News of European pancreatology
(by materials of the 50th meeting of European Pancreatic Club)

N. B. Gubergrits[1], N. V. Byelyayeva[1], G. M. Lukashevich[1], A. Y. Klochkov[1], P. G. Fomenko[1], L. A. Yaroshenko[1], A. V. Yuryeva[1], V. S. Rakhmetova[2]

[1]*Donetsk National Medical University, Ukraine*

[2]*Medical University Astana, Kazakhstan*

Key words: European Pancreatic Club, Ukrainian Pancreatic Club, diagnostics and treatment of chronic pancreatitis, pancreatic insufficiency, Creon

June 13-16, 2018 in Berlin (Germany), the jubilee 50th meeting of the European Pancreatic Club was held. About 500 oral and poster presentations were presented at the meeting [1].

Let's start with the achievements of the Ukrainian Pancreatic Club. Our Club is still the most numerous in Europe. The delegation of Ukraine consisted of 24 pancreatologists. At the meeting in Berlin we presented about 40 papers in the form of oral and poster presentations. The President of the Ukrainian Club was awarded an honorary mark for active work.

Now briefly tell about the results of some studies that attracted our attention. Let's start with the first session of the meeting devoted to hypertriglyceridemic pancreatitis.

Professor E. Steinhagen-Thiessen (Germany) delivered a lecture on hereditary disorders of lipid metabolism and their connection with pancreatitis. Hypertriglyceridemia is divided into 3 categories (Figure 1). The frequency of hypertriglyceridemia has been studied in a number of studies, for example, in a large population study conducted in Copenhagen, in which 108,711 adults were analyzed (Figure 2). A European register of patients with genetically determined variants of hyperlipidemia (more than 200 mutations) was created, including hypertriglyceridemia. The manifestations of high hypertriglyceridemia, in the first place, are xanthomas and chiles (Figure 3). However, pancreatitis, joint pain, tendonitis, hepatosplenomegaly, retinal lesions, and neurologic manifestations are

also possible. The highest content of triglycerides is characteristic of chylomicrons (Fig. 4).

At present, alipogen (Glibera preparation) is used to treat a genetically determined lipoprotein lipase deficiency accompanied by hypertriglyceridemia. The drug is a product of genetic engineering, its mechanism of action is shown in Fig. 5. Lecture by Professor H. U. Klor (Germany) was devoted to the pathogenesis and treatment of hypertriglyceridemic pancreatitis.

Possible mechanisms for the development of pancreatitis with a high level of chylomicrons in the blood are presented below:

- decreased blood flow in the capillaries of the pancreas, which increases the risk of enzymatic attack with lipase, phospholipase A2 on lecithin and chylomicron triglycerides directly in the vascular bed of the pancreas;

- products of enzymatic attack (free fatty acids, lysoceletin, monoglycerides) — detergents that cause platelet aggregation and ischemia;

- "lipolytic storm" can occur in the vessels of other organs (kidneys, lungs, brain), causing multi-organ failure;

- with hypercholesterolemia, the risk of pancreatitis is not increased, because cholesterol-esterase hydrolysis of cholesterol esters in the vascular bed of the pancreas does not occur because of the need to activate the enzyme by bile acids.

The likelihood of pancreatitis increases with fatty foods, alcohol, and obesity. A survey of 899 patients with hypertriglyceridemia revealed a relationship between the level of triglycerides in the blood and the risk of pancreatitis, diabetes, and cholelithiasis (Figure 6).

Professor H. U. Klor outlined the hypothesis of the pathogenesis of pancreatitis in the metabolic syndrome, which he developed for many years and which he repeatedly published (Figure 7). First of all, the development of metabolic syndrome, and pancreatitis, both acute and chronic, is facilitated by excessive consumption of fatty foods, alcohol. This is promoted by the modern "American" style of food in the McDonald’s bistro, etc. When the metabolic syndrome develops, the hormonal profile is broken with an increase in the level of estrogens or androgens in the blood.

With an increase in the content of estrogens in the blood, an antiatherogenic lipid profile of blood is formed, and the cholesterol that comes with food is mostly secreted into bile. As a result, bile is supersaturated with cholesterol, microliths are formed in it, and then stones are formed. When the microliths of the fatal nipple region are injured for a long time, papillostenosis is formed. It, in turn, promotes the development of intra-flow pancreatic hypertension, chronic obstructive pancreatitis. It is clear that the pancreatitis progresses functional failure of the pancreas, including endocrine. It is included in the pathogenesis of the metabolic syndrome, exacerbating the manifestations of diabetes mellitus. Thus, the first closed pathogenetic ring is formed. With the predominant increase in the level of androgens in the blood, an atherogenic lipid profile is created, which contributes to the progression of atherosclerosis. Violation of the trophism of the pancreas, as well as of other organs of the abdominal cavity, accelerates its fibrosis and the progression of pancreatic insufficiency. In this case, newly emerging pancreatogenic diabetes aggravates the manifestations of the metabolic syndrome (the second pathogenetic ring). In general, obesity as a component of the metabolic syndrome and in itself helps to reduce the external secretion of the pancreas, probably due to fatty degeneration of the acinar cells and/or lipoidosis of the organ. Outer-secretory pancreatic insufficiency develops in about a third of cases in obese patients. In addition to papillostenosis, which was mentioned above, the development of pancreatitis is facilitated by cholelithiasis, which is a recognized etiological factor of acute and chronic pancreatitis. This hypothesis, largely confirmed by the results of scientific research, should be taken into account in practice when drawing up a plan for examining and treating patients.

Immediate therapeutic measures include fasting and plasmapheresis. A comparative evaluation of the treatment of hypertriglyceridemic pancreatitis is presented in Table 1.

Table 1

Comparative evaluation of treatment methods for hypertriglyceridemic pancreatitis (N. Ewald et al., 2009 [7])

A special session was devoted to autoimmune pancreatitis. In the lecture of Professor M. Lohr (Sweden), features of autoimmune pancreatitis of the 1 st and 2 nd types were highlighted.

Autoimmune pancreatitis of the 1st type:

- lymphoplasmocytic sclerosing pancreatitis;
- increase in IgG4 in the blood and in the tissue of the pancreas (more than 10 in n/sp at a high magnification);
- absence of neutrophils in the infiltrate;
- storyiform fibrosis;
- periductal inflammation;
-obliterating phlebitis.

Autoimmune pancreatitis of the 2nd type:

- idiopathic centroprotective pancreatitis;
- granulocyte epithelial lesions;
- absence or minimal amount of IgG4 in the blood and in the pancreas tissue (less than 10 in sp. At high magnification);
- CD4 + lymphoplasmatic infiltration.

The pathogenesis of autoimmune pancreatitis has not been elucidated. The participation of molecular mimicry (Cag A Helicobacter pylori with type II carbonic anhydrase) is supposed. However, in the pancreas tissue, Helicobacter pylori DNA is not detected. Possible involvement in the pathogenesis of the retrovirus, the Varicella Zoster virus, is studied, but they are also not detected in the pancreas tissue.

The epidemiology of autoimmune pancreatitis in Europe has not been studied. However, in Europe, autoimmune pancreatitis of type 2 occurs more often than in Asia (Figure 8).

The distribution of patients with autoimmune pancreatitis by age is shown in Figure 9.

The frequency of involvement of other organs, according to P. A. Viachou et al., 2011 [11], is as follows:

- bile ducts (sclerosing cholangitis) — 77%;

- kidneys — 35%;
- lymph nodes — 33%;
- gall bladder — 16%;
- salivary glands — 14%;
- thyroid pancreas — 12%;
- arteries — 12%;
- retroperitoneal space — 9%;
- lungs — 5%;
- orbits or tear glands — 3%;
- mesentery — 3%.

External exocrine pancreatic insufficiency (EPI) develops in 64% of cases of autoimmune pancreatitis of type 1 and in 20% of cases of autoimmune pancreatitis of type 2 [11].

Corticosteroids take the leading place in the treatment, the effectiveness of ursodeoxycholic acid is studied. It is important that under the influence of corticosteroid therapy, not only the diameter of the pancreatic and common bile ducts is normalized, but the external secretion of the pancreas is improved (Figure 10) [8].

Information about the risk of cancer of various organs in autoimmune pancreatitis is contradictory.

S. Wyszkovski et al. (Poland) studied the informative value of the immunohistochemical determination of the IgG4 biopsy specimens of the falcon nipple for the diagnosis of type 1 autoimmune pancreatitis. We examined 175 patients with suspected autoimmune pancreatitis. The disease was diagnosed in 31 patients, with immunohistochemically IgG4 in the fecal nipple tissue being determined in 67.7% of cases (in 21 patients). As for autoimmune pancreatitis of type 2, only 5 patients were diagnosed with this diagnosis, and immunogistochemically IgG4 in the fecal nipple tissue was determined in 20.0% of cases (in 1 patient). The authors believe that the immunohistochemical examination of the fetal nipple biopsy specimens is more accessible than the pancreas biopsy and is quite informative for the diagnosis of type 1 autoimmune pancreatitis.

A great interest was caused by the Abbott Symposium, dedicated to the issues of diagnostics and treatment of EPI. Professor L. Frulloni (Italy) gave a lecture on the diagnosis of EPI. First of all, the need for hormonal control and synchronization of pancreatic secretion, evacuation from the stomach, production of bile for normal digestion in the duodenal module of the digestive tract was emphasized (Figure 11).

