THE ORGANISM AND THE HABITATION ATMOSPHERE

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Annotation

This monograph examines experimental data on the study of the influence of the different parameters of the atmosphere on the organism for the purpose of making a physiological determination of the permissible oxygen concentrations in inhabited airtight compartments and considering the application of high oxygen concentrations for respiration for medical purposes.

The author presents data on the evolution of the atmosphere and of the role of O_2 in the process of the evolutionary development of living beings, on the influence on an organism of an artificial atmosphere and an atmosphere containing high and low oxygen concentrations, the laws of oxygen permeation into the fluid media of the organism, the biological role of inert gases, and so forth.

The relationship between the gas medium of habitation and the reactivity of the organism is determined.

The book is intended for physiologists, pathophysiologists, and physicians working in the field of aviation and space medicine.

Foreword

The study of the problem of the interrelation of the organism with the environment and its adaptability to the constantly changing conditions of the external world remain the most important task of scientific investigations. In this regard the evolutionary principle is one of the most important ones to be considered in studying the functioning of the different systems of the organism and their regulation. /3

The problem of the biological expediency and harmony of organism and environment in the evolutionary aspect has been considered in the works of I. N. Sechenov, I. P. Pavlov, K. A. Timiryazev, and other Soviet scientists.

The effect of a certain environmental factor on the organism has minimum and maximum limits. Life is possible only within these limits and beyond their bounds severe disturbances of the different functional systems begin. The normal existence of the organism is unthinkable outside the atmosphere—the air sea covering the entire terrestrial sphere. The oceans, seas, and rivers, plants, animals, and human beings—all these not only live in air but also live by air.

In the course of many millenia man has adapted to existence in the conditions of the earth's surface. These conditions are characterized by very insignificant changes in barometric pressure and a stable composition of the atmospheric air.

As a result of the evolution of the organic world, the most important energy source for the performance of physiological processes proved to be aerobic processes connected with oxidation. The respiration of organic substances in turn determined the entire course of evolution of the animal world and contributed to the development of a complex system of organs and mechanisms providing for the absorption of oxygen from the environment, its transportation to the tissues, the nervous and humoral mechanisms for controlling the different component elements of the respiratory process, and so forth. The partial pressure of oxygen in the lungs and its pressure in the cells, blood, and tissue fluids is the /4 most important factor determining the level of oxygen absorption from the external environment necessary for normal life activity of living things, and its use by the tissues.

In recent years conclusive **facts** have been obtained on the favorable influence of adaptation to hypoxia and acclimatization to high mountain conditions, on resistance to the effects of carbon monoxide and organic peroxides, high temperature, to severe burns and deep cooling, to radial acceleration, on increasing radiation resistance, and so forth.

Numerous clinical and experimental investigations have indicated the promising nature of the use of increased oxygen pressure in curing decompression sickness (the bends), hemic forms of oxygen deficiency, in the case of disturbances of the brain and coronary blood circulation, in the case of anaerobic infection and for improving the results of radiation therapy of malignant neoplasms.

In recent years great attention has been given to the study of the effectiveness of using high oxygen pressure during the performance of operations requiring complete or partial exclusion of blood circulation.

Although hyperbaric oxygen therapy has been quite well developed and has essentially become an independent division of medical science, the physiological theory of the oxygen regime is still little developed. Establishment of the limit of the permissible oxygen concentrations, clarification of the biological role of inert gases and development of the substances increasing the organism's resistance to the effects of hypo- and hyperoxia are important problems for medical science.

Many of the above-indicated actual physiological problems have been experimentally analyzed over the years in the laboratory directed by N. A. Agadzhanyan. Numerous experiments of different durations (from one to 100 days) have been conducted to discover the optimal parameters of the gas medium and artificial atmosphere for a man occupying an airtight compartment for an extended period of time and for studying the physiological mechanisms of disturbances arising in the conditions of a changed gas environment.

From 1964 to 1970 the author set up scientific experiments in the region of the Central Tyan-Shan and the Caucasus and personally directed them. The investigations were conducted in order to es- /5
tablish the relation between the medium of habitation and the ability to endure such extreme conditions as hypoxia, hyperoxia, hypercapnea, acceleration, explosive decompression, and great physical loads. All these problems are illuminated in the present book and not only have important significance for the theory and practice of medicine but also are of general biological interest.

The further study of the physiological mechanisms of adaptation of the organism to a changed gas medium makes makes it possible to control compensatory-adaptive physiological reactions, to discover the essential nature of many pathological states, to present the possibility of extensive regulation of energy exchange in the organism, and consequently to find methods for increasing the resistance of the organism to different unfavorable influences.

Academician V. V. Parin

TABLE OF CONTENTS

CHAPTER I

THE EARTH'S ATMOSPHERE AND THE EVOLUTION OF LIVING THINGS

The earth's atmosphere is one of the products of the general process of the creation and development of the earth in the course of its geological history, beginning many billions years ago and continuing to the present time. The problem of the evolution of the atmosphere is closely connected with the problems of the formation of the earth and the appearance of life on our planet. /6*

In the opinion of the majority of scientists, the earth's atmosphere consisted, in the first stages, of hydrogen, helium, nitrogen, ammonium, and methane, and also compounds of hydrogen with bromine, chlorine, flourine, and sulfur. The predominance of high temperatures made the rate of motion of the molecules of these gases very high, and therefore they rapidly left the atmosphere.

Having lost its original atmosphere, the boiling mass of our planet also gradually lost its heat. The underground gases which appeared in this period were similar to the gases ejected during modern volcanic eruptions. Thus, for example, the content of the gases erupting from the volcano Halemaumau on the Hawaiian Islands was the following: 68% water vapor, 13% carbon dioxide, 8% nitrogen. The remainder consisted of sulfurous fumes. Among these gases there is no free oxygen and there probably was no oxygen earlier (V. A. Sokolov, 1966).

When the earth cooled further the loss of gases decreased and, finally, completely ceased. Water vapor, upon condensing, filled the oceans with hot water. The carbon dioxide partially dissolved in the water and part of it was absorbed by carbonaceous rocks. The earth again acquired an atmosphere and was now in a position to retain it. However, the earth's atmosphere significantly differed from that which surrounds us today—it did not have the free oxygen necessary for life. A. I. Oparin (1968) connects the appearance of life with the synthesis of biologically important compounds from substances of inorganic origin and attributes great significance to the presence of CH_4 and NH_3 in the earth's "secondary" atmosphere. /7

Oxygen was gradually liberated into the atmosphere, evidently as a result of the processes of photosynthesis in which carbon dioxide gas and the primitive plant world participated. Carbon was deposited in the form of coal and oil. Nitrogen continued to accumulate in the atmosphere. Oxygen arose anew in the atmosphere

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*Numbers in righthand margin indicate pagination of foreign text.

under the influence of photochemical reactions or the activity of organisms. Since oxygen compounds—water and carbon dioxide—were always present in the primeval atmosphere, the formation of free oxygen in the atmosphere as a result of photodissociation of water and carbon dioxide is not excluded. However, this process proceeded very slowly. Easily oxidizing substances of volcanic origin inhibited the accumulation of oxygen in the primeval atmosphere. Great amounts of oxygen appeared in the atmosphere around three billion years ago with the beginning of the photosynthetic activity of plants and the oxygen balance of the atmosphere became more stable. Free oxygen began to participate in the overall cycle of substances on the surface of the earth. The history of oxygen can be reconstructed on the basis of isotope composition. Oxygen has several isotopes—O^{16}, O^{17}, and O^{18}. The heaviest is the oxygen of air and carbon dioxide gas and the lightest is the oxygen of fresh water.

