hypertension and gastrointestinal hemorrhages that recur

### **Control of initial knowledge level**

1. Patient complains on nausea, pain in right hypochondrium, diarrhea, and frequent abdominal distension. In anamnesis: systematic alcohol consumption. Objective data: subnutrition, tongue covered with white film, belly is soft, sensitive to palpation in paraumbilical area. Liver and spleen are not enlarged. Feces analysis: steatorrhea, creatorrhea. What diagnosis of the listed below is the most probable one?

- A.** Chronic hepatitis
- B.** Helminthiasis
- C.** Chronic recurrent alcoholic pancreatitis
- D.** Chronic enterocolitis
- E.** Chronic cholecystitis

2. Patient complains on the pain in the epigastrium and left subcostal area; repeated vomiting which doesn't bring relief, abdominal distention, diarrhea, weight loss. Objective data: tongue is wet, covered with white film near the root. During profound belly palpation an insufficient painfulness is found in epigastrium and Mayo-Robson's point. What disease should you think of in the first turn?

- A.** Ulcer
- B.** Chronic atrophic gastritis
- C.** Chronic pancreatitis
- D.** Chronic cholecystitis
- E.** Chronic enteritis

3. A female patient has been suffering from chronic pancreatitis during previous 5 years. She complains on frequent watery excrements, loss of 12 kg during 2 months. What syndrome does the patient have?

- A.** Astheno-neurotic
- B.** Malabsorption
- C.** Dyspeptic
- D.** Pain
- E.** Epigastric

4. A woman, 32 years old, complains on the pain in the left hypochondrium emerging in 2 hours after meal, nausea, abdominal distention, tendency to diarrhea. Objective data: subicteric sclera, painful belly during palpation in Gubergrits-Skulsky's point. The level of which enzymes should be determined?

- A.** Amylase
- B.** Lactate dehydrogenase
- C.** Creatine phosphokinase
- D.** Gammaglutamyltranspeptidase
- E.** Aspartaminotransferase

5. A patient complains on the pain in the upper right area of belly emerging in an hours after meal and irradiating to lumbus on the right side. During belly palpation there is painfulness in Chauffard's zone. What part of pancreas is damaged in this patient?

- A.** Head of pancreas
- B.** Body of pancreas
- C.** Tail of pancreas
- D.** Total pancreas damage
- E.** Focal damage

6. A patient with chronic pancreatitis has an increased level of blood serum glucose.  
What pancreatic function disorder does the patient have?

- A.** Exocrine
- B.** Endocrine
- C.** Absorption disorder
- D.** Acid-forming
- E.** Pepsinogenous

7. What hormones stimulate pancreatic activity?

- A.** Cholecystokinin-pancreozymin
- B.** Insulin
- C.** Thyrotropic
- D.** Counterinsular
- E.** Adrenalin

8. Which type of pancreatic juice secretion is the most typical for chronic pancreatitis?

- A.** Hyposecretory
- B.** Ductular
- C.** Upper obturative
- D.** Lower obturative
- E.** Hypersecretory

9. Which changes are typical for endocrine pancreatic insufficiency?

- A.** Jaundice
- B.** Nausea, vomiting
- C.** Hypoglycemic state, pancreatic diabetes development
- D.** Dyspeptic
- E.** Vitamin deficiency

10. Which clinic syndrome is associated with exocrine pancreatic disorder?

- A.** Pain
- B.** Maldigestion
- C.** Allergic
- D.** Epigastric
- E.** Right reactive vegetative

Correct answers:

- 1. C
- 2. C
- 3. B
- 4. A
- 5. A
- 6. B
- 7. A

- 8. A
- 9. C
- 10. B

### **Control of final knowledge level**

1. Which of these etiologic factors prevail in formation of primary chronic pancreatitis?
  - A.** Alimentary factors
  - B.** Alcoholism
  - C.** Heredity
  - D.** Medication
  - E.** Allergy
2. Which pathogenetic mechanisms are responsible for the development of chronic pancreatitis of alcoholic genesis?
  - A.** Pancreatic juice composition change with deposition of protein lumps in ducts
  - B.** Production of antibodies to the gland tissue
  - C.** Reflux of duodenal content to Wirsung's ducts
  - D.** Reflux of bile to Wirsung's ducts
  - E.** Inflammatory changes in gland
3. What causes pain syndrome in case of chronic pancreatitis?
  - A.** Fibrosis formation in the gland
  - B.** Necrotic changes
  - C.** Rise of pressure in ducts
  - D.** Gland edema
  - E.** Duct blocking
4. Which food products can cause pain syndrome in case pancreatitis?
  - A.** Salty food
  - B.** Alcohol, sweets, cakes
  - C.** Solid protein food
  - D.** Acrid and fried food
  - E.** Milk products
5. What evidences of dyspeptic syndrome are typical for chronic pancreatitis?
  - A.** Bitter taste, heartburn
  - B.** Nausea, vomiting without relief, gaseous eructation
  - C.** One time vomiting with relief
  - D.** Heartburn, sour eructation, nausea
  - E.** Food eructation, bitter taste
6. Which clinical evidences are typical for exocrine pancreatic function disorder?
  - A.** Constipation
  - B.** Diarrhea with blood in feces
  - C.** Imperative urge to defecate
  - D.** Abdominal distention, constipation
  - E.** Meteorism, rumbling, more frequent defecation
7. Which irritators are used for generation of pancreatic juice?

- A.** Histamine
- B.** Insulin
- C.** Aminophylline
- D.** Cholecystokinin-pancreozymin
- E.** Sulfurous magnesia

8. Which pancreatic enzyme is determined in blood of patients with chronic pancreatitis during the first hours?

- A.** Lipase
- B.** Tripsin
- C.** Chymotripsin
- D.** Nuclease
- E.** Amylase

9. Which pancreatic ferment stays increased during a long time when chronic pancreatitis exacerbates?

- A.** Tripsin
- B.** Lipase
- C.** Amylase
- D.** Nuclease
- E.** Chymotripsin

10. Which treatment method should be used during the first 2-3 days of chronic pancreatitis exacerbation?

- A.** Diet, spasmolytics, enzymes
- B.** Diet, M-cholinolytics, antienzymatic agents
- C.** Hunger, antienzymatic agents, H<sub>2</sub>-histamine receptor blockers
- D.** Diet, alkali, spasmolytics
- E.** Diet, spasmolytics, enzymes, vitamins

Correct answers (final knowledge level):

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

### **Case-based questions**

1. A female patient, 37 years old, complains on constant dull pain in hypochondrium with irradiation to the back that gets intensified after meals. Other complaints: abdominal distention, frequent defecation with indigested food. Objective data: moderate abdominal distention, painfulness in Chauffard's zone, Desjardin's point, Mayo-Robson's points. What study method is the most informative for proving of exocrine pancreatic insufficiency?

- A.** Esophagogastroduodenoscopy
- B.** Peroral cholecystography
- C.** Retrograde pancreatography
- D.** Coprogram

**E. Ultrasonography of abdominal organs**

2. A man, 45 years old, complaints of the aching pain in the left subcostal area, nausea, gaseous eructation, diarrhea after ingestion of fatty food, meteorism, abdominal rumbling, weight loss. He suffers about 25 years when he started noticing the pain in the left subcostal area, gaseous eructation because of improper food, and later, diarrhea, stinking fatty feces. Which preliminary diagnosis is the most probable?

- A. Ulcer**
- B. Chronic gastritis**
- C. Chronic cholecystitis**
- D. Gastroesophageal reflux**
- E. Chronic pancreatitis**

3. A man, 46 years old, complains on the severe pain in the upper half of the abdomen, mainly on the left, nausea, vomiting without relief on the 2-nd day after a banquet. Such condition is regularly observed after the diet problems. Objective data: temperature 37°C, pale and wet skin, pulse - 88 beats per 1 min, rhythmic, the belly is moderately distended, acute pain in the pancreas projection. CBC: L -  $18 \cdot 10^9/l$ , urine diastase - 256 un. after Wolgemut. What would be the most correct management of this condition by general practitioner?

- A. Urgent hospitalization to the surgery department**
- B. Ambulatory therapy**
- C. Home ward**
- D. Planned hospitalization to the therapeutics unit**
- E. Gastroenterologist consultation**

4. A man, 35 years old, complaints on the permanent dull pain in the left hypochondrium after fatty and smoked food, vomiting without relief. Feces look shiny and malodorous. Patient have been suffering from this condition for 8 years, he drinks too much alcohol, smokes a lot. Objective data: reduced nutrition. Pale and dry skin. Foul tongue with white film. The belly is moderately inflated, pain in Chauffard's, Gubergrits-Skulsky's zone, Desjardin's, Mayo-Robson's points. Which disease should you think of first of all?

