

State petroleum company of the Republic of Azerbaijan

Central hospital for petroleum workers



REPORT

on the clinical trials of the preparation "VIUSID" in the immunological prophylaxis of purulent complications in abdominal surgery

Central hospital for petroleum workers

Report

**on the clinical trials of the preparation "Viusid" in the immunological
prophylaxis of purulent complications in abdominal surgery**

Author

**Head of Surgery Department
Prof. R. A. Kuliev**

**Under the direction of -
Hospital**

**Head Doctor of the Central
for petroleum workers
F. G. Dzhavadov**

Contents

<u>INTRODUCTION</u>	3
<u>RESEARCH OBJECTIVES</u>	8
<u>MATERIALS AND METHODS</u>	8
1. <u>CLINICAL CHARACTERISTIC OF THE PATIENTS</u>	8
2. <u>RESEARCH METHODS</u>	11
<u>RESULTS OBTAINED</u>	14
1. <u>RESULTS OF THE MICROBIOLOGICAL RESEARCH</u>	14
2. <u>RESULTS OF IMMUNE MONITORING</u>	17
3. <u>DYNAMICS OF THE LIPID PEROXIDATION SYSTEM</u>	22
4. <u>CLINICAL INDICATORS OF THE EVOLUTION OF THE PROCESS AND COMPLICATIONS</u>	24
<u>BIBLIOGRAPHY</u>	27
<u>CONTACT DETAILS</u>	39

INTRODUCTION

One of the factors that slows down the development of contemporary surgery is purulent surgical infection. This problem affects up to 15% of surgical operations and contributes to the development of serious complications, the increase in treatment times and the growth of costs. For this reason, the fight against post-operational infections constitutes one of the most important challenges of contemporary surgery, and therefore any activity directed towards the reduction of this type of complications is welcome. During recent years, the problem of intra-hospital infections has acquired great importance for all the countries of the world, not only developing countries, but also for industrially developed ones. In this sense, our country is no exception. The numerous factors such as the accelerated rhythm of growth of medical institutions, the creation of new types of equipment and medical instruments (of a therapeutic and diagnostic nature), the application of the most modern medications with immunodepressive properties, the artificial reduction of immunity in the transplant of organs and tissues increase the danger of distribution of infections among the patients and personnel of medical institutions.

It has been shown that in official statistics the data regarding the frequency of purulent inflammatory complications appear notably reduced: in cases of acute appendicitis – 5.8 times; in the case of hernias – 9.7 times; in the case of benign pathologies of the bile ducts – 8.2 times and in the case of ulcerous disease – 4.7 times. It has also been observed that the frequency of purulent inflammatory complications is influenced by the age of the patient, the presence in the patient of diabetes mellitus, the persistence of the infection, the duration of the surgical operation, the qualification of the surgeon, etc. The time of year in which the operation is carried out also has a certain influence. In particular, the frequency of post-operational complications increases notably in March-April. The second peak is observed in July-August. In the first case the phenomenon is related to avitaminosis, the general decrease in immunity and hormonal changes in the

organism, while in the second case it is related to the conditions appropriate for the development of microorganisms in the environment and with the holiday season.

Contemporary scientific data presented in the work of foreign and national researchers, allow the assertion that purulent inflammatory complications arise in at least 5-12% of the patients who are admitted to medical institutions. In the USA, according to the data of R. Dixon (1976), up to 2,000,000 cases of purulent inflammatory complications are registered annually in hospitals, in the FRG (Federal Republic of Germany) between 500,000 and 700,000, in Hungary 100,000 which represents around 1% of the population of these countries. In the USA, of the 120,000 patients affected by purulent inflammatory complications around 25% of patients die which, according to the evaluation of experts, including the most conservative, constitutes the principal cause of lethal cases. The data obtained in recent years demonstrate that purulent inflammatory complications considerably increase the stay of patients in hospitals and the damages caused reach in the USA from 5-10 billion dollars, in the FRG 500 thousand euros and in Hungary 100-180 million forint.

The problem of the prophylaxis of purulent inflammatory complications can only be resolved by acting on the main links of the pathogenesis of the purulent surgical infections.

Three main factors participate in the pathogenesis of purulent surgical infections:

- 1 the pathogenic agent
- 2 microflora present in the patient's organism
- 3 reactivity (immunity).

For the appearance of the inflammatory process it is necessary that the antigenic irritation inside the organism exceeds the protective capacity of the immune system. This happens when the pathologic agent multiplies excessively inside one of the natural recipients of the organism that host microflora (gastrointestinal tract,

respiratory tract, skin) and its translocation to the affected organ takes place.

In nature no pathogenic agents exist which are specific to purulent infection. All of them in a certain quantity and adopting one form or another vegetate in the natural recipients of the organism. However, in certain circumstances the degree of their pathogenicity changes. Among the pathogenic agents of the purulent infection we find (in order of the frequency of their appearance): - the staphylococcus aureus and the streptococcus from the group of Gram-positive microorganisms, and an ample group of Gram-negative microorganisms – the bacillus pyocyaneus, Proteus, intestinal bacillus, Klebsiella, cytotobacteria, Serratia, non clostridial anaerobic flora. In 60% of cases the flora at the point of infection is mixed. The fact that the pathological agents possess diverse aggressive ferments (hialuronidase, fibrinolysin, coagulase), endotoxins (haemolysin, leucocidin, lethal toxin, enterotoxin, etc.) facilitates its penetration in tissues and organs and conditions the variety of forms of the disease and their different severity. The application point of the endotoxin produced in the organism by the gram-negative flora is the endothelium of the capillaries and the vegetative nervous system. According to morphological studies the inflammatory response is different for the different types of microorganisms. For the staphylococcus the most characteristic are cutaneous lesions, and those to the subcutaneous adipose tissue, the bones, the lungs, the gastrointestinal tract. For the agents of the Gram-negative group the usual symptom is lesions of the intestine, the joints, the urinary tract. The Gram-negative microflora play a predominant role in the development of post-operational complications and in the pathogenesis of post-resuscitation disease.

The impression was given that to combat the microflora it was sufficient to administer antibiotics. Therapy with antibiotics has been applied in clinical medicine for 50 years. Initially great hope was placed in antibiotics, which was fulfilled. It is difficult to imagine, but in the 1950s all patients suffering from acute haematogenous osteomyelitis were cured in a conservative manner, by administering them penicillin. With time, the efficiency of antibiotics began to be reduced owing to the mutations of the microorganisms and the variation of the

microbial composition. This circumstance caused unsatisfactory results in therapy with antibiotics and stimulated the incessant search and the synthesis of new antibiotics. The microbial composition of surgical infections changes quite quickly and the appearance of the new pharmaceutical developments does not always keep pace with this change. The hopes placed in therapy with antibiotics for the prophylaxis of surgical infections are constantly being reduced. The attention of the researchers has focused on methods of treatment and prophylaxis aimed at increasing the immunological strength of the organism and the stabilisation of the metabolic alterations.

Lipid peroxidation (LP) continually takes place normally in all tissues and to a certain degree of intensity it is one of the types of normal metabolic process. There is a well-determined stationary level of lipoperoxidation. This level is a vital link in the regulation of the lipidic composition of the biomembranes and of the membranous ferments, it participates in the regulation of the permeability and of the transport of substances through the membrane, in the transportation of electrons in the chain of the respiratory ferments, in the synthesis of prostaglandins and leucotriens, in the metabolism of catecholamines and steroid hormones, in the differentiation and in the speed of cellular division.

In recent years many researchers have emphasised the direct dependence that exists between the intensity of LP and hypoxia, which leads to the destabilisation and degradation of the membranes. Throughout the evolution process antioxidant mechanisms have been formed, intended for protection from the destructive action of the products of LP.