The principal mechanisms for the development of the National Institute of Natural Resources are as follows:

- decrease in the volume of the parenchyma of the pancreas (pancreatitis, pancreas tumor, resection of the pancreas, etc.);
- obstruction of the pancreatic duct (calcifications, tumor, stenosis, etc.);
- a violation of mixing chyme and digestive secretions in the duodenal lumen (after surgical interventions, the presence of biliary pathology, etc.);
- decrease in pH in the duodenal lumen (gastrinoma).

Steatorrhea develops with a decrease in the production of pancreatic lipase to 10% and lower from the physiological level. In this case, the need for substitution enzyme therapy is beyond doubt. But with a light and moderate EPI there are questions (Figure 12):

- Does the mild/moderate EPI have clinical significance?
- Does substitution therapy improve the clinical outcome of mild/moderate HIV/AIDS?
- When should we start treatment?

Indications for the appointment of replacement therapy are presented in Table 2.

Table 2

Indications for substitution enzyme therapy in patients with EPI according to different consensus [6, 13, 19, 21]

Guidelines	Year	EPI	Quantitative estimation of steatorrhea	Symptoms of malabsorption	Weight loss
Italian	2010	+	-	-	-
German	2012	+ +	7–15 g/day > 15 g/day	+ -	+ -

Spanish	2013	+	-	+	+
Unified European	2017	+	-	+	+

Taking into account the European recommendations for the treatment of EPI (Table 2), as well as the effect of EPI on the life expectancy of patients (Figure 13), substitution therapy should be prescribed already with light EPI.

The most common methods for diagnosing EPI are quantitative determination of fat in the stool, triglyceride respiratory test and fecal elastase test. The first method is labor-intensive and is used for scientific research. The respiratory test is highly informative, but it is not available everywhere, it takes considerable time. The most common practice is a fecal elastase test. Its advantages:

- non-invasive (no-probe);
- elastase-1 — pancreatic-specific enzyme;
- elastase-1 undergoes minimal changes in intestinal transit;
- elastase-1 is stable;
- eastase-1 is easily measured in feces;
- there is no need to abolish enzyme preparations;
- low cost of research.

It is also important that there is a correlation between the amount of fat in the feces and the rates of fecal elastase-1 (Figures 14, 15).

All over the world, magnetic resonance imaging with secretin is increasingly used to evaluate the exocrine function of the pancreas.

The lecture of Professor J. E. Dominguez-Munoz (Spain) was devoted to the clinical manifestations and new aspects of the treatment of EPI. EPI is an inadequate secretion of pancreatic enzymes and/or bicarbonates to ensure normal digestion. With malaria, malabsorption of nutrients and symptoms of nutritional insufficiency develop. Malnutrition is accompanied by a decrease in the indices of essential amino acids, fatty acids, fat-soluble vitamins and micronutrients circulating in the blood, high-density lipoproteins, and apolipoprotenes A and AI. In patients with EPI, high morbidity and mortality, the incidence of complications associated with malnutrition.

In these patients, the risk of spontaneous fracture of the femoral neck was increased 9.2 times compared to the general population, 5.8 times the vertebral fracture, and 2.8 times the fracture of the wrist bone [10].

With EPI sarcopenia develops. R. Shintakuya et al. (2017) [20] examined 132 patients with diseases of the pancreas. Using computerized tomography, the volume of muscle mass (skeletal muscle), subcutaneous and visceral adipose tissue was measured. It was found that the risk of sarcopenia with EPI increased by 7.39 times compared with the general population (p□0.001). A decrease in the volume of adipose tissue was not found.

D. de la Iglesia et al. (2017) [12] examined 430 patients with chronic pancreatitis, follow-up continued 8.3±4.6 years. Cardiovascular diseases during this period developed significantly (p0.001) more often in patients with EPI (23.0%) compared with patients without EPI (5.3%). Cardiovascular events, except for EPI, were associated with diabetes mellitus, hypertension and smoking. Mortality in patients with chronic pancreatitis is significantly higher than in the general population, while mortality in chronic pancreatitis with EPI is significantly higher than without EPI (Figure 16). The risk of death was increased not only with EPI, but also with pancreatitis of alcoholic etiology, the presence of cirrhosis and/or respiratory diseases.

Treatment of EPI includes full nutrition and substitution therapy with minimally encroached enzyme preparations with an acid-resistant coating (Creon). Substitution therapy is indicated in the presence of clinical symptoms or laboratory signs of malabsorption. The purpose of the substitution enzyme therapy is to eliminate (prevent) steatorea and malabsorption-associated symptoms, complications and lethality, and also to provide a normal nutritional status. Enzyme preparations should be taken while eating, as shown in a cross-sectional study by J. E. Dominguez-Munoz et al. (2005) [5] (Figure 17).

The dose of the enzyme preparation should be such that not only eliminate the symptoms of EPI, but also normalize the nutritional status of the patient, because it is proved that in the elimination of clinical symptoms (diarrhea, flatulence), a

deficiency of nutrients remains in a significant part of the cases (Figure 18). This dose is 40,000-50,000 Ph.U for the main meal and 20,000-25,000 Ph.U for an intermediate meal.

If the effectiveness of substitution treatment is inadequate, you should increase the dose of the enzyme preparation (double or triple) and/or add a proton pump inhibitor (Figure 19A). The reason for the insufficient effect may be a syndrome of excess bacterial growth in the small intestine, at which acidification of the lumen of the gut occurs (Fig. 19B).

Among patients with EPI, attention should be paid to those patients who, when carrying out substitution therapy, although nutritional parameters are within the limits of the norm, but their level is below 25% of the norm and, especially, below 10% of the norm. Such patients have a higher risk of death than patients with a higher level within the norm (Figure 20).

Professor K. Roberts (UK) gave a lecture on substitution enzyme therapy for pancreas cancer. First of all, it was noted that the EPI inevitably develops in pancreatic cancer due to compression of the pancreatic duct, the destruction of the parenchyma.

Cachexia also develops due to intoxication, decreased appetite, chemotherapy and radiation therapy, violation of physiological interrelations of the digestive organs after surgical interventions, etc. In unresectable cancer of the head of the pancreas, the rates of fecal elastase-1 decrease by an average of 10.2% per month [18]. After surgical treatment, EPI is usually aggravated by resection of the pancreas tissue. At the same time, special attention should be paid to substitution enzyme therapy with a minimosphere enzyme preparation (Creon). Based on the evidence, the lecturer concluded that substitution therapy improves survival, lengthens life, reduces symptoms and improves the quality of life of patients with resectable and non-resectable pancreas. S. Olesen et al. (Denmark) conducted a one-center study, which included 186 patients with chronic pancreatitis. Performed bioimpedanceometry, dynamometry, anthropometry, quality of life was assessed. The observation lasted 12 months. Sarcopenia was detected in 18.3% of cases, and a reduced body mass index

was defined only in 29% of patients with sarcopenia. In the remaining 71% of cases, the body mass index was normal or elevated. Sarcopenia was associated with the presence of EPI, smoking, opioid treatment. In the identification of sarcopenia in patients, the indicators of overall health and physical functioning were reduced. When observing patients, it was found that in the presence of sarcopenia, the frequency of hospitalizations, the length of stay in the hospital, lethality increased. Erchinger et al. (Norway) studied in 10 patients with chronic pancreatitis with EPI and 12 healthy volunteers the fat absorption coefficient and energy absorption coefficient before and after substitution enzyme therapy for 5 weeks in increasing doses up to 200,000 Ph.U per day. It is shown that enzyme therapy contributes to a significant increase in both coefficients in patients, but does not affect the indices of healthy patients (Figure 21). The work of A. Sheel et al. (UK) on the progression of minimal changes in the pancreas in endosonography before the development of chronic pancreatitis. In a retrospective single-center cohort study, 40 patients with minimal pancreatic changes were examined. The observation lasted more than three years. In 12 (30%) patients developed chronic pancreatitis. 8 (67%) of them abused alcohol, 10 (83%) were intense smokers. The same patients more often needed surgical treatment, they developed EPI, had a higher mortality rate than those patients with chronic pancreatitis who did not abuse alcohol and did not smoke. H. Kang et al. (South Korea) studied the relationship of the hyperechoogenicity of the pancreas in obesity endosonography. A total of 248 patients with pancreatic hyperechogenicity were examined. The volume of visceral adipose tissue was assessed by computer tomography. Obesity, age over 60 years, steatosis of the liver, diabetes mellitus, hypercholesterolemia appeared to be independent risk factors for the pancreatic hyperechoinality. An increase in visceral fat also proved to be a risk factor for pancreatic hyperechoinality. Research A. Szentesi et al. (Hungary) was devoted to the components of the metabolic syndrome as risk factors for the deterioration of acute pancreatitis. 1435 patients with acute pancreatitis and various components of the metabolic syndrome were examined. Arterial hypertension and hyperlipidemia are independent risk factors for complications of acute pancreatitis. In addition,

