

AZERBAIJAN REPUBLIC

in the right of the manuscript

A B S T R A C T

of the presented dissertation
to obtain a doctorate scientific degree in medical sciences

**CHANGES OF SOME IMMUNE INDICATORS, MEDIATORS
AND LITHIUM MICRONUTRIENT LEVELS AND THEIR
CORRECTION DURING ALLERGIC REACTIONS**

Specialty: 3243.01 - Pathological physiology

The field of science: Medicine

Applicant: **Tarana Rzagulu Aliyeva**

Baku – 2024

The dissertation work was performed at the Department of Pathological Physiology of Azerbaijan Medical University.

Official opponents:

Doctor of Medical Sciences, Professor,
Vladimir Ivanovich Karandashov

Professor dr. **Muhammet Chalik**

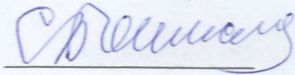
Professor dr. **Sare Sibal**

Doctor of Medical Sciences,
Rashad Farhad Sholan

Dissertation Council BED 4.20 of the Supreme Attestation Commission under the President of the Republic of Azerbaijan operating at Azerbaijan Medical University

Chairman of the Dissertation Council:

Corresponding member of ANAS,
Honored Scientist, Doctor of
Medical Sciences, Professor
Sudeif Bashir Imamverdiyev



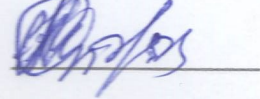
Scientific Secretary of the Dissertation Council:

Doctor of Medical Sciences, Professor
Habil Kamil Muradov



Chairman of the scientific seminar:

Doctor of Medical Sciences
Fazil Ikram Aliyev



The actuality of the theme. The high level and ever-increasing development of allergic diseases has become a global problem of the present period. According to the literature, 20% of the world's population suffers from allergic diseases. According to the World Health Organization (WHO), one in every three people in the world has an allergic processes.

Currently, allergies are one of the most common diseases after cardiovascular and tumor diseases. Widespread use of therapeutic serums, various drugs, increases the number of drug allergies. Allergic reactions are also an important factor in the pathogenesis of collagenosis. The allergic component plays an important role in the development of hypertension, atherosclerosis, certain types of arrhythmias, diabetes, and radiation diseases. It is known that autoimmune processes develop in the necrosis site during myocardial infarction. According to some researchers, the blood circulation system diseases and intake of beta-adrenoblockers increase the risk of complications of anaphylaxis.

There is information of some trace elements, in particular the increase and decrease of the amount of lithium during allergic reactions. In the studies which conducted by S.J.Aliyev and J.H.Tagdisi at the Department of Pathological Physiology, Azerbaijan Medical University have revealed that lithium micronutrients have hyposensitizing and antiallergic effects [55].

Although the immune system changes in the developing mechanism of allergic reactions have been studied in detail, these changes have not been investigated comparatively in the case of anaphylactic shock, immune complex, Arthus or Overi phenomenon of atopic reactions. On the other hand, the study of the role of lithium micronutrients in changes in blood and lymphatic immune indicators and the presence of allergic mediators, and the correction of these changes remain a relatively controversial issue. One of the main problems in this case is the development of effective treatment methods that eliminate allergic pathology and immune dysfunction and the proper choice of antihistamines¹.

¹ Tagdisi D.G. The Role of Trace Elements in the Pathology of the Cardiovascular System/D.G. Tagdisi, S.D. Aliyev, I.G. Musaev [et al.]//Abstracts of Reports of the III Republican Conference "Trace Elements in Agriculture and Medicine," November 27-28, 1991, p.189.

The aim of the work. The aim of the work was the study of the role of lithium micronutrients during anaphylactic shock which is atopic reaction, Artyus of immune complexes and Overi phenomenon of skin-anaphylactic reaction the immune indicators in the blood and lymph (interleukins - IL-4 and IL-6, IgE, and IgG, circulating immune complexes-DIC, the tiration of the complement) in alterations of allergic mediators (serotonin and histamine) and the development of adequate correction methods.

Research objectives:

1. In animals that have developed appropriate experimental models of systemic and local allergic reactions (anaphylactic shock, Artyus and Overi phenomenon), during the stages of these reactions the comparative study of changes of the immune indicators (Interlekin-4, interleukin-6, immunoglobulin E, immunoglobulin G, circulating immune complexes, titration of the complement) in blood and lymph

2. In animals that have developed appropriate experimental models of systemic and local allergic reactions (anaphylactic shock, Artyus and Overi phenomenon), during the stages of these reactions the comparative study of the mediators' concentration (histamine and serotonin) in blood and lymph

3. In animals that have developed appropriate experimental models of systemic and local allergic reactions (anaphylactic shock, Artyus and Overi phenomenon), during the stages of these reactions the determination of the amount of the lithium micronutrient

4. In animals that have developed appropriate experimental models of anaphylactic shock, Artyus and Overi phenomenon, study of some immune indicators in blood and lymph before and after sensibilization as well as in the sensibilization and desensibilization stages of anaphylactic shock, after injection of correctors (lithium-oxybutyrate and cetirizine)

5. In animals that have developed appropriate experimental models of anaphylactic shock, Artyus and Overi phenomenon, study of histamine and serotonin in blood and lymph before and after sensibilization as well as in the sensibilization and desensibilization

stages of anaphylactic shock, after injection of correctors (lithium-oxybutyrate and cetirizine)

6. In animals that have developed appropriate experimental models of anaphylactic shock, Artyus and Overi phenomenon, study of changes in the amount of lithium micronutrient in the blood and lymph, within 24 and 48 hours after the injection of the correction lithium-oxybutyrate

Scientific novelty of the research

1. For the first time, in animals that have developed appropriate experimental models of systemic and local allergic reactions (anaphylactic shock, Artyus and Overi phenomenon), it has done the comparative study of changes of the immune indicators (Interlekin-4, interleukin-6, immunoglobulin E, immunoglobulin G, circulating immune complexes, titration of the complement) in blood and lymph

2. In the blood and lymph of the animals that have developed appropriate experimental models of anaphylactic shock, Artyus and Overi phenomenon, it has determined the concentration of the allergic mediators: histamine and serotonin

3. In the blood and lymph of the animals that have developed appropriate experimental models of anaphylactic shock, Artyus and Overi phenomenon, it has determined the amount of the lithium micronutrient

4. In the blood and lymph of the animals that have developed appropriate experimental models of anaphylactic shock, Artyus and Overi phenomenon, it has determined the role of the lithium micronutrient during the changes of the immune indicators (Interlekin-4, interleukin-6, immunoglobulin E, immunoglobulin G, circulating immune complexes, titration of the complement)

5. In the blood and lymph of the animals that have developed appropriate experimental models of anaphylactic shock, Artyus and Overi phenomenon, it has studied the effect of the lithium micronutrient to the secretion of the allergic mediators - histamine and serotonin

6. In the blood and lymph of the animals that have developed appropriate experimental models of anaphylactic shock, Artyus and Overi phenomenon, for the correction of the changes of the immune indicators (Interlekin-4, interleukin-6, immunoglobulin E,

immunoglobulin G, circulating immune complexes, titration of the complement), and allergic mediators was used cetirizine as an antihistamine drug, and the results were investigated.

7. It has been established that small doses of lithium micronutrients and their compounds have anti-allergic effects.

8. During the appropriate experimental models of anaphylactic shock, Artyus and Overi phenomenon, it has determined the lymph flow rate (LFR)

Main provisions for defense:

1. Although the level of interleukin-4 increased in all three allergic reactions, this rise was more prominent during anaphylactic shock.

2. Changes of the interleukin-6 level were more prominent during the Artyus phenomenon.

3. Although there was an increase in serotonin and histamine levels in all 3 allergic reactions, this rise was more prominent during anaphylactic shock.

4. The concentration of the circulating immune complexes (CIC) has increased in all 3 allergic reactions and decreased the titration of the complement. In the anaphylactic shock phase, the titration of the complement have not been identified.

5. The levels of IL-4 and IL-6 have reduced by the effect of lithium-oxybutyrate in all 3 allergic reactions.

6. The levels of IgE and IgG have reduced by the effect of lithium-oxybutyrate in all 3 allergic reactions.

7. The concentration of serotonin and histamine has reduced by the effect of lithium-oxybutyrate in all 3 allergic reactions.

8. During all 3 allergic reactions, the levels of the interleukin IL-4 and IL-6, immunoglobulin E and G, serotonin and histamine, and circulating immune complexes (CIC) have reduced and the titration of the complement have increased by the effect of certizine which include to the antihistamine drugs.

Materials and methods of research. The experiments were conducted on 7 series of rabbits which belong to «Shinshilla» genus weighing 2.0-3.0 kg, and three models of allergic reaction, such as anaphylactic shock and the phenomenon of Artyus and Overi (Table 1).

In these animals, immune indicators: levels of IL-4 and IL-6, "E" and "G" immunoglobulins, CIC concentration and titration of the complement, histamine and serotonin from the mediators, and lithium from the micronutrients were investigated. Lithium-oxybutyrate 10ml / kg, and cetirizine 2.5mg / kg , were used as a correction agent.

The division of experimental animals into groups dependent on the purpose of the research

In the experiment was sensitized by injecting 0.1ml of horse serum under the skin of the rabbit to create anaphylactic shock, and the decisive dose was injected into the heart cavity at 1ml on the 21st day of sensibilization.

In order to create the Artyus phenomenon in the experiment, the hair of a certain area in the rabbit's scapula area was cleared, and 1 ml of blood serum was injected under his skin once in every five days for 25 days. The first and second injections of the horse serum were virtually absorbed without trace, and after the 3rd injection, the area in which the serum was administered showed swelling and hyperemia. After the fifth injection, necrosis has already developed in the area, indicating the occurring of the Artyus phenomenon.

A decisive dose of horse serum was injected under the skin of a pre-sensibilization animal to obtain the Overi phenomenon, and Evans's forte was injected into the ear vein. In this case the injection area was painted blue.

Methods of obtaining blood and lymph. The blood was obtained from the peripheral vein of the rabbit's ear, and the lymph from the breast lymph drainage by A. Kornienko (1977) drainage methods in modification by M.Kh.Aliyev and V.G Mammadov [1989] [53]. The rate of the lymph flow from the lymph node of the breast is determined based on the amount of lymph per kilogram of rabbits collected in this node at a unit time².

Levels of interleukin-4 and interleukin-6 were determined by rigorous immunoenzyme analysis method in blood and lymph. Sandwich method - "IFA" is carried out on 96-well plates.

² Kornienko A.A., Kulikovskiy N.N., Sorokaty A.E., Catheterization of the thoracic duct in experiment/- Moscow: Topical issues of topographic anatomy and operative surgery. -1977. No. 1, - p. 22-26.

Monoclonal antibodies against cytokine molecular epitopes are immobilized on the inner surface of the wells. This research was carried out with the help of the German firm "IBL" test-system and a semi-automatic analyzer Stat-fax (USA).

The immunoferrment analysis method (IFA) was used to determine the levels of IGE and IgG. The determination of the immunoglobulins were performed with the help of the US firm «Farmingen» test systems set and a semi-automatic analyzer. **The levels of total IgE were carried on a sandwich method of two-stage immunoenzyme analysis method.**

Serotonin levels in blood and lymph was determined by Fujino et al. (2003) method of liquid chromatography . This method is based on deproteination with the help of saturated uranilacetate (Sartorius-, 045 m).

Determiration of histamine concentration was performed by fluorometric method. The basis of this method is the acquisition of 0.1% orthophthalate aldehyde fluorophore in methanol. The study was carried out with the help of a «Bian-130» fluorimeter device^{3,4,5}.

Determiration of lithium micronutrient concentration in blood and lymph

The determiration of lithium micronutrient in the blood and lymph was carried out by atomic absorption method. The method is based on the removal of proteins in the blood by 96% ethanol [255].

Determiration of the concentration of circulating immune complexes (CIC) and complement activity

The method for determining the concentration of CIC is based on the principle of the non-specific presipitation of the CIC in the polymerization buffer and then the testing of the samples ability of

³ Kudaeva O.T., Nenasheva E.V., Kozlov V.A. Determiration of immunoglobulins content in whole blood//Moscow: Immunology, -2005. T.26, No. 3, - p.189-191

⁴ Fujino K. Determiration of 5-hydroxyindoles and catechols by high-performance liquid chromatography with fluoescence detection following derivatization with benzylamine and 1,2-diphenylethylenediamine./ K. Fucino, T. Yoshitake, J. Kehr [et al.] // Journal Chromatography, - Philadelphia: Elsevier, - 2003. 1012 (2) - p.169-77.