The LP – antioxidant system is well balanced and works according to the retro-alimentation principle. The action mechanism of the antioxidants against the lipidic peroxides and free radicals consists of the substitution of the active radical for a less active radical of the antioxidant and in its inactivation.

The substances able to stop LP belong, according to their chemical nature, to a large group of compounds of different types, the most important of which are the

tocopherol preparations. They are able to interact directly with the radicals in the stage of the “breaking” of the chains, diminishing the concentration of peroxide radicals. It is for this reason that the correction of LP with antioxidants has been widely used in clinical practice in cases of numerous diseases in which an alteration of this system is observed. LP products define one of the primary mechanisms of action against alien cells and constitute an important factor in immunological defence – phagocytosis. The analysis of LP without taking cellular factors and humoral factors into consideration is incapable of completely revealing the whole depth of metabolic alterations and the possibilities of correcting them.

The question regarding the development of the immunological response in the case of infiltrations of pathogenic flora has been quite well studied and described in detail in the work of numerous authors. The alteration of the metabolism leads, according to the opinion of a series of authors, to modifications in the structure of the lymphocytes. Alterations have been pointed out to the membrane of the lymphocytes, moreover, in the neutrophils, monocytes and macrophages of the blood of patients an insufficiency of lysosome ferments has been discovered which indicates a low antibacterial activity of the neutrophils.

The question regarding the status of the T and B immune systems is hotly debated. A series of researchers shows the reduction in the quantity of functional activity of the T-lymphocytes. The generalised tendency towards the reduction in functional activity of T-lymphocytes in patients after operations is observed, especially, among persons prone to bacterial infections. At the same time there are reports which indicate that after surgical operations the percentage of T-lymphocytes in patients does not vary, the percentage of helper T-cells increases, while the number of suppressor T-cells declines.

Other researchers publish data regarding the increase in the level of immunoglobulins A and M, as well as regarding the decrease in the level of immunoglobulin G. The researchers relate this increase in the levels of immunoglobulins A and M, with the humoral hypersecretion of B-lymphocytes that arises as a consequence of the alteration of the functions that control their

suppressor T-cells.

From the data in the publications it is possible to reach the conclusion that a single common opinion does not exist regarding the state of the immune system during the post-operational period. However, taking into consideration the opinion of the majority of authors, it is possible to point to the presence of secondary immunodeficiency.

Therefore, to carry out the prophylaxis of purulent inflammatory complications in patients, it is necessary to correct their immunodeficiency. A notable improvement in the results of treatment and the decrease in post-operational complications is achieved on the basis of a preparation previous to the operation, which includes a medication based therapy with immunomodulators. It is precisely this aspect to which it has been decided to dedicate this research.

RESEARCH OBJECTIVES

To carry out a comparative evaluation of the prophylaxis of purulent inflammatory complications in abdominal operations with the preparation "Viusid", on the one hand, and with antibiotics, on the other. To determine which of these methods of prophylaxis is the most effective.

MATERIALS AND METHODS

1. Clinical characteristic of the patients

In total 227 patients have been investigated upon whom some abdominal operation has been practised. The group is made up of patients whose operations were relatively clean, that is to say, those operations during which the opening of organs with natural cavities has been practised (stomach, intestine, bile ducts). The patients were of both sexes, with ages of between 22 and 69 years. The patients

were divided into 2 groups according to their preparation previous to the operation:

- 1 The main group (112 patients),
- 2 The control group (115 patients).

During 5 days previous to the operation, the patients of the main group received the preparation "Viusid" the dose of which was 1 sachet (4.5 grams) 3 times a day.

1 hour before the operation and 3 days after the operation, the patients of the control group were given intramuscular or intravenous injections of one of the 3rd generation cephalosporinic antibiotics, the dose being 1-2 grams per day.

Table 1. Distribution of the patients according to sex and age

Age	Group, sex and number of patients				Total
	main		control		
	men	women	men	women	
22-30	21	2	21	1	45(19.8%)
31-40	22	7	27	3	59(26.0%)
41-50	16	4	19	7	46(20.2%)
51-60	17	6	14	5	42(18.5%)
61-70	14	3	15	3	35(15.4%)
Total	90	22	96	19	227(100%)

During treatment both the general clinical indices and the laboratory results were evaluated.

There were 41 women (18.1%) and 186 men (81.9%). The distribution according to ages was as follows: from 22 to 30 years – 45 (19.8%), from 31 to 40 years 59 (26%), from 41 to 50 years – 46 (20.2%), from 51 to 60 years – 42 (18.5%) and from 61 to 70 years – 35 (15.4%).

Thus, according to the data presented, no pre-selection has been carried out according to anamnesis or concomitant diseases. All clinical material within the groups is uniform and no advantage is observed in either of the groups, by virtue of which it is perfectly possible to carry out a comparatively reliable analysis.

Table 2. Distribution of the patients according to the type of treatment

Type of operation	Group and number of patients		Total
	main	control	
On the gall bladder	39	44	83
On the bile ducts	14	15	29
On the stomach	15	12	27
On the duodenum	11	11	22
On the small intestine	17	14	31
On the large intestine	16	19	35
Total	112	115	227

Table 3. Distribution of the patients according to the type of treatment and the concomitant diseases

Concomitant disease	Group and number of patients		Total
	main	control	
Hypertonia	11	11	22
Chronic ischaemic heart disease	9	10	19
Atherosclerosis	7	8	15
Urogenital diseases	7	6	13
Thrombophlebitis	6	7	13
Diabetes mellitus	6	5	11

Glaucoma and cataract	6	6	12
Chronic diseases of the bones and joints	6	5	11
Cholecystopancreatitis	3	4	7
Gastrointestinal Diseases	2	3	5
Hernias	2	3	5
Rheumatic carditis	2	3	5
Fistulas	2	2	4
Oncological diseases	1	2	3
Dermatitis	2	1	3
Chronic lung diseases	1	2	3
Neurological diseases	1	0	1
TOTAL:	74	78	152

2. Research methods

During the treatment both general clinical indices and laboratory results have been evaluated.

A blood sample was taken from patients to investigate a series of laboratory indices. The general clinical analyses have been analysed by calculating the leucocyte intoxication index of Kal-Kalif (LII) and the intoxication index neutrophils / lymphocytes (N/L).

$$LII = \frac{(S+2P+3J+4Mi) \cdot (PI+1)}{(M+Li) \cdot (E+1)}$$

S - leucocytes with segmented nucleus;

P – leucocytes with rod-shaped nucleus;

J – young leucocytes;

Mi – myelocytes;

PI – plasmocytes;

M –monocytes;

Li – lymphocytes;

E – eosinophils.

The normal values of LII vary between 0.6 and 1.2. Values higher than 1.2 correspond to: localised infection without toxicosis (1.2 – 2.5); localised infection with grade I toxicosis – 2.5 – 5.0; the same with grade II toxicosis – 5.0 – 10.0, and grade III – more than 10.0.

The study of the reactivity of patients forms part of the methods of laboratory investigation. According to the formula of the blood it is possible to judge the degree of definition of the inflammatory process and especially the character of the pathogenic agent. For a staphylococcal infection in the acute phase of the disease the moderate increase of leucocytes is characteristic, accompanied by lymphocytosis and neutropenia, while for Gram-negative infections lymphopenia and neutrophilia are characteristic.

Also analysed was the state of the lipid peroxidation and the antioxidant protection of the organism. For the evaluation of these factors the concentration of lipid hydroperoxides was studied according to the method of V. B. Gavrilov and M. M. Mishkorudnaya. Currently, with the increase in the tolerance of the strains of numerous pathogenic agents towards antibiotics and other medicinal preparations, when the reactivity of the organism has decreased and the possibility of the

atypical course of the purulent infection has appeared, immunological monitoring has become a method of many perspectives in clinical practice for the forecast of the future of the clinical process on the basis of some immunological indices.