hypertension is associated with greater severity of the disease course. The more components of the metabolic syndrome occur in the patient, the more severe the course of acute pancreatitis. Blaho et al. (Czech Republic) studied the condition of the pancreas in the metabolic syndrome. 35 patients were examined, 21 (60%) of whom were diagnosed with non-alcoholic fatty disease of the pancreas (hyperechoinality of the pancreas, hypertriglyceridemia). According to the authors, this problem is urgent and requires further study. The information on the determination of pancreatic blood isoamylase for the diagnosis of chronic pancreatitis was noted by S. S. Olesen et al. (Denmark). The study included 121 patients with chronic pancreatitis and 94 healthy. The level of pancreatic isoamylase below 17.3 U/l was specific (94%) and moderately sensitive for the diagnosis of chronic pancreatitis (56%). A correlation was found between the indices of blood isoamylase and the duration of pancreatitis, the presence of EPI and diabetes mellitus (Figure 22). It is concluded that the pancreatic-specific isoamylase is informative for the diagnosis of chronic pancreatitis and EPI. D. V. Balaban et al. (Romania) examined 102 patients with pancreatogenic diabetes mellitus. Of these, 46 (45%) suffered from chronic pancreatitis, 45 (44%) with pancreatic tumors (33 solid tumors, 12 cystic tumors), 6 (6%) suffered resection of the pancreas, and 5 (5%) indicated pancreatic necrosis in the anamnesis. The authors noted that about two-thirds of patients with pancreatic cancer develop impaired glucose tolerance. In a third of cases of pancreas cancer diagnose newly diagnosed diabetes mellitus. Patients over the age of 60 years with newly diagnosed diabetes should be screened for pancreas cancer. Y. A. Shekhovtsova et al. (Kharkov, Ukraine) in an oral report reported on the relationship between adipocytokinemia and anthropometric data in patients with a combination of chronic pancreatitis and type II diabetes mellitus. Sixty patients and 20 healthy patients were examined. Correlations have been found between the body mass index and blood serum indices. Report by A. V. Rotar et al. (Chernivtsi, Ukraine) was devoted to the prognosis and early diagnosis of infectious complications of acute necrotizing pancreatitis. In 70 patients, the parameters of endotoxin, presepsin (a highly sensitive marker of bacterial complications of pancreatitis), procalcitonin, C-

reactive protein, secretory CD14, interleukin-6 in the blood serum when admitted to hospital and in treatment dynamics were compared with the assessment of the severity of pancreatitis according to the APACHE II scale, the results of bacteriological examination of the pancreas tissue. It turned out that a high level of secretory CD14 upon admission to the hospital and 72 hours after the onset of the disease is associated with the development of infected necrotic pancreatitis. The 50th meeting of the European Pancreatic Club in Berlin was interesting, informative, saturated both scientifically and with point of view of communication with colleagues. Meeting in Kiev in 2022 is coming soon. Let's begin our preparations.

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[1]*Donetsk National Medical University, Ukraine*

[2]*Medical University Astana, Kazakhstan*

Key words: European Pancreatic Club, Ukrainian Pancreatic Club, diagnostics and treatment of chronic pancreatitis, pancreatic insufficiency, Creon

Article represents the results of main scientific researches in pancreatology conducted in 2016–2017. There are stated achievements of leading pancreatologists of Europe regarding study of etiology, pathogenesis, diagnostics and treatment of pancreatitis and tumors of the pancreas.

Подписи к рисункам:

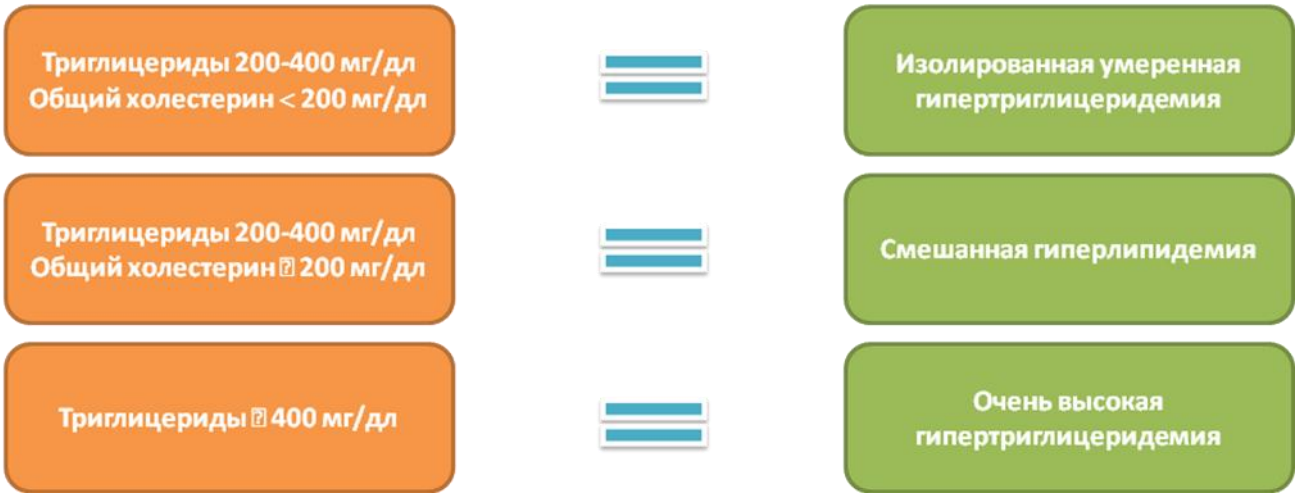


Fig. 1. Categories of hypertriglyceridemia, depending on its degree and combination with hypercholesterolemia (E. Steinhagen-Thiessen, 2018 [1]).

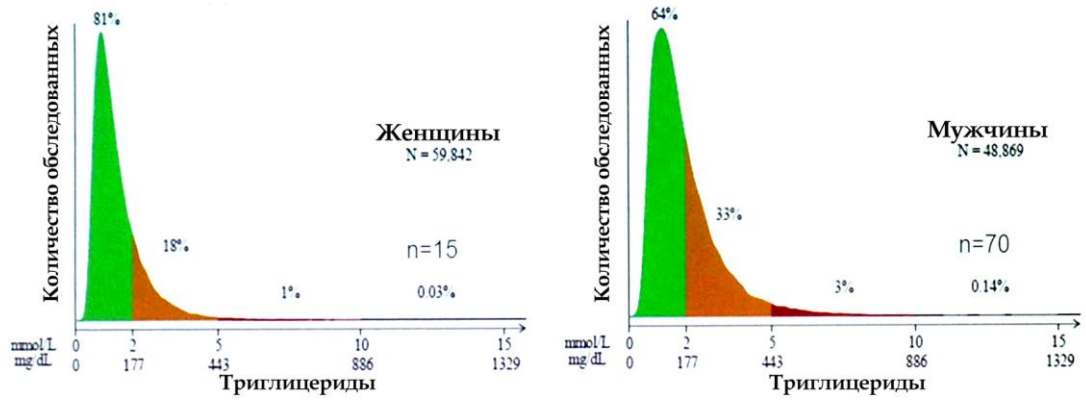


Fig. 2. Frequency of different levels of triglyceridemia (S. B. Pedersen et al., 2018 [3]).