- A. Chronic pancreatitis**
- B. Chronic cholecystitis**
- C. Ulcer**
- D. Chronic gastroduodenitis**
- E. Chronic enterocolitis**

5. A woman, 48 years old, complains on the periodic pain in the right hypochondrium with irradiation to lumbar region, nausea after any kind of food, frequent fluid excrements. She lost 12 kg in 2 months. Objective data: reduced nutrition, soft belly, significant pain in the Desjardin's point. Liver goes beyond the costal margin for 1 cm, unpainful. Defecations 3 - 4 times a day with additives of neutral fat. Gastric analysis: hydrochloric acid - 30 un. Urine diastase - 16 un. Which pathology causes such picture most probably?

- A. Gluten enteropathy**
- B. Chronic pancreatitis**
- C. Chronic hepatitis**
- D. Chronic enterocolitis**
- E. Autoimmune gastritis**

6. A woman, 32 years old, complains on the pain in the left hypochondrium which occurs 2 hours after meal, nausea, abdominal distention, frequent liquid stool. Objectively: subicteric scleras, painful belly during palpation in the Gubergrits-Skulsky's point. Liver - on the edge of

costal margin. In blood: amylase - 288 g/h\*1, total bilirubin- 20 micromol/1. What is the most possible diagnosis?

- A.** Chronic gastritis
- B.** Chronic hepatitis
- C.** Chronic enterocolitis
- D.** Chronic cholecystitis
- E.** Chronic pancreatitis

7. A patient suffers from chronic relapsing pancreatitis with marked exocrine function disorder. After fatty, spicy food, alcohol consumption a defecation with fatty excrements occurs. Deficiency of what factor is the most probable cause of steatorrhea?

- A.** Amylase
- B.** Trypsin
- C.** Gastric acidity
- D.** Lipase
- E.** Alkaline phosphatase

8. A patient complains on the permanent pain in the upper half of the belly, more on the left, intensifying after meal. Other complaints: diarrhea, weight loss. Alcohol overusage. He had acute pancreatitis two years ago. Blood amylase - 4 mg (ml per hr.). Coprogram - steatorrhea, creatorrea. Blood sugar - 6,0 mmol/1. Which treatment is indicated for this patient?

- A.** Contrical
- B.** Insulin
- C.** Gastrozepinum
- D.** Panzynom forte
- E.** No-shpa

9. A patient, 62 years old, suffers from periodic episodic pain in the left hypochondrium with irradiation to the back during 32 years, due to that he had to follow a strict diet with the limitation of fatty, fried, spicy, smoked food. During the last 18 months he observes emerging of abdominal distention, more frequent defecations - 2 - 3 times a day. The excrements are thick, stinking, with shiny surface, residues of indigested food. The change of the patient's symptomatology is caused by:

- A.** Exocrine pancreatic insufficiency
- B.** Endocrine pancreatic insufficiency
- C.** Cholestatic syndrome
- D.** Irritable bowel syndrome
- E.** Pancreatic insufficiency

#### CORRECT ANSWERS

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



**Control Questions:**

1. Give the definition of the chronic pancreatitis.
2. Principal clinical syndromes in case of the chronic pancreatitis.
3. Characteristics of the physical examination of a patient with the chronic pancreatitis.
4. Name the methods of diagnostics of the chronic pancreatitis.
5. Name the evidences of exocrine and endocrine pancreatic insufficiency.
6. Name the types of exocrine pancreatic secretion disorders.
7. Give the classification of the chronic pancreatitis.
8. Name the characteristics of the chronic pancreatitis course.
9. Name the complications of the chronic pancreatitis.
10. Name the causes of the CP development and characteristics of the diseases depending on its etiologic factor.
11. Name the pathogenesis of the CP main forms.
12. Principles of the chronic pancreatitis treatment.
13. Lifestyle changes and diet therapy in case of the chronic pancreatitis.
14. Drug treatment of the chronic pancreatitis at different stages of the disease course.
15. Indications for surgery.
16. CP prevention.

**Practical Tasks:**

1. Supervise patients with chronic pancreatitis.
2. Interpret the obtained laboratory data.
3. Interpret the obtained data of instrumental study.
4. Write a prescription for the chronic pancreatitis treatment.

**Further reading:**

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