⁵ Proshina L.Ya. Histamine and serotonin study in a single blood sample/-Moscow: Laboratory work, -1991. No. 1, -c. 90-93.

the emitting light from the spectrophotometer [75, 214]. The optical density of the solutions in the test glass was measured on a spectrophotometer at the Department of Biochemistry (Spekol, Germany) at wavelengths of 450 nm and expressed in conventional units (c.u).

The activity of the complement: The activity of the complement was determined by 50% hemolysis by the method of L.S. Reznikova (1967) [172]. The principle of the method is based on the immune hemolysis of erythrocytes in the presence of hemolysis and complement. The results are shown in hemolytic units (h.u.).

Monitoring and recording of the functions of the vital organs of experimental animals are measured using Arterial Pressure (AP) method. Silicone catheter containing 3.8% sodium-citrate solution is inserted into the femoral artery and attached to the «E-167» additional block of the «BMT-401» (Germany) biomonitor attached to the «Mingograph 34» (Switzerland-Germany) apparatus. We recorded the pneumogramma (PG) in the "Mingograph-34" apparatus via «W-401» (Germany) a breathing transformer attached to the nasal cavity^{6, 7, 8}.

Statistical processing of the research results was conducted using a non-parametric method - Wilcoxon (Manna-Whitney) criterion (U).

Results and Discussion. In the blood and lymph of the animals that have developed appropriate experimental models of anaphylactic shock, Artyus and Overi phenomenon, it has been studied the levels of IL-4 and IL-6, IgE and IgG, circulating immune complexes, complement, serotonin, histamine and lithium

⁶ Lehmann WD., Bahr U., Schulten H.R. Determination of lithium in microlitre amounts of human body fluids at therapeutic and normal levels by stable isotope dilution and field desorption mass spectrometry // - UK: John Wiley and Sonsinc: Biomedical Mass Spectrometry - 1978. 5 (9) - p. 536-539.

⁷ Grinevich Yu.A., Alferov A.N. Determination of immune complexes in the blood of cancer patients// - Moscow: Laboratory work, -1981. No. 8, -p.493-495.

⁸ Reznikova L.S. Complement and its significance in immunological reactions - Moscow: Medicine, -1967. -272p.

micronutrients, also correctors: lithium-oxybutyrate and cetirizine in animals that were injected before the sensibilization phase of allergic reactions, during sensibilization and after decisive phase, were studied in blood and lymph.

The changes of the levels of IL-4 and IL-6, IgE and IgG, circulating immune complexes, complement, serotonin, histamine and the concentration of the lithium micronutrients in the blood and lymph of the animals that have developed appropriate experimental models of anaphylactic shock, Artyus and Overi phenomenon

In the first control series of experiments, in the blood and lymph of 9 intact rabbits IL-4, IL-6, E and G-immunoglobulin levels, the concentration of CIC, titration of complement, the concentration of the histamine and cerotonin, and the level of the lithium micronutrients were determined. It has been found that the levels of investigated indicators in blood of the intact animals are higher than the corresponding indicators in lymph. It is clear from the literature that the lowest levels of immunoglobulins belong to IgE (which can be maximized in atopic-allergic reactions) and the results of our studies overlap with this data.

It was determined that A / T and respiratory activity did not change significantly during the sensibilization phase of anaphylactic shock. During the anaphylactic shock phase, the A / T fell sharply and the number of respiratory movements increased. Thus, AT decreased rapidly by 2.7 times, and TS increased by 2.0 times. In animals which were free from anaphylactic shock, AT was 1.4 times less than intact indicator, and TS was closer to intact indicator. During the desensibilization phase, both the A / T and the minutes number of the breath are closer to the norm.

Despite increasing levels of cytokines, immunoglobulins and allergic mediators, the levels of lithium micronutrients are decreasing in the course of allergic reactions. In the anaphylactic shock phase, this decrement is more sharply. Complement activity is also reduced in the dynamics of allergic reactions, and is generally not determined in the course of anaphylactic shock.

In the second control series of experiments, in the animals that have developed appropriate experimental models of anaphylactic shock, Artyus and Overi phenomenon, in the seventh days of the sensibilization IL-4, IL-6, E and G-immunoglobulin levels, the concentration of CIC, histamine and cerotonin, lithium micronutrients and the activity of the complement were determined. It has been found that the levels of investigated indicators in blood of the intact animals are higher than the corresponding indicators in lymph. It is clear from the literature that the lowest levels of immunoglobulins belong to IgE (which can be maximized in atopic-allergic reactions) and the results of our studies overlap with this data.

The results of the study show that although the changes of the immune and other indicators in blood and lymph are similar, the difference in quantitative changes is significant. Although levels of IL-4 and IL-6 synthesized by Th2-lymphocytes increased during the anaphylactic shock, the Arthyus and Overi phenomena, this rise was particularly high on the 21st day of sensibilization in the blood of the animals with anaphylactic shock. Thus, the level of IL-4 in the blood of 9 animals taken as a control group increased by 3.8 times ($p < 0.001$) than the intact indicator in the sensibilization phase of the anaphylactic shock (day 7), and by 11.9 times on the 14th day ($p < 0.001$). In the anaphylactic shock phase, the level of IL-4 was 31 times higher ($p < 0.001$) compared to the intact index. 30 minutes after shock, IL-4 levels were 30.0 times higher than the intact indicator, this is 1.6 times less than the shock period.

Level of IL-6 increased 3.0 times ($p < 0.001$) on the 7th day of the sensibilization period compared to intact indicator, and 6.2 times ($p < 0.001$) on the 14th day. At the shock stage, the level of IL-6 was 22.3 times ($p < 0.001$) higher than the intact indicator.

The results show that the level of IL-4 during anaphylactic shock increased more than IL-6, which is probably due to the accelerated IL-4 secretion by T2 helper during atopic reactions. The secretion of IL-4, in turn, accelerates IgE synthesis. During anaphylactic shock, it has been observed itching, coughing, waking, involuntary urinary and fecal excretion in the animals.

In the blood IgE levels increased 3.5 times compared to control group on day 7 of the sensibilization phase of the anaphylactic shock, reaching 35.6 ME/l ($p < 0.001$), and increased to 151.1 ME/l in the shock phase ($p < 0.001$). IgG levels increased up to 8 g / l ($p < 0.001$) during the sensibilization phase (day 7) and decreased up to 4.5 g / l in shock phase; these may be due to the reduction of IgM and IgG synthesis in B lymphocytes during atopic reactions and an increase in IgE synthesis. The concentration of the CIC during the shock phase increased up to 23 c.u., while the complement titration has not been identified because of a dramatic decrement.

As we know, atopic reactions develop with the occurring of antibodies in the blood against antigens that enter the organism and the re-entry antigen with these antibodies formed the antigen-antibody complex. These complexes are fixated on the mast cells, causing their degranulation and, consequently, secretion of allergic mediators such as histamine and serotonin. Histamine plays a key role in the development of allergic reactions and clinical symptoms. In addition, histamine and serotonin contribute to the acceleration of some immunoglobulins, especially IgG synthesis [48]. For this reason, we investigated histamine and serotonin levels in blood and lymph from allergic mediators in series IV of our study in 27 animals which created 3 different allergic reactions - anaphylactic shock, Artyus and Overi phenomenon (9 rabbits in each). At the same time, these indicators were determined at the sensibilization, the decisive and the desensibilization stages of the anaphylactic shock.

The results of the study show that the concentration of allergic mediators - serotonin and histamine increases in the blood and lymph in the animals with anaphylactic shock and in the animals that have been created by the phenomenon of Artyus and Overi. However, this increment was more prominent in the blood and lymph of the animals with created anaphylactic shock model, and the changes of the histamine's concentration in lymph were more significant than serotonin. Thus, on the 7th day of the sensibilization in the blood of control group of the animals, the serotonin levels increased 1.7 times compared to the indicators of the intact animals

and 5.8 times in the anaphylactic shock phase and were 4,093 mmol / l ($p < 0.001$). The animals which go out the shock, after 30 minutes, ie during desensibilisation phase, the serotonin levels were 2.7 times higher than in intact animals Table №2⁹.

In some animals, the symptoms of shock may be severe, but in others, there is only shortness of breath and involuntary urinary excretion. In this time some animals had 220 heartbeats, and had 140 respiratory movements. A / T reduced up to 40. Decreasing of the interleukin levels in shocked animals is associated with a decreasing of the number of T-lymphocytes, which in turn affects to the levels of immunoglobulin E and G. After shock, the number of heartbeat and respiration in animals decreased, and the A / T increased up to 70.

The study revealed that in the animals with the anaphylactic shock and with created Artyus and Overi phenomenon the concentration of lithium has reduced in both the sensibilization and in the decisive stages. However, this decrement is more prominent during anaphylactic shock. Thus, at the sensibilization stage of anaphylactic shock (7 days), the lithium concentration in the blood decreased by 1.5 ($p < 0.05$) compared with the intact indicator, and 2.2 times ($p < 0.001$) on the 14th day. In the anaphylactic shock phase (21st day) there was a sharply decreasing of the lithium concentration, ie, to 0.33 mmol / l. This is 4.8 times less than the indicators of intact animals.

In the animals which created the Artyus phenomenon model for immunocomplex reactions was established during the sensibilization phase (day 5), level of IL-4 in the blood 2.3 ($p < 0.001$) times increase, IL-6 -3.4 times ($p < 0.001$) increase compared to the control group. On the 25th day, the level of IL-4 during the Artyus phenomenon increased 13.3 ($p < 0.001$) and the level of IL-6 increased 15.6 ($p < 0.001$) times compared to the control group.

Although the IgG level increased during the sensibilisation phase of the Artyus phenomenon (5th and 15th days), this growth

⁹ .Gushin I.S. Mediated IgG release of histamine from human basophils / I.S. Gushin, A.I. Zebrev, V.A. Aleshkin and [others] // Pathological physiology and experimental therapy, Moscow: - 1983. T.4, No. 4, -p.18-22.

was more prominent in animals with the Artyus phenomenon model, whereas the IgE levels were dramatically reduced. We assume that increased levels of IgG are due to the superiority of the inflammatory response to these reactions. Thus, IgE levels decreased during the Artyus phenomenon compared with the control group, when it was equal up to 10.6 mE / l ($p < 0.001$), and IgG, by contrast, increased up to 23g / l. At the Artyus phenomena stage, the concentration of the CIC increased by 11.8 times compared to the intake index and reached 38.14 c.u. ($p < 0.001$). The titration of the complement was 8.5 times less than the intake and was 4.8 h.u. ($p < 0.001$).

Permin H. and other authors have shown that the concentration of allergic mediators are altered depending on the dose of antigen [57]. It was found from our study, that serotonin concentration depends on the way in which antigen enters to the organism. Thus, when the decisive dose is injected directly into the animal's vein or heart, there is a greater increasing of the concentration of the serotonin and histamine.

The levels of IL-4 and IL-6 were increased 4.1 times ($p < 0.001$) and 2.6 times ($p < 0.001$) in the blood of the animals in which the Overi phenomenon was created. Although IgE and IgG levels have increased, this growth has been more prominent at IgE levels. The concentration of the CIC increased by 4.8 times compared to the sensibilization phase and equaled 15.37 c.u., the complement titration decreased by 3.6 times and was 11.3 h.u. Both the serotonin and the histamine concentration increased during the Overi phenomenon, which is belong to the skin-anaphylaxis reaction.

Changes in immune indicators of the lymph of the animals in which the anaphylactic shock model was created were slightly weaker than in blood. Thus, the levels of IL-4 and IL-6 in the lymph at the sensibilization stage of anaphylactic shock (day 7) were 2.6 ($p < 0.001$) and 2.7 times, and at the shock stage were respectively 2.6 ($p < 0.001$) and 21.3 times ($p < 0.001$) more than control group.

Although the levels of IgG immunglobulin increased during the shock phase compared to the intact indicator, IgG decreased in comparison with the sensibilisation phase. The serotonin levels in lymph increased by 1.4 times on the 7th day of the sensibilization,

and by 1.6 times on the 14th day compared to the indicators of the intact animals, were 1.01 and 1.11 mmol/l ($p < 0.001$), while in the anaphylactic shock stage 3.6 times higher than the intact indicator and was 2.56 mmol / l ($p < 0.001$), but after 30 minutes of shock, ie, during the desensitizing phase, after 30 minutes the shock, in the desensibilisation phase this indicator decreased up to 1.20 mmol, which is 1.7 times higher than the intact indicator.

