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**RISK FACTORS FOR PROGRESSION OF DIABETIC RETINOPATHY
IN PATIENTS WITH TYPE 2 DIABETES MELLITUS**

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A high prevalence of diabetes mellitus (DM) has emerged as a worldwide public health problem in the past 20 years. Type 2 diabetes (T2DM) is the most common form of DM, estimated to account for 85–90% of DM. T2DM affects over 246 millions of people worldwide and it is estimated to increase around 380 million until 2025.

Diabetic retinopathy (DR) is a major microvascular complication of diabetes, and it is the commonest cause of blindness in people of working age in the world. Risk factors for development and progression of DR include hyperglycaemia, nephropathy, genetic predisposition, hypertension and lipid metabolism.

A continuous relation exists between glycemic control and the incidence and progression of microvascular complications. Hypertension and smoking also have an adverse effect on microvascular outcomes.

Hyperglycemia is regarded as a major cause of DR. Improved glycemic control retards the development and progression of retinopathy in both type 1 and type 2 DM. However, worsening of retinopathy has been reported after rapidly improved glycemic control.

In the UK prospective diabetes study of patients with T2DM, an intensive glucose control policy that lowered glycated haemoglobin concentrations by an average of 0.9% compared with conventional treatment (median HbA1c 7.0% v 7.9%) resulted in a 25% reduction in the overall microvascular complication rate. It was estimated that for every 1% reduction in HbA1c concentration there is a 35% reduction in microvascular disease. It was shown (F.E. Shadracheva 2008) that for patients with type 2 diabetes, high HbA1c level is a predictor of rapid transition pre-proliferative stage DR to proliferative DR.

Among patients suffering from MD a significant number of cases (96%) were also diagnosed with diabetic microvascular retinal damage. The association of microalbuminuria with DR has been proved in the results of population-based study WESDR (Wisconsin epidemiological study).

Microalbuminuria is associated cross-sectionally with the presence of retinopathy in persons with diabetes and with the presence of proliferative disease in younger-onset individuals. These data suggest that microalbuminuria may be a marker for the risk of proliferative DR developing.

The UKPDS has further shown the value of an accurate blood pressure control in delaying the development of DR complications as well as other microvascular endpoints. Researchers in JAMA (Emdin C.A., 2014) concluded that people with DM who reached systolic blood pressure below 130 mm/Hg had 25% lower risk of stroke than those with higher blood pressure levels and also had a lower risk of retinopathy and albuminuria.

Nonetheless, DR occurs even with optimal glucose and blood pressure control. Currently, the contribution of genetic factors in the development of T2DM is not in doubt. Some patients with poor control of glycemia or blood pressure do not develop diabetic retinopathy even over prolonged periods of time, while others may develop diabetic retinopathy in relatively short periods of time despite good risk factor control. This was prominently illustrated in Joslin Medalist study which found that almost 50% of older diabetic participants in their study had no evidence of retinopathy despite surviving over 50 years with type 1 diabetes.

These findings emphasize the importance of careful long-term monitoring for people with DM to control blood pressure, decrease of cholesterol level in the blood serum, eliminating cigarette smoking, as well as the importance of integrating food and hygienic approaches on a large scale, to prevent the development of diabetes and its complications.

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**MULTIMODAL TREATMENT AND PREVENTION OF SEPTIC COMPLICATIONS OF ACUTE
DESTRUCTIVE CHOLECYSTITIS**

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During the last decades, there has been found a growing number of patients with acute destructive (necrotizing) cholecystitis. Especially there has been increase in the number of entities found with various kinds of complicated septic conditions. According to the literature reports, the number of patients operated in recent years with acute destructive cholecystitis complicated with abdominal sepsis is 12-20% of total patient operated on this pathology.

Tactics of surgical treatment of this disease is not always favorable, that's why mortality and postop morbidity remains high. The principles of surgical management of septic complications in acute destructive cholecystitis have not changed for a century. At the same time significant changes in the management of septic complications have affected the means and methods of treatment of septic complications in acute destructive cholecystitis.

The objective of the study is to reduce the incidence of postoperative complications, improve the results of treatment and prevention of septic complications in acute destructive cholecystitis, establishing patterns of development and progression of this disease.

The research consisted of an experimental part, which was performed on inbred white rats and also the clinical and laboratory examinations of patients with septic complications of acute destructive cholecystitis. All animals were



obtained from the vivarium of Bukovinian State Medical University. The experiment included 50 white rats weighing 200-250 g without obvious signs of the disease and with normal rates of laboratory tests (complete blood and urine). The clinical material included 45 patients who were treated at the Emergency Clinical Hospital of Chernivtsi with various forms of acute destructive cholecystitis. Among the surveyed patients there were 11 men (24.44%) and 34 women (75.56%). The mean age of patients was for men – 56.69 years, for women – 53.84 years.