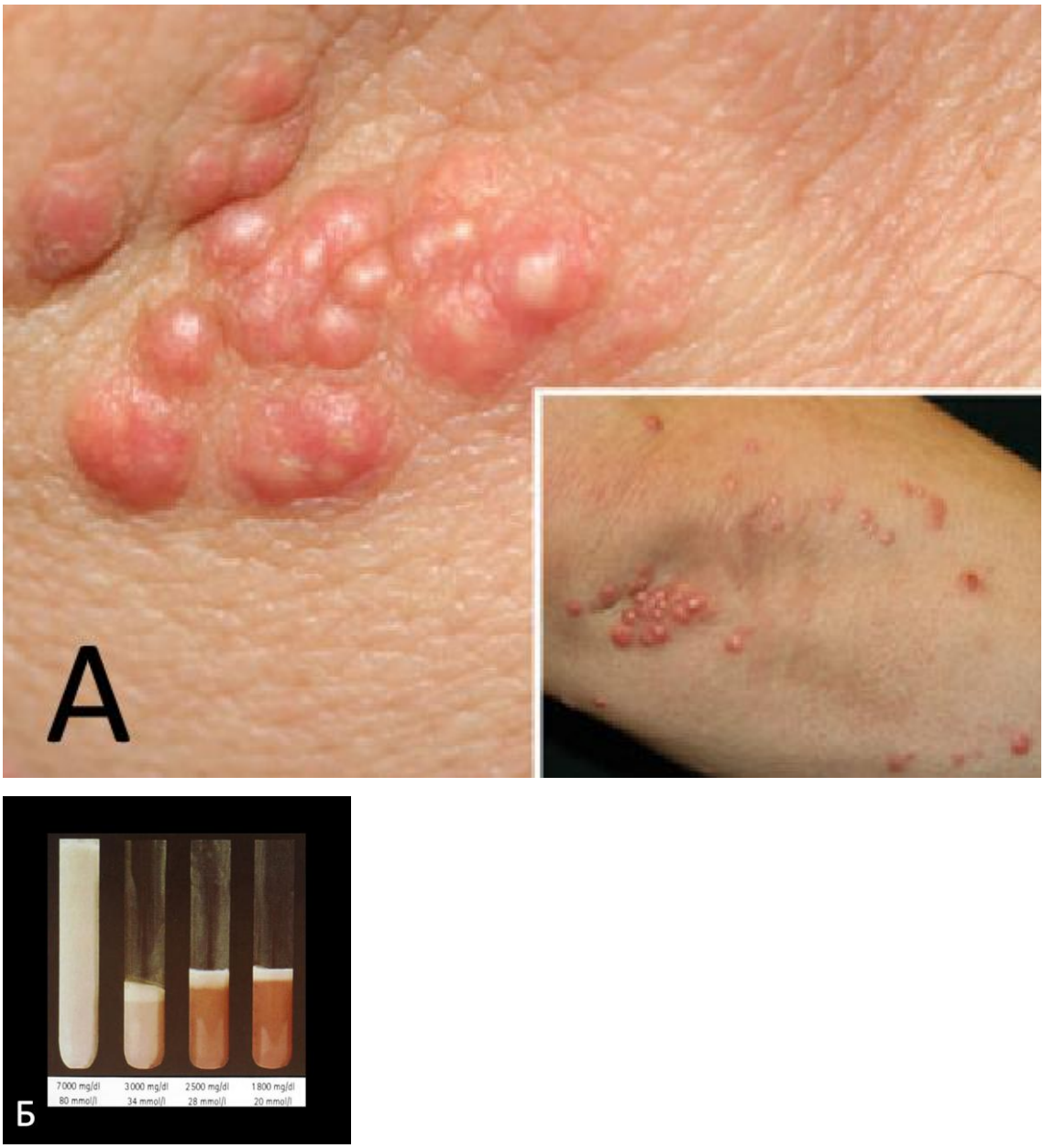
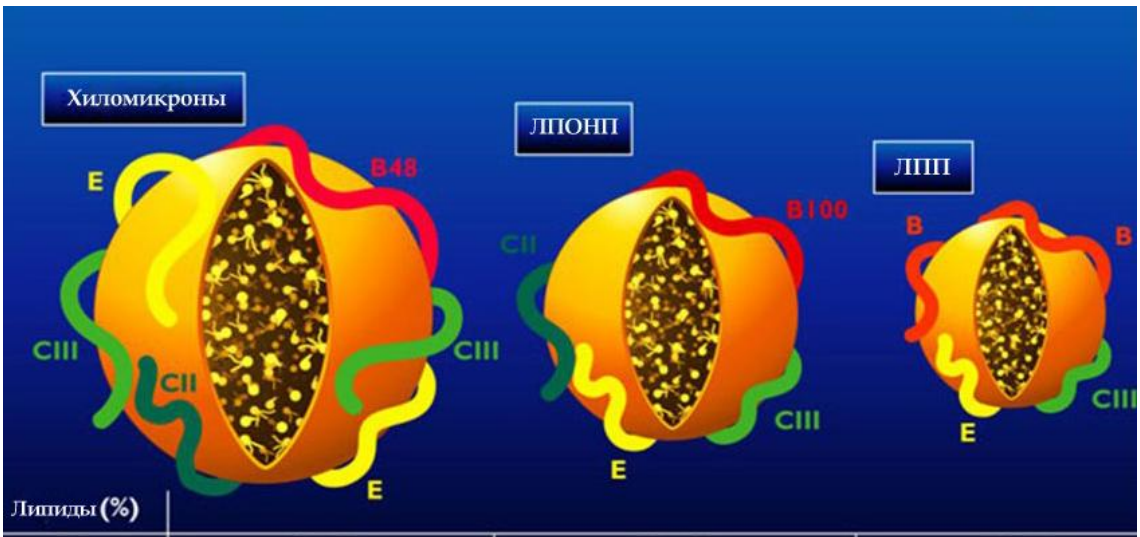


Fig. 3. Xanthoma (A) and chylosis, depending on the level of chylomicrons in serum (Б) (E. Steinhagen-Thiessen, 2018 [1]).



Липиды (%)			
Триглицериды	85–90	50–60	18–25
Холестерин	2–6	14–22	30–38
Фосфолипиды	6–9	12–20	20–28
Размер, А	800–5000	300–800	200–350

Fig. 4. Characteristics of different lipoproteins (E. Steinhagen-Thiessen, 2018 [1]).

ЛПОНП — very low density lipoproteins

ЛПП — intermediate density lipoproteins

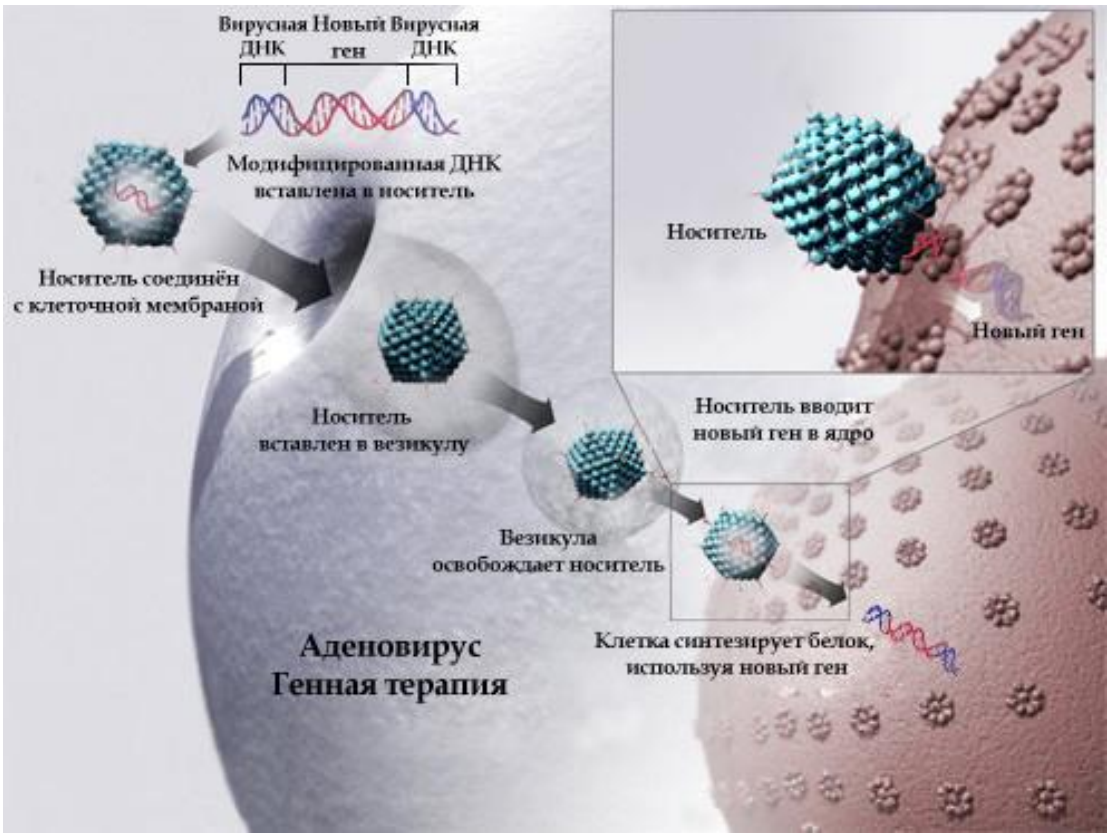


Fig. 5. Mechanism of action of alipogen (E. Steinhagen-Thiessen, 2018 [1]).

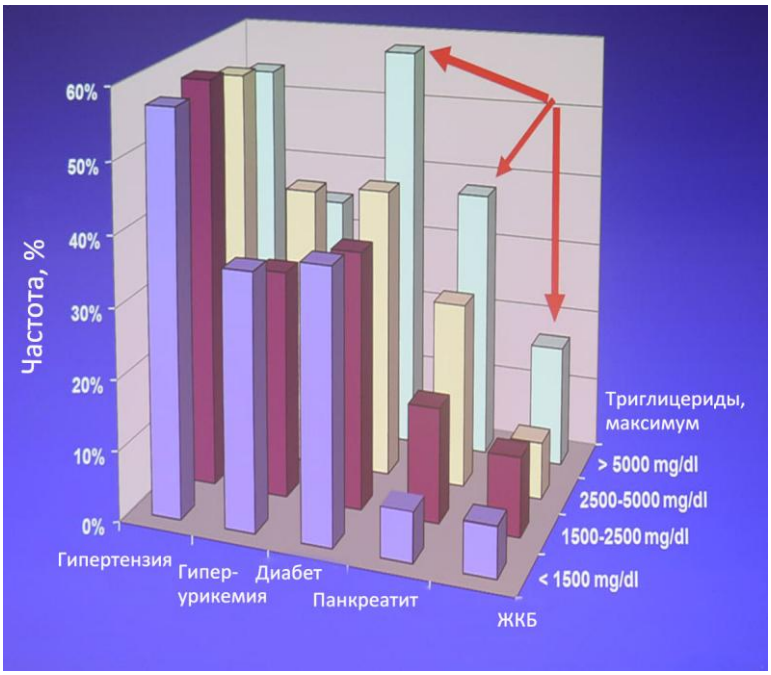


Fig. 6. The dependence of the risk of comorbid pathology on the level of triglycerides of blood (H. U. Klor, 2018 [1]).