The concentration of the histamine was 1.4 times greater than the intake rate on the 7th day of the sensibilization, and 1.6 times higher on the 14th day ($p < 0.001$), and in anaphylactic shock stage again increased and was 2.12 mmol/l ($p < 0.001$), this is 3.3 times higher than the intake indicator.

As a result of the study, it became clear that the concentration of the CIC increases along the line in the dynamics of the anaphylactic shock model¹⁰.

Thus, in the blood of the animals in which the anaphylactic shock model was created, the concentration of CIC in the blood during the anaphylactic shock stage was 7.1 times higher than the intact indicator ($p < 0.001$) and was 23 c.u.. The complement titration decreased sharply, and it was not possible to detect it, after 30 minutes of shock it increased up to 2.5 h.u., this is 16.6 times less than the intake indicator (Table 3.16).

In the lymph, the concentration of the CIC in the sensibilization stage of the anaphylactic shock (day 7), increased by 2.2 times ($p < 0.001$) and 3.6 times ($p < 0.001$) on the 14th day compared with the intact animals indicators, while the complement titration decreased by 1.4 and 2.7 times, were respectively 21.9 and 11.6 h.u ($p < 0.001$). In the anaphylactic shock phase, the concentration of CIC in the lymph was 6.2 times higher than indicators of the intact animals, and the complement titration was not detectable due to the dramatic reduction.

According to some researchers, the damaging effects of immune complexes depend on the antibodies contained in them, and

¹⁰ Permin H., Stahl Skov P., Norn S. Basophil histamine release induced by leukocyte nuclei in patients with rheumatoid arthritis. // - Nyu York, USA: The Journal of Allergy, -1983. 38 (4) -p.273-281.

the complement linking activity depends on their concentration in blood and the molecular mass of the immune complex [7]. It has also been established that the pathological process in immunocomplexes diseases is mainly occurred in the microcirculatory vessels. During this time, the immune complexes attach to the receptors of the endothelial cells, causing their damage and desquamation. This promotes the entry of immune complexes into the vessel wall and surrounding tissues, increases the activity of labrocytes and basophils, leads to their degranulation, release of histamine, serotonin, and other biologically active substances from the cells, which subsequently cause dystrophy and necrosis in the vessel wall. According to some authors, the concentration of CIC and the level of IgE in people with allergic diseases increase from the early stages of the disease [2]. According to other researchers, increased levels of the IgE lead to the decreasing of the concentration of CIC [50]^{11,12}.

Although our study showed that CIC increased during anaphylactic shock and Artyus and Overi phenomena, this increment was more prominent during the Artyus phenomenon. Thus, the concentration of CIC in the blood of animals in the model of Artyus phenomenon on the 5th day of the sensibilization increased by 4.5 times, on the 15th day of the sensibilization increased by 7.7 times than intact indicator and were 14.6 c.u. ($p < 0.001$) and 24.88 c.u. ($p < 0.001$) respectively. At the stage of the Artyus phenomenon, the CIC increased by 11.8 times compared to the intact indicator and was 38.14 c.u. ($p < 0.001$). The complement titration on the 5th day of sensibilization was 1.1. times lower than intact indicator, on the 15th day was 1.5 times lower and were respectively 36.4 h.u. and 26.6 h.u. ($p < 0.001$). At the Artyus phenomenon stage, this indicator was 8.5 times less than the intact, and was 4.8 h. Uu. ($p < 0.001$) [27].

¹¹ Aliyev S.J., Akhundov I.A. Change of immune parameters in anaphylactic reactions and its correction with trace elements// -Baku: Scientific and pedagogical news of Odlar Yurdu University, - 2005. No. 14, - p.86-91.

¹² Vozqoment O.V., Krivenko E.I. Version of the mechanism for the development of a severe complication of vaccination against tick-borne encephalitis// - Moscow: Immunology, -2002. T.23, No. 1, -p. 42-43.

It should be noted that some animals with the Artyus phenomenon model the necrosis in the injection site developed poorly, while others showed only acute hyperemia. According to the literature, III type allergic reactions are associated with increased IgG levels by the effects of IL-6, this is consistent with our results.

During the shock phase, the lymph flow rate was reduced by 2 times. 30 minutes after shock, there was a decrease in interleukin-4 and -6, immunoglobulin E and G, and the concentration of CIC, and complement titration increased than to intact indicator.

In the lymph of the animals in which the Artyus Phenomena was created, the levels of IL-4 and IL-6 in the Artyus Phenomena stage were respectively 11.8 ($p < 0.001$) and 13.7 ($p < 0.001$) times higher than the intact indicators. At this stage, the level of immunoglobulin G was higher than immune globulin E. The concentration of CIC increased significantly, and the growth in complement titration was less significant.

It has observed that in the lymph of the animals which created Overi Phenomenon increasing of the level of IgE was more prominent than IgG in the changes of the levels of IgE and IgG. Also increment of IL-4 level in lymph was significant¹³.

Thus, at this stage, the increment of IL-4 from interleukines and IgE from the immune globulin was more important. Some researchers, however, have shown that the concentration of CIC decreased during anaphylactic shock.

According to the literature, in the sensibilized organism when the titration of IGE increases dramatically at that time an atopic reaction develops, and the increasing of the IgG leads to normal immune response, which results the scavengang of the allergic reactions. This coincides with our research's results. The IL-4 regulation of the synthesis of IgE and IgG antibodies occurs through differentiation. Thus, it has a dose-dependent effect on these immunoglobulins. High levels of IL-4 stimulate IgG synthesis. It can

¹³ Aliyeva T.R. Determination of the level of complement and the concentration of circulating immunocomplexes in blood and lymph in experimental anaphylactic shock and the Overi phenomenon// -Almaats: Therapeutic Bulletin, -2012. No. 2, - p. 38-41.

be assumed that the acceleration of IgG synthesis develops as a compensatory reaction [11].

It has been found that lymph drainage disorders cause increasing of the some interleukin levels and slowing of others. Thus, Konenkov V.I. and others, while investigating lymph drainage disorders during thermal burn of the skin in Wistar-type mice, observed that IL-1 β , IL-2, and SNF- α activity decreased, and IL-4 activity was increased [55]. On the 30th day of the disease, after lymph drainage recovery, inflammatory IL-1 β , SNF- α activity began to increase, and IL-4 activity decreased. Thus, lymph drainage disorders lead to a gradual alteration of cytokines. Low levels of interleukines in the stage of desensibilization of the animals which undergoing shock are associated with a decreasing of the number of T-lymphocytes, which in turn leads to a decrease in the levels of immunoglobulin E and G^{14,15,16}.

It has been shown that some micronutrients in the cells have the ability to influence AMF levels, such as lithium, molybdenum and others. It has been shown that, the lithium salts inhibit the proliferation of T-suppressors by increasing the level of s.AMF in lymphocytes. Also, the therapeutic effect of lithium salts in bronchial asthma is explained of the increasing of ts. AMF levels due to decreasing of the adenylacyclase activity and so inhibit of the muscular contraction. Some authors note that lithium micronutrients have the ability to inhibit of the releasing of histamine from the mast cells. According to results of C.H. Tagdisi and S.C. Aliyev research, the amount of some micronutrients, especially lithium in the blood, have been reduced by 2.5 times during anaphylaxis reactions.

In our study, the level of lithium decreased in comparison

¹⁴ Konenkov V.I., Makarova O.P., Bhatova N.P. The role of lymphatic drainage in changing of the activity of cytokines and neutrophil functions in the blood of rats after thermal skin burn //- Moscow: Pathological physiology and experimental therapy, -2012. T.38, No. 4, - p.98-101.

¹⁵ Aliyeva T.R. – The comparative analysis of IgE and IgG levels in blood and lymph during in the experimental anaphylactic shock and Overy phenomenon. Journal "Health," 2009, No. 4, p.138-142

¹⁶ Podkolzin A.A., Dontsov V.I. Factors of low intensity in bioactivation and immunocorrection. -Moscow: Medical newspaper, -1995. -p.165, -p.88-95.

with intact animals indicators on the 7th and 14th of the sensibilization stage in the blood of animals in which the anaphylactic shock model was created. In the stage of anaphylactic shock, the lithium level decreased dramatically, and was three times less than the intact indicator. This is due to its weak anti-allergic properties. 30 minutes after shock, the lithium concentration increased in comparison with the shock phase. Although the level of lithium on the 5 and 15 days of sensibilization in the blood of the animals which created Artyus phenomenon model decreased compared with the indicators of the intact animals, this was less noticeable compared with the indicators of animals which undergoing anaphylactic shock. The concentration of lithium micronutrients in animals with the Artyus phenomenon model was increased compared with the intact indicator. At this stage, the reduction of the lithium concentration was less than in the shock phase.

The concentration of lithium at the sensibilization stage in the blood of animals in the Overi phenomenon was slightly decreased ($p < 0.001$) compared to the intact indicator, whereas in the stage of Overi phenomenon the decrement was more significantly¹⁷.

Changes of IL-4 and IL-6, IgE, IgG levels, the concentration of CIC, complement, serotonin and histamine, lithium micronutrient in the blood and lymph of the animals which injected the corrective agents in the anaphylactic shock, before the sensibilization stage of Artyus and Overi Phenomenons.

In this study series, animals were injected with 3% lithium-oxybutyrate and 2.5 mg / kg cetirizine suspension for 7 days in advance. It was injected Li-oxybutyrate into the ear vein of the 4 animals out of 9 animals, and cetirizine-hydrochloride to the

¹⁷ Aliyev S.D., Tagdisi D.G. Musaev I.G. and others. Trace elements as endo- and exogenous immunomodulators//I World Congresses on Immunopathology and Respiratory Allergy, International Journal on immunorehabilitation- Moscow: Meditsina -Zdorovye, Singapore: -2002, dec. 2-6, Vol.4, No 1, - p. 96.

abdominal cavity of the 5 animals out of 9 animals, and then the animals were sensibilised with horse serum. Modifications of the immune indicators in the blood and lymph of the animals which created anaphylactic shock, the Arthus and Overi phenomena were compared with both intact (I control group) and control group indicators (II control group).

Thus, before the sensibilization phase of the anaphylactic shock model, the changes in the lymph of the animals which injected corrective agents were as follows: on the 7-day of the sensibilization phase IL-4 levels were 1.9 times increased compared to levels of the intact animals, during the anaphylactic shock phase, the level of IL-4 increased 9.7 times and was 23.20 ($p < 0.001$) pg / ml. These are 1.77 and 2.7 times less than in the control group.

The post-shock indicator was 5.2 times higher than the intact, and 3.3 times less ($p < 0.001$) than the according indicator of the control group.

Although the levels of IgE and IgG and the concentration of the CIC increased compared with the intact indicator, it decreased relatively to the control indicator, which could also be attributed to the anti-allergic effects of lithium-oxybutyrate and cetirizine. The complement titration decreased in comparison with intact indicator, but increased compared to control indicator. The levels of IgE and IgG and the concentration of CIC increased in comparison with the intake indicator and decreased relatively to the control indicator. The complement titration decreased in comparison with the intact indicator and increased relatively to the corresponding control indicator.

Although in our study, an increase in the level of DIC was recorded in the blood and lymph of all three models, the Arthus phenomenon model has been more pronounced which created in animals [2]¹⁸.

¹⁸ Aliyeva T.R. Analysis of the concentration and level of IgE of circulating immunocomplexes in the blood and lymph during experimental anaphylactic shock and Overi phenomenon // - Baku: Azerbaijan Journal of Oncology and Hematology, - 2012.№1, -p.78-81.

It was found that the high levels of IgG are observed over a period of 3 weeks, while the maximum IgE levels are observed at earlier times and then begin to decrease []. In all three models of the animals during our study, the levels of immune globulin varied depending on the way in which the antigen was injected into the organism. Thus, if the antigen is injected directly into the vessel or into the heart cavity of the sensitized body occurs anaphylactic shock and while is injected into subcutaneous the Artyus and Overi phenomena may occur.

On the 21st day of sensitization, immediately after the anaphylactic shock, IL-4 levels increased 10.1 times compared to the intact indicator, and reaches high level, and were 3.1 times lower than the indicators of the control group animals. It is associated with anti-allergic and anti-inflammatory effects of lithium-oxibutyrate and cetirizine drugs.

Although IL-6 levels increased 7.6 times compared to indicators of the intact animals, it decreased by 2.9 times compared to the indicators of the control group. Although IgE and IgG levels, the concentration of CIC increased in comparison with the intact indicator, decreased compared with the control indicator. At this stage, the level of IgG was partly reduced in the background of the maximum increasing of IgE levels. The complement titration also decreased dramatically at this stage compared to the intact indicator, and increased compared with the control indicator. The symptoms of shock in the pre-injected animals were slightly weaker, the animals were more easily affected by shock, and 2 animals died of shock. This was more pronounced in the animals injected with cetacean suspension.