In 1936 the American chemist Malcolm Dole observed that the isotropic composition of atmospheric oxygen and oxygen obtained from the electrolysis of water is not identical. "Water" oxygen is approximately 3% lighter than atmospheric oxygen. If the amount of the heavy isotope O^{18} in water is taken as 100%, then in the oxygen of the air it proves to be 103%. This surprising discovery is called the Dole effect.

Where does this 3% come from? Atmospheric oxygen is the product of photosynthesis and is obtained from water in the process of dehyrogenation. In building complex organic substances, a plant uses carbon dioxide gas and hydrogen separate from water, and the liberated oxygen passes into the atmosphere.

Long-term studies have shown that the light isotope O^{16} is more active than the heavy one; it enters into reactions more easily than the heavy isotope, and therefore the atmosphere is gradually /8
enriched with the isotope O^{18}.

The chief creators of the Dole effect are the plankton and algae of the ocean. They regenerate the greater part of atmospheric oxygen.

The processes of respiration and other oxidizing reactions occurring on the earth also influence the isotope composition of atmospheric oxygen. However, it has not yet been possible to establish the complete balance necessary for a definitive solution of the Dole effect.

Thus, the atmosphere does not contain significant amounts of gases of primary cosmic origin. The main body of these gases --- hydrogen, inert gases and others were lost during the formation of the solid matter of the earth; some gases were scattered into outer space.

The amount of loss of the gases depended on their physical properties and on the mass of the forming planet. Despite the great speed of the molecules (hundreds of meters per second), their numerous collisions hindered them from being forced out into the upper layers of the atmosphere. Nonetheless, the migration of gas molecules from the lower layers of the atmosphere into the upper layers still takes place. At high altitudes where the atmosphere is extremely rarefied, individual molecules fly out from it into outer space. This phenomenon is called the escape of gases.

The total mass of the atmosphere is equal to approximately $5 \cdot 27 \cdot 10^{15}$ tons, which amounts to around one millionth of the mass of the earth.

The following basic layers of the atmosphere are distinguished: troposphere, stratosphere, mesosphere, thermosphere, and exosphere. The troposphere is the lowest, most studied layer of the atmosphere with an altitude in middle latitudes up to 10-12 km, in polar regions 9-10 km, and in the equatorial belt 16-18 km. The bulk of the atmosphere (approximately 80%) and almost all the water vapor are concentrated in the troposphere. The existence of an atmosphere is an important condition for life on earth. The atmosphere participates in the water cycle on the earth and in heat exchange. The presence of water vapor and carbon dioxide gas in the atmosphere exerts a great influence on the thermal conditions of the earth. The atmosphere absorbs around 15% of the solar radiation (the earth's surface, around 43%). In the higher layers ozone, which absorbs a significant amount of the ultraviolet radiation of the sun, has a strong influence on the thermal condition of the atmosphere.

The composition of the atmosphere is practically constant up /9
to an altitude of 85-100 km. The earth's atmosphere is a physical mixture of the basic gases: oxygen, carbon dioxide, and nitrogen. The atmosphere contains around 1% of other gases. The oxygen of the air is necessary for the respiration of living organisms and the carbon dioxide gas for feeding plants. The circulation of carbon is one of the chief biochemical cycles. There are around 2500 billion tons of carbon dioxide gas in the earth's atmosphere. Two-hundred-thousand trillion tons of carbon dioxide is stored in the earth's crust in the form of calcium carbonate.

The chemically inactive nitrogen enters into combination with other substances only under special conditions and at the same time nitrogen is one of the basic elements for feeding all life on earth. If nitrogen easily combined with other elements, such as the ocean waters, then the nitric acid formed would make life impossible.

Nature regulates the amount of nitrogen. The nitrogen-fixing and nitrifying bacteria present in the soil combine free atmospheric nitrogen into organic compounds which then serve as food materials for plants and animals. Denitrifying bacteria decompose dead organisms and return nitrogen into the atmosphere.

The small amounts of nitric oxide and ammonia, formed as a result of lightning discharges and delivered from the upper layers of the atmosphere by rains, are also an important source for restoring the fertility of the soil. All these processes enabled the earth to acquire a sufficiently stable atmosphere, the gas composition of which has been preserved to the present time. Thus, atmospheric air appeared from the depths of our once lifeless planet.

However, the continuous leaking of nitrogen into the atmosphere creates a serious problem for all life on earth. The conversion of nitrogen into food products for animals and plants at the present time depends almost 100% on nitrogen-fixing bacteria. In contrast to nitrogen, oxygen is highly active. It is necessary both for supporting the process of fuel combustion in a furnace and for the "burning" of the carbon, hydrogen, and nitrogen contained in our food and for converting them into water, urea, and carbon dioxide gas.

Hydrogen and helium are the most wide-spread elements in the /10
universe. Of the total number of atoms, hydrogen makes up around 93% and helium 6-7%. The other elements comprise, in all, around 1%. In the first stage of the earth's formation, oxygen, due to its chemical activity, probably was present only in the form of compounds with other elements (oxygen compounds of silicon, oxides of magnesium, and other metals).

If, in the formation period of the earth gases were not preserved on it, then life would not have arisen because water and gases are necessary for the formation and existence of living matter. Consequently, geological phenomena had a definite influence on the evolution of organisms. Great transformations of the earth's surface in the process of historical development are accompanied by the transformation not only of the plant but also of the animal world: change in the blood pigment of animals, the appearance of air respiration, the appearance of warm-blooded animals, and so forth.

In different periods of the earth's formation, significant changes took place in the organic world—the trilobites died out, the first triploblastic organisms (arthropods) appeared, and then dipnoid fishes.

Stable air respiration arises in the Devonian period—the vertebrates appear. Up to this point, organisms, in which the respiratory pigment of the blood—specifically adapted for oxygen transfer—was the copper-containing protein hemocyanin, prevailed in the plankton of the world ocean. However, as soon as such organisms found themselves in conditions of insufficient oxygen, hemocyanins could no longer provide them with this element. In the families of molluscs and crayfish, burrowing in the ground, there appear individuals, the blood of which contains hemoglobin and provides a better delivery of oxygen to the tissues of the organisms. The conversion from gill respiration to air respiration evidently produced the active influence of carbohydrase promoting the liberation of carbon dioxide from the tissues of organisms. For billions of years the sun has been feeding the biosphere with life energy, producing biogeochemical processes of enormous intensity on the earth and an infinite number of changes in living organisms. Scientists have established four great eras in geological history: the Archean, the Paleozoic, the Mesozoic, and the Caenozoic. The ocean basins were formed in the Archean period. The /11
first marine organisms appeared toward the end of this period.

In the Paleozoic era a great number of more complicated plant and animal organisms developed and the first living creatures began to leave the sea and settle the dry land. The Mesozoic era is the era of reptiles. This period also gave rise to the first mammals, which reached their evolutionary flowering in the following, Caenozoic, era of mammals, including man.