For this reason the immune status of the organism has been studied, investigating the indices of cellular and humoral factors of immunological protection.

The investigation of the level of immunoglobulins (Ig) of class A, M, G has been carried out using the radial immunodiffusion method of Mancini. The circulating immune complexes (CIC) were obtained according to the method of V. Haskova. The level of rosette shaped cells, helper T-cells and suppressor T-cells was evaluated using the express method.

The functional capacity of the lymphocytes was evaluated in the reaction of blastotransformation of the lymphocytes (RBTL) with the action of non specific mitogen. The reaction was carried out with the use of phytohemagglutinin (PHA) of the company Difco Inc. & Company (USA) according to the Bach F methodology.

The bacteriological analysis of the of the samples taken from the pharynx and the exudation of the wound were carried out on solid cultivation media. The tolerance of the microflora segregated towards the antibiotics was determined via normal paper discs. The statistical treatment of the data obtained was carried out on a personal computer PC/XT of the company IBM (USA). For the statistical treatment packets of mathematics programs of the company Microtest (Canada) were used, as well as statistical and statistical-graphic programs of the companies Electronics Industrial Co, Ltd and Promoting Enterprise Co, Ltd (USA). When carrying out the statistical analysis additional algorithms of statistical tables in surgery by E.Kohutova were used. For the writing of texts and the creation of graphic images the MS Office package of the company Microsoft (USA) was used.

RESULTS OBTAINED

1. Results of the microbiological research

The predominant cause of post-operational purulent complications is not so much hospital strains, as the microbial flora which was already present in the organism of the patient before hospitalisation. This circumstance plays an important or, perhaps, decisive role in the interpretation of the causes of post-operational complications, which are in essence the reflection of the microbial fauna endogenous in the patient, which has demonstrated its aggressive properties owing to the weakness of the defence factors against infections, provoked by the main disease, the trauma of the operation or the loss of blood.

Table 4. Frequency of appearance of microflora in cultivations originating in the pharynx

SPECIES OF MICROORGANISMS	Number of cultivations	%
Gram-positive:		
- staphil.aureus	117	35.2
- staphil.epiderm.	49	14.8
-staphil.spp.*	26	7.8
-strept.spp.*	10	3.0
Gram-negative:		
- enterobact.spp*	14	4.2
-e.coli	14	4.2
-citrobacter	13	3.9
klebsiella	12	2.6
-proteus.spp*	12	3.6
-providencia	8	2.4
-pseudomonas	6	1.8
-maraxella	2	0.6

-alcaligenes	1	0.3
-acinetobacter	1	0.3
Microbic associations	47	14.2
TOTAL:	332	100

*- spp. – all species

However, the role of hospital strains in the development of post-operational complications via wounds cannot be denied. This is confirmed, in particular, by the data on the majority dependence of the structure of the agents of the infections via wounds after exhaustive unitary surgical treatment of the intra-hospital nature of the infection. A bacteriological analysis of microflora was carried out on the research patients.

According to our data, in the cultivations with higher frequency the staphylococcus aureus, the staphylococcus epidermis and microbial associations were discovered. The resistance to antibiotics is characteristic of the segregated hospital strains. Resistance to the most used antibiotics can reach figures of 70-90%. A high resistance has been observed towards penicillin as well as a high sensitivity towards fluoroquinolones.

According to one point of view antibiotics have a negative influence on the functional state of the immune system. The attempts to use antibiotics for the prophylaxis of post-operational complications often lead to immunodepression and the exacerbation of the infectious process. This affirmation, somewhat categorical, lacks convincing arguments. However, it is true that an incorrect application of antibiotics can be accompanied by the manifestation of infections via wound during the post-operational period. The first thing upon which attention centres when discussing questions related to intra-hospital infectious complications, is the importance of hospital strains of microbial infections.

The sanitary bacteriological control is the most accessible and most significant test that describes the level of microbial contamination of clinical institutions and shows

the predominance of particular hospital strains.

Table 5. Sensitivity of microflora to antibiotics

Antibiotic	Sensitiveness in %
Penicillin	32.2
Streptomycin	41.5
Levomycesin	57.4
Erythromycin	22.6
Tetracycline	37.1
Monomycin	62.8
Neomycin	54.2
Linkomycin	58.5
Oleandomycin	19.7
Oxacillin	42.3
Methicillin	39.7
Kanamycin	62.4
Karbenicillin	66.3
Polymyxin	54.7
Ampicillin	43.3
Ristomycin	67.2
Ampicid	63.7
Nevaxon	72.8
Tabanik	97.1
Abaktal	92.4

The state of the hospital environment undoubtedly determines the probability of development of a hospital infection. However its role is mainly seen in intestinal

and respiratory infections, as well as the development of purulent infections in new born babies and parturient women. Regarding post-operational complications via wounds, their relationship with the state of the hospital environment is much weaker.

2. Results of immune monitoring

When evaluating the factors that influence in the frequency of post-operational complications via wounds, the importance of alterations to immunological reactivity should not be forgotten.

The research carried out during various years by members of our team on the role of immunodeficiency in the development of post-operational complications has not only allowed the definition of the prime importance of a small number of the immunological status indices, but they have also suggested a concept that is wider than the protection against infections as a system of adaptation that includes a wide number of indices of the immune, endocrine and vegetative nervous systems and of their interdependent relationships.

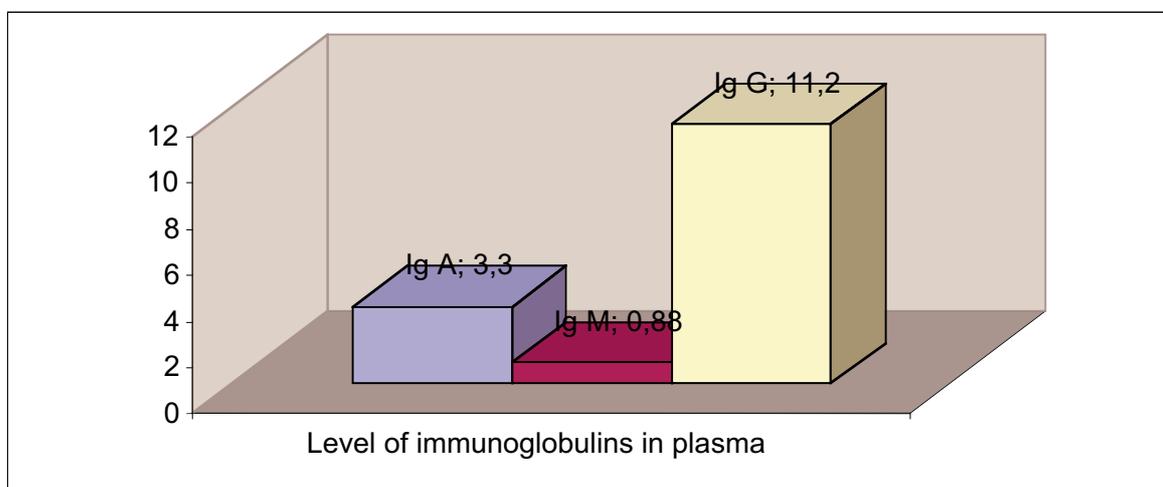


Figure 1.

The development and progress of a purulent process is closely linked to changes in the immunological resistance of the organism. At the same time, the analysis of

the cellular and humoral factors of immunity allow the discovery of the selective action of the curative agents employed.

The initial immunological status was studied in the 2 groups of patients before the operation.