The symptoms of shock in the pre-injected animals of the correctors were slightly weaker, the animals were more easily go out the shock, and 2 animals died due to shock. This was more prominent in the animals injected with cetirizine suspension. It can be assumed that cetirizine reduces the level of IL-4 by inhibiting Th-2 cell activity, causing hyposensitization by lowering concentration of IgE. According to A.A. Podkolzin and V.I. Dontsov's research, anti-allergic effect of Li-oxibutyrate is associated increasing of cyclic AMF levels

by inhibition of the adenylylase enzyme in cells [57]. Some researchers have suggested that IgE synthesis is replaced by IgA and IgG under the influence of this micronutrient^{19, 20}.

In animals who underwent anaphylactic shock 30 minutes after shock, IL-4 levels were 5.1 times higher than in intact animals, but were 4.0 times lower than the control group indicators. The level of IL-6 was 4.6 times higher than intact animals, which was 3.9 times lower than indicators of the control group animals. Although IgE and IgG levels and the concentration of CIC were lower than in the shock phase, this was higher than the intact indicator. Thus, on the 7th day of the sensibilization phase of the anaphylactic shock model, IgE levels increased 2.2 times compared to intact animals, these were 1.6 and 1.8 times less respectively than the indicators (35.6ME / mL) and (73.22ME / mL) of the control group animals. During anaphylactic shock, IgE levels were 110.3ME / ml, which is 10.8 times higher than the intact indicator, and 1.4 times less than indicator (151.2 ME / ml) of the control group ($p < 0.001$). In the anaphylactic shock phase, the CIC was 20.50 c.u. ($p < 0.001$), which is 6.4 times higher than the intake indicator and 1.1 times lower than the indicator of the control group. 30 minutes after the shock, the CIC concentration was 15.64 c.u. ($p < 0.001$). This is 1.1 times lower than the control indicator as in the shock phase.

The complement titration values was 1.1 h.u in the anaphylactic shock phase, which was 36.6 times less than the intact indicator ($p < 0.001$). Thirty minutes after the shock, the complement titration increased slightly and was 1.8 h.u., this is 22.8 times less than the control indicator.

Decreasing of IL-4 and IL-6 levels in animals with anaphylactic shock may be due to a delay in T-lymphocyte activity. Decreased IL-4 levels in the blood and lymph can lead to a decrease in IgE levels in parallel.

¹⁹ Podkolzin A.A., Dontsov V.I. Factors of low intensity in bioactivation and immunocorrection. -Moscow: Medical newspaper, -1995. -p.165, -p.88-95.

²⁰ Osakovsky V.L., Fedorov A.I., Krivoschapkin V.G. Content of some cytokines at various levels of serum IgG // - St. Petersburg: Ecological immunology, -2002. V.4, No. 1, -p.125-128.

Initially the lithium-oxybutyrate and cetirizine were injected for 7 days, and then the Artyus phenomenon created, the immun indicators - IL-4, IL-6, IgE, IgG, CIC in the blood of these animals and the changes in the complement levels were different than the indicators of the animals with anaphylactic shock model. Changes in IL-4 were more prominent, although the levels of each interleukin in the blood of animals with Artyus phenomenon were reduced after injection of lithium-oxybutyrate and cetirizine within 7 days prior to sensibilization. On the 15th day of sensibilization, after the III injection, the increase in IL-4 and IL-6 concentrations was more significant than that of Day 5, the complement titration was decreased 2 times. During the Artyus Phenomena, IL-6 and IgG levels were significantly increased, while IL-4 and IgE levels decreased. The concentration of the CIC increased at this stage, and was more significant than the indicators of the animals with shock model. Complement titration has decreased.

In the half-series of this study, one animal died before going out the shock and another one died during taking blood in the desensibilization phase.

In the pre-injected animals of the corrective agents, despite a significant increase in IgG at the Artyus phenomenon stage, it has been noted the poor development of hyperergic inflammation and a smaller size of necrosis region. This is due to the fact that, according to the literature, not all ICs activate complement and cause inflammation. In our view, the decreasing of the IgE level is due to the substitution of IgE synthesis by the synthesis of IgG due to the effect of lithium-oxybutyrate, which is coincides with the results of A.A. Podkolzin and VI. Dontsov and others [46].

After exposure to the correctors for 7 days in advance, on the 5th day of sensibiliization in the lymphs of the animals which created Artyus phenomenon model increased both IL-4 and IL-6 levels inaccurately in comparison with indicators of the intact animals. In Lymph, the IL-6 levels were higher than IL4. IgE and IgG levels increased, the concentration of CIC increased, and the complement titration decreased. On the 15th day of sensibilization, both IL-4 and IL-6 levels increased in comparison with indicators of

the intact animals, and IL-6 growth was significantly higher than IL-4. Although the level of IgE and IgG increased in comparison with the intact indicator, the increase in IgG levels was more significant. The concentration of CIC increased in comparison with the intact indicator, and the complement titration decreased. All of the above immune indicators, except of complement titration, were reduced in comparison with the control group²¹.

On the 25th day of the sensibilization, that is, in the Artyus phenomenon stage, the higher levels of IL-6 and IgG may be attributed to the superiority of the inflammatory processes of immune complexes reactions. Due to the effect of lithium-oxybutyrate and cetirizine, IL-4 and IL-6, the levels of IgE and IgG, and the concentration of CIC decreased relatively to the control indicator, and complement titration was relatively increased.

It has been observed the decreasing of the intensity of the hyperergic inflammation, which develops during the Artyus phenomenon by the effects of lithium-oxybutyrate and cetirizine, In some animals, the inflammatory symptoms are poorly developed.

Initially the lithium-oxybutyrate and cetirizine were injected for 7 days, and then the Overi phenomenon created, in the sensibilization phase (day 6) in the blood of these animals IL-4 and IL-6 levels was increased compared with the indicators of the intact animals (I control group), decreased compared with the indicators of the control group II. At that time, the growth of IL 4 was more significant than IL 6. Although both IgE and IgG levels increased relatively to the intact indicator, the increase of the IgE level was more significant. There was a decrease in this indicator compared with control ($p < 0.001$). The concentration of the CIC increased in comparison with the intact indicator and was 1.5 times lower than the control indicator. Complement titration decreased in comparison with intact indicator, and increased 1.3 times as compared to control indicator. Although we suppose that the increase in IL-6 and IgG levels in the blood of the animals in the model of the Overi

²¹ Dontsov V.I., Ismailov T.A. Use of lithium trace element in the treatment of bronchial asthma//Moskva: Pathological physiology and experimental therapy, - 1984. V.5, No. 5, -p. 65-66.

phenomenon would be more prominent, on the contrary, it has been observed that IL-4 and IgE levels were higher [46].

The initially injection of the lithium-oxybutyrate and cetirizine for 7 days, in the lymph of the animals which the Overi phenomenon created, caused decreasing of the IL-4 and IL-6 levels. Thus, the level of IL-4 increased in both the sensibilization and at the stage of the Overi phenomenon compared with the indicator of the intact animals, while decreased during the sensibilization phase and at the stage of the Overi phenomenon compared with the control group. The levels of IL-6 increased in both the sensibilization and at the stage of the Overi phenomenon compared with the indicators of intact animals and decreased compared with the control indicator. The levels of IgE and IgG, and the concentration of CIC increased compared to the intact indicator, decreased compared with the control indicator. Complement titration was slightly higher due to the effect of correctors on both the sensibilization stage and at the stages of the Overi phenomena, but was less than the intact indicators. The pre-injection of the correctors for 7 days resulted in a partial reduction in dyspnea and tachycardia and poor coloration of the injection area with the Evans blue²².

In animals with pre-injection of the correctors and then created anaphylactic shock model, on the 7th day of sensibilization, both serotonin ($p < 0.001$) and histamine concentration were increased compared with the indicators of the intact animals. The concentration of both allergic mediators has been reduced relatively to control indicator, which is also correlated with the anti-allergic effects of lithium-oxybutyrate and cetirizine drugs. Thus, during the sensibilization phase of the anaphylactic shock model (day 7), serotonin concentration decreased by 1.3 times compared to the intact indicator, but increased 1.7 times on the 14th day of the sensibilization. In the anaphylactic shock phase, it again increased and was 2.32 mmol / l ($p < 0.001$), which was 3.3 times higher than the indicator of the intact animals and 1.8 times less than the indicator of the control group.

²² Aliyeva T.R. Effect of lithium-oxybutyrate on some cytokine parameters during experimental anaphylactic shock and Overi phenomenon // -Baku: Azerbaijan Journal of Pharmacy and Pharmacotherapy, -2008. №2, -p.52-58.

On 21st day of the sensibilization, the concentration of the serotonin and histamine increased dramatically, and the concentration of both mediators was lower than the indicator of the control group ($p < 0.001$), but the concentration of the histamine was most lowest. 30 min after the shock the concentration of both allergic mediators decreased.

In the blood of the animals which initially the lithium-oxybutyrate and cetirizine were injected, and then the Artyus phenomenon created, the serotonin and histamine concentration was inaccurately increased than the intact indicator and decreased accurately than the control indicator on the 5th day of sensibilization. On the 15th day of sensibilization, the concentration of both mediators was increased accurately in comparison with indicators of intact animals, and decreased accurately with relatively to the indicator of the control group. On the 25th day of sensibilization, that is, at the stage of the Artyus phenomenon both serotonin and histamine concentration increased with relatively to the indicators of the intact animals, and decreased accurately relatively to the indicator of the control group.

Although the concentration of serotonin and histamine in lymph increased compared with the indicators of the intact animals in the 7th day of sensibilization, the increasing of the histamine levels was more prominent. Compared to the indicator of the control group, the concentration of both allergic mediators decreased. On the 14th day of sensibilization, the concentration of each two mediators increased relatively to the indicator of the intact animals and decreased compared to the indicator of the control group. During the anaphylactic shock phase, both serotonin and histamine concentration were increased in comparison with intact indicator, and decreased compared to control indicator ($p < 0.001$).

On day 5 of the sensibilization phase, in the lymph of the animals which the Artyus phenomenon created, the concentration of serotonin increased slightly compared with indicators of intact animals, and histamine levels significantly increased. The concentration of both allergic mediators decreased compared with indicators of intact animals. On the 25th day of sensibilization, that

is, in the stage of Artyus Phenomenon, the concentration of serotonin and histamine in the lymph was increased, and the concentration of histamine was slightly higher than serotonin. The concentration of both allergic mediators ($p < 0.001$) decreased compared to the indicators of the control group. Changes of the concentrations of the indicators which studied at the lymph were less prominent in comparison with the indicators in the blood.

At the lymph which the model of the Overi Phenomenon created at the sensibilization stage, also at the stage of the Overi Phenomenon, the serotonin and histamine concentrations were increased compared with the indicators of the intact animals and were decreased in comparison with the control group.

According to the results, although the concentration of histamine and serotonin in both blood and lymph increased during the experimental anaphylactic shock, Artyus and Overi phenomena, it was reached a higher level during anaphylactic shock. As for the comparison of the concentration of mediators in the blood and lymph, it was observed that the indicators are slightly higher in the lymph. Studies by Podkolzin and Dontsov have also shown that histamine concentrations are higher in lymph [58].

The changes of IL-4 and IL-6 levels, changes of IgE, IgG levels, DIC, complement, serotonin and histamine concentrations in the blood and lymph of animals injected of correctors during the sensibilization phase of anaphylactic shock, Artyus and Overi phenomena.

In the II experiment series of the study, 9 rabbits sensibilized with 0.1 ml of horse blood serum and were injected 3% lithium oxybutyrate and cetirizine for 7 days from the 13th day of sensibilization to the shock phase. Lithium-oxybutyrate was injected into 4 of the correctors and cetirizine into 5 of them. Although the level of interleukins in this series increased during the sensibilization phase, it decreased compared to the control indicator in the critical phase, which is due to the antiallergic effect of the correctors.

Thus, on the 7th day of sensibilization in animals with an anaphylactic shock model, the level of IL-4 increased 4.2 times

compared to intact animals ($p < 0.001$) after 7 days of injection of lithium-oxybutyrate and cetirizine in the shock phase was 12.4 times (39.90 pg / ml) ($p < 0.001$) higher than the intact indicator²³.

However, in I control group animals, this indicator was 31 times higher than intact indicator. Thirty minutes after the shock, the level of IL-4 was 7.2 times higher than the intact value and 4.2 times lower than the corresponding value of the control group.

