
REVIEWS

Lipid Distress-Syndrome in Surgery

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The paper reviews the results of treatment of lipid distress-syndrome manifested in obliterating atherosclerosis, gallbladder cholesterosis, chronic abdominal ischemia, lipid pancreatitis, and lipid hepatosis. New diagnostic methods for these diseases are described. The efficiency of partial ileal bypass and conservative treatment with mineral oil-pectin emulsion Fishant in correcting dyslipoproteinemia is demonstrated. The therapeutic results are confirmed by radioisotopic and ultrasonic studies.

Key Words: *dyslipoproteinemia; lipid distress-syndrome; partial ileal bypass; blockade of enterohepatic circulation of bile acids*

During last decades, disturbances of lipid metabolism (lipid distress-syndrome, LDS) have been in the focus of therapeutic research. The contribution of surgeons in the study of this problem was not particularly large, although they regularly deal with various manifestations of LDS, which are considered as the individual nosologic forms [1,7,9,13-15,19-22]. Paradoxically, the primary cause of pathological process is usually ignored in the local surgical treatment of involved organs.

This review is not intended to discuss LDS comprehensively. Our aim was to describe a novel surgical approach to a number of pathological states caused by disturbances in lipid metabolism.

S. I. Spasokukotskii Faculty Surgery Clinic has a rich experience in the treatment of more than 1,000 patients with lipid metabolism disturbances. It made possible to consider some diseases as a pathology of lipid metabolism. These nosologic forms were (in percents of the total number of patients): obliterating atherosclerosis (64.2%), gallbladder cholesterosis (24.2%), chronic ischemia of digestive organs (4.5%), lipid pancreatitis (4.4%), and lipid hepatosis (2.7%). We started to accumulate evidence with obliterating atherosclerosis.

Diagnosis of LDS

Diagnosis of LDS includes two components: description of the cascade of disturbances in lipid homeostasis and evaluation of pathological changes in the target organ.

The first diagnostic task is solved by analyzing blood plasma lipids, blood rheology, lipid peroxidation (LPO), antioxidant protection, *etc.* Without depreciating the virtues of these methods, it should be noted that studies focused on the function of the reticuloendothelial system in the liver and interaction of organism with its autochthonous microflora are of primary importance in diagnosing of LDS. In our study this interaction is assessed on the basis of microbial and metabolic analysis of the large intestine.

Pathology in the target organ and the organic surgical manifestation of LDS are diagnosed with the help of various ultrasonic methods (in particular, echodensitometry) and x-ray contrast angiography, which allow to determine localization and the nature of vascular diseases in the majority of cases. In addition, the radioisotopic methods used to study the vascular system and some physiological functions (for example, biligenesis in the liver) help to effectively assess pathological processes in the target organ involved in LDS [2,5,8].

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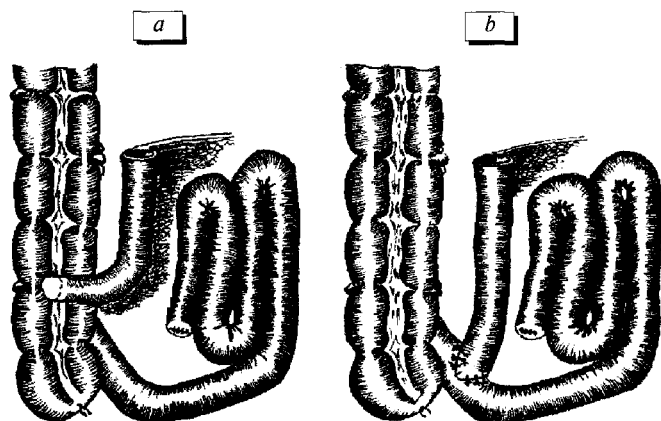


Fig. 1. Classical (a) and modified (b) partial ileal bypass operation.

Vital radioisotopic study of microcirculation and capillary bed in the target organ helps to exclude bias evaluation of the obtained data. This method was the most informative in the study of microcirculation in the stomach and in duodenum.

Treatment of LDS

Treatment of LDS includes procedures aimed at correction of lipid homeostasis pathology and normalization of function of involved organ. This subdivision is rather conventional and mainly relates to the diseases with pronounced vascular abnormalities: obliterating atherosclerosis, chronic ischemic abdominal disease, i.e. the pathologies that often require vascular intervention.