Ожирение
Инсулинорезистентность
Гипертриглицеридемия
Богатая жирами и холестерином пища
Метаболический синдром
Высокий уровень эстрогенов
Высокий уровень андрогенов
Антиатерогенный метаболический профиль (ЛВП↑, ЛНП↓)
Атерогенный метаболический профиль (ЛВП↓, ЛНП↑)
Насыщение желчи холестерином (литогенность) (Ж>М)
Накопление холестерина в артериальной стенке
Образование микрокристаллов в желчном пузыре (2–3 мм)
Атеросклероз
Выделение микрокристаллов в общий желчный проток
Образование камней в желчном пузыре, холелитиаз
Раздражение микрокристаллами ампулы приводит к хроническому папиллиту с фиброзом
Папиллярный стеноз
Индуцирование панкреатической секреции (жирная пища, алкоголь)
Легкие рецидивирующие панкреатические атаки с вовлечением экзокринных (эндокринных) тканей вследствие повышения внутрипротокового давления
+ аутоиммунное индуцирование экзокринными и эндокринными антигенами
Деструкция островкового аппарата, сахарный диабет

Fig. 7. Hypothesis of pathogenesis of pancreatitis in metabolic syndrome (H. U. Klor, 2018 [1]).

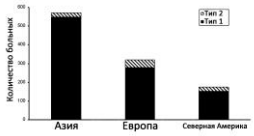


Fig. 8. The number of patients and their distribution according to the types of autoimmune pancreatitis in the various regions included in the study by P. A. Hart et al., 2013 (totally 1064 patients with autoimmune pancreatitis) [14].

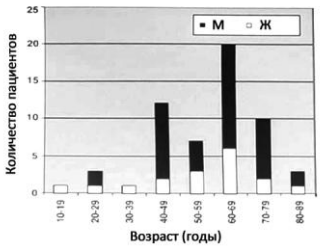


Fig. 9. Distribution of patients with autoimmune pancreatitis by age (A. Schneider et al., 2017 [16]).

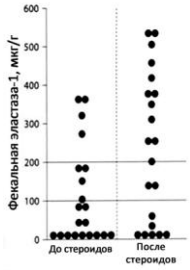


Fig. 10. Dynamics of the exocrine function of the pancreas under the influence of corticosteroid therapy in autoimmune pancreatitis (L. Frulloni et al., 2010 [8]).

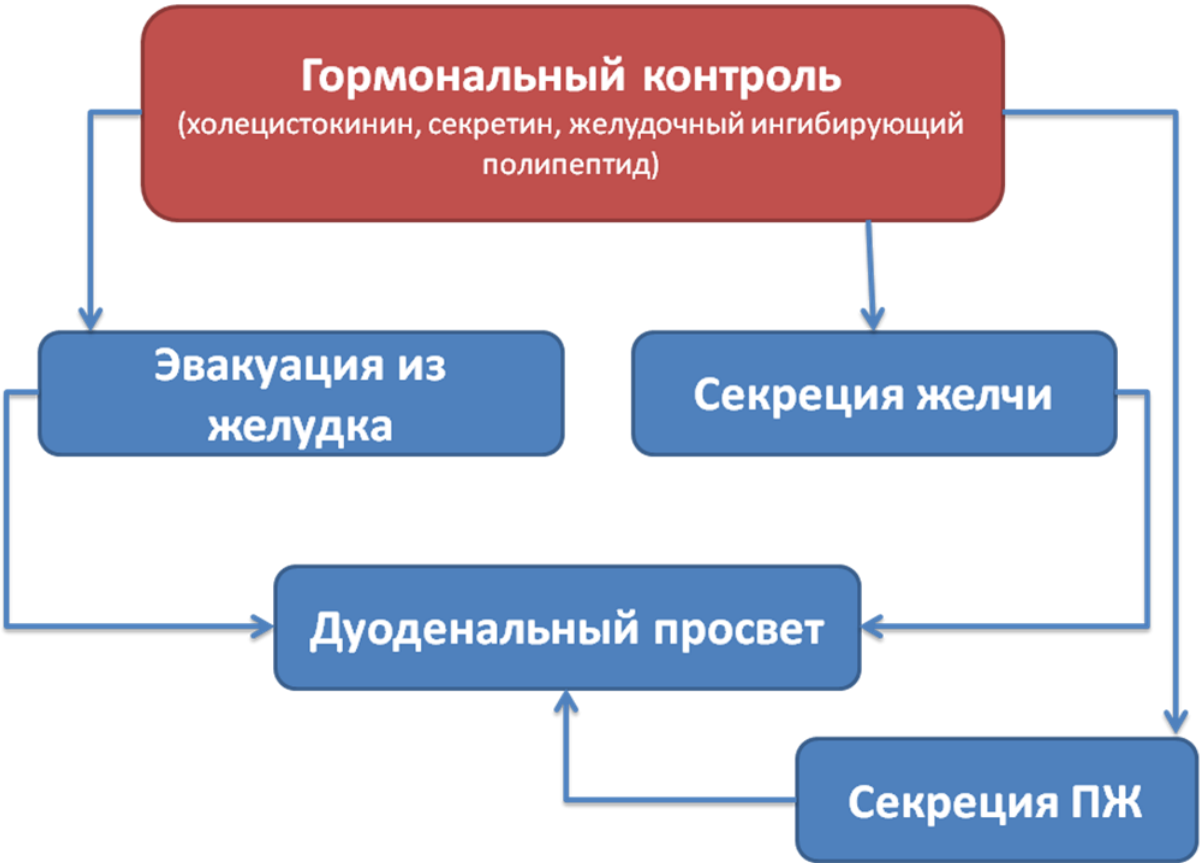


Fig. 11. The need for hormonal control and synchronization of pancreatic secretion, evacuation from the stomach, production of bile to ensure normal digestion in the duodenal module of the digestive tract (L. Frulloni, 2018 [1]).

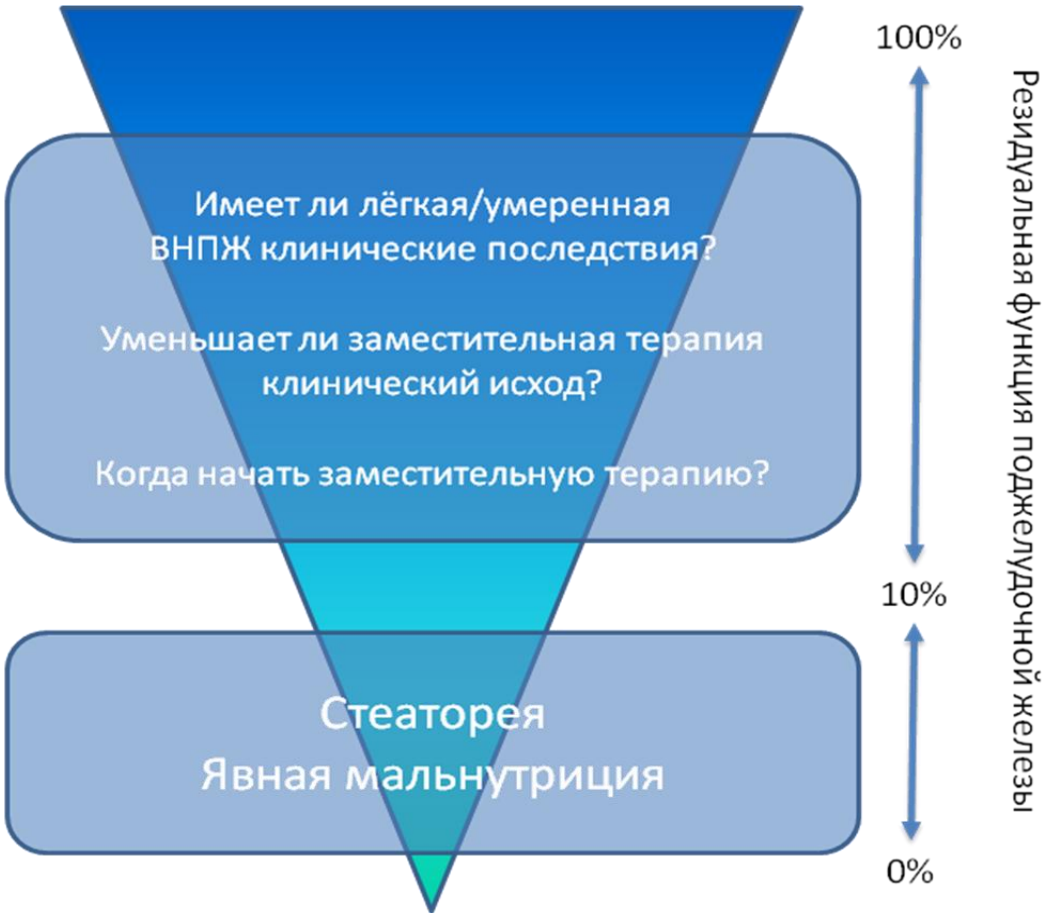


Fig. 12. The relationship between the degree of EPI and treatment tactics (L. Frulloni, 2018 [1]).