On the 7th day of sensibilization, IL-6 levels increased 2.7 times ($p < 0.001$) compared with intact animals indicators, and was 9.0 times higher in the anaphylactic shock phase after the injection of correctors, was equal to 33.28 pg / ml ($p < 0.001$). This is 2.5 times less than the indicators of the control group of animals (22.3). 30 minutes after the shock, the level of IL-6 was 5.9 times higher than the intact value, and 2.9 times lower than the corresponding value of the control group.

IL-4 level in lymph increased 2.7 ($p < 0.001$) and 6.1 ($p < 0.001$) times on days 7 and 14, compared with the indicators of the intact animals and were 6.44 and 14.56 pg / ml respectively, after 7 days injection of lithium-oxybutyrate and cetirizine was 9.2 times more in the shock phase, and was 5.0 times more 30 minutes after shock, which is respectively 2.8 and 3.5 times less than the according values of the control group animals.

On the 7th day of sensibilization, the level of IL-6 was 2.9 times higher than the indicators of intact animals ($p < 0.01$), and 12.4 times ($p < 0.001$) higher in the anaphylactic shock phase after 7 days of injection of lithium oxybutyrate and cetirizine. Since 2 animals perished while taking lymph, in the lymph of the 7 animals the level of IL-6 was 7.6 times more than the intact indicator and 2.4 times less than the indicator of the control group which we identified during the desensibilization phase 30 minutes after the shock.

Correctors - lithium-oxybutyrate and cetirizine in the blood of animals injected during the sensibilization phase of the Artyus phenomenon model, on the 5th day of sensibilization, the level of IL-

²³ Podkolzin A.A., Dontsov V.I. Low-intensity factors in bioactivation and immunocorrection. –Moscow: Medical newspaper, -1995. -p.165, -p.88-95.

4 was 1.9 times ($p < 0.001$) more compared with indicators of the intact animals, after the effect of lithium-oxybutyrate and cetirizine was 6.5 times ($p < 0.001$) more at the stage of the Artyus phenomenon. This is 2 times less than the indicators of the control group of animals (13.3pg / ml).

IL-6 level was 2.4 times ($p < 0.001$) more on the 5th day of sensibilization compared to the indicators of the intact animals, and was 7.4 times higher on the 25th day of sensibilization after injection of lithium oxybutyrate and cetirizine. This is 2.1 times less than the indicators of the control group animals.

On the 5th day of the sensibilization in the lymph, the level of IL-4 was 1.3 times higher than the indicators of the intact animals (g/d), and after 7 days of injection of the correctors increased up to 15.83 pg / ml in the phase of Arthus phenomenon, this is 6.6 times more than the intact index, and 1.8 times less than the corresponding indicators of the control group animals. Lymph flow rate was 1.0 times lower than the intact indicator in the sensibilization phase (on the 5th and 15th days) and 1.1 times lower in the Artyus phenomenon. The levels of IL-6 in the lymph were 3.5 and 6.1 times higher than the indicators of the intact animals on the 5th and 15th days of sensibilization, and increased to 15.08 pg / mL at the Artyus stage after 7 days injection of the correctors, this is 8.7 times more than the indicators of the intact animals and 1.2 times less than the corresponding control indicator.

It was determined that the increase in the interleukin levels in the blood and lymph of the animals in which the Overi phenomenon model was studied was not as noticeable as in the animals with the anaphylactic shock, Artyus phenomenon model.

IgE and IgG levels decreased in the decisive phase after 7 days of injection of lithium- oxybutyrate and cetirizine in the animals during the sensibilization phase. When determining the concentration of circulating immunocomplexes (CIC) and complement activity in this half-series, it was found that although the CIC density increases during both anaphylactic shock and Artyus phenomenon, this increase is more noticeable during Artyus phenomenon. Thus, in the sensibilization phase of the II control series of the anaphylactic shock

model (7th day), the concentration of CIC in the blood was 4.4 ($p < 0.001$) times higher compared to intact animals, and 7.1 times higher in the anaphylactic shock stage ($p < 0.001$). The titer of complement was 1.4 times higher than the intact value on the 7th day of sensibilization, it was not determined in the shock phase due to a sharp decrease, and increased slightly 30 minutes after the shock was 16.6 times lower than the intact value. In the lymph, in the sensibilization phase of the anaphylactic shock (in the 7th day), the concentration of CIC was 2.2 times ($p < 0.001$) higher and in the shock phase was 6.2 times higher than the indicators of the intact animals, and the complement titer was not determined due to a sharp decrease. 30 minutes after the shock, during the desensibilization phase, the concentration of CIC in the lymph was 4.9 times higher than the indicators of the intact animals, and the titer of complement was 39 times lower ($p < 0.001$).

On the 5th day of sensibilization, the concentration of CIC in the blood of animals which created by the Artyus phenomenon model increased by 4.5 times compared to the intact index, and at the stage of the Artyus phenomenon increased by 11.8 times and was 38.14 c.u. The titer of complement was 1.1 times lower than the intact value on the 5th day of sensibilization, and 8.5 times lower than in the Arthus phenomenon and was 48.93 h.u. ($p < 0.001$). In some of the animals in which the Artyus phenomenon model was created, necrosis at the injection site covered a small area, while in others it manifested itself only with intense redness.

On the 6th day of the sensibilization phase in the animals of the Overi phenomenon model, the concentration of CIC increased by 1.9 times compared to the intact index and reached to 4.84 c.u. The titer of complement decreased 1.5 times and was 27.4 h.u. At the stage of the Overi phenomenon, the concentration of CIC increased by 4.8 times compared to the sensibilization stage, reaching 15.37 c.u. the titer of complement decreased by 3.6 times and reached to 11.3 h.u. In some animals in which the Overi phenomenon model was developed, the staining of the injection site was poor.

In the next half-series of the study, lithium-oxybutyrate and cetirizine were injected for 7 days during the sensibilization phase in

animals with anaphylactic shock, Artys and Overi phenomena, serotonin and histamine concentrations were investigated. At the same time, on the 7th day of sensibilization in the blood of animals with anaphylactic shock model, the concentration of both serotonin and histamine increased accurately compared to the indicators of the intact animals. On the 14th day of sensibilization, the concentration of both mediators increased relative to the indicators of the intact animals, but decreased relative to the indicators of the control group.

As a result of 7 days of injection of lithium oxybutyrate and cetirizine in animals before the 21st day of sensibilization, the concentration of serotonin and histamine increased compared to the indicators of the intact animals, but decreased compared to the indicators of the controls. Also, the increase in histamine was more significant. Thus, in the stage of anaphylactic shock, ie after the effect of correctors, the concentration of serotonin in the blood increased by 2.7 times compared to intact indicator and was equal to 1.92 mmol / l, and was recorded 2.1 times lower than the control indicator. During the desensibilization phase, the concentration of serotonin was 1,235 mmol / l ($p < 0.001$). This is 1.8 times more than the intact index, but 1.5 times less than the control index.

As for the level of histamine, on the 7th day of sensibilization, its level in the blood was 1.3 times higher than the indicators of intact animals, and increased to 1.486 mmol / l ($p < 0.001$) in the stage of anaphylactic shock, which is 3.0 times higher than intact index, and was 1.3 times lower than the control index. 30 minutes after the shock, the histamine level decreased up to 0.92 mmol / l, which was 1.9 times higher than the intact index and 1.4 times lower than the control index [11]²⁴.

In the sensibilization phase of anaphylactic shock in the lymph, the concentration of serotonin was 1.6 times higher than the intact value, but in the shock phase was 2.2 times higher than intact value and was 1.57 mmol/l ($p < 0.001$). This was 1.6 times lower than control indicator. The histamine concentrations at lymph were 1.4

²⁴ Aliyeva T.R., Aliyev S.C. Comparative analysis of serotonin and histamine levels in blood and lymph during anaphylactic shock and Overi phenomenon // - Baku: Azerbaijan Medical Journal, - 2011. № 1, -p. 38-41.

and 1.6 times higher than the intact value on the 7th and 14th day of sensibilization, and in the anaphylactic shock stage was 2.2 times higher than the intact value.

The concentration of serotonin in the blood of animals injected with correctors in the sensibilization phase of the Artyus phenomenon model, was 1.4 times higher than the intact value on the 5th day of sensibilization, and in the Artyus phenomenon phase was 1.43 mmol / l ($p < 0.001$), which is 2,0 times more than intact indicator and 1.8 times lower than the control indicator. On the 5th day of sensibilization, the concentration of histamine was 1.3 times higher than the intact value, almost indistinguishable from the control group, and in the Artyus phenomenon stage it was 2.5 times higher than the intact value and 1.4 times lower than the control value.

On the 5th day of the sensibilization, at the lymph of the animals with the Artyus phenomenon model the concentration of serotonin increased both in relation to the indicators of the intact animals and in comparison with the indicators of the II control group. Because of animals were injected with lithium oxybutyrate and cetirizine for 7 days before the Artyus phenomenon, the concentration of the studied allergic mediators was higher than the indicators of the intact animals and lower than the indicators of the II control group.

There were no significant changes in the concentration of serotonin and histamine in the blood and lymph of the animals in which the Overi model was created at the sensibilization stage and at the Overi phenomenon stage.

Changes in IL-4 and IL-6, IgE, IgG levels, CIC, serotonin, histamine concentration and complement activity in the blood and lymph of animals exposed to correctors agents during 7 days after the decisive phase.

In the next series of studies, after the creation of anaphylactic shock, Artyus and Overi Phenomenon, the animals were injected at a dose of 3% Li-oxybutyrate 10 mg / kg for 7 days into the ear vein, , and a suspension of cetirizine 2.5 mg / kg into the abdomen. Immune parameters were compared comparatively both in the stages of

anaphylactic shock, Artyus and Overi phenomena, and after injection of correctors. In animals with an anaphylactic shock model, IL-4 levels in the shock phase were 31.6 times higher than the indicators of the intact animals, and only 4 times higher after 7 days injection of the lithium-oxybutyrate and cetirizine suspension. This is 7.5 times less than the shock phase. The level of IL-6 increased 22.6 times compared to the indicators of the intact animals, and after 7 days of injection of correctors it was 12 times higher than the intact value. This is 1.8 times less than the shock phase. Decreases in IgE and IgG levels were also observed due to the antiallergic effect of correctors. It should be noted that the level of IgE is much lower. The concentration of CIC in the shock phase was significantly higher than the intact index, and after injection of correctors was 2 times lower than in the control group. The titer of complement was sharply reduced at this stage compared to the intact value, which was 1.2 times higher than the control value after 7 days of injection of correctors.

Although IL-4 levels in the lymph of the anaphylactic shock phase were higher than the indicators of the intact animals, they were still higher ($p < 0.001$) than intact value after 7 days injection of the lithium-oxybutyrate and cetirizine suspension, but were approximately 10 times lower than in the shock phase. IL-6 levels increased than the indicators of the intact animals and decreased after injection of lithium oxybutyrate and cetirizine ($p < 0.001$). IgE levels in the lymph also increased accurately compared to the intact value during the shock phase ($p < 0.001$). Although IgG levels increased accurately compared to this indicator, they were lower than IgE. After 7 days of the injections of the correctors, both IgE and IgG levels decreased compared to the shock phase. The level of IgE in the blood of animals studied in the anaphylactic shock stage increased by 16.1 times compared to the indicators of the intact animals and was 165.1 ME / ml ($p < 0.001$), and after 7 days of injection of correctors decreased up to 62.33 ($p < 0.001$) ME / ml, which is 6.1 times more than the intact value; 2.6 times less than the control indicator [5]²⁵.

²⁵ Aliyeva T.R. Changes in some immune parameters in the blood and lymph during atopic reactions and immunocomplex reactions // -Baku: Azerbaijan Medical Journal, -2012. №1, - p.36-39.

IgG levels decreased up to 5.73 g / l (p-g / d) after 7 days of injection of correctors in the anaphylactic shock phase.

The concentration of CIC increased in the anaphylactic shock phase compared to the intact index, decreased after the effect of correctors and was 2 times higher than the intact index, and 2.5 times less than in the shock phase. The titer of complement decreased in the anaphylactic shock phase compared with the intact index and increased accurately after the injection of correctors. When determining the concentration of serotonin and histamine in the blood of animals with anaphylactic shock, it was found that in the shock phase, the concentration of serotonin and histamine increased relative to intact values (I control group) and was maximum, but did not differ from II control values. The concentration of serotonin was much higher than the histamine. After 7 days of injection of lithium oxybutyrate and cetirizine, the concentration of these allergic mediators decreased by 3.5 times compared to the shock phase.