In other clinical forms of LDS (lipogenic pancreatitis, gallbladder cholesterosis, and lipid hepatosis) normalization of lipid metabolism always leads to recovery of physiological functions of the target organ.

In this paper we summarize our experience in surgical ($n=53$) and conservative ($n=1500$) treatment of LDS [11,18,23]. The treatment included administration of mevacor and its analogs ($n=258$), which were later excluded because of side effects, and our original mineral oil-pectin emulsion (MOPE) Fishant ($n=1057$) [20,21].

It should be emphasized that we do not use statines since 1995 because of numerous complications

in patients with dyslipoproteinemia, which were treated with hydroxymethylglutaryl coenzyme A-reductase for a long time [11].

We modified the classical Buchwald's partial ileal bypass (PIB) operation and applied ileo-ileal bypass near the ileocecal valve instead of ileocecal shunt (Fig. 1) [6]. In this modification the operation has at least three advantages: the colointestinal reflux is prevented by the ileocecal valve, a small fragment of the ileum is preserved, where vitamin B₁₂ is absorbed, which makes it needless to administer this vitamin in the delayed postoperation period, and the most important feature is the absence of diarrhea after modified PIB due to dosed in contrast to massive bile entry into the colon after Buchwald's operation.

One could expect a decrease in hypolipidemic effect of PIB due to the presence of a functioning ileal fragment. However, the biochemical effect of modified PIB did not differ from that of the classical Buchwald's operation.

Long-term and persistent normalization of plasma lipids was accompanied by a significant improvement in the blood rheology and erythrocyte elasticity against the background of LPO inhibition, increase in antioxidant protection, and normalization of all primarily important liver functions. According to the long-term follow-up (10 years), these positive changes were maintained at the same level [12].

We observed no complications after PIB and documented a positive biochemical effect and positive clinical dynamics. At the same time, this operation is rather traumatic and often leads to various complications (in particular, the bypass syndrome, etc.). Therefore, the patients were carefully selected and the operation was made only in cases when conservative treatment was not indicated.

Similarly to PIB, the new drug MOPE Fishant blocks enterohepatic circulation of bile acids [3]. We compared the efficiency of known hypolipidemic drugs and our preparation (Table 1). The principal advantages of MOPE Fishant were the absence of contraindications and complications during long-term (more than year) treatment with equal biochemical effect (in some patients MOPE Fishant was superior to statines), a decrease in atherogenic lipoproteins to

TABLE 1. Efficiency of Various Methods of Treatment of Dyslipoproteinemia

Drug, mean therapeutic dose	Biochemical indices, %		HDL	LDL	Reference
	cholesterol	triglycerides			
Lovastatin, 40 mg/day	-28.0	-12.0	+6.0	-35.0	[24]
PIB operation	-51.6	-67.5	+75.5	-46.2	[16]
MOPE "Fishant"	-44.5	-25.6	+14.4	-61.7	[16]

60%, an increase in antiatherogenic HDL by 25%, and a decrease in plasma cholesterol by 40-50%.

The effects of MOPE Fishant and PIB on lipid metabolism are similar, although surgical intervention is more effective, especially for HDL cholesterol.

On the basis of our long-term experience of application of various hypolipidemic drugs, we prefer MOPE Fishant because even modern statines produce a great number of complications during long-term administration. In addition, long-term treatment (which is life-long in a number of patients) is rather expensive.

Let us consider specific features of the treatment of some specific forms of LDS.

**Target organ: arteries of lower limbs.
Disease: chronic arterial insufficiency**

Recently, correction of dyslipidemia, generally considered culprit of atherosclerosis progression, becomes a usual component of the complex therapy of chronic arterial insufficiency.

We have experience in conservative and surgical correction of dyslipidemia in 720 patients with obliterating atherosclerosis. Among them, 32 patients were subjected to PIB operation, while 688 were treated conservatively with MOPE Fishant.