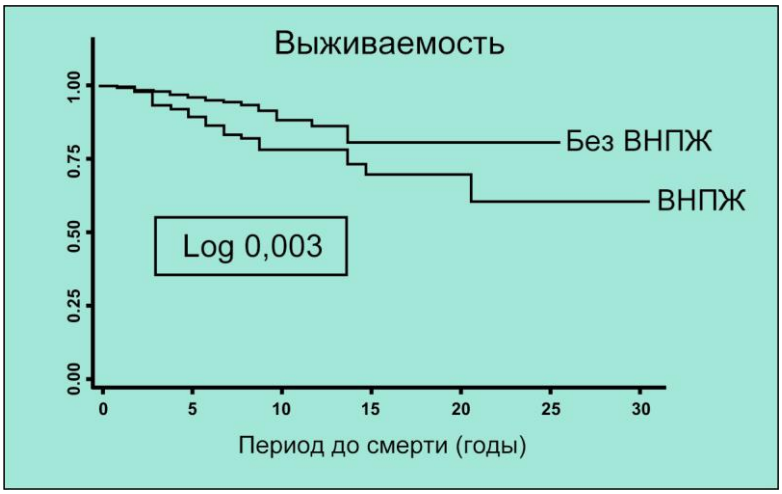


Fig. 13. Life expectancy of patients with chronic pancreatitis, depending on the presence of EPI (N. Vallejo-Senra et al., 2016 [2]).

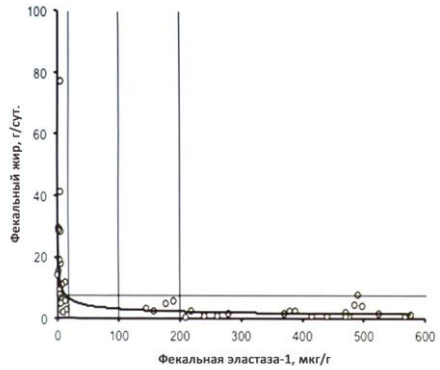


Fig. 14. Correlation between the amount of fat in the feces and the results of the fecal elastase test (L. Benini et al., 2013 [9]).

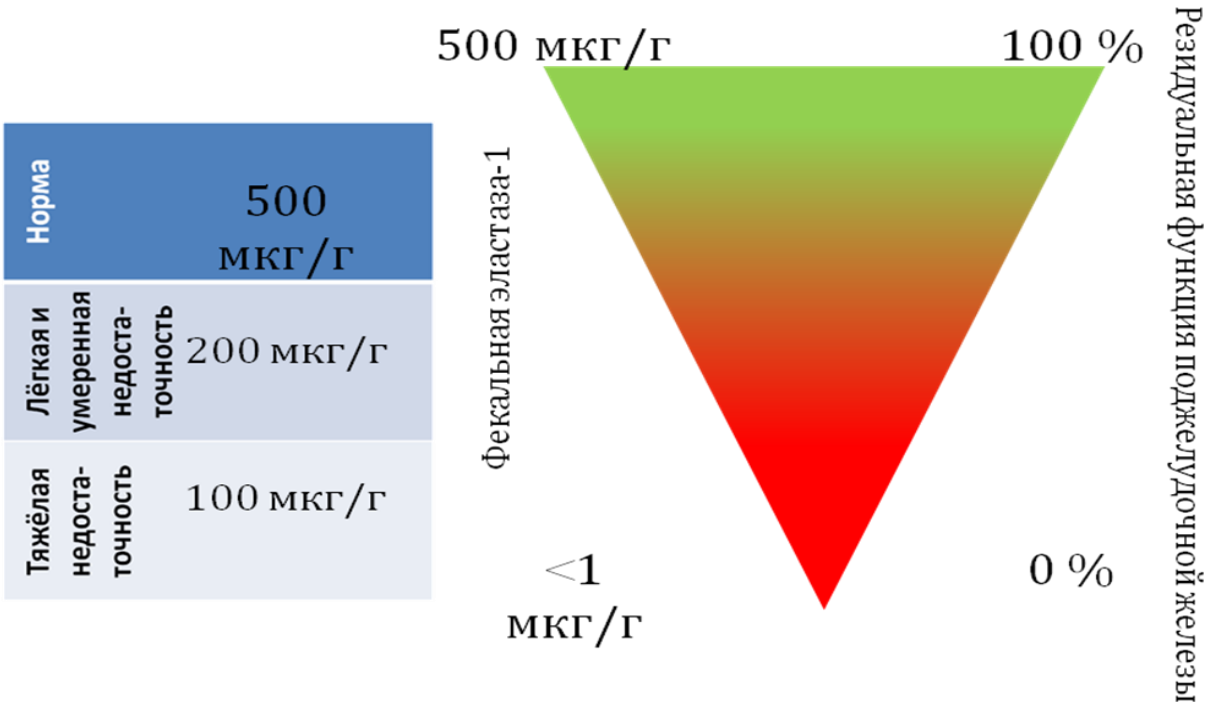


Fig. 15. The degrees of EPI in accordance with the results of the fecal elastase test (L. Frulloni, 2018 [1]).

Fig. 16. Mortality in chronic pancreatitis, depending on the presence of EPI (D. de la Iglesia et al., 2017 [12]).

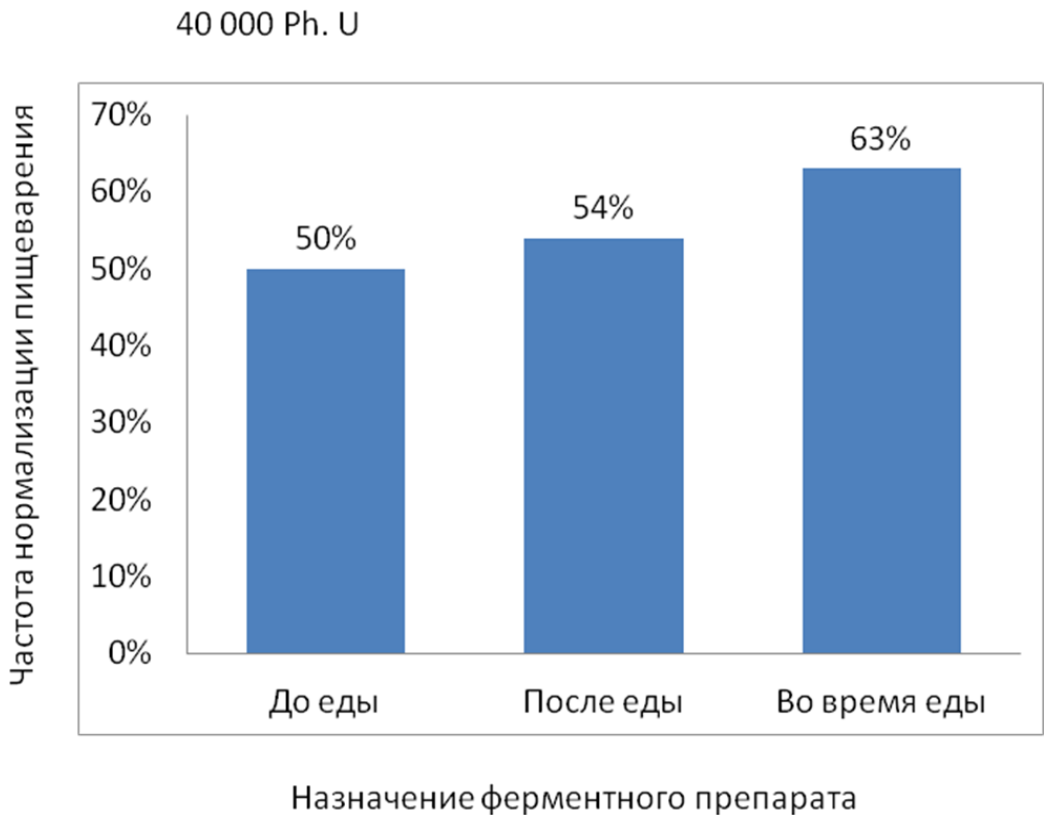


Fig. 17. Normalization of digestion is achieved more often when taking enzyme preparations during meals (J. E. Dominguez-Munoz et al., 2005 [5]).

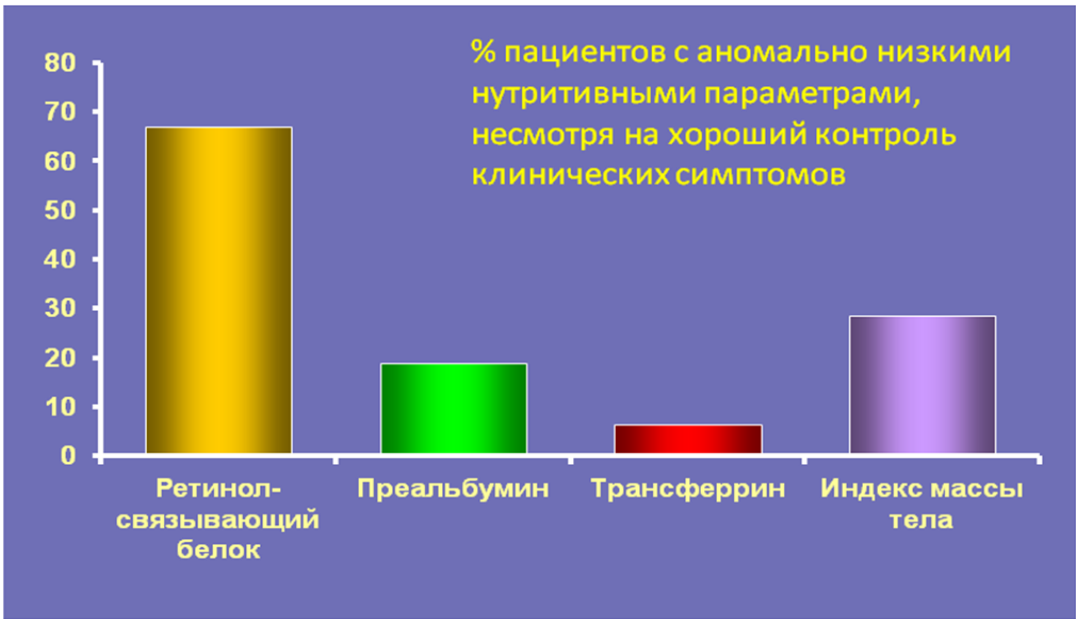


Fig. 18. The frequency of nutrient deficiency in patients with EPI with the appointment of a dose of enzyme preparations that eliminates clinical manifestations (J. E. Dominguez-Munoz et al., 2007 [4]).