The concentration of histamine and serotonin in the lymph increased relative to the intact values and did not differ much from the control values. After 7 days of injection of correctors, the concentration of both serotonin and histamine decreased relative to intact values. It is clear from the literature that changes in serotonin metabolism affect the intensity of shock development [46]. That is, as anaphylactic shock develops, the concentration of serotonin in some lymphoid organs decreases. The study of this helps to obtain rapid therapeutic effects by affecting individual systems in the pharmacological correction of shock conditions. In our study, we determined the concentration of serotonin and histamine only in the blood and lymph [21]. In the result of the study, it is found that the increase in the concentration of histamine in the blood and lymph was more noticeable than in serotonin.

The level of IL-4 in the blood of animals in which the Artyus phenomenon model was created was higher than according indicators of the intact animals, and even after 7 days of injection of lithium-oxybutyrate and cetirizine was higher thanthe intact indicators. Levels of IL-6 were higher than the indicators of the intact animals at both the Artyus stage and after 7 days of injection of correctors. The

level of IgE and IgG in the blood of animals created the Artyus phenomenon model was increased compared to the intact index ($p < 0.001$)²⁶.

Although a decrease in the level of both immunoglobulins was observed after injection of lithium oxybutyrate and cetirizine, the decrease in IgE levels was more noticeable ($p < 0.001$). The concentration of CIC in the blood at this stage was 11.4 times higher than the intact value ($p < 0.001$), and after 7 days of injection of correctors was 7.2 times higher ($p < 0.001$). This is 1.6 times less than the control indicator. The titer of complement was 6.4 times lower than the intact index ($p < 0.001$), increased after injection of correctors and was 22.9 h.u. ($p < 0.001$).

In the lymph of animals in which the Artyus phenomenon model was created, the level of IL-4 increased compared to the indicators of the intact animals, and decreased sharply compared to intact values after 7 days of injection of lithium-oxybutyrate and cetirizine. IL-6 levels increased 3 times compared to the indicators of the intact animals ($p < 0.001$) and decreased after injection of lithium-oxybutyrate and cetirizine. Immunoglobulins IgE and IgG levels increased relative to the intact index, but the increase in IgG levels was more pronounced. After 7 days of injection of correctors, the level of both immunoglobulins decreased ($p < 0.001$). When determining the concentration of CIC in the lymph of the animals which Artyus Phenomenon model created, it was found that this increased 10.3 times ($p < 0,001$) than the intact values and did not differ from the control index. A 7-day injection of lithium oxybutyrate and cetirizine resulted in a 5.1 times increase in the concentration of CIC in the animal's lymph compared to the intact value and a 2.0 times decrease compared to the control value. The titer of complement decreased by 6.6 times ($p < 0.001$) compared to the intact index, and increased slightly after 7 days of injection of correctors, was 13.9 h.u. ($p < 0.001$), which is 2.2 times less than the

²⁶ Alieva T.R., Aliev S.D. Determination of serotonin levels in the blood with indicators of immunoglobulins E and G in experimental anaphylactic shock and the phenomenon of Artyus // - Moscow: Natural and technical sciences, -2011. №1, - p.49-51.

intact index and 2.9 times more than the control. The concentration of serotonin and histamine in the blood of animals created by the Artyus phenomenon increased relative to intact values, but this increase was slightly weaker than in animals created by shock. After 7 days of injection of lithium oxybutyrate and cetirizine, the concentration of allergic mediators decreased by about 3 times compared to the stage of the Artyus Phenomenon.

After 7 days of injection of the correctors, the concentration of histamine, which decreased up to 0.83 mmol / l ($p < 0.001$), was 1.3 times higher than the intact value and 2.3 times lower than the control value.

Although lymph flow decreased during the Arthus phenomenon, it accelerated under the influence of correctors.

As a result of the injection of correctors, hyperergic inflammation in some animals was more rapidly absorbed, and the process of replacing necrotic tissue with new tissue was accelerated. In others, these symptoms gradually disappeared. As a result of injection of correctors, hyperergic inflammation in some animals is more rapidly absorbed, and the process of replacing necrotic tissue with new tissue is accelerated. In others, the symptoms gradually disappeared.

The levels of IL-4 and IL-6 in the blood of animals created in the Overi phenomenon model increased compared to the corresponding indicator of intact animals, and the level of IL-4 was higher than in IL-6. After 7 days of injection of correctors lithium oxybutyrate and cetirizine, the level of IL-4 decreased by 2.16 times compared to the stage of the Overi phenomenon, and the level of IL-6 decreased by 2 times. Although the levels of IgE and IgG in the blood of animals in which the Overi phenomenon model was created were higher than intact, the increase in IgE levels was more pronounced. At this stage, the concentration of CIC increased accurately and the titer of complement decreased ($p < 0.001$). After 7 days of injection of correctors, the concentration of CIC decreased relative to the intact index, and the titer of complement increased. At the stage of the Overi phenomenon, the concentration of serotonin and histamine in the blood increased accurately compared with the

indicator of intact animals (I control group), the concentration of histamine decreased significantly after 7 days of the injection of lithium oxybutyrate and cetirizine, while the serotonin concentration was insignificant. This is due to the antiallergic effect of these drugs.

The concentration of serotonin and histamine in the lymph increased compared to the intact index, and the concentration of both serotonin and histamine decreased slightly after 7 days of injection of correctors. In the phase of the Overi phenomenon, LAS remained almost unchanged compared with the intact rate, it increased under the influence of correctors.

After the creation of the Overi Phenomenon, the injection of correctors led to rapid healing of the injected area of the skin and the disappearance of signs of inflammation. Heart beats and respiratory rate returned to normal from the second day of injection.

Changes in the concentration of lithium in the blood and lymph after 24 and 48 hours in animals in which anaphylactic shock, Artyus and Overi phenomenon models were created and lithium-oxybutyrate was injected.

In the VIII series of the study, the concentration of lithium in the blood and lymph of animals injected with lithium-oxybutyrate after 24 and 48 hours was studied. It was found that the level of lithium in the blood of animals with anaphylactic shock was 0.33 mmol / l, 24 hours after injection of lithium-oxybutyrate increased up to 2.10 mmol / l, which is 1.3 times higher than the intact values. After 48 hours, the lithium level dropped up to 1.87 mmol / l. This is 1.2 times higher than the intact value. On the 21st day of the sensibilization, 24 hours after lithium oxybutyrate injection, the concentration of this microelement increased 1.5 times compared to the intact value, which is 4 times higher than in the shock phase. 48 hours after lithium oxybutyrate injection, the level of this trace element was close to the intact index (I control group).

After 24 hours of lithium-oxybutyrate injection in animals after the Artyus phenomenon stage, the lithium concentration in the blood increased up to 1.87 Mmol/l, which was 1.2 times higher than the intact value. After 48 hours, this value decreased up to 1.62

Mmol / l, which almost coincided with the intact value. After 24 and 48 hours, the study of its concentration showed that after 24 hours the concentration of lithium was 1.2 times higher than the intact value, and after 48 hours it approached the intact state.

After the phase of the Overi Phenomenon, the level of lithium in the blood of animals was 1.21 mmol / l, and 24 hours after injection of lithium-oxybutyrate increased up to 1.59 mmol / l. Over 24 hours after lithium-oxybutyrate injection, the concentration of lithium in the blood of animals with Overi Phenomenon was 1.0 times lower than the intact value, and 48 hours later it was 1.1 times lower than the intact value.

The concentration of this micronutrient in the lymph was 1.2 times higher than the intact value after 24 hours of the injection of lithium oxybutyrate in the animals which go out the shock, and did not change after 48 hours. This is 1.3 and 1.8 times higher than the control indicators, respectively. Although the level of lithium in the lymph during the Artyus phenomenon was 0.86 mmol / l, after 24 hours of the lithium oxybutyrate injection, the level of this microelement increased up to 1.60 mmol / l, which is 1.2 times higher than the intact value and 1.3 times more compared to the control group.. The concentration of lithium, which decreased up to 1.52 mmol / l after 48 hours was 1.2 times higher than the intact value and 1.5 times higher than the control value. In the Overi Phenomenon phase, the concentration of the lithium at the lymph was 1.13 mmol / l, increased to 1.41 mmol / l after 24 hours injection of the lithium oxybutyrate, and was 1.1 times higher than the intact values and 1.2 times higher than the control values (p. <0.05). After 48 hours, it decreased up to 1.25 mmol / l, was 1.0 times less than the intact index and 1.1 times more than the indicators of the control group.

In this study, the micronutrient lithium and its compound, lithium oxybutyrate, reduced IL-4 and IL-6, IgE and IgG levels in the blood and lymph, and decreased the concentration of CIC, serotonin and histamine, slightly increasing the titer of complement, this proves antiallergic effect of its. It has also been noted that lithium compound injection makes the shock phase easier and the animals come out of the shock more easily. According to the literature, the

synthesis of IgG is directly dependent on the dose of the injected antigen. It was found that high IgG levels are observed within 3 weeks, and maximum IgE levels are observed earlier, and then begin to decline. In our study, the levels of immunoglobulins in all three models animals varied depending on the route of entry of the antigen into the body. Thus, if the antigen is repeatedly injected directly into a vein or into the heart cavity of the sensitized organism directly, anaphylactic shock occurs, and if injected subcutaneously, Artyus and Overi phenomena occur. In our study, increased levels of IgE and IgG were observed in animals with anaphylactic shock. Also, the levels of immunoglobulins, the concentration of CIC changed depending on the nature of the allergic reaction. Thus, the concentration of IgE and IL-4 was reached maximum during anaphylactic shock, and the concentration of IgG and CIC was reached maximum during the Artyus phenomenon [29]. As we know, on the surface of lymphocytes have receptors against of the various biologically active substances - catecholamines, prostaglandins, histamine, etc. Although histamine receptors have been identified as H₁ and H₂, H₂-receptors have been found to play a more important role [62]^{27,28}.

Mediator secretion from the target cell is one of the main reasons for the development of allergic diseases. The secretion of these mediators occurs as a result of the interaction of specific allergens and antibodies with receptors on the surface of mast cells and blood basophils. In this case, the secreted histamine inhibits its subsequent secretion by acting on the mast cells by H₂-receptors associated with the adenylate cyclase enzyme.

Histamine plays a key role in the development of allergic reactions and the development of clinical symptoms. Also, histamine and serotonin itself accelerate the synthesis of some

²⁷ Aliyeva T.R., Allahverdieva L.I. Change in the concentration of lithium trace element in blood and lymph depending on the level of histamine and serotonin in experimental anaphylactic shock and the Arthus phenomenon// - Moscow: Immunology, - 2015, V.36, No. 1, -p.19-22.

²⁸ Sorbo J., Jakobsson A., Norrby K. Mast-cell histamine is angiogenic through receptors for histamine I and II // International Journal Experimental Pathology, - USA: NCBI, Bethesda MD. -1994. 75 (1) -p.43-50.

immunoglobulins, especially IgG [23]. For this reason, we compared the concentrations of histamine and serotonin in the blood and lymph of animals in the anaphylactic shock, Artyus, and Overi phenomenon models in series IV of the study, both in the sensitization, decisive, and desensitization stages.

In the sensitization phase of anaphylactic shock in the series of the I control (day 7), the concentration of both serotonin and histamine in the blood increased accurately compared with the indicators of the intact animals (I control group), but this increase was more pronounced in serotonin levels. On the 14th day of sensitization, the concentration of serotonin and histamine increased accurately compared to the indicators of the intact animals. Although the concentration of both allergic mediators increased during the anaphylactic shock phase compared with intact indicators, the concentration of serotonin was higher than the histamine. 30 minutes after the shock, both histamine and serotonin levels decreased relative to the shock phase.

The concentration of both mediators in the lymph increased accurately than the indicators of the intact animals. Thus, on both the 7th and 14th days of sensitization, the levels of histamine and serotonin increased, but this was not noticeable. In the anaphylactic shock phase, the concentration of both allergic mediators is significantly increased. It should be noted that the concentration of serotonin in the lymph, as well as in the blood, was higher than in histamine. Lymph flow rate is also reduced. According to our study, a greater increase in the concentration of serotonin and histamine is observed when the decisive dose is injected directly into an animal's vein or heart [9]^{29, 30}.

On the 5th and 15th days of sensitization, the concentration of both serotonin and histamine in the blood of animals

²⁹ Aliyeva T.R. Determination of serotonin level in blood with immunoglobulins E and G in experimental anaphylactic shock and Overi phenomenon // -Harkov: International Medical Journal, -2011. V.17, No. 2, - p.48-52.