We established that long-term normalization of lipid metabolism produces positive stabilizing effect on the development of atherosclerosis. It is confirmed by changes in damaged arteries, which we observed during reparative plastic operation after long-term (as a rule, no less than 6 months) normalization of plasma lipids. The arteries were elastic, their lumens contained loose atherosclerotic masses with sites of recanalization. Atherosclerotic plaques were easily removed with forceps without trauma to the intima. Histological examination showed that the cholesterol inclusions were virtually absent in the arterial wall, while the endothelial lining was not attached to intraluminal masses.

Duration of lipid-correcting treatment of patients with occlusion-stenotic atherosclerotic lesions in lower limbs is a key factor in correction of dyslipidemia. Observation of stenotic sites during long-term correction of dyslipidemia showed moderation of stenosis and loosening of atheromatous masses.

These features underlie our original and clinically beneficial method of catheter aspiration deobliteration (CAD) aimed at the restoration of the patency of damaged arteries [3,10]. At the first stage, dyslipidemia is corrected by PIB with subsequent dynamic echodensitometry of the damaged region of the artery [4]. When density coefficient of the damaged region became almost normal (1.17), which occurred no earlier

than 6-8 months postoperation, CAD was performed. To this end, the artery was catheterized and loose intraluminal masses were removed from occluded region. Finally, balloon angioplasty of the stenotic regions was accomplished. The aspiration is recommended to perform from distal to proximal regions to reduce the risk of thrombosis in the case of intima detachment. For atherosclerotic plaques in the region of femoral artery bifurcation a semienclosed method is used: isolation of the femoral artery by conventional technique, arteriotomy with regard to plaque location, removal of the plaque, and endovascular angioplasty.

Localization of damaged regions in the arterial bed subjected to CAD was different: common iliac artery ($n=5$), external iliac artery ($n=4$), common femoral artery ($n=2$), superficial femoral artery ($n=6$), popliteal artery ($n=1$). In 16 patients catheterization was accomplished transcutaneously by the method of Seldinger, in 2 patients operation was performed by semienclosed method after preliminary isolation of the artery.

The semienclosed method of CAD is indicated in cases when preliminary attempts of endovascular deobstruction failed due to catheter impasse into the obliterated artery (usually before correction therapy). After PIB operation or MOPE Fishant treatment (for at least 6 months) catheterization of the obstruction region and aspiration of the loosened endovascular substrate become possible (Fig. 2).

Thus, under condition of long-term lipid correction therapy, a minor traumatic intervention restored patency of the main arteries in a certain category of patients. However, indications for CAD should be determined with due regards for individual dynamics of the ischemic manifestations in the damaged limb, results of dyslipoproteinemia correction, repeated ultrasonic data on the length of occluded region, the state of arterial wall, and the density of intraluminal structures.

The tactical problem in atherosclerosis and hyperlipidemia is solved as follows. Correction of hyperlipidemia is indicated in all patients with obliterating atherosclerosis irrespective of indication for vascular surgery. In case of mild chronic ischemia of the lower limbs, hyperlipidemia correction is indicated (PIB operation or conservative treatment with MOPE Fishant during at least 6 months) followed by CAD of the occluded artery. In the case of failure of the endovascular intervention, angioplasty is indicated.

**Target organ: gallbladder.
Disease: gallbladder cholesterosis**

According to current views, gallbladder is the target organ of LDS. Logically, gallbladder cholesterosis can