The formation of the seas and oceans, which are the chief suppliers of moisture into the atmosphere, greatly contributed to the appearance and flourishing of life on earth. Thus, 449,000 km^3 of moisture evaporates from the surface of the oceans, and 62,000 km^3 in all from the land surface, i. e., 7 times less. The oceans additionally provide around 37,000 km^3 of precipitation to the continents. The amount of precipitation falling in different physicogeographical regions is closely connected with the features of the general atmospheric circulation and the local topography. In some regions of the Sahara, Chile, and Peru, the total annual precipitation does not exceed 10 mm, while in Cherrapunji it is around 11,000 mm and some years reaches 22,000 mm.

The gases of the earth, which even today have vast significance, played an important role in the formation of our planet.

All the organic substances of the vegetable world are primarily created from gases absorbed from the atmosphere by the plants.

Animal organisms exist by feeding on plants. After the death of a living organism the bulk of its substance returns to the atmosphere in the form of gases. In the rocks and water of the earth gases are continuously being formed - the products of chemical, bio-chemical, radio-chemical and nuclear processes. Air is one of our principle natural resources. The coal and oil which we extract today basically consist of carbon extracted by plants from the air in ancient times. Even today it would be impossible to use these resources if the air lacked the oxygen necessary to burn them.

During the entire history of civilization around thirty-three billion tons of oil, one hundred twenty-five billion tons of coal and around one billion tons of natural gas have been extracted. /12
Around two hundred and seventy five billion tons of oxygen, i.e., some 0.02 percent of the entire oxygen content in the atmosphere, was used for burning this fuel. During the last fifty years the oxygen content in the atmosphere has remained practically unchanged but this does not at all mean that we should not be concerned about its preservation and the protection of the green cover of the earth. Plant resources must be increased in every way possible since plants are the basic regulator of the oxygen-carbon dioxide ratio in the atmosphere.

In the course of a day a man eats on the average 1.24 kilograms of food and drinks around two liters of water but breathes in more than 9 kilograms of air. He may refuse low quality food or water of questionable purity but he must breathe the air in which he is found at a given moment even if it is polluted or dangerous for health. The air envelope of the earth, while scattering sunlight, causes the blue color of the sky and produces the glows of the morning and evening skies, the aurora and other majestic and enchanting natural spectacles.

As V.I. Vernadskiy notes, with man, a vast new geological force appeared on the surface of our planet. Mankind took into the sphere of its consumption all resources available to it, and into the sphere of its influence the entire biosphere of the earth. Huge cities and industrial complexes grew up; an extensive network of roads was laid out. The once clear air of the great cities was filled with clouds of industrial dust and automobile gases. The problem of "man and his environment" sharply arose before contemporary man.

A large part of the population of the globe, especially of the the industrial centers and great cities, is forced to live and work in air, polluted with smoke, dust and chemical substances thrown into the atmosphere by plants and factories, heating systems and motor vehicles. The problem of preserving the purity of the air has become an acute social problem. It is not by accident that so much attention has been given to this problem in this country and that special government decisions directed toward protecting the atmospheric air from pollution have been taken.

Polluted air damages the skin, has a destructive effect on the lungs, blocks a significant amount of solar radiation, promotes the multiplication of microbes and lowers an organism's resistance to diseases. According to the data of K. Orr (1964), /13 every year more than fifty million tons of different impurities enter the atmosphere over the territory of the USA. It is well known that a man cannot endure carbon monoxide gas if its concentration is one-hundred parts per million, nitric oxide - twenty five parts per million, sulfur dioxide - ten parts per million, ozone - one part per million etc. Polluted air stops the development of plants and destroys them. As a result of the extreme air pollution in many places, several species of plants have disappeared.. In the outskirts of Los Angeles the destruction of plants is observed as far as 80 kilometers from the center of the city. In other cities - New York, San Francisco, London, Paris and Copenhagen - this phenomenon extends to a distance of 24 kilometers from the city.

In a single large industrial city motor vehicle engines give off into the atmosphere around two million liters of harmful substances a day. As a result of nuclear weapons testings, there is around one ton of radioactive substances in the atmosphere.

As K. Orr notes, in the course of the last twenty years the incidence of ling cancer has increased by 400 %. Lung cancer is particularly wide-spread in cities and industrial regions. Scientists in Great Britain have established a geographical relationship between the frequency of lung cancer cases and the number of smoke stacks per hectare of area. In the same country a relationship has been observed between the distribution of lung cancer and the duration of motor transport operation.

One of the results of the bombardment of the atmosphere with cosmic rays is the transformation of ordinary molecules of carbon into one of its isotopes, C^{14}, which is found in atmospheric carbon dioxide and finally enters the tissues of animals and plants. While organisms live, they accumulate this isotope of carbon; after their death the radioactive carbon decays gradually. It has been established that every 5500 years the amount of C^{14} is reduced by half. And since this is so, radioactive carbon serves as a unique clock, making it possible to obtain a precise chronology of historical events. Measuring the percentage of radioactive carbon in living organisms and also in ancient remains of plant or animal origin, it is possible to calculate the time which has passed since these plants or animals died.

Now as a result of nuclear weapons testing the stratosphere contains around eighteen kilograms of radioactive strontium (Sr^{90}), the most dangerous of all products of radioactive decay. According to scientists at Columbia University, at the present time Sr^{90} is present in all human organisms irrespective of age or place of habitation. The ability of some animals and plants to accumulate great amounts of radioactive elements presents a serious danger for man. /14

Only the peaceful solution of international problems will free mankind from the ever-increasing danger of air pollution. The food, drinking water and air which we breathe must be pure. "It is impossible to tolerate," wrote Joliot-Curie, "that people should apply to their own annihilation those forces of nature which they were able to discover and subdue." Soviet medical scientists together with progressive scientists of the whole world alertly stand guard over the health of the people, the duty of each man is to aid them in this.

1. THE ROLE OF OXYGEN IN THE PROCESS OF EVOLUTION OF THE ANIMAL WORLD

The living nature surrounding us gives us a colossal number of examples of the amazing adaptation of organisms to the varied conditions of their existence.

The evolution of living creatures proceeded along two paths. The internal environment of some organisms conformed to changes in inanimate nature by means of cellular adaptation to the new conditions. Thus, if the salt composition of these habitat changed, then, correspondingly, the composition of the internal environment also changed. If the changes exceeded a certain critical value, the animals perished. In other living creatures, new systems were created in the organism, which made it possible to pass through geological epochs without changing the stable conditions of the cellular existence; i.e., the creatures' own evolution countered the evolution of inanimate nature.

Having defended themselves against the influence of changes which the habitation environment underwent, these organisms continually complicated and perfected their organization. The transition to a terrestrial existence marked an important stage /15 in the development of vertebrate animals. When representatives of some species of animals succeeded in going onto dry land there was first of all formed in them an air breathing organ in contact with the atmosphere. The lung of mammals is the most perfect such organ. In man the diffusion surface of the lungs is approximately 100 meters. Whatever degree of perfection a water-breathing organ achieved it could not provide for the development of the highest forms of life which are characterized by a constant body temperature as a result of the intensive metobolism (A. G. Ginetsinskiy, 1963). Changes in the structural-physiological characteristics of the organism were caused by biological expediency.

As I. V. Davydovsky (1962) noted, "Adaptation to an external environment is often bought at the cost of significant morphological and functional shifts, passing into the region of nosology".