³⁰ Aliyeva T.R. Comparison of the concentration of circulating immune complexes, levels of some immunoglobulins and histamine in blood and lymph in anaphylactic shock and the Artyus phenomenon in the experiment // Kazan Medical Journal, Kazan, 2018, No. 1 -p.58-61

in which the Artyus phenomenon model was created increased accurately relative to the indicators of the intact animals. During in the stage of the Artyus phenomenon, the concentration of serotonin and histamine increased accurately compared to the indicators of the intact animals ($p < 0.001$), and the concentration of serotonin was higher than histamine.

On the 5th and 15th day of the sensibilization at lymph, the concentration of both allergic mediators increased accurately, and although the levels of both histamine and serotonin increased during the stage of the Arthus phenomenon, the increase in serotonin concentration was more significant than the histamine.

During the sensibilization phase, the concentration of histamine and serotonin in the blood of animals in which the Overi phenomenon model was created was accurately increased compared to the indicators of the intact animals ($p < 0.001$). Although there was a accurately increase in the concentration of both allergic mediators during in the stage of the Overi phenomenon, the concentration of serotonin was significantly higher than that of histamine.

The concentration of serotonin and histamine in the lymph of animals in which the Overi phenomenon was created was accurately higher than the indicators of the intact animals, and this increase was more pronounced in the concentration of serotonin. At the stage of the Overi Phenomenon, the concentration of both serotonin and histamine increased accurately compared to the indicators of the intact animals.

In the semi-series of the V series of the study, the animals were pre-injected with lithium oxybutyrate and cetirizine for 7 days, then sensibilized with horse serum to create models of anaphylactic shock, Artyus phenomenon, and Overi phenomenon.

Correctors were first injected, and then in animals with an anaphylactic shock model, on the 7th day of sensibilization, the concentration of serotonin was accurately increase than the indicators of the intact animals ($p < 0.001$), and the concentration of histamine was incorrectly increased. The concentration of both allergic mediators decreased accurately compared to the control indicator, which is associated with the antiallergic effect of lithium-

oxybutyrate and cetirizine. The effect of lithium oxybutyrate and cetirizine was weak on some days of sensibilization. Thus, on the 14th day of sensibilization, the concentration of both serotonin and histamine increased accurately relative to the intact values ($p < 0.001$) and decreased accurately relative to the control value. On the 21st day of sensibilization, the concentration of serotonin and histamine increased sharply, while the concentration of histamine decreased inaccurately compared to the indicators of the control group, and the concentration of serotonin decreased accurately ($p < 0.001$). 30 minutes after the shock, the concentration of both allergic mediators decreased. The level of this decline was almost the same.

On the 7th day of the sensibilization at lymph, the concentration of serotonin was inaccurately increased compared to the indicators of the intact animals, and histamine was accurately increased. The concentration of both allergic mediators was accurately reduced compared to the indicators of the control group. On the 14th day of the sensibilization, the concentration of both mediators increased accurately relative to the indicators of the intact animals and decreased accurately compared to the indicators of the control group. In the anaphylactic shock phase, both serotonin and histamine concentrations increased accurately relative to the intact values and decreased accurately relative to the control values ($p < 0.001$). Thirty minutes after the shock, the concentration of allergic mediators decreased accurately compared to the shock phase.

Lithium-oxybutyrate and cetirizine were pre-injected, and then on the 5th day of sensibilization, the concentration of serotonin and histamine in the blood of animals in which the Artius phenomenon model was created increased inaccurately compared with intact values and decreased accurately relative to control values. On the 15th day of the sensibilization, the concentration of both mediators increased accurately compared to the intact animals, and decreased accurately compared to the indicators of the control group animals. On the 25th day of sensibilization, ie during in the stage of the Artyus phenomenon, the concentration of both serotonin and histamine increased relative to the indicators of the intact animals and decreased inaccurately compared to the indicators of the control group.

On day 5th day of the sensibilization at lymph, the serotonin concentration increased inaccuracy compared to the indicators of the intact animals, and histamine levels increased accurately. The concentration of both allergic mediators was significantly reduced compared to the indicators of the intact animals. On the 15th day of sensibilization, the concentrations of both serotonin and histamine increased accurately relative to the indicators of the intact animals and decreased accurately compared to the indicators of the control group. On the 25th day of sensibilization, ie during in the stage of the Arthus phenomenon, the concentration of serotonin and histamine in the lymph increased accurately, and the concentration of histamine was slightly higher. The concentration of both allergic mediators was accurately reduced compared to the indicators of the control group ($p < 0.001$). Changes in the concentrations of the parameters studied in the lymph were less noticeable than in the blood. V.A. Tomilets and V.I. Dontsov showed that ambrosia extract, as a specific antigen, prednisolone, platinum and palladium salts have a significant effect on histamine secretion [70]³¹.

In order to obtain accurate information of the number of histamine cell receptors, other authors have found that immunogplexes containing aggregated IgG stimulate the secretion of some mediators from basophils, as well as stimulate the secretion of histamine from target cells []. In our study, the concentration of histamine depends on the route of entry of the antigen into the body [].

According to some authors, the weakening of the sensitivity of the receptor apparatus of lymphocytes in animals with anaphylactic shock proves the role of allergic mediators that interact with immune mechanisms in the pathogenesis of allergic reactions [].

Studies have also shown that changes in the serotonin metabolism in the body are reflected in the development of shock [150]. Thus, the development of anaphylactic shock in guinea pigs with the injection of horse serum leads to a sharp decrease in the concentration of serotonin in the spleen, which leads to shock

³¹ Dontsov V.I., Ismailov T.A. Use of lithium trace element in the treatment of bronchial asthma//Moscow: Pathological physiology and experimental therapy, - 1984. V.5, No. 5, -p. 65-66.

damage to this organ (shock organ). It was found that the concentration of serotonin in the blood and some lymphoid organs is an indicator of the intensity of shock. In our study, the concentration of serotonin and histamine was determined only in the blood and lymph, and not in the lymphoid organs. According to the results, during the experimental anaphylactic shock, Artyus and Overi phenomena, the concentration of histamine and serotonin in both blood and lymph increased, but the increase in these mediators reached a higher level during anaphylactic shock. As for the comparison of the concentration of mediators in the blood and lymph, it was observed that the indicators are slightly higher in the lymph. Studies by Podkolzin and Dontsov also show that the concentration of histamine in the lymph is higher^{32, 33, 34}.

RESULTS

1. In animals with an anaphylactic shock model, a sharp decrease in AP and an increase in TS were observed from vital signs; in animals with Artyus and Overi phenomena model, the AP did not change, and the number of breaths increased [2,4].

2. In animals with both anaphylactic shock and Artyus and Overi phenomena, increased levels of IgE and IgG in both blood and lymph during the sensibilization phase but were not noticeable [6,7,8].

3. At the beginning of the anaphylactic shock, the level of immunoglobulin E in the blood of animals increased 14.7 times compared to intact values, and only 1.3 times during the Artyus phenomenon, while the level of immunoglobulin G, on the contrary,

³² Gushhin I.S. Mediated IgG release of histamine from human basophils / I.S. Gushhin, A.I. Zebrev, V.A. Aleshkin and others // Pathological physiology and experimental therapy, Moscow: - 1983. V.4, No. 4, -p.18-22.

³³ Eliseeva L.S., Stefanovich L.E., Popova V.S. The effect of immunization on serotonin binding by cells of immunocompetent tissues of mice// - Moscow: Immunology, -1983. V. 4, No. 4 -p.45-48.

³⁴ Aliyeva T.R., Aliyev S.C. Comparative analysis of serotonin and histamine levels in blood and lymph during anaphylactic shock and Overi phenomenon // - Baku: Azerbaijan Medical Journal, - 2011. № 1, -p. 38-41.

increased 1.4 times during anaphylactic shock and was 4.3 times more in the Artyus phenomenon. The changes in the Overi phenomenon were not so noticeable. Changes in these parameters in the lymph were weak [5,7].

4. The level of IL-4 in the blood of animals with an anaphylactic shock model increased 31 times compared to intact indicators, and the level of IL-6 increased 22.6 times, while in animals with the Artyus phenomenon model, on the contrary, the level of IL-6 has increased 21, 6 times, and IL-4 - 13.3 times. Changes in the blood parameters of animals in which the Overi phenomenon was created were less noticeable. In the lymph, the changes in these parameters were not significant compared to the blood [3,9].

5. In the experiment, the concentration of CIC in the blood and lymph of animals with anaphylactic shock, Artyus and Overi phenomena increased, and the titer of complement decreased. The maximum level of CIC was observed during the Artyus phenomenon, and the lowest level of complement was observed during anaphylactic shock[10,17].

6. In the experiment, the concentration of serotonin in the blood of animals with anaphylactic shock, Artyus and Overi phenomena increased by 1.5 times compared to histamine. The increase in these parameters in the lymph was more noticeable than in the blood[21,22].

7. Although the concentration of lithium in the blood and lymph of animals with anaphylactic shock and Artyus and Overi phenomena decreased, this change was more noticeable during anaphylactic shock[23,25].

8. It was found that injection of lithium-oxybutyrate and cetirizine causes a decrease in the level of immune parameters which we studied, but this was more pronounced at the level of IL-4 and IL-6. The complement titers, on the contrary, increased due to the effect of correctors[18,26,27].

9. Lithium micronutrient has a desensibilizing effect and has a delaying effect on the development of anaphylactic shock. As a result of the action of lithium in the sensitized organism, the titer of

IgE and the secretion of histamine decreases, and the level of IgG increases. The use of cetirizine had a more effective anti-allergic effect and made it easier for animals to recover from the shock[42,43,45].

PRACTICAL RECOMMENDATIONS

1. Considering of the desensibilizing effect of the lithium trace element, its compounds can be used in the prevention of some allergic diseases.

2. Considering of the micronutrient lithium reduces the titer of IgE, increases the titer of IgG and inhibits the secretion of histamine, its compounds can be used in the treatment of some allergic diseases.

3. In addition to local allergic reactions, the use of cetirizine after anaphylactic shock may also have some effect.

4. In order to accelerate the excretion of toxic, chemical substances entering the body, to increase the activity of cytokines, practitioners are advised to accelerate lymphatic drainage in patients.

Dissertasiya mövzusunə aid elmi işlərin siyahısı

1. Əliyeva T.R., Əliyev S.C. Ümumi və yerli allergik reaksiyalar zamanı immun göstəricilərin pozulmaları. "Sağlamlıq" jurnalı, 2008, № 1.s.7-11

2. Алиева Т.Р. Влияние оксипутирата- лития на цитокиновые показатели при общих и местных аллергических реакциях у кроликов. "Экспериментальная и клиническая медицина". № 3, 2008. С.12-15

3. Алиева Т.Р. Влияние оксипутирата - лития на цитокиновые показатели при экспериментальной сенсбилизации. "Экспериментальная и клиническая медицина" № 4, 2008. с.40-42

4. Əliyeva T.R. Ümumi və yerli allergik reaksiyalar zamanı bəzi sitokin göstəricilərinin müqayisəli təhlili. Allerqologiya, immunologiya və immunoreabilitasiya üzrə III Azərbaycan milli konqresi, 2008,s.142-145

5. Əliyeva T.R. Ümumi və yerli allergik reaksiyalar zamanı bəzi sitokin göstəricilərinin qanda və limfada müqayisəli təhlili. "Sağlamlıq" jurnalı, № 7, 2008, s.132-135

6. Əliyeva T.R. Litium-oksibutiratın eksperimental anafilaktik şok və Overi fenomeni zamanı bəzi sitokin göstəricilərinə təsiri. Azərbaycan Əczaçılıq və Farmakoterapiya jurnalı, 2008, № 2, s.30-34

7. Əliyeva T.R. Anafilaktik şok və Artyus fenomeni zamanı litium-oksibutiratın sitokin göstəricilərinə təsirinin müqayisəli təhlili Azərbaycan Tibb jurnalı, 2009, №1.s.49-53

8. Əliyeva T.R. Eksperimentdə anafilaktik şok və Artyus fenomeni yaradılmış heyvanlarda litium-oksibutirat inyeksiyasından 24 və 48 saat sonra litium mikroelementinin səviyyəsinin dəyişiklikləri. Azərbaycan təbabətinin müasir nailiyyətləri, 2009, № 1, s.131-133

9. Əliyeva T.R. Anafilaktik şok və Artyus fenomeni zamanı qanda və limfada bəzi immunqlobulinlərin səviyyəsi. Azərbaycan Tibb Jurnalı, 2009, №3, s.26-29

10. Əliyeva T.R. Eksperimental anafilaktik şok və Overy fenomeni zaman qanda və limfada IgE və IgG-nin səviyyəsinin müqayisəli təhlili. "Sağlamlıq" jurnalı, 2009, № 4, s.138-142

11. Алиева Т.Р. Сравнительный анализ влияния препарата зиртека на уровень IgE и IgG в периоде сенсibilизации и шока при анафилактическом шоке и феномена Артюса. "Metabolizm" jurnalı, № 3, 2009, с.6-11

12. Алиева Т.Р. Определение уровня иммуноглобулинов Е и G у животных после инъекции зиртека, перенесший анафилактический шок. XIV Международный конгресс по реабил. в медицине и иммунореабил., Аллергология и иммунология, Москва, 2009, Т.11, №1. с.31

13. Алиева Т.Р., Алиев С.Д. Уровень IgE и IgG в крови и лимфе животных с предварительной инъекцией зиртека, Биомедицина, 2009, № 2., s.27-31

14. Əliyeva T.R. Ümumi və yerli allergik reaksiyalar zamanı litium mikroelementinin səviyyəsinin dəyişiklikləri. Azərbaycan Onkologiya və Hematologiya jurnalı, 2010, № 1., s.156-161

15. Əliyeva T.R., Əliyev S.C. Anafilaktik şok və Overi fenomeni zamanı zirtek preparatı qanda və limfada serotoninin səviyyəsinə təsiri. Azərbaycan Əczaçılıq və Farmakoterapiya jurnalı, 2010, № 2, s.28-32

16. Əliyeva T.R. Anafilaktik şok və Artyus fenomeni zamanı IgE və IgG -nin səviyyəsinin interleykin-4 və interleykin-6-dan asılı dəyişiklikləri. Azərbaycan Tibb jurnalı, 2010, № 1, s.65-68.