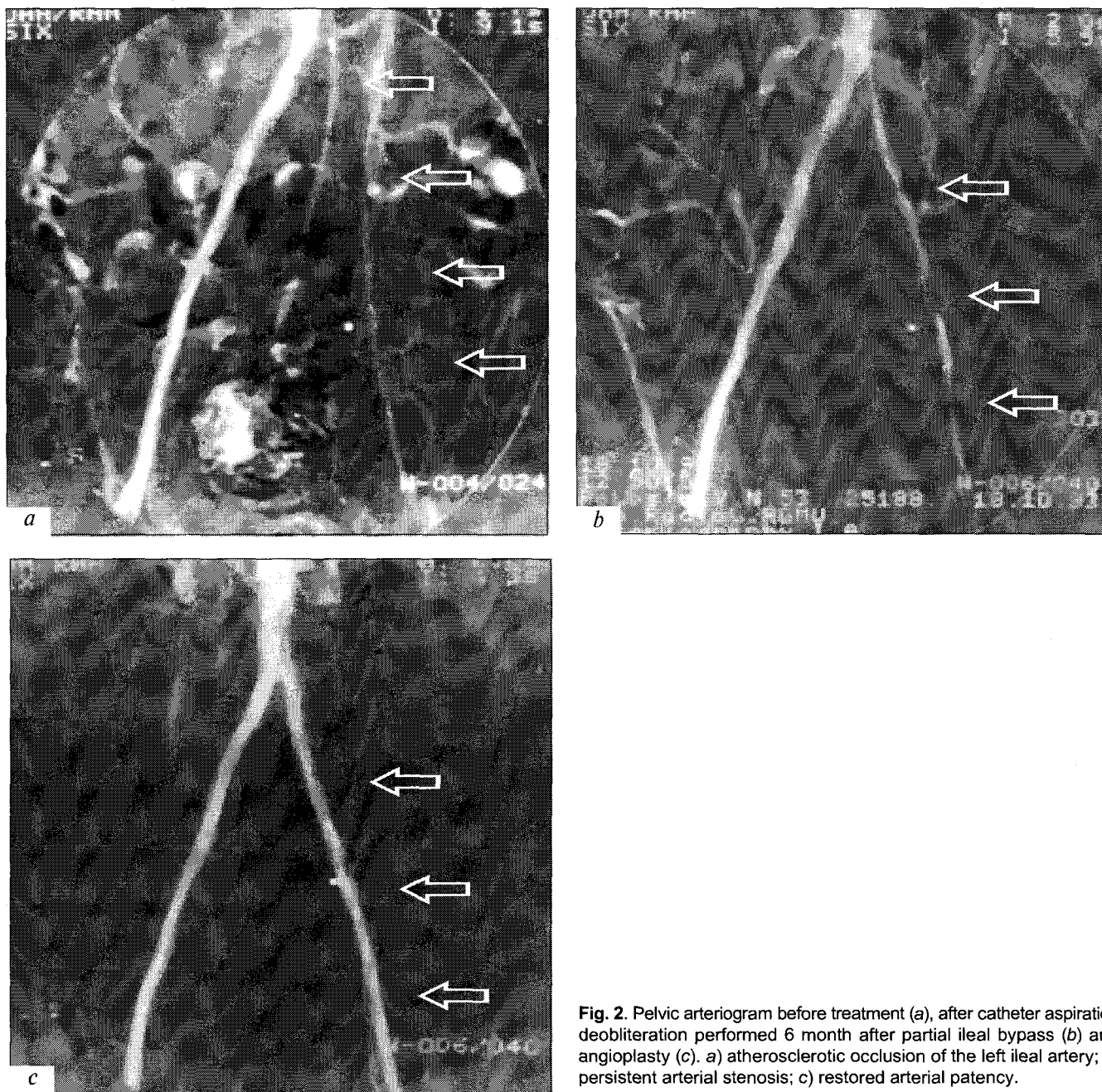


Fig. 2. Pelvic arteriogram before treatment (a), after catheter aspiration deoblation performed 6 month after partial ileal bypass (b) and angioplasty (c). a) atherosclerotic occlusion of the left ileal artery; b) persistent arterial stenosis; c) restored arterial patency.

be defined as a preliminary stage of cholelithiasis, and cholelithiasis as the calculus form of cholesterosis.

All conventional methods to treat gallbladder cholesterosis are based on cholecystectomy for the calculus cholesterosis and treatment of gallbladder dyskinesia for acalculus cholesterosis. In other words, they are not based on pathogenetic approach, prevention of lithogenic bile formation, alterations of the gallbladder wall, and gallstone formation, i.e. correction of lipid metabolism disturbances, which usually takes long time.

Our experience in the treatment of gallbladder cholesterosis is based on the data of 251 patients with

acalculus ($n=108$) and calculus ($n=143$) forms of the disease. The patients with acalculus cholesterosis were treated conservatively with MOPE Fishant for 2-6 months. After treatment, the patients with single gallstones ($n=76$) were subjected to extracorporeal biliary lithotripsy, while the patients with multiple gallstones ($n=67$) were subjected to conventional cholecystectomy.