Comparative physiological studies have shown that the evolution of the respiratory function of the blood of cold-blooded animals proceeded along the lines of increasing the oxygen-binding properties of hemoglobin and, consequently, of increasing the oxygen capacity. With the transition to the terrestrial form of life the change in the oxygen binding properties (as a mechanism of adaptation to the new conditions of a gas) takes place mainly in the stage of embryo genesis (Barcroft, Rotschild, 1932; A. G. Ginetsinskiy, 1936). Such a type of adaptive reaction was also preserved in several high-mountain animals and birds.

The migration of vertebrate animals onto dry land was connected with a sharp intensification of energy losses not only in movement but also in supporting the body itself. It is known, for example, that inhabitants of a water environment, like fish suspended state (their specific gravity is 0.955—1.040) do not expend energy in supporting

A water environment is unfavorable for the appearance of organisms with a high intensity of oxidizing processes. Whereas not more than ten milliliters of oxygen can be dissolved in one liter of water, one liter of air can contain 210 milliliters of oxygen.

The extensive periods of time spent under water without access to the atmosphere by such diving animals as the whale, seal and others, are possible only because of the low metabolic intensity and not as a result of great oxygen reserves in their organisms. P. S. Korzhuyev (1966) notes that the quantitative relationships between the body weight and blood volume in the whale are approximately /16 the same as in man (in a whale having a total weight of 122,000 kilograms the amount of blood is 8,000 liters).

During intensive muscular work, a man may require up to six liters of oxygen per minute. For this, around 120 liters of air must pass through his lung, and in a polluted atmosphere, still more. If there existed an analogous organism with water respiration, then up to 2,000 liters of water would have to pass through its gills, i.e., around 30 liters kilogram of body weight (A. G. Ginetsinskiy, 1963). It is impossible to imagine a respiratory system of such capacity. Such significant amounts of oxygen may be obtained only by an organism with a more perfect organ of respiration.

The vegetable world, necessary for animal life developed and was perfected at the same time as the evolutionary development and perfection of living creatures on our planet. Thanks to plants there appeared vast supplies of organic food on the earth. It is sufficient to note that the vegetable world of the earth daily requires around 550 billion tons of carbon dioxide gas, combines 150 billion tons of carbon dioxide with 25 billion tons of hydrogen, liberates 400 billion tons of oxygen and creates 450 billion tons of organic substances, i.e., approximately 180 tons per person, wherein around 90% of these supplies are created as a result of the photosynthesis of single-celled algae inhabitating the world ocean.

The area of our planet earth is 510 million km^2, of which 149 million km^2 is land and the rest is ocean. In the atmosphere, water, and earth's crust are found more than 2 million species of animals, 0.5 million species of plants and also around 3 billion human beings. If there were any severe disturbance of the precise balance between the photosynthetic production of oxygen and its consumption, this would inevitably lead to a catastrophic decrease in oxygen concentration in the surrounding atmosphere. The oxygen would completely disappear from the atmosphere within 2,000 years if its supply were not constantly renewed by plants (including algae).

In the twentieth century, particularly in the last fifty years, /17
the carbon dioxide content in the atmosphere has somewhat increased since it began to be formed more intensively. At the present time around ten billion tons of carbon dioxide are introduced into the atmosphere just from the combustion of fossil fuel. It must be assumed that this process will progress even further. Calculations indicate that by the year 2000 the amount of carbon dioxide gas in the air will rise by 20%. This is seen as producing a significant increase in temperature over the entire globe since carbon dioxide

gas possesses the property of absorbing a certain portion of solar energy.

2. THE OXYGEN REQUIREMENT OF THE ORGANISM AND THE WAYS OXYGEN PERMEATES THE LIQUID MEDIA OF THE ORGANISM

Of all the gases entering into the composition of the atmosphere, that most vitally necessary for the organism is oxygen. The oxygen atom is an unbelievably efficient energy source. In fulfilling its function in the respiratory process it liberates 674 calories for each gram of molecular weight. For comparison, we note that in another chemical process capable of supporting life—fermentation—an average of 15 calories per gram are liberated, i.e., 45 times less. Only a small number of species of invertebrate animals (inhabitants of ooze deposits on the bottom of bodies of water) are capable of performing a full life cycle in the absence of oxygen.

The greatest specialist in the area of the physiology of respiration, Joseph Barcroft (1937), wrote: "Of the substances necessary for maintaining life and activity, perhaps the most important is oxygen. It is remarkable that the organism has so few reserves of such a necessary element. Moreover, the dependence of the organism on a direct oxygen supply increases according to the degree of transition to the more highly organized forms of life: anaerobes can live forever without oxygen, frogs for days, and man for minutes."

As a result of the evolution of the organic world, oxidation /18 proved to be the most important source of energy for performing physiological processes. On as much as the struggle for oxygen determined to a great degree the entire course of the evolution of mammals and the development of a complex system of specialized and interconnected organs and mechanisms responsible for oxygen exchange. It is sufficient to note that one erythrocyte contains around 280 million molecules of hemoglobin, and each molecule consists of approximately 10,000 atoms of hydrogen, carbon, nitrogen, oxygen, sulfur, and four atoms of iron. If hemoglobin were not present in the blood, one liter of arterial blood could dissolve and carry not more than 3 ml of oxygen, while with hemoglobin present, this amount increases by seventy times. The iron-containing component of hemoglobin—hemin—acquires the property of high solubility as a result of combination with a protein—globin. The capacity of hemoglobin to bind and give off oxygen is characterized by its dissociation curve.

Between the partial pressure of the oxygen in plasma and the degree of saturation of the blood with oxygen there exists a direct dependence, which is graphically expressed in the form of the oxyhemoglobin dissociation curve, which is S-shaped for the whole blood of man and animals (Fig. 1). The true form of the oxyhemoglobin dissociation curve was first obtained by Bohr in 1904.

The upper portion of the dissociation curve is sloping owing to which blood is easily arterialized even in cases where pO_2 in the alveolar air is significantly decreased. In the central portion of the dissociation curve, i.e., in the zone of lower values of pO_2, there is a significant evolution in the capillaries with a certain drop in the oxygen pressure in them. This is very important for the normal flow of oxidation processes in the tissues.

Physiological functions are provided with energy as a result of using the energy accumulated in the form of compounds rich in energy.

The process of anaerobic decomposition of hydrocarbons—the process of glycolysis, or glycogenolysis—is a phylogenetically ancient, relatively inefficient, and quite complex process formation of energy-rich phosphorus compound bonds. A significantly

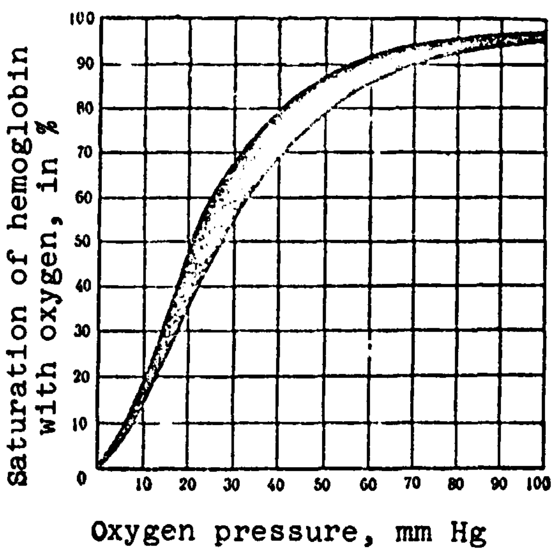

Fig. 1. Oxyhemoglobin dissociation curve.

more efficient means of forming high-energy compounds, in particular of adenosine triphosphate (ATP), is by means of oxidizing phosphorylation. In this case, the oxygen consumption of the cells is partially transformed into the energy of the phosphate bonds of ATP and other organic phosphorus compounds (V. A. Engel'gardt, /19

1930, 1959; V. A. Belitser, Ye. T. Tsybakova, 1939). At the present time the mechanism of oxidizing phosphorylation is widely studied in many laboratories here and abroad. However, the nature of the intermediate products of the process remains insufficiently investigated.