The initial level of immunoglobulins class A, M and G is presented in figure 1. During the post-operational period the development of hypimmunoglobulinemia A and G has been observed. It is evident that this is favoured by the predominance of the processes of protein catabolism, dehydration, including that caused by the exudation of the wound, as well as proteolysis. With regard to immunoglobulin M, our research showed an insignificant and uncertain growth of the level of IgM during the beginning of treatment. This could be explained by the fact that during the treatment the polymerisation of the IgM molecules takes place, as a result of which the de IgM monomers do not segregate, but are incorporated into the cell membrane.

The dynamics of the change of level of IgA and of IgG that depended on the type of pre-operational preparation, are presented in figure 2. In the main group of patients, the change in the level of IgA and IgG after the operation was less pronounced and it stabilised before that of the control group.

The initial level of phagocytosis was evaluated using the general level of phagocyte activity of the neutrophils. The percentual content of the phagocytosing cells at the beginning of treatment in the patients of all groups was 41.3%. No marked difference has been observed in the level of phagocytes between the groups ($P > 0.05 > 0.1$).

The reduction in the number of phagocytosing cells after the operation points to the depression of the resistance of the organism. Resistance was stabilised more dynamically and in a more definite manner in the patients of the main group.

The content of rosette shaped T-lymphocytes (E-POK) before the operation was 61.1%. The content of B-lymphocytes at the beginning of treatment was 13.2%

which is less than the norm. During the treatment after the operation a reliable decrease of E-POK and M-POK was observed. Subsequently a tendency towards the normalisation of indices was observed. Normalisation in the main group was more rapid and in earlier periods than in the control group.

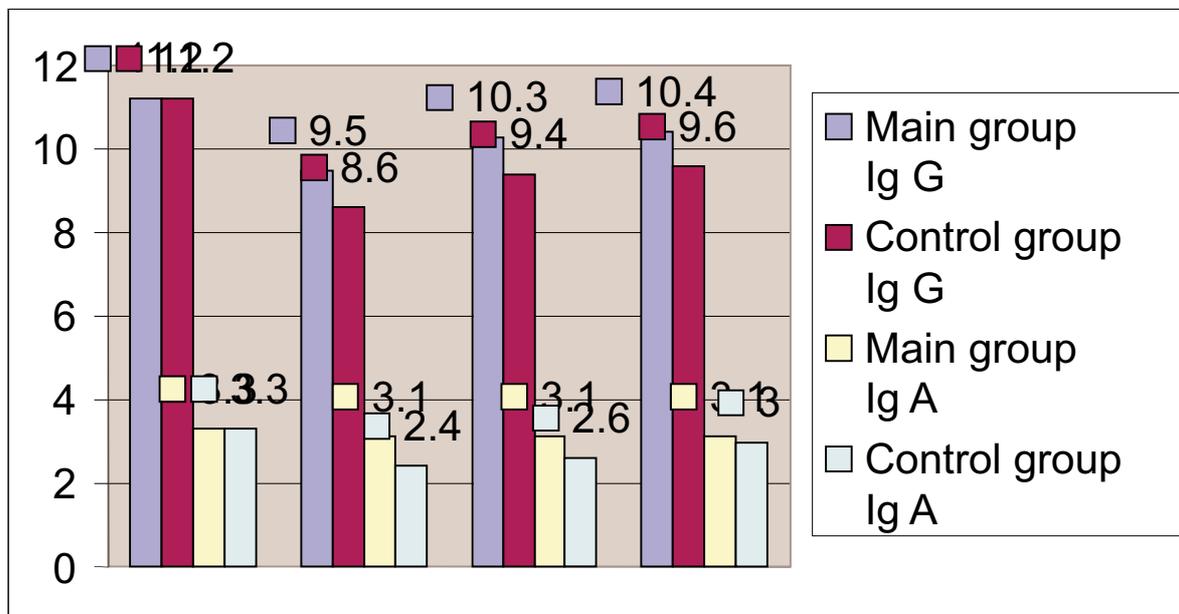


Figure 2.

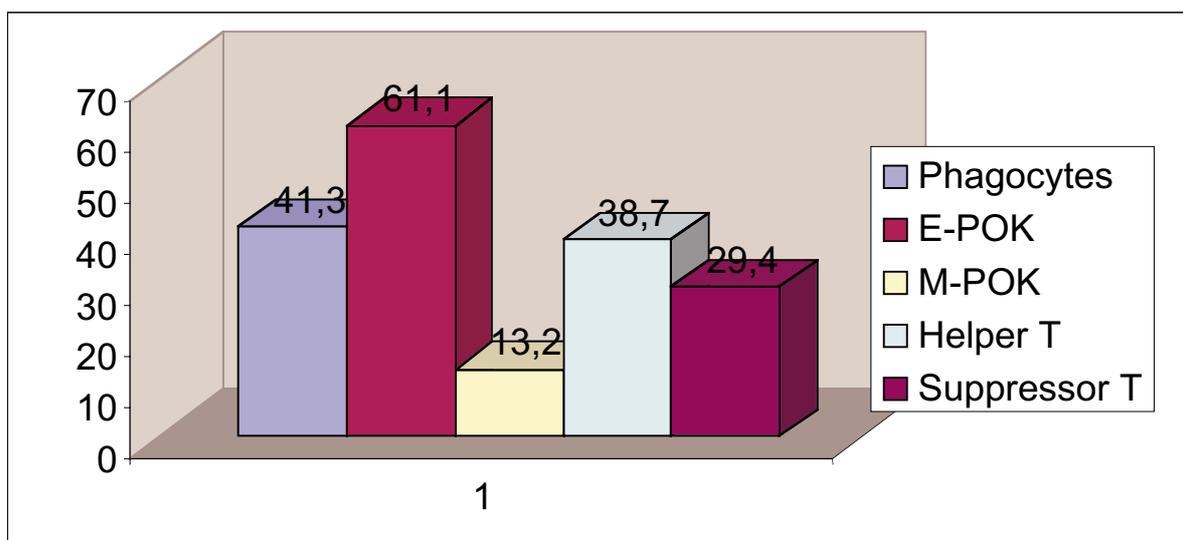
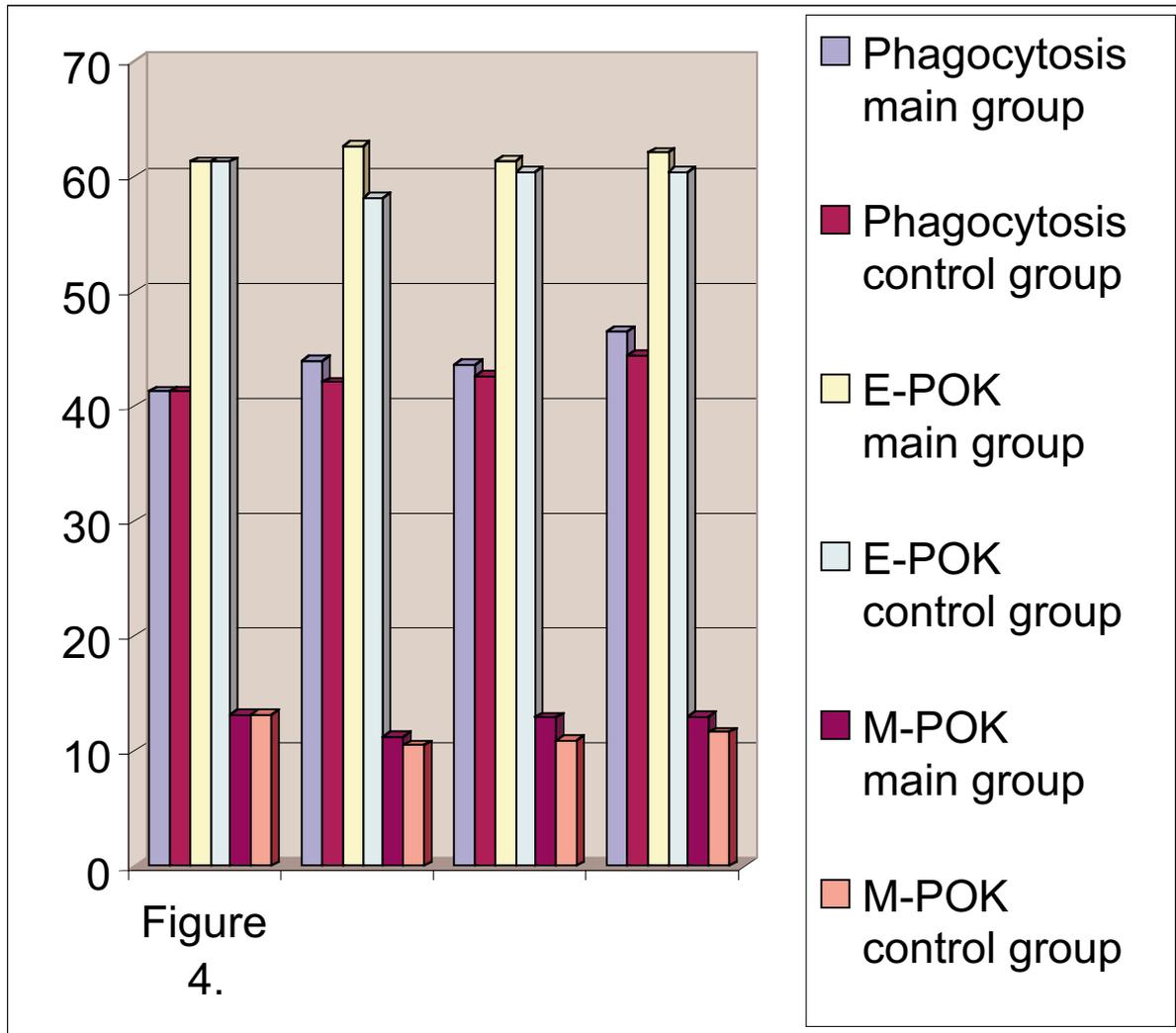