17. Алиева Т.Р. Сравнительный анализ уровней иммуноглобулинов Е,G и микроэлемента лития в крови и лимфе при анафилактическом шоке, феноменах Артюса и Овери. Аллергология и иммунология, Москва, 2010, Т.11, № 2, с. 38-42

18. Əliyeva T.R., Əliyev S.C. Anafilaktik şok və Overi fenomeni zamanı qanda və limfada serotonin və histaminin səviyyəsinin müqayisəli təhlili. Azərbaycan Tibb jurnalı, 2011, № 1, s.44-48

19. Алиева Т.Р. Effect of lithium-oxubutyrate on cytokine indices in experimental anaphylactic shock and the Arthus phenomenon in rabbits. Актуальные проблемы гуманитарных и естественных наук, Москва, 2011, № 3, с. 167-169

20. Алиева Т.Р., Алиев С.Д. Определение уровня серотонина в крови с показателями иммуноглобулинов Е и G при экспериментальном анафилактическом шоке и феномене Артюса. Естественные и технические науки. Москва, 2011, № 1.с.136-139

21. Алиева Т.Р. Определение уровня серотонина в крови с показателями иммуноглобулинов Е и G при экспериментальном анафилактическом шоке и феномене Овери. Международный медицинский журнал, Харьков, 2011, № 2, т. 17.с.79-81

22. Алиева Т.Р. Сравнительный анализ уровней иммуноглобулинов Е и G и циркулирующих иммунокомплексов в крови и лимфе при экспериментальном анафилактическом шоке и феномене Овери. Curierul medical, Молдова, 2011, № 6.с.3-6

23. Əliyeva T.R. Atopik reaksiyalar və immunkompleks reaksiyaları zamanı qanda və limfada immun sistemin bəzi göstəricilərinin dəyişiklikləri. Azərbaycan Tibb jurnalı, 2012, № 1, s.41-46

24. Əliyeva T.R. Eksperimental anafilaktik şok və Overi fenomeni zamanı qanda və limfada dövr edən immunkomplekslərin qatılığının və immunqlobulin G-nin səviyyəsinin təhlili. Azərbaycan Onkologiya və Hematologiya jurnalı, 2012, № 1, s.73-76

25. Алиева Т.Р. Определение уровня гистамина и иммуноглобулинов Е и G при экспериментальном анафилактическом шоке. Аллергология и иммунология, Москва, 2011, Т.12, № 2, с. 217

26. Əliyeva T.R. Anafilaktik şok və Artyus fenomeni zamanı qanda və limfada bəzi immun göstəricilərin dəyişiklikləri və allergik mediatorların qatılığının müqayisəli təhlili. Azərbaycan təbabətinin müasir nailiyyətləri, 2012, № 2, s.102-109

27. Алиева Т.Р. Определение уровня комплемента и концентрации циркулирующих иммунокомплексов в крови и лимфе при экспериментальном анафилактическом шоке и феномене Овери. Терапевтический вестник, Алматы, 2012, № 2, с.79-82

28. Алиева Т.Р. Влияние зиртека на некоторые цитокиновые показатели при анафилактическом шоке, феномене Артюса и Овери. Цитокины и воспаление. 2012, Т.11, № 4, с. 41-44.

29. Əliyeva T.R., Əliyev S.C., Əbilova R.Q. Eksperimental anafilaktik şok və immunkompleks reaksiyaları zamanı dövr edən immunkomplekslərin və komplementin fəallığının immunqlobulin E və -G-dən asılı dəyişiklikləri. Allerqologiya, immunologiya və immunoreabilitasiya üzrə IV Azərbaycan milli konqresi, 2012, s.27-30

30. Əliyeva T.R. Anafilaktik şok və Artyus fenomeni zamanı qanda və limfada bəzi immun göstəricilərin, litium mikroelementinin miqdarının və allergik mediatorların qatılığının müqayisəli təhlili. Azərbaycan təbabətinin müasir nailiyyətləri, 2013, № 3, s. 102-109.

31. Алиева Т.Р. Определение уровней иммуноглобулина Е и G при экспериментальном

феномене Артюса и феномене Овери. Збірник матеріалів міжнародної науково-практичної конференції "Медичні та фармацевтичні: науки: стратегічні пріоритети розвитку та інноваційні рішення". 6-7 грудня 2013 р. м. Дніпропетровськ 2013. "Solutem" 120 с. С.3-7

32. Алиева Т.Р. Сравнительный анализ влияния препарата зиртека на уровень IgE и IgG при экспериментальном анафилактическом шоке и феномене Овери Azərbaycan allergologiya və klinik immunologiya jurnalı T 2, N2,2014,c.74-78

33. Алиева Т.Р., Алиев С.Д., Талышинская М.Б. Определение уровней интерлейкина-4 и интерлейкина-6 в периоде сенсibilизации и разрешения при анафилактическом шоке и феномене Овери Аллергология и иммунология Т 16,№1, 2015

34. Алиева Т.Р., Аллахвердиева Л.И. Изменение концентрации микроэлемента лития в крови и лимфе в зависимости от уровня гистамина и серотонина при экспериментальном анафилактическом шоке и феномене Артюса Иммунология Т-36, №1, 2015, с. 19-22

35. Алиева Т.Р., Алиев С.Д., Аллахвердиева Л.И. Изменение концентрации циркулирующих иммунных комплексов активности комплемента и уровней IgE и IgG в крови и лимфе в зависимости при экспериментальном анафилактическом шоке и феномене Артюса, Иммунология Т-36, №2, 2015, с. 107-110

36. Алиева Т.Р., Аллахвердиева Л.И. Сравнительная характеристика уровня гистамина и иммуноглобулинов класса Е и G при экспериментальном анафилактическом шоке и феномене Артюса, Патологическая физиология и экспериментальная терапия Т.59, №3, 2015, с.76-80

37. Əliyeva T.R., Əliyev S.C. Anafilaktik şok və Artyus fenomeni zamanı histamin və DİK-in qatılığının müqayisəli təhlili

Allerqologiya, immunologiya və immunoreabilitasiya üzrə V Azərbaycan milli konqresi, 2016, c.42-45

38. Əliyeva T.R., Əliyev S.C., Talışinskaya M.B. Eksperimental Artyus fenomeni zamanı E və G immunqlobulinlərinin qanda və limfada tədqiqi / Ə.Əliyevin anadan olmasının 120 illik yubileyi münasibətilə ATU-da keçirilən elmi-praktik konfransın materialları, görkəmli elm və dövlət xadiminə həsr olunmuş xatirələr, 2016, s.419-420.

39. Əliyeva T.R. Artyus və Overi fenomeni zamanı qanda və limfada interleykin 4,6-nın səviyyələrinin təhlili //Azərbaycan Onkologiya Jurnalı, Bakı, 2017, s. 111-113.

40. Алиева Т.Р. М.В.Тalışinskaya, Р.А.Ахундов Изучение уровней иммуноглобулина Е, G и интерлейкина-4 в крови и лимфе при анафилактическом шоке и феномене Артюса в эксперименте // Биомедицина , Бақы, 2017, с. 47-50

41. Əliyeva T.R. , İbrahimova G.H. Анафилактик şok və Artyus fenomeni zamanı E və G immunqlobulinlərinin səviyyələrinin qanda və limfada müqayisəli təyini, //Azərbaycan təbabətinin müasir nailiyyətləri, Bakı, 2018, №1, c.19-22.

42. Алиева Т.Р. Сравнение концентрации циркулирующих иммунных комплексов, уровней некоторых иммуноглобулинов и гистамина в крови и лимфе при анафилактическом шоке и феномене Артюса в эксперименте // Казанский медицинский журнал, Казань, 2018, №1, с.58-61

43. Алиева Т.Р. Сравнительное определение концентрации микроэлемента лития, циркулирующих иммунных комплексов и активности комплемента в крови и лимфе при экспериментальном анафилактическом шоке и феномене Артюса // Казанский медицинский журнал, Казань, 2018, №3, с.39-42

44. Aliyeva T.R. Determining the level of histamine in the experimental anaphylactic shock / International Conference on Applied Biosciences (İCAB-2019) December 5-6, 2019, №3, с. 85

45. Əliyeva T.R. Artyus fenomeni zamanı dövr edən immun komplekslərin və E immunqlobulininin səviyyələrinin qanda və limfada müqayisəli təhlili /Allerqologiya, immunologiya və immunoreabilitasiya üzrə V Azərbaycan milli konqresi, Bakı, 2019, s.20

46. Aliyeva T.R. Activity of Complement comparatively in the Blood and Lymph in the experimental Arthus and Overy Phenomenon // International Journal of Immunology, USA, 2019, T.7, №3, c. 43-46

47 Aliyeva T.R. Determination of the Levels of IgE and IgG and the Complement activity

Relatively in the Blood and Lymph // Journal of Immunology Research and Therapy, USA, 2020, №5 s. 198-199

48. Əliyeva T.R. E.Ç.Əkbərov, A.Ş. Qasımoğlu Bəzi allergik reaksiyalar zamanı dövr edən immunkomplekslərin (DİK) qatılığının dəyişiklikləri // Azərbaycan Tibb Jurnalı , 2021,№1, s. 114-116

49. Aliyeva T.R., İbişova A.V., İsayeva V.A., Yaquboba S.M. Study of IL-4 and IL-6 levels and complement activity comparatively in blood and lymph in experimental anaphylactic shock and Arthus phenomenon //Clinical Immunology and Research, İndia, 2023, V.7, №1 p. 1-3.

50. Aliyeva T.R., Akbarov E.Ç. Determination of circulating immune complexes and complement levels in some allergic reactions // American Journal of Medical and Clinical Research & Reviews , İndia 2023, V 2, № 10, p. 1-5.

51. Əliyeva T.R. Artyus fenomeni zamanı komplementin fəallığının tədqiqi / Professor Zərifə Ağarza qızı Zeynalovanın anadan olmasının 90 illik yubileyinə həsr olunmuş elmi konfransın materialları, Bakı ,Elm və təhsil 2023, 1s.

52. Əliyeva T.R. Eksperimentdə anafilaktik yaradılmış heyvanların qanında və limfasında bəzi immun göstəricilərin dəyişiklikləri / Ümummilli lider Heydər Əliyevin anadan olmasının 100 illiyinə həsr olunmuş “Təbabətin aktual problemləri” Beynəlxalq elmi-praktik konqresin materialları, Bakı, 3-6 may, 2023, 1s.

The defense of the dissertation will be held at the meeting of the Dissertation Council at BED 4.20 on "01" march 2024 at "14:00".

Address: AZ 1022, Baku city, A.Gasimzade Str., 14
(conference hall)

The dissertation can be found in the library of Azerbaijan Medical University.

Electronic versions of the dissertation and abstract are posted on the official website of the Azerbaijan Medical University (www.amu.edu.az).

The abstract was sent to the necessary addresses on "26" yanuary 2024.

Signed for print: 22.01.2024
Paper format: 60x84¹/₁₆
Volume: 68624 characters
Number of hard copies: 20