In the study by Boyer and colleagues (1962), experiments are described which explain the presence of mitochondrial formation in the cells of substances capable of serving as intermediate products of oxidizing phosphorylation. It has been established that oxidizing enzymes are concentrated in the mitochondria—cellular organelles—the chemical composition, morphological structure, and physiological function of which have now been studied in detail. However, the oxidizing processes, concentrated in the mitochondria, are diverse in nature.

In Boyer's opinion, the energy-rich bond initially forming in the respiratory chain does not belong to phosphorus but to some other compounds. The author experimentally separated a water soluble protein from mitochondria which was capable of oxidizing phosphorylation in a cell-less system. S. Ye. Severin (1964) considers that conversions taking place in the citric acid cycle and also during the transfer of hydrogen and electrons in the respiratory chain, have the greatest significance for cell energetics. The point of view of V. P. Skulachev (1958) is that the transport of hydrogen and electrons is to be attributed to the adenine of adenosine diphosphate (ADP). According to this view, adenine nucleotides fulfill the role not only of the carriers of phosphoric acid radicals, but also of hydrogen. /20

It is established that oxygen molecules in the tissues follow a complicated path until, having run into a flow of electrons, they acquire the ability to unite with ionized hydrogen, forming water as the end product of biological oxidation. It is shown that the last process takes place in the mitochondria of the cells. Up to this point, all the preceding oxygen compounds are temporary, having only a transport significance, and under certain conditions are easily decomposed.

V. N. Chernigovskiy (1971) is correct when he says that "a cell could not be a cell if at any moment it were not surrounded by a very thin membrane possessing selective permeability."

Specific quantitative relationships have been established between the oxygen consumption and the expenditure of energy in the organism.

It is known that a man at rest with a minimum gas exchange requires around 250 ml of oxygen per minute and gives off around

TABLE 1. RESPIRATION OF A MAN UNDER A LIGHT PHYSICAL LOAD.

Oxygen consumption	25 liters/hour 36 grams/hour 0.864 kg/day
Liberation of carbon dioxide gas	20 liters/hour 40 grams/hour 0.96 kg/day
Liberation of water vapor	50 grams/hour 1.2 kg/day
Energy consumptions (according to gas exchange)	130 kcal/hour 3120 kcal/day

200 ml of carbon dioxide. These factors almost double in the case of a light physical load (Table 1). In the case of heavy muscular work the oxygen requirement increases to ten times more (Table 2). This statement is also confirmed by data obtained by determining the level of the oxygen requirement of individual organs (Table 3). /21

TABLE 2. HUMAN OXYGEN REQUIREMENT AND EXHALATION OF CARBON DIOXIDE GAS DEPENDING ON THE INTENSITY OF PHYSICAL WORK (ACCORDING TO M. Ye. MARSHAK).

Intensity of work	Oxygen requirement, liters/hr	Exhalation of carbon dioxide gas
Lying	14.2	10.2
Standing	19.7	15.8
Walking at a speed of (km/hr)		
2	46.8	39.7
3	63.9	44.3
4	95.7	83.5
5	152.5	143.1

TABLE 3. THE OXYGEN REQUIREMENT OF DIFFERENT ORGANS (IN ml PER kg OF WEIGHT OF THE ORGAN) PER MINUTE (ACCORDING TO A. M. CHARNYY).

Organ	State of rest	Intense activity
Gastrointestinal tract	35	350
Heart	18	36
Kidney	85	840
Liver	15.2	50
Salivary gland	40	160
Muscles	4	32

A study of the fundamental physical properties of oxygen and the laws of its permeation into the fluid media of the organism showed that the most important factor determining a normal activity of living creatures is the partial pressure of the oxygen in the blood cells and the tissue fluids.

According to Dalton's law, the pressure of any gas in a mixture does not depend on the content of other components in it and is equal to that pressure (partial) which this amount of gas would have if it completely filled the given volume. /22

The entry of oxygen into an organism is subject to the laws of permeation of gases through the pulmonary membrane and their diffusion into fluids. Given the condition that there are around 725 million alveoli in the human lungs, the respiratory surface of the lungs is around 100 m^2. Bohr introduced the concept of the envasion coefficient—the quantity of gas which at 760 mm of mercury passes through 1 cm^2 of surface in one minute. Further investigations have shown that the absorption of gases by a fluid, the molecular weight, the pressure on the boundary layers of the fluid, the mass of the individual gas molecules, etc. all have significance for the diffusion of gases.

If we take all the above-mentioned factors into account, then the rate of diffusion of a gas (V) is expressed by the formula:

$$V = \frac{a(P_I - P_{II})K}{760d},$$

where a is the Bunsen absorption coefficient (the amount of gas absorbed by a unit volume of a liquid at atmospheric pressure); K is Stefan's diffusion coefficient (a constant depending on the nature of the diffusing gas, the liquid, and the temperature);

d is the thickness of the septum (according to the data of numerous investigators this is 0.004 mm); P is the partial pressure of oxygen.

From the formula given it is obvious that the rate of diffusion of a gas is directly proportional to the absorption coefficient, to the pressure difference of the diffusing gas on both sides of the fluid, and to the diffusion constant, and is inversely proportional to the barometric pressure and the thickness of the septum.

Further experimental investigations showed that diffusion through the pulmonary tissue takes place two times faster than through water and instead of the diffusion coefficient, the so-called diffusion factor (C) was proposed, which is derived from the diffusion coefficient by multiplying it by the square root of the molecular weight of the gas. The diffusion factor for the lungs is 0.139 and for the water it is half of that — 0.065. On the /23 basis of these data it was calculated that for a man during normal respiration 0.006756 ml of oxygen permeates through 1 cm^2 of the alveolar wall into the blood per minute, and through the entire pulmonary surface (90 m^2) — 6080 ml of oxygen.

If we consider that the oxygen requirement of a mature man at rest is 250-300 ml per minute, then it is obvious that at normal pressure the lungs provide the organism with an excess of oxygen.

As is known, in calculating the amount of oxygen required, and the carbon dioxide exhaled, and in determining the energy expenditure it is necessary to reduce the value of the respiratory minute volume (RMV) to standard conditions, i.e., to the dry state (0° and 760 mm of mercury) (A. G. Dembo, Ye. M. Kreps, 1959).