Figure 3.

Our research demonstrated that during treatment the low initial level of helper T-cells and suppressor T-cells decreases after the operation and then shows a tendency to normalisation.



Special interest was presented by the study of lymphocyte blastotransformation. The RBTL determined the capacity of the lymphocytes upon transformation into blasts. BTL is constantly observed in lymphoid tissues as a result of antigenic stimulation. It is the primary reaction of the lymphoid tissue and the initial step of the immune response. For this reason the RBTL allows the researcher to establish the disposition of the lymphocytes to immune response and to determine the

disposition of the lymphocytes to proliferation. In our patients of all groups, at the beginning of treatment the index in question varied between 35% and 43%. During treatment reliable changes were not detected.

In this way it is possible to state that the use of Viusid in integrated treatment positively influences the stabilisation process of the level of immunoglobulins A and G. No influence was detected on the variations in the concentration in the blood of IgM.

Considering that immunoglobulins are the basis of the immune response of the organism and that, according to the very graphic expression of V. I. Struchkov, "the immune response begins with the immunoglobulins and ends with them", it is reasonable to affirm that the use of Viusid in the preparation previous to the operation supplies the immune response with new possibilities.

The phagocytosis indices point to the state of the anti-infection resistance of the organism. The increase in the degree of phagocytosis allows the researcher to reach the conclusion regarding the increase in resistance and constitutes a favourable prognosis factor .

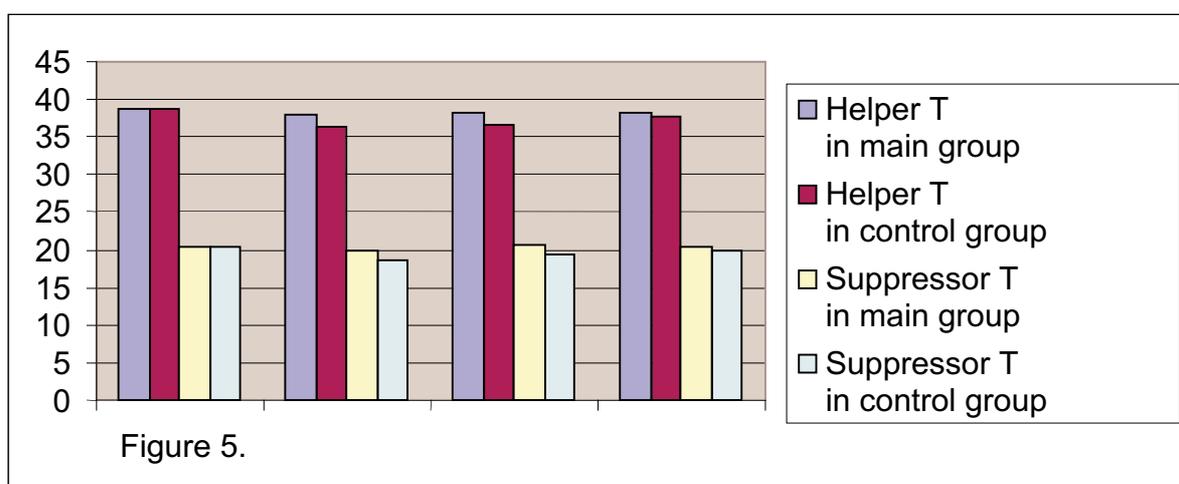
The alterations to the immune response system in patients after surgical operations also affect the T and B lymphocyte systems and their populations, as well as their functional state.

In this way, based on the study of the previously listed indices of the cellular link of the immunological protection of the organism, it is possible to state that during treatment the said indices have a tendency to stabilisation, becoming fully normalised in a series of cases. The dynamics of the behaviour of the said indices are correlated with the preoperational preparation. The most positive correlation when studying the levels of E-POK and M-POK is observed in cases where Viusid was used in the treatment.

According to the opinion of a series of investigators, the exclusive study of the general populations of T and B lymphocytes provides a degree of information

which is limited in cases of both local and generalised infections. Much more information is provided by the study of the different sub-populations of lymphocytes, especially the helper T and the suppressor T, as well as the capacity of lymphocytes to transform into blasts.

In this way it is possible to classify the state of immunological reactivity of the organism of patients who have undergone relatively clean surgical operations, according to the method of pre-operational preparation.



We have detected that the use of Viusid has a positive influence on the normalisation process of the immune protection system of the organism. When using Viusid in all the indices studied a faster and more complete normalisation of the immune status was detected.

The administration of therapy with antibiotics was less efficient, since it did not lead to the express normalisation of the indices of the immune protection level of the organism.