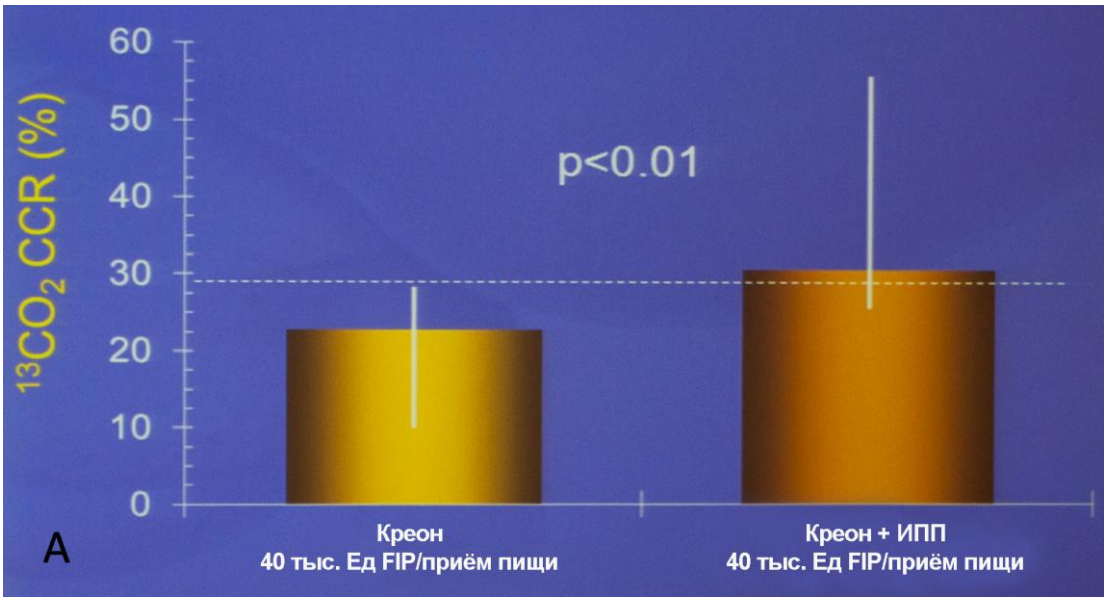
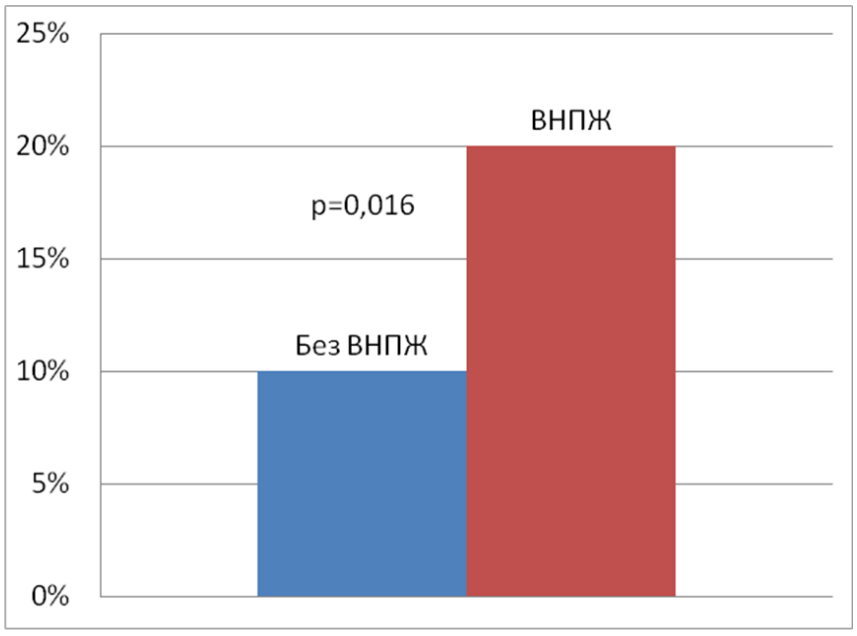


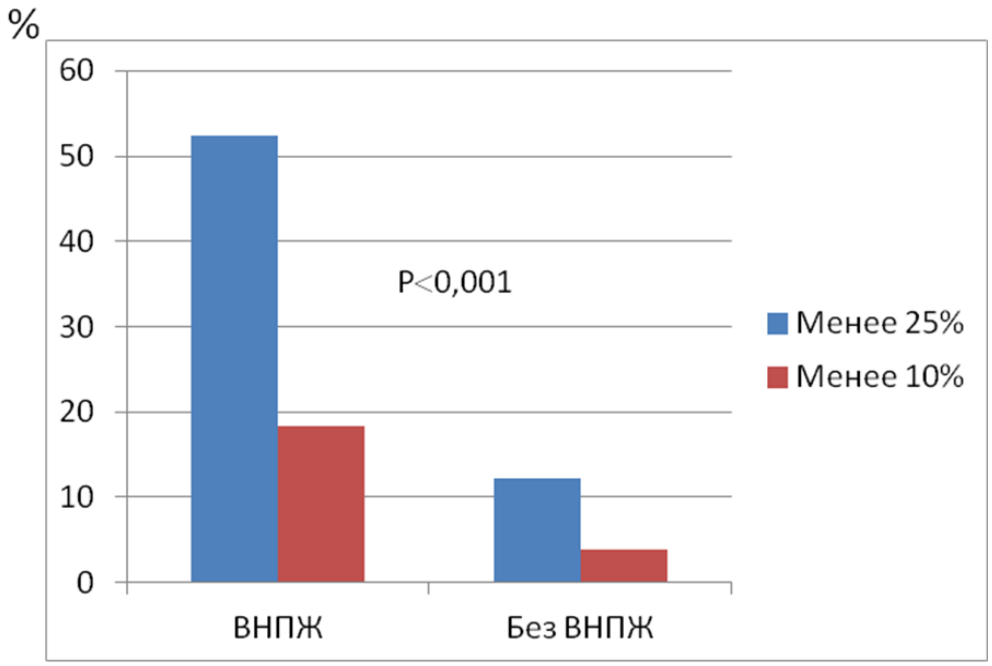
Fig. 19. Insufficient effectiveness of enzyme preparations.

A. Increase in the effectiveness of substitution enzyme therapy in the appointment of a proton pump inhibitor (PPI) (based on the triglyceride respiratory test) (J. E. Dominguez-Munoz et al., 2006 [15]).

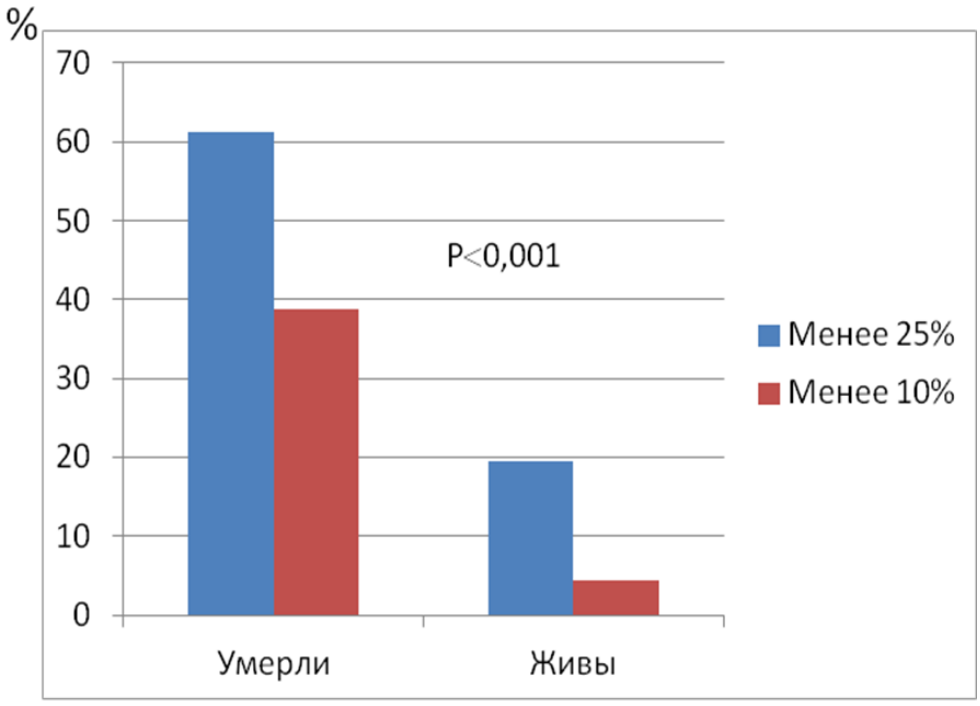


Б

Б. The frequency of the syndrome of excessive bacterial growth in chronic pancreatitis (H. M. Ni Chonchubhair et al., 2018 [17]).