We developed two diagnostic criteria of cholesterosis: the probabilistic and deterministic. The probabilistic ultrasonic criteria are:

- ◆ increased gallbladder wall density ($L>24$ gray-scale units),

- ◆ decreased homogeneity of gallbladder wall (homogeneity index 2.5-3.0),
- ◆ reduced gallbladder contractility (<50%),
- ◆ high density of bladder bile ($L > 4$ gray-scale units),
- ◆ thickening of the gallbladder wall (0.3-0.6 cm).

The deterministic ultrasonic criterion of gallbladder cholesterosis is regression of the above probabilistic criteria against the background hypocholesterolemic therapy.

It should be noted that the earliest manifestations of gallbladder cholesterosis are the decrease in its contractility and increase in the density of gallbladder wall.

Treatment of gallbladder cholesterosis should be performed differentially depending on the form of the disease. In acalculus cholesterosis conservative therapy is indicated, while the treatment of calculus form depends on the number and size of gallstones. When extracorporeal lithotripsy is indicated, the treatment consists of two stages: conservative therapy (decholesterolization of the gallbladder wall) and, after normalization of the contractile function, the gallstones are fragmented by distant shock-wave lithotripsy.

Recently, this method was popular in physicians and patients, but then its disadvantages were revealed:

- ◆ resistance of gallstones to lithotripsy even when this procedure was clearly indicated;
- ◆ slow and often incomplete elimination of stone fragments after lithotripsy;
- ◆ frequent recurrences of stone formation in the gallbladder.

These shortages can be explained by gallbladder cholesterosis, impairment of its contractile function, and high density of bladder bile, which was proven in our experiments by ultrasonic examination of gallbladder motility, as well as echodensitometry of the gallbladder walls, bile, and stones.

Taking into consideration the analogy of atherosclerotic lesion in arteries and gallbladder cholesterosis in hypercholesterolemia, we used MOPE Fishant during 4-6 months before lithotripsy under dynamic ultrasonic control (Fig. 3). The treatment normalized lipid metabolism due to a decrease in the concentration of total cholesterol and atherogenic LDL, the level of HDL being increased. Dynamic echodensitometry revealed a decrease in the gallbladder wall thickness, restoration of its contractility, a decrease in bladder bile density, and in some cases loosening of gallstones, which became less dense and homogenous.

This treatment facilitated removal of gallstones (several hundreds pulses instead of usual thousands pulses were needed). Stone fragments were eliminated within 2-4 months (vs. 6 months and more after conventional treatment). The treatment with MOPE Fishant was resumed after lithotripsy.

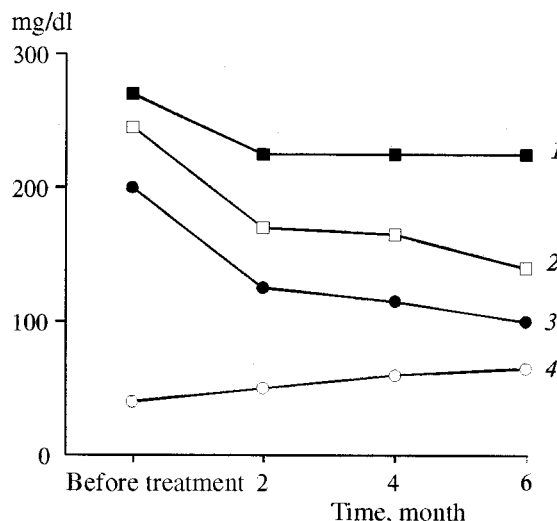


Fig. 3. Indices of lipid metabolism in patients with gallbladder cholesterosis treated for dyslipoproteinemia. 1) cholesterol; 2) triglycerides; 3) LDL; 4) HDL.

Target organ: pancreas.

Disease: lipogenic pancreatitis

Disturbances in lipid metabolism are the key elements in the pathogenesis of acute pancreatitis in 30% patients. The first report on chylous character of serum in a patient with acute pancreatitis was made in 1846. However, until now the term "lipogenic pancreatitis" is not generally accepted.