3. Dynamics of the lipid peroxidation system

One of the most profound and until now little studied metabolic processes is the

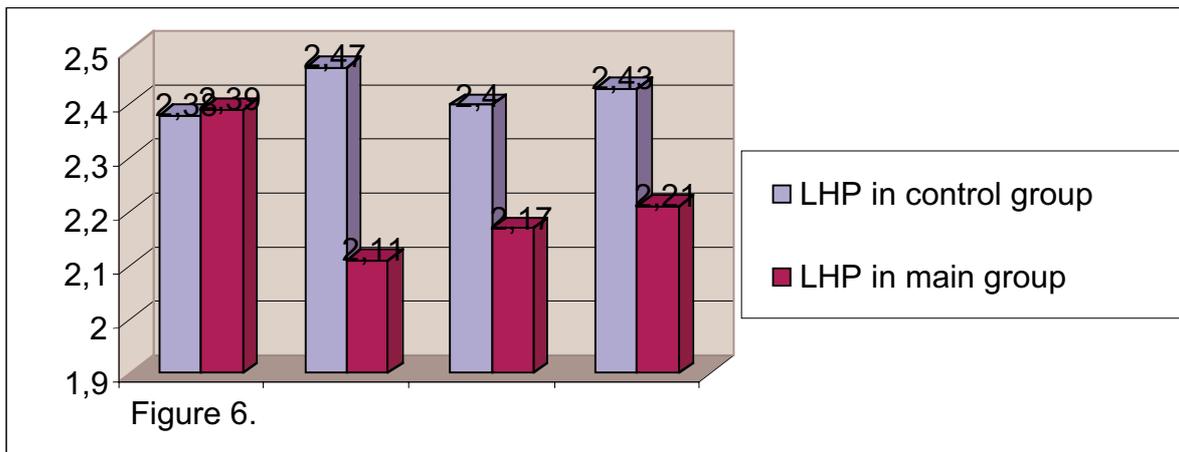
system of lipid peroxidation. It has already been demonstrated that the peroxidation system is directly related to the kinetic of accumulation of symptoms and the seriousness of the pathological process. This relationship mainly arises due to the toxic products of the LP acting on the cellular membranes. Within the physiological processes, LP plays an important role in the regulation of the permeability of the cellular membranes and the stability of their lipoproteic complex. Related to LP are the speed of cellular division, the state of oxidative phosphorylation, the activity of a series of ferments, and progesterone, prostaglandin and thromboxin synthesis. LP defines one of the primary mechanisms of action on alien cells and constitutes an important factor of phagocytosis.

An excessive concentration in the organism of LP products leads to the development of lipid peroxidation syndrome which includes a series of pathogenic components: the deterioration of the lipids of the membrane, of lipoproteins and proteins, the intumescence of the destruction of mitochondria and lysosomes, the deactivation of ferments and the alteration of cellular division and phagocytosis.

The level of lipid hydroperoxides (LHP) bears a direct relationship with the alterations to the metabolism at cellular level caused by the formation of LP products with their subsequent expulsion to the surrounding environment. At this stage of LP its products, influencing the cellular metabolic processes, will surely obstruct the stability of the cellular immunity mechanism. From our point of view, this is the circumstance that explains the conjectures of some investigators regarding the tense state of the phagocyte defence mechanisms in cases of destabilisation of LP.

Thus, based on the study of the behaviour of the indices of lipid hydroperoxides in the plasma, it is possible to evaluate the effectiveness of the methods of treatment from the point of view of the stabilisation of the LP processes.

The initial state of lipid hydroperoxides (LHP) was reviewed in the two groups of patients (figure 6).



After the operation, the behaviour of LHP in the two groups was different.

In the control group the level of LHP invariably rose until it subsequently became stabilised at below normal levels. In the main group a proven decrease of LHP products took place, which also underwent subsequent stabilisation. This process can be explained by the fact that the patients in the main group had received an antioxidant preparation prior to the operation. Thus, based on the data obtained and generalising them, it can be considered that the stabilisation of LP is more complete and occurs in shorter periods when using the preparation Viusid in the pre-operational preparation, as part of the set of curative activities.

4. Clinical indicators of the evolution of the process and complications

For the comparative evaluation of the treatment methods we have registered the values of the clinical indicators, via which it was possible to judge the evolution of the process and of its complications (tables 6 and 7).

Table 6. Dynamics of clinical indicators

Clinical indicator	Group and value of indicator	
	Main group	Control group
Normalisation of body temperature	3.2+0.3	3.6+0.4

Improvement of general condition	3.6+0.4	4.3+0.4
Pain relief	3.6+0.5	4.0+0.3
Reduction of oedema of tissues	4.4+0.6	5.0+0.5
Number of days	8.4	10.2

When registering the normalisation of the patients' body temperature, no significant difference was confirmed between the groups ($P>0.05$). Therefore, the treatment methods did not influence the normalisation time for body temperature.

For all other clinical indicators there was a real differentiation according to the group. The improvement of general condition, pain relief and the decrease in oedema of tissues in the main group certainly took place in shorter periods than in the control group ($P<0.05$).

Perhaps the most objective indicator is the duration of treatment in hospital. The patients in the main group stayed in hospital for fewer days.

In 38 patients different complications have been detected, the structure of which is presented in table 7.

Table 7. Post-operational complications

Type of complication	Group and quantity	
	Main group	Control group
Cystitis, urethritis	2	4
Phlebitis	2	4
Pneumonia	2	3
Infiltration	2	2
Haematoma of the wound	2	2
Serum leakage from the wound	2	2
Suppuration of the wound	-	2
Tracheobronchitis	1	1
Allergic reactions	-	1

Thromboembolism	-	1
Inconsistency of the sutures	-	1
Peritonitis	-	1
Eversionation	-	1
Total:	13	25

The number of complications in the groups was not distributed in a uniform manner, which became evident when calculating the percentage of complications of each group.

Therefore, it can be considered that the specific registered weight of the complications depends on the pre-operational preparation and diminishes considerably when using immunotherapy and antioxidant therapy.

- _____ // _____. II _____ - _____. _____
 _____, 1999; 28-9.
5. I.A.Bezruk. Infección intrahospitalaria en un centro quirúrgico (premisas inmunológicas e inmunoprofilaxis: problemas de diagnóstico, clínica, tratamiento y profilaxis) // Autoepítome de la tesis doctoral en medicina. Almá-Atá, 1991; 23 p.
- _____ : _____
 (_____ : _____
 _____, _____, _____) // _____, _____, _____, _____
 _____ - _____, 1991; 23 _.
6. V.D.Beliakov, A.P.Kolesov, P.B.Ostroúmov y otros. Infección hospitalaria. - Leningrado: Medicina. - 1976. - 232 p.
- _____ : _____
 _____ - 1976. - 232 _.
7. B.S.Briskin. Acción colateral de antibióticos en la clínica quirúrgica // Autoepítome de la tesis doctoral en medicina. Moscú, 1959; 21.
- _____ //
 _____, 1959; 21.
8. B.S.Briskin, Z.I.Savchenko, N.N.Khachatryan. Mecanismos de defensa y adaptación en casos de peritonitis y posibilidades de corrección farmacológica de sus alteraciones // Materiales del I Congreso internacional de cirujanos de Moscú. Moscú, 1995; 80-1.
- _____ // _____
 I _____, 1995; 80-1.
9. O.V.Evstifeeva. Regulación de la inmunidad mediante glucocorticoides y su papel en el tratamiento de peritonitis // Autoepítome de la tesis doctoral en medicina. Moscú, 1996; 25.
- _____ // _____, 1996; 25.
- 10.E.G.Brusina. Evolución del proceso epidémico de las infecciones hospitalarias

sépticas purulentas en la cirugía. Resumen de 20 años // Tesis del informe. II Conferencia científica práctica de Rusia con la participación internacional. Moscú, 1999; 47-8

_____ _____
_____ 20 // ____ . ____ . II _____ .
_____ _____ , 1999; 47-8

11. I.F. Vilenskaya, P.E. Sheprinskiy., A.N. Osipova y otros. Particularidades de las complicaciones post-operatorias en un centro quirúrgico // Tesis del informe. II Conferencia científica práctica de Rusia con la participación internacional. Moscú, 1999; 51-2.

_____ _____ _____
_____ _____ // ____ . ____ . II _____ .
_____ _____ , 1999; 51-2.

12. O.A. Vitkova, A.G. Shatashvili. Control epidemiológico de las infecciones intrahospitalarias // Tesis del informe. II Conferencia científica práctica de Rusia con la participación internacional. Moscú, 1999; 54-5.