The available tables of the coefficient F for reducing gas volumes to standard conditions are calculated for changes in barometric pressure from 711 to 790 mm of mercury (R. P. Ol'nyanskaya, L. A. Isaakyan, 1959). For conditions of rarefaction from 760 to 198 mm of mercury (from 0-10,000 m) we compiled a table of the coefficients F (N. A. Agadzhanyan, I. R. Kalinichenko, 1965). The calculations for Table 4 were made according to the formula

$$\frac{B - b}{760(1+Lt^{\circ})},$$

where B is the barometric pressure at the moment of investigation; b is the vapor pressure (in mm of mercury) of the vapor saturating the space at the given temperature; L is the universal gas constant (1/273); t° is the air temperature (in degrees Celsius, according to N. S. Savchenko, 1936).

Reducing the gas volume in a rarefied atmosphere to standard conditions we obtain a value reduced by approximately as much as the barometric pressure is reduced. These calculations are not reflected ·· the coefficients of gas exchange. A determination of the oxygen requirement and liberation of carbon dioxide in the laboratory (barometric pressure 760 mm of mercury) and in a chamber pressurized to an altitude of 7000 m (barometric pressure 308 mm of mercury) showed that in both cases the pulmonary ventilation equalled 7 liters per minute and the temperature of the exhaled air was 20°.

1. Reducing the volume of air to standard conditions: /24

$$(RMV \cdot F) = 7000 \cdot 0.910 = 6370 \text{ ml/min.} \quad (1)$$

2. Since the volume of exhaled carbon dioxide is less than the volume of absorbed oxygen (in the case of a respiratory coefficient—RC—less than unity), it is necessary to introduce a correction connected with the effect of RC

$$X = \frac{N_2 \cdot O_2}{N_1},$$

where N_2 is the value exerted on the part of the nitrogen in the exhaled air [in our example, 100%—(3.4 + 17) = 79.6%]; N_1 is the value exerted on the part of the nitrogen in the inhaled air [100%—(0.05 + 20.91) = 79.04%]; O_2 is the oxygen content in the inhaled air (in percent).

Having substituted the values obtained into the formula /25

$$X = \frac{79.6 \cdot 20.91}{79.4} = 21.05\% \quad (2)$$

and subtracting the oxygen contained in the exhaled air (17%) from 21.05%, we obtain the percentage of oxygen absorbed by the organism (21.05 - 17 = 4.05).

3. Knowing the respiratory minute volume (RMV), it is possible to determine the amount of absorbed oxygen (in milliliters):

$$X = \frac{6370 \cdot 4.05}{100} = 258 \text{ ml/min.} \quad (3)$$

4. Calculation of the amount of carbon dioxide exhaled is made according to the difference between the percentage of CO_2 contained in the exhaled and inhaled air (3.04 - 0.05 = 3.35%), multiplied by the value of the RMV: /26

$$X = \frac{6370 \cdot 3 \cdot 35}{100} = 213.4 \text{ ml/min.} \quad (4)$$

TABLE 4. THE COEFFICIENT F FOR REDUCING A GAS SATURATED WITH VAPOR TO THE DRY STATE, 0° C AND 760 mm OF MERCURY FOR CONDITIONS OF RAREFACTION.

Altitude, m	Pressure B, mm Hg	760/B	Vapor pressure, mm Hg															
			[illegible]	[illegible]	14,45	[illegible]	16,37	[illegible]	18,50	19,66	20,88	22,18	23,55	24,99	26,50	[illegible]	29,78	31,55
			temperature, °C															
			15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30
10 000	198,18	3,83	0,231	0,230	0,227	0,225	0,223	0,221	0,219	0,215	0,214	0,212	0,210	0,203	0,205	0,202	0,200	0,197
9 500	213,82	3,55	0,250	0,248	0,247	0,244	0,242	0,240	0,238	0,236	0,234	0,231	0,229	0,227	0,224	0,221	0,219	0,216
9 000	230,45	3,29	0,271	0,269	0,267	0,265	[illegible]	0,261	0,259	0,256	0,254	0,251	0,249	0,247	0,244	0,241	0,238	0,235
8 500	248,13	3,06	0,293	0,290	0,289	0,287	0,285	0,282	0,281	0,278	0,275	0,273	0,270	0,268	0,265	0,262	0,259	0,256
8 000	266,89	2,84	0,316	0,314	0,312	0,310	0,308	0,306	0,303	0,301	0,298	0,296	0,293	0,290	0,287	0,285	0,282	0,279
7 500	286,79	2,65	0,341	0,339	0,337	0,335	0,332	0,330	0,327	0,325	0,322	0,320	0,317	0,314	0,311	0,308	0,305	0,302
7 000	307,87	2,46	0,368	0,365	0,363	0,361	0,358	0,356	0,353	0,350	0,348	0,345	0,343	0,339	0,336	0,333	0,330	0,328
6 500	330,18	2,30	0,393	0,391	0,388	0,385	0,383	0,380	0,380	0,379	0,375	0,372	0,369	0,366	0,364	0,360	0,357	0,354
6 000	353,77	2,14	0,425	0,422	0,420	0,417	0,414	0,412	0,409	0,406	0,404	0,401	0,399	0,395	0,391	0,388	0,385	0,381
5 500	378,71	2,06	0,456	0,453	0,451	0,418	0,445	0,443	0,440	0,437	0,434	0,431	0,427	0,425	0,421	0,418	0,415	0,411
5 000	405,09	1,87	0,489	0,486	0,484	0,481	0,478	0,475	0,472	0,469	0,466	0,463	0,459	0,456	0,453	0,449	0,446	0,442
4 500	432,9	1,75	0,524	0,520	0,518	0,515	0,512	0,509	0,506	0,503	0,500	0,496	0,493	0,490	0,486	0,482	0,479	0,475
4 000	462,26	1,64	0,560	0,556	0,554	0,551	0,548	0,545	0,542	0,539	0,535	0,532	0,528	0,525	0,521	0,517	0,514	0,510
3 500	493,19	1,54	0,598	0,595	0,593	0,589	0,586	0,583	0,579	0,576	0,573	0,569	0,565	0,462	0,558	0,554	0,551	0,547
3 000	525,79	1,44	0,639	0,635	0,633	0,629	0,626	0,623	0,619	0,616	0,612	0,609	0,605	0,601	0,597	0,593	0,590	0,585
2 500	560,11	1,35	0,682	0,678	0,676	0,672	0,668	0,665	0,661	0,658	0,654	0,650	0,646	0,643	0,639	[illegible]	0,630	0,626
2 000	596,23	1,27	0,727	0,723	0,720	0,716	0,713	0,709	0,705	0,702	0,698	0,694	0,690	0,686	0,682	0,677	0,673	0,669
1 500	634,15	1,19	0,775	0,770	0,767	0,763	0,759	0,756	0,752	0,748	0,744	0,740	0,735	0,732	0,727	0,722	0,719	0,714
1 000	674,09	1,12	0,824	0,819	0,817	0,813	0,808	0,805	0,801	0,796	0,793	0,788	0,783	0,779	0,775	0,770	0,766	0,761
500	715,99	1,06	0,877	0,871	0,869	0,864	0,860	0,856	0,852	0,848	0,843	0,839	0,834	0,830	0,825	0,820	0,817	0,811
0	760	1,0	0,932	0,928	0,923	0,919	0,915	0,910	0,906	0,901	0,897	0,892	0,888	0,883	0,878	0,873	0,869	0,864

In the study by A. P. Apollonov and V. G. Mirolyubov (1938) it is shown that the oxygen consumption by the tissues during elevation to an altitude remains unchanged in rather wide limits and decreases only in conditions of extreme degrees of rarefaction of the atmosphere.