We accumulated experience of treatment of 53 patients with chronic postnecrotic lipogenic pancreatitis. The diagnosis was verified either operatively or during laparoscopy. To correct lipid metabolism, the patients were subjected to PIB ($n=12$) or were treated with MOPE Fishant ($n=41$).

Long-term and persistent normalization of plasma lipids (after surgical or conservative treatment) activates complex metabolic mechanisms and restores function of the reticuloendothelial system in the liver,

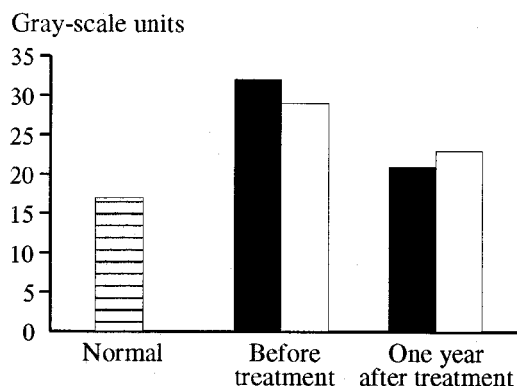


Fig. 4. Density of the pancreas involved in lipogenic pancreatitis after partial ileal bypass (solid bars) and treatment with mineral oil-pectin emulsion Fishant (light bars).

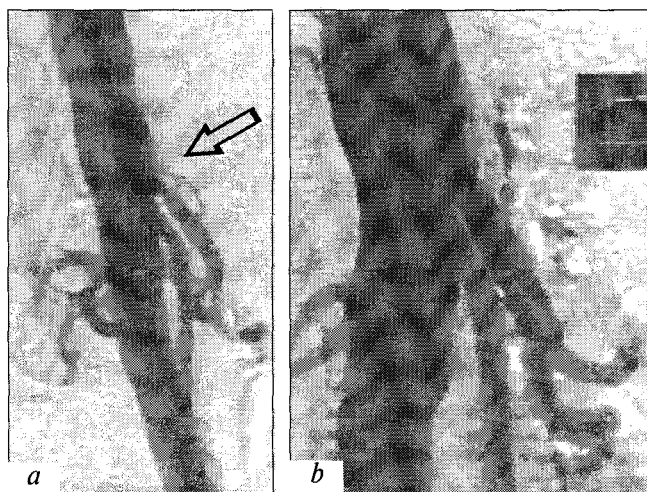


Fig. 5. Celiac trunk stenosis in a female patient with chronic ischemia of digestive organs (a) and restoration of vascular patency after endovascular angioplasty (b).

reduces cholesterosis in the gallbladder and major duodenal papilla, improves intra- and extrahepatic bile dynamics, enhances expression of receptors, modulates apoptosis in the pancreas and restores its excretory function, and improves metabolism in the host-microbiotic system. These positive factors make it possible to normalize liver function and prevent the development of irreversible changes in the pancreas, which is confirmed by ultrasonic densitometry (Fig. 4).

Long-term treatment of dyslipoproteinemia improves absorption in the small intestine, which was revealed during the study of absorption with ^{131}I -albumin. The basic index of visceral circulation, alimentary blood flow in the portal vein considerably increased. Thus, correction of lipid metabolism prevents

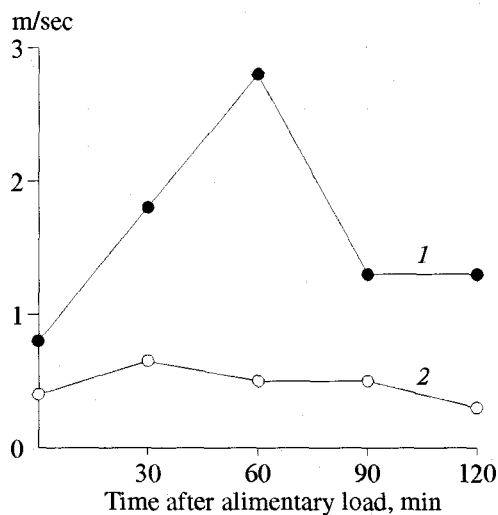


Fig. 6. Blood flow rate in portal vein after alimentary load in healthy subject (1) and in female patient with chronic ischemia of digestive organs (2).

recurrences of acute lipogenic pancreatitis and greatly improves the quality of patient life.