_____ _____ _____
_____ _____ // ____ . ____ . II _____ .
_____ _____ , 1999; 54-5.

13. N.I. Vladimirov, P.S. Oparin. Infecciones sépticas purulentas en un centro quirúrgico // Tesis del informe. II Conferencia científica práctica de Rusia con la participación internacional. Moscú, 1999; 55-6.

_____ _____ _____
_____ _____ // ____ . ____ . II _____ .
_____ _____ , 1999; 55-6.

14. Infecciones intrahospitalarias: Trad. de inglés/ Bajo redacción de R.P. Ventsel. - Moscú: Medicina. - 1990. - 656 p.

_____ : ____ . ____ . / _____
_____ - 1990. - 656 p.

15. E.P. Volynchik, O.S. Belorusov, V.I. Sorokina y otros. Problema de la infección

intrahospitalaria en los enfermos con trasplante de riñón // Tesis del informe. II Conferencia científica práctica de Rusia con la participación internacional. Moscú, 1999; 58-9

_____ // _____. II _____, 1999; 58-9

16. R.A.Galkin, V.V.Pavlov, A.A.Bykov y otros. Monitoreo microbiológico en el control epidemiológico de las infecciones intrahospitalarias // Tesis del informe. II Conferencia científica práctica de Rusia con la participación internacional. Moscú, 1999; 62-3.

_____ // _____. II _____, 1999; 62-3.

17. L.S.Gladkova, Yu.I.Tiurnikov, A.V.Skorobulatov. Problema del registro de la sepsis nosocomial // Tesis del informe. II Conferencia científica práctica de Rusia con la participación internacional. Moscú, 1999; 65-6.

_____ // _____. II _____, 1999; 65-6.

18. F.S.Glumcher, A.V.Makarov, S.A.Dubrov (2003) Profilaxis y tratamiento de la neumonía post-operatoria. Cirugía clínica, 4-5: 15-16.

_____ (2003) _____, 4-5: 15-16.

19. V.K.Gostishchev. Medios y posibilidades de la profilaxis de las complicaciones infecciosas en la cirugía // Recomendaciones metodológicas: Enfoques racionales y profilaxis de las complicaciones infecciosas en la cirugía. Moscú, 1997; 2-11.

_____ // _____. _____, 1997; 2-11.

20. Yu.M.Grinzand, V.I.Melnikova, A.Yu.Vasilenko. Inmunomodulación con factores

físicos en la profilaxis de las infecciones post-operatorias // Tesis del informe. II Conferencia científica práctica de Rusia con la participación internacional. Moscú, 1999; 75-6.

_____ // _____ II _____, 1999; 75-6.

21. G.N.Gubina. Complicaciones intrahospitalarias inflamatorias purulentas tras operaciones radicales en casos de cáncer de estómago // Autoepítome de la tesis doctoral en medicina. Moscú, 1979; 20 p.

_____ // _____, 1979; 20 p.

22. E.I.Gudkova, A.A.Adarchenko, O.P.Sobeshchuk y otros. Dinámica del estructura etiológico de la infección hospitalaria por herida en los centros quirúrgicos de quemados de la República de Belarús // Tesis del informe. II Conferencia científica práctica de Rusia con la participación internacional. Moscú, 1999; 78-9.

_____ // _____ II _____, 1999; 78-9.

23. N.V.Dmitrieva, I.N.Petukhova, A.Z.Smolyanskiy. Estructura etiológico y la sensibilidad hacia los antibióticos de los agentes principales de las complicaciones infecciosas en la clínica oncológica // Moscú, 1999; 65.

_____ // _____, 1999; 65.

24. V.I.Dontsov, T.A.Popova, N.M.Bashkova, A.I.Yurovskaya. Infecciones intrahospitalarias en la ciudad de Ekaterimburgo en los años 90 del siglo XX // Tesis del informe. II Conferencia científica práctica de Rusia con la participación internacional. Moscú, 1999; 87-8.

- _____ 90- __. XX ____ // __. __. II ____.
_____, 1999; 87-8.
25. V.V.Zhebrovskiy, G.T.Menshikova, V.G.Medishchev. Complicaciones precoces por la herida operatoria tras la apendectomía por las formas destructivas de apendicitis // Fisiología y patología de los órganos de la digestión. Simferopol, 1978; 50-94.
- _____ // _____, 1978; 50-94.
26. V.V.Zhebrovskiy, K.D.Toskin. Problema de las complicaciones post-operatorias en la cirugía abdominal // Complicaciones post-operatorias y los peligros en la cirugía abdominal. Moscú: Medicina, 1990; 5-181.
- _____ // _____, 1990; 5-181.
27. G.A.Ivanov, V.F.Lebedev, O.P.Sidelnikov, T.N.Suborova. Frecuencia de la secreción de los agentes de complicaciones infecciosas de las heridas de distinta origen // Problemas actuales de la infección en la cirugía. Moscú, 1999; 155-7
- _____ // _____, 1999; 155-7
28. V.M.Kliuzhev, V.G.Akimkin. Infecciones intrahospitalarias y el papel del personal médico en la profilaxis de éstas // Asistencia médica. - 1997. - N 4.- P. 27-31.
- _____ // _____. - 1997. - N 4.- P. 27-31.
29. V.M.Kliuzhev, V.G.Akimkin. Aspectos epidemiológicos y de organización en la profilaxis de las infecciones intrahospitalarias // Revista médica militar. - 1996. - N 8. - P.23-28.

_____ // _____ - 1996. - N 8.
- 23-28.

30. V.I.Knysh, V.S.Ananyev. Complicaciones post-operatorias en los enfermos de cáncer de colon // Problemas de oncología. 1985; 5: 42-7.

_____ // _____. 1985; 5: 42-7.

- 31 T.K.Korneva, Yu.A.Shelygin, E.A.Konovich, S.V.Nezhikova, I.A.Liagina. Etiología de las infecciones intrahospitalarias en la clínica proctológica // Tesis del informe. II Conferencia científica práctica de Rusia con la participación internacional. Moscú, 1999; 122-3.

_____ // _____. II
_____, 1999; 122-3.

32. M.I.Kuzin, T.M.Kostiuchenok. Heridas y la infección por herida. Moscú: Medicina, 1981; 678.

_____, 1981; 678.

33. M.I.Kuzin, T.M.Kostiuchenok, S.Ya.Kuleshova. Infección anaeróbica no clostridial en la cirugía supurativa // Heridas y la infección por herida. - I Conferencia nacional – Tesis del informe. Moscú, 1986; 201-2.

_____ // _____ - I _____ -
_____, 1986; 201-2.

34. V.G.Kulaevskaya. Inconsistencia de suturas de la esofagogastroanastomosis y la esofagoeterostomía // Autoepítome de la tesis doctoral en medicina. Moscú, 1980; 20 p.

_____ // _____, 1980; 20 p.

35. D. Loshonci. Infecciones intrahospitalarias. - Moscú: Medicina. - 1978. - 452 p.

_____ - 1978. - 452 p.

36. C.Marshall. Infecciones quirúrgicas y complicaciones infecciosas tras quemaduras // Infecciones intrahospitalarias / Bajo redacción de R.P.Ventsil. _oscú: Medicina, 1990; 259-338.

// _____ / _____, 1990; 259-338.

37. O.T.Milonov, K.D.Toskin, V.V.Zhebrovskiy. Complicaciones post-operatorias y peligros en la cirugía abdominal. _oscú: Medicina, 1990; 560.

_____, 1990; 560.

38. V.Yu.Moroz, R.P.Terekhova, V.V.Galkin y otros. Infección hospitalaria en la clínica quirúrgica // Infección intrahospitalaria – problemas epidemiológicos. - Tesis del informe. II Conferencia científica práctica de Rusia con la participación internacional. _oscú, 1999; 161-2

_____, 1999; 161-2

39. S.V.Oleynik, N.A.Baúlin. Sobre el análisis epidemiológico de la patología purulenta post-operatoria en los centros quirúrgicos // Revista de microbiología, epidemiología e inmunología. 1992; 4: 26-8.