Experimental studies showed that for normal oxygen supply to the organism the partial pressure of oxygen in the gas mixture at different altitudes must be maintained at a level somewhat exceeding the sea level value at a pressure of 760 mm of mercury. For this it is necessary to know the nature of the calculation of the percentage of oxygen in the cabin of the flying vehicle. As is known, in absolutely dry air at sea level the partial pressure of oxygen (pO_2) is determined according to the formula:

$$pO_2 = \frac{a \cdot B}{100} = \frac{20.93 \cdot 760}{100} = 159 \text{ mm of mercury}$$

where a is the percentage of oxygen in the air; B is the total barometric pressure.

However, inhaled air is rapidly saturated with water vapor and is heated to body temperature. It is assumed that the water vapor pressure at high altitudes does not change and amounts to 47 mm of mercury.

For a long time aviation doctors were of the opinion that for normal oxygen supply to the organism it is sufficient that the partial pressure of oxygen in cabins at different altitudes be maintained at a level of 159 mm of mercury. However, it was subsequently shown that with equal partial pressures of oxygen in inhaled air the pO_2 in the alveolar air in conditions of lowered barometric pressure will be lower than in the case of normal atmospheric pressure. This phenomenon results from the fact that the alveolar air is saturated with water vapor. And since the water vapor pressure does not change at high altitude, then with a decrease in the total pressure the pressure exerted on the water vapor will be correspondingly increased.

This circumstance must be considered when determining the partial pressure of respiratory gases in the organism. Thus, in order to obtain the value of the partial pressure of oxygen in tracheal air, the above-given formula will appear as follows: /27

$$pO_2 = \frac{a(B - 47)}{100} = \frac{20.93(760 - 47)}{100} = 149.2 \text{ mm Hg.}$$

Hence the percentage of oxygen is:

$$a = \frac{149.2 \cdot 100}{B - 47}.$$

In order to maintain the normal partial pressure of oxygen in the tracheal air (equal to 149.2 mm Hg), and consequently also in the alveolar air (100 mm Hg) at different altitudes it is necessary, as we indicated above, to increase the percentage of oxygen in the inhaled air. The calculation is performed according to the formula:

$$a = \frac{pO_2 \cdot 100}{B - 47}$$

The values obtained according to this formula for altitudes up to 10,000 m are given in Table 5.

TABLE 5. THE RELATIONSHIP BETWEEN THE PERCENTAGE OF OXYGEN AND NITROGEN FOR MAINTAINING A pO_2 IN INHALED MOIST AIR EQUAL TO 149.2 mm Hg AT HIGH ALTITUDES.

Altitude, m	Atmospheric pressure mm Hg	pO_2 in dry air, mm Hg	Percentage in inhaled gas mixture	
			oxygen	nitrogen
0	760	159,07	20,93	79,04
1 000	674,09	159,74	23,7	76,3
2 000	596,23	162,1	27,2	72,8
3 000	525,79	163,6	31,1	68,9
4 000	462,26	165,8	35,9	64,1
5 000	405,09	168,5	41,6	58,4
6 000	353,77	172,0	48,6	51,4
7 000	307,87	176,2	57,2	42,8
8 000	266,89	181,0	67,8	32,2
9 000	230,45	187,4	81,5	18,5
10 000	198,18	195,6	98,8	1,1

As an example, Fig. 2 presents data characterizing the gas ratio in inhaled and alveolar air in man in a laboratory study and in conditions of an artificial atmosphere in a pressure chamber (altitude 6900 m, O_2 58%). /28

As is seen from Fig. 2, in order to have an identical partial pressure of oxygen in the alveolar air (100 mm Hg) it is necessary to increase the pO_2 in the inhaled air from 154.6 mm Hg (at sea level) to 178 mm Hg (at an altitude of 6900 m).

Figures 3 and 4 show the gas ratio in the blood and in the air in the case of breathing at sea level and at an altitude of 4250 m atmospheric air (Fig. 3) and pure oxygen at 760 mm Hg and at an altitude of 10,400 m (Fig. 4).

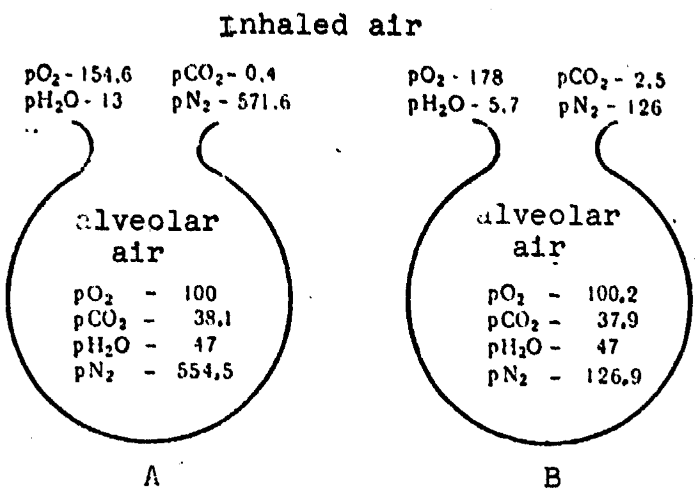

Fig. 2. Ratio of gases in inhaled and alveolar air (in mm Hg) in the case of breathing atmospheric air at sea level (A), and a gas mixture containing 58% oxygen at an altitude of 6900 m (B).

The knowledge of the characteristics of an investigation of gas exchange has important practical significance not only for conducting laboratory studies in pressure chamber conditions but also in developing new oxygen breathing apparatus and high altitude equipment and for developing an artificial atmosphere in the cabins of

In recent years fundamental work on the further study of the theory of the oxygen dynamics in the tissues of a living organism has appeared at home and abroad. The application of electronics in physiology and the creation of instruments (oxyhemom- /30
eters, polarographs, and so forth) have made it possible to more precisely determine the dynamics of the oxygen parameters with simultaneous recording of the indicators of the activity of physiological systems participating in oxygen exchange.

According to contemporary concepts, the paths of entry of oxygen into the organism are considered to be a continuously decreasing cascade of levels of the partial pressure of oxygen in the alveoli, the arterial, capillary,

In scientific literature there have appeared the concepts the oxygen budget of the organism", the "total oxygen gradient", the oxygen cascade", and the oxygen regime of the organism", which reflect the drop in the partial pressure of oxygen at the

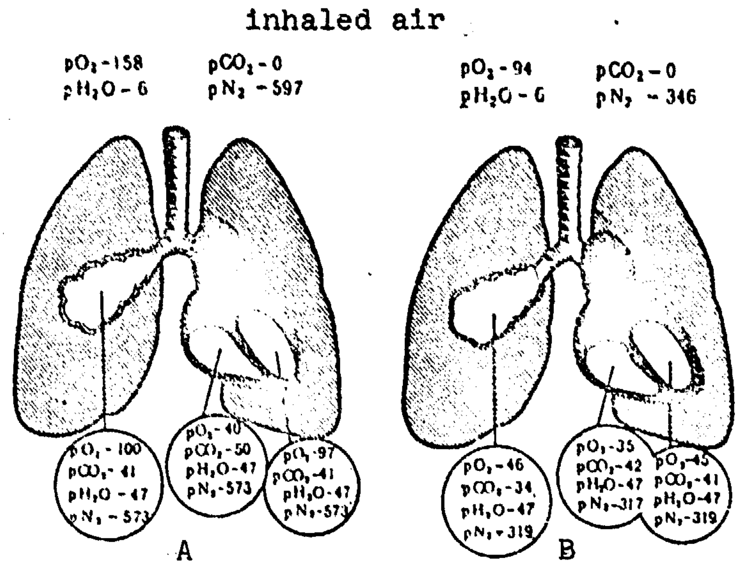

Fig. 3. Gas ratios in the blood and in inhaled air (in mm Hg) in the case of breathing atmospheric air at sea level (A), and at an altitude of 4250 m (B).