**Target organ: abdominal visceral arteries.
Disease: chronic ischemic disease
of digestive organs**

Fifty-one patients with chronic ischemic disease of digestive organs were examined. Correction of lipid metabolism was performed by PIB operation ($n=9$) or with MOPE Fishant ($n=37$). In 5 patients angioplasty of critical stenosis of the celiac trunk was performed after normalization of lipid metabolism.

The accumulated experience can be summarized in the following conclusions.

1. Abdominal angina occurs more often than generally assumed, because morphological and functional alternations in various organs of the abdominal cavity typical of this pathology are often considered as "trivial" chronic inflammation.

2. Etiopathogenetically, LDS should include also chronic ischemia caused by circulation disturbances due vascular wall lesions, in addition to disturbances produced by external compression.

3. Pathology of celiac trunk is easiest for diagnostics and can be corrected by angioplasty. In our clinics, stenosis of the celiac trunk was diagnosed and corrected by angioplasty in 5 patients (Fig. 5). Other patients (90%) had a particular form of arterial bed pathology: disturbances in the microcirculatory bed of abdominal organs (stomach and intestine).

Vital examination revealed severe disturbances of microcirculation in the stomach and duodenum. This method of examination can become indispensable in the study of vascular pathology of the upper subdivisions of the gastrointestinal tract. In the small and large intestine, regional blood flow was assessed with ultrasonic technique. In patients with pronounced clinical manifestations of abdominal angina, this method can establish the absence of postprandial blood flow increase in the portal vein even when celiogram was "normal", which is a significant indication of the pathology of intramural blood flow (Fig. 6). The study of absorption in the small intestine by radioisotopic method confirmed considerable impairment of abdominal microcirculation in these patients.

Another significant objective criterion is visceral vascular resistance index identical to the conventional total vascular resistance index. In the peripheral form of chronic abdominal ischemia this index is considerably increased.

Microcirculatory disturbances in the target organ persisted even after removal of celiac trunk pathology and complete recovery of macrohemodynamics. They can be removed by long-term treatment of dyslipi-

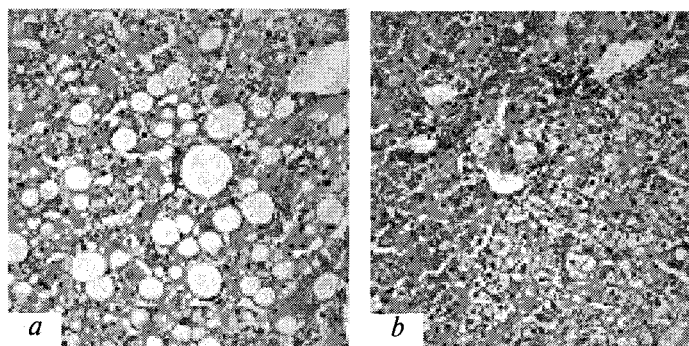


Fig. 7. Liver biopsy specimen from a patient with lipid hepatitis before (a) and 4 months after treatment with mineral oil-pectin emulsion Fishant (b). $\times 70$. Staining with hematoxylin and eosin.

demia. In addition, normalization of lipid metabolism improves microcirculation in the stomach and duodenum, restores visceral vascular resistance index and the hemodynamic parameters in the portal vein, and alleviates pain syndrome.

Target organ: liver.

Disease: lipid hepatitis

Practically all our patients with disturbances in lipid metabolism had the signs of fatty liver degeneration. At the early stages, this disease (as all others related to disturbances in lipid metabolism) is reversible. It is confirmed by the results of treatment of 31 patients with dyslipoproteinemia by MOPE Fishant. The diagnosis of lipid hepatitis was established by radioisotopic scintillography and paracentetic hepatic biopsy.

As a rule, no less than 4 months of MOPE Fishant application are required for normalization of functional activity of cells in the reticuloendothelial system and for improvement of indices of hepatic blood flow. Histological examination of hepatic biopsy specimens confirmed the radioisotopic data (Fig. 7).

Summing up the results of surgical study of LDS, it should be noted that many diseases caused by disturbances of lipid metabolism, can be considered as LDS. This approach may help to choose the optimal method for correction of dyslipoproteinemia and tactics of treating individual organs.

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