_____. 1992; 4: 26-8.

40. V.I. Pokrovskiy. Preámbulo al manual “Profilaxis de las infecciones intrahospitalarias”. _oscú, 1993; 3.

_____, 1993; 3.

41. T.A.Pertseva, R.A.Bontsevich (2003) Particularidades del diagnóstico etiológico y tratamiento de la neumonía nosocomial. _____, 4: 31-34.

_____. (2003)

48. T.D.Savchuk. Peritonitis purulenta. _oscú: Medicina, 1979; 188 p.
 _____, 1979; 188 _.
49. V.T.Smolovskiy. Estudio de la difusión de las enfermedades hospitalarias sépticas purulentas en las instituciones curativo-profilácticas tanto urbanas como rurales de distintas regiones del país // Infecciones hospitalarias y la resistencia de microorganismos a la medicina. – Recopilatorio de obras científicas, _oscú, 1992; 7-10.
 _____ // _____
 _____, 1992; 7-10.
50. Guía del epidemiólogo de un centro hospitalario. _oscú, 1999; 335.
 _____, 1999; 335.
51. V.N.Stepanov. Profilaxis perioperatoria de las infecciones. Posibilidad de introducción de bactericidas una sola vez. // Nueva revista médica. 1998; 2: 23-4.
 _____ // _____
 1998; 2: 23-4.
52. K.D.Toskin, V.V.Zhebrovskiy, F.G.Bereznitskiy. Abscesos intra-abdominales y extra-abdominales post-operatorios // Complicaciones post-operatorias y peligros en la cirugía abdominal. _oscú: Medicina, 1990; 84-133.
 _____ // _____
 _____, 1990; 84-133.
53. N.N.Filatov, I.A.Khrapunova, S.I.Matveev. Problema de las infecciones sépticas purulentas en los centros hospitalarios quirúrgicos // Tesis del informe. II Conferencia científica práctica de Rusia con la participación internacional. _oscú, 1999; 254-5.

- _____ // _____. II _____.
_____, 1999; 254-5.
54. D. Shevola, N. V. Dmitrieva. Profilaxis con antibióticos en la medicina práctica. Moscú, 1998; 128 p.
- _____, 1998; 128 p.
55. V. P. Yakovlev, S. V. Yakovlev. Terapia antibacteriana moderna en tablas // Concilio. 1999; 1(1): 18-36.
- _____, 1999; 1(1): 18-36.
56. R. Kh. Yafaev, L. P. Zueva. Epidemiología de la infección intrahospitalaria. - Leningrado: Medicina. - 1989. - 168 p. V. V. Shkarin, N. A. Davydova, O. V. Kovalishina y otros. "Particularidades epidemiológicas de la infección séptica purulenta en un centro hospitalario de cardiocirugía", Revista de microbiología, epidemiología e inmunología. 1998; 43-7
- _____, 1989. - 168 p. V. V. Shkarin, N. A. Davydova, O. V. Kovalishina y otros. "Particularidades epidemiológicas de la infección séptica purulenta en un centro hospitalario de cardiocirugía", Revista de microbiología, epidemiología e inmunología. 1998; 43-7
57. G. A. J. Eyeliff, E. A. Burganskaya, J. M. Weber y otros. Fundamentos del control de infección: Manual práctico para médicos (1997) – Moscú.
- _____, (1997) - ____.
58. Brachman P. S. Nosocomial infection control: An overview. - Rev. infect. Pis., 1981. - Vol. 3. - N 4. - P. 640-648.
59. Brachman P. S., Dan B. B., Haley R. W. et al. Nosocomial surgical infections: Incidence and cost // Surg clin North Am. 1980; 60: 1
60. Cruse P. I. E., Foord R. The epidemiology of wound infection: a ten-year prospective study of 62939 wounds // Surg clin North Am. 1980; 60: 27-40.
61. Dixon R. Effect of infections on hospital care. - Ann. intern. Med., 1978. - Vol.

89. - P.749-753.
62. Haley RW. (1986) Managing infection control for cost-effectiveness. Chicago, American Hospital Association.
63. Vincent JL, Bichari DJ, Suter PM, et al. (1995) The prevalence of nosocomial infection in intensive care units in Europe. *JAMA*, 274: 639-644.
64. Fagon J-Y, Chastre J, Domart Y, et al. (1999) Nosocomial pneumonia in patients receiving continuous mechanical ventilation. *Amer J resp Dis*, 139: 877-884.
65. Leu HS, Kaiser DL, Mori M, Woolson RF, Wenzel RP (1989) Hospital-acquired pneumonia: attributable mortality and morbidity. *Am J Epidemiol*, 129: 1258-1267.
66. Maki DG. (1989) Risk factors for nosocomial infection in intensive care. *Arch Intern Med*, 149: 30-35.
67. Leroy O, Meybeck A, D'Escrivan T, et al. (2003) Impact of adequacy of initial antimicrobial therapy on the prognosis of patients with ventilator-associated pneumonia. *Intensive Care Med*, Sep 12 [Epub ahead of print]).
68. Paterson DL, Rice LB. (2003) Empirical antibiotic choice for the seriously ill patient: are minimization of selection of resistant organisms and maximization of individual outcome mutually exclusive? *Clin Infect Dis*, 36(8): 1006-1012.
69. Kane SL, Weber RJ, Dasta JF. (2003) The impact of critical care pharmacists on enhancing patient outcomes. *Intensive Care Med*, 29(5): 691-698.
70. Levi M, Schultz MJ, Rijneveld AW, van der Poll T. (2003) Bronchoalveolar coagulation and fibrinolysis in endotoxemia and pneumonia. *Crit Care Med*, 31(4 Suppl): S238-42.
71. Stone H.H., Haney B.B., Koeb H.D. Prophylactic and preventive antibiotic therapy. Timing, duration and economics // *Ann Surg*. 1979; 189: 691-9.
72. Wellinger R.C., Mc Langhlin S. Unique epidemiology of nosocomial infections in a children's hospital // *Amer J Dis Child*.1984; 138: 131-5.
73. Wenzel R.P. Surveillance and reporting of hospital-acquired infections // *Handbook of Hospital Aquired infections* - Boca Raton, F.L. Cre Press. 1981; 44.
74. Niederhauser U., Vogt M., Genoni M. et al. Cardiac surgery in a high risk group of patients - is prolonged postoperative antibiotic prophylaxys effective? *J Therac Cardiovasc Surg*. 1997; 114: 162.

75. Rebollo M., Bernal G., Lorca J. et al. Nosocomial infections in patients having cardiovascular operations - a multivariate analysis of risk factors. J Thorac Cardiovasc Surg. 1996; 112: 908-13.
76. Soyer R., Bessou J., Bouhart F. et al. Surgical treatment of infected composite graft after replacement of ascending aorta. Ann Thorac Surg. 1994; 58: 425-8.

Contact details

Autor:

Rauf Kuliev (hijo de Alefser) – doctor en ciencias de medicina, profesor, jefe de cirugía del Hospital central de los trabajadores de petróleo de la Compañía estatal petrolera de Azerbaiján.

Dirección para correspondencia: Hospital central de los trabajadores de petróleo, Dpto. de cirugía. C/ul. Yu.Safarova, 17, 370025, ciudad de Bakú, República de Azerbaiján

370025, _____, _____, _____, _____, _____ **17,** _____
_____, _____.

Tel. Oficina (+994 50) 314 7099

Móvil (+994 12) 4902944

E-mail rquliyev@lycos.com