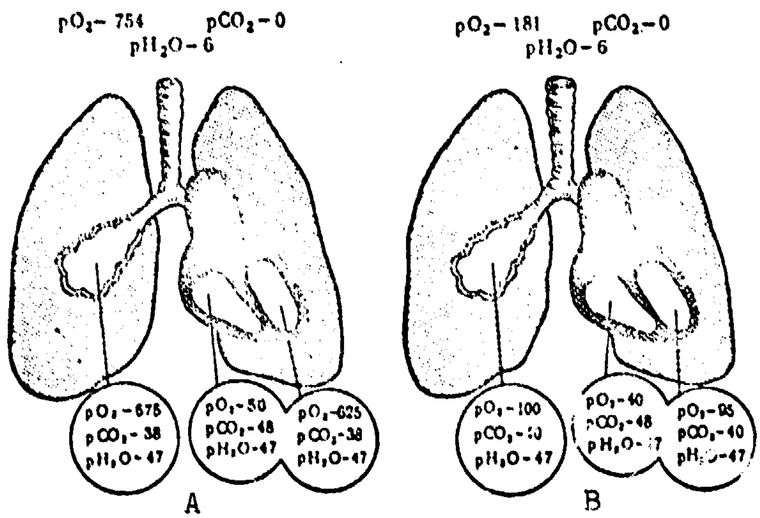

Fig. 4. Gas ratio in the blood and in air (in mm Hg) in the case of breathing pure oxygen at sea level (A), and at an altitude of 10,400 m (B).

various stages of its distribution in the organism (A. M. Charnyy, 1947, 1961; Luft, Armstrong, 1962; Hurtado, 1963; A. Z. Kolchinskaya, 1964). In addition, this indicator is compared with the respiratory minute volume, the alveolar ventilation, the rate of oxygen diffusion, the oxygen capacity of the blood, the dissociation curve of oxyhemoglobin and carbon dioxide, and so forth (Fenn, Rahn, Otis, 1946, 1959; Hurtado, 1963).

The concept of the "total oxygen gradient", being one of the integrating indicators of the oxygen exchange, not only creates an idea of those physical conditions in which oxygen exchange takes place at the different levels of the oxygen cascade, but also makes it possible to determine the nature of physiological shifts in the conditions of a changed gas medium, for example in the process of acclimatization to a high mountain climate. Studying the processes of the adaptation of the organism to high mountain conditions, Hurtado (1963) determined the basic values (gradients) of oxygen pressure in simultaneously taken samples of alveolar air, arterial blood, and mixed venous blood from the pulmonary artery (with the aid of catheterization of the right heart) in subjects living at sea level (Lima) and in inhabitants of Marococho (central Andes, altitude 4540 m). Analysis of the results obtained made it possible to draw the conclusion that the high degree of acclimatization of the local inhabitants to hypoxia is explained by the fact that in them the total drop in the oxygen pressure gradient is half of that which is observed in people living at sea level. Such an economy takes place as a result of physiological adaptation pro- /31
cesses (increasing long ventilation, decreasing the alveolar-arterial gradient, polycythemia, and so forth). In inhabitants of Marococho, for example, lung ventilation is 20% higher than in people living at sea level, and if we recalculate for weight or body area, then this value is raised to 40%.

Investigations (Hurtado, 1963; M. M. Mirrakhimova, 1964; K. Yu. Akhmedova, 1967; N. A. Agadzhanyan, M. M. Mirrakhimova, 1970) showed that acclimatized mountain **residents, together with a higher degree of** ventilation, have a greater volume of alveolar air and an increased functional residual capacity and diffusion surface of the lungs. Moreover, in an anatomical investigation of specimens of human lung, expansion of the capillary channel was always observed (Campos, Iglesias, 1956). All these materials indicate that the great capacity for oxygen diffusion observed in mountain aborigines is a result not only of functional but also anatomical characteristics of their organs and systems providing for control of the oxygen exchange between the organism and the surrounding environment. The expanded vascular channel of the capillaries observed in the tissues of mountaineers is an important mechanism of adaptation as a result of the greater ease of passage (diffusion) of oxygen along them. The myoglobin content also has a definite influence on the oxygen utilization by the tissues. In 1937 Hurtado mentioned the higher myoglobin content in the muscles of dogs which were born and lived in the mountains. Quite recently these data were confirmed in human beings through a muscle biopsy performed on high-mountain dwellers (Reynafarie, 1962).

In connection with the experimental data received in recent years it appears to us that the above-mentioned general formulas for the rate of gas diffusion and the general laws of oxygen permeation into the liquid media of the organism, as they relate to aborigines who have lived for centuries in high mountain conditions, probably require appropriate correction and refinements.

A significant step forward as regards oxygen exchange as a whole was made by A. M. Charnyy (1947) in proposing the term "oxygen budget of the organism." The concept of an "oxygen budget" includes a whole complex of questions relating to the need of an organism for oxygen, the laws of oxygen permeation into the cells and fluids of the organism, its transportation through the circulatory system, and the mechanism of oxygen use by the tissues. /32
Thus, the very concept of an "oxygen budget" provides for a total quantitative evaluation of the oxygen exchange.

N. V. Lauer and A. Z. Kolchinskaya (1966) made an attempt to establish the oxygen parameters which would successively reflect the amount of oxygen entering in a unit of time with the inhaled air (q_1O_2), reaching the alveoli (q_AO_2), transported by the arterial blood to the tissues (q_aO_2), removed by the venous blood after a time from the tissues (q_vO_2), and required by the tissues themselves (q_tO_2).

Comparison of the cascade qO_2 and pO_2 shows that at different stages of the exchange, the above-mentioned parameters have a definite interdependence which makes it possible to speak of the "oxygen regime of the organism".

Thus, authors take the term "oxygen regime of the organism" as meaning the combination of interconnected oxygen parameters (pO_2 and qO_2) of the inhaled alveolar air, the arterial and venous blood, and the tissues, determined by the level of functioning of various systems of the organism directed toward maintaining the balance between the oxygen need and suppy of the tissues.

However, the concept of an oxygen regime proposed by N. V. Lauer and A. Z. Kolchinskaya also does not completely exclude those procedural difficulties which investigators ran into earlier and which are now found in studying the qualitative interdependence of the values of the parameter values at various stages of the cascades.

It seems to us that the essence of the concepts "oxygen budget of the organism" (A.M. Charnyy, 1947), "total oxygen gradient", "oxygen cascade" (Luft, Armstrong, 1962; Hurtado, 1963), "oxygen regime of the organism" (N. V. Lauer, A. Z. Kolchinskaya, 1966) do not contradict one another in principle, but rather mutually complement and refine one another, being a step forward in the solution of the problem of oxygen exchange