Obtained results were indicative of the fact that intraoperative bile duct sanitation for three times by introduction of antibiotics prevented the development of septic complications like suppurative cholangitis in the early postoperative period. In addition, development of local septic complications, which are sources of generalized sepsis, can be prevented by early surgery in the period of 48 hours after hospitalization of patients.

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COMPARATIVE DYNAMICS OF CHANGES OF INTESTINAL SUTURES'S MICROBIOTA UNDER THE CONDITIONS OF THEIR LEAK DEVELOPMENT

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Intestinal sutures leak (ISL) is an urgent problem in abdominal surgery related with the increase of duration of inpatient treatment and rehabilitation, frequent disability and mortality, the rate of the last one is up to 50% in the case of postoperative peritonitis development. A microbial contamination of the sutures line is one of the initiative factors of ISL occurrence. However, the patterns of local changes of the intestinal anastomosis microbiota and its impact on healing of junction zone remain obscure.

Objectives: to investigate the peculiarities of dynamics of quantitative and qualitative changes of microflora composition in the region of rats' intestinal sutures on the experimental model of their leakage.

The research was carried out on 80 albino nonlinear male rats, weighing 180 ± 20 g, they were undergone the resection of caecum with suturing the defect of intestinal wall by means of interrupted sutures (polyamide 5-0). ISL was modeled by the way of excessive mobilization of the junction area and twice as much rare application of sutures. Bacteriological tests of smears from line of the sutures were performed aseptically during chronological periods (12, 24, 48, 72 hours and 5 days following surgical interference). Indices of microbial count (MC) and numbers of the most significant types of intestinal microflora were determined: *E. coli*, *Enterococcus* spp., *Bacteroides* spp., *Clostridium* spp. were determined in concentrations equal to Lg CFU/ml. The relevance of changes in the compared groups was determined by Mann-Whitney t-test and Pearson's correlation coefficient (r).

It has been established that the MC index was statistically higher ($p < 0,001$) in the animals of experimental group in comparison with the control data during the entire period of observation. Etiologically significant concentrations of microorganisms (> 5 Lg CFU/ml) were detected in the sutured tissues of the intestine in the animals with AL beginning with 24 h. after surgery to the end of the fifth day their total number increased up to $7,10 \pm 0,038$ Lg CFU/ml. An exponential increasing of MC index was observed in case of unfavourable postoperative period, but the decrease of microbial contamination of the sutures line was proved in the animals of control group at the end of observation ($p < 0,001$).

While analysing the dynamics of changes of the population structure of microbiota in the region of applies sutures it has been established that in 12 h. the increase of MC was mainly due to the growing number of *E. coli* ($r = +0,98$). The macroscopic signs of biological leakage of junction zone were friable adhesions involving infiltrated flushed omentum, loops of small intestine and adjacent parts of the colon. In 24 h. powerful positive relation was detected between the increasing MC and the number of *E. coli* ($r = +0,97$) and the moderate negative one – between the index MC and the number of *Enterococcus* spp. ($r = -0,37$). In 48 h. increasing MC was correlated with increasing numbers of *E. coli* ($r = +0,97$) and *Bacteroides* spp. ($r = +0,37$). In 72 h. a moderate positive relationship was detected between the index MC and the number of *E. coli* ($r = +0,32$) and a negative one – to the number of *Bacteroides* spp. ($r = -0,38$). In 5 days the increase of index MC was in a moderate positive relationship with the numbers *Bacteroides* spp. ($r = +0,39$) and *Clostridium* spp. ($r = +0,41$) and in a negative one with the numbers of *E. coli* ($r = -0,49$) and *Enterococcus* spp. ($r = -0,53$). The mechanical disruption of junction zone was registered in all animals of the experimental group during this period in the form of necrosis of the bowel wall in the area of applied sutures on the background of separated or general accumulation of fibrinous-purulent fluid in the abdominal cavity.

An exponential increase of the total quantity of microorganisms with the changes of the population structure of intestinal microflora occurs in the sutured tissues of intestine under the conditions of anastomotic leakage. In the early terms (12-24 h. after the sutures application) the increase of the microbial number is mainly caused by the number of an autochthonous microflora (*E. coli*) and later (after 3-5 days of the anastomotic leakage initiation) – by the increased number of obligate anaerobes (*Bacteroides* spp. and *Clostridium* spp.) along with the decreasing of concentration of facultative anaerobic microorganisms (*E. coli* and *Enterococcus* spp.). Such dynamics of changes in quantity and species composition of microbiota in the area of the line of sutures affirms that the disorder of colonization resistance of the intestinal tissues due to synergy and antagonistic effects of some representatives of intestinal microflora under conditions of anastomotic leak development.