А



Б

Fig. 20. The frequency of nutritional indices is below 25% and below 10% of the norm in patients with chronic pancreatitis with and without EPI (A), and the association of these indices with death and survival (Б) (D. de la Iglesia et al., 2017 [12]).

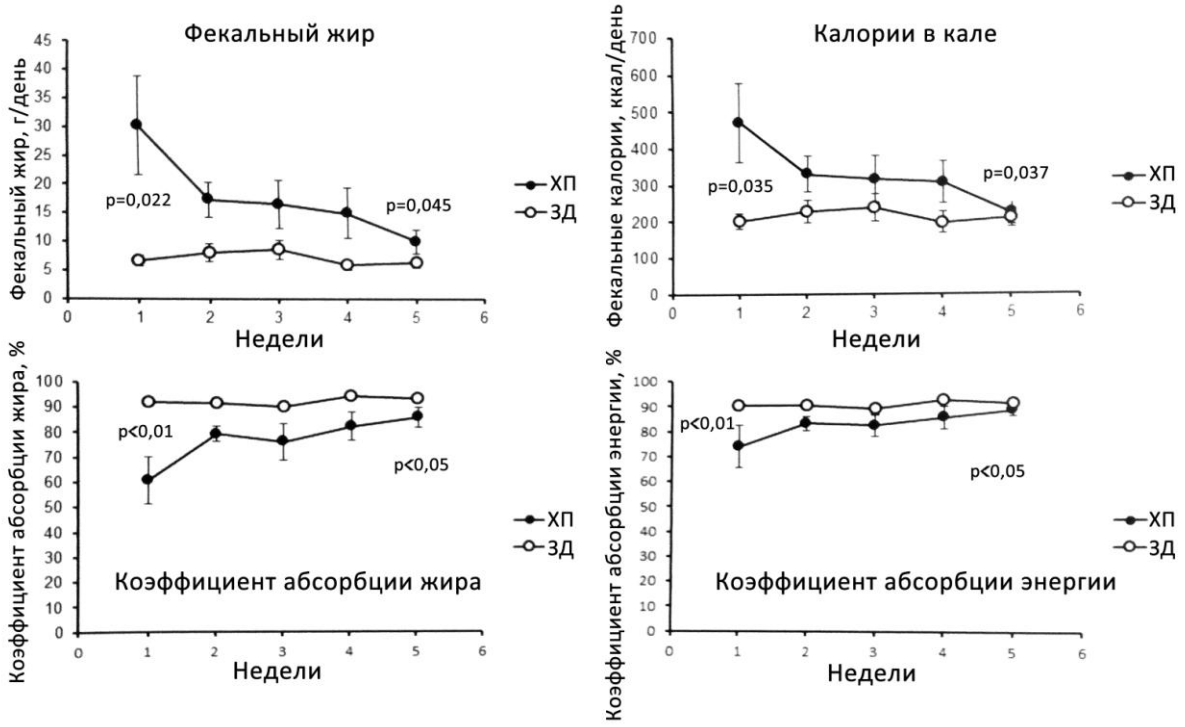


Fig. 21. Dynamics of loss and absorption of fat and energy in patients with chronic pancreatitis and healthy when taking enzyme preparations in increasing doses (F. Erchinger et al., 2018 [1]).

ХП — chronic pancreatitis

ЗД — healthy volunteers

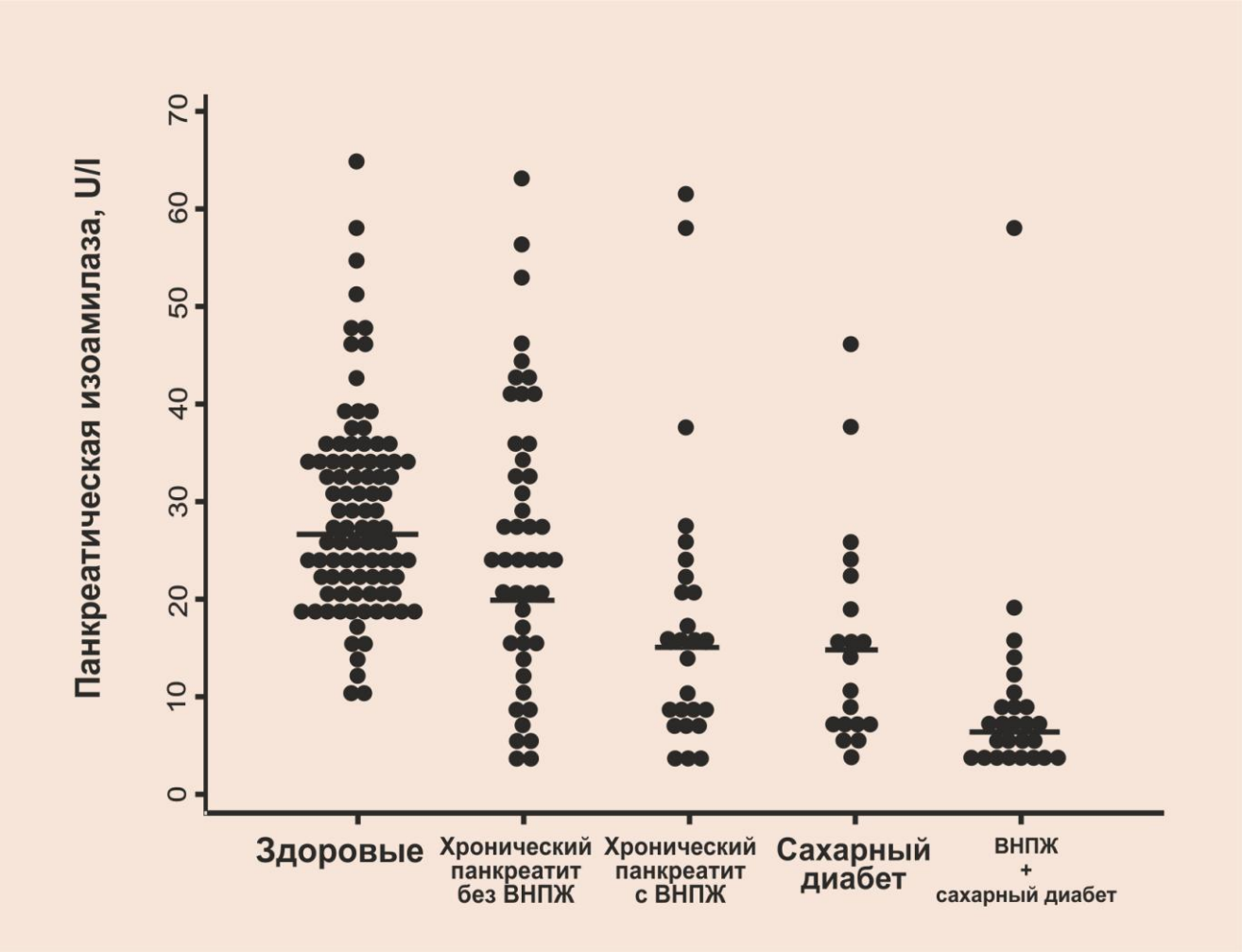


Fig. 22. Indicators of pancreatic isoamylase of blood in healthy, with chronic pancreatitis, diabetes mellitus (S. S. Olesen et al., 2018 [1]).

Treatment	Mechanism of action	Comments	Restrictions
Plasmapheresis	Direct removal of triglycerides as a causative factor	The obvious effect, it is necessary to apply in the early stage of pancreatitis	Accessibility is limited, invasive and expensive method
Insulin	Activation of lipoprotein lipase, which contributes to the degradation of chylomicrons	A useful method, especially in patients with poorly controlled diabetes mellitus with high triglyceride levels in the blood	Effectiveness is limited
Heparin	Stimulation of the release of I endothelial lipoprotein-lipase	Not recommended as a monotherapy	Increased lipoprotein lipase degradation and depletion of reserves ee plasma
Fibrates	Increased levels lipopro those in — lipase, decreased production of triglycerides in the liver put e m e induction oven overnight oxidation of free fatty acids and stimulate reverse cholesterol transport	Preparations of the first choice	Slow start of decrease in triglycerides
Omega-3 fatty acids	Reduction of triglyceride synthesis in liver, yc and Leniye β — oxidation in peroxisomes, increased synthesis lipopro those yn-lipase and ee expression in adipose tissue	Powerful immediate effect without side effect	No restrictions

A nicotinic acid	Reduced secretion lipoprotei d s very low density	Significant long-term effect on lowering triglyceride levels	Side effects (skin reddening), slow onset of effect per level of triglycerides
Statins	Inhibition of cholesterol synthesis	Only in combination with other drugs (fibrates) to achieve synergistic effect	Risk of myopathy, do not belong to first choice drugs
Medium chain triglycerides	Blockade of formation of chylomicrons, induction of mitochondrial β — oxidation of fatty acids	Immediate onset of action on triglyceride levels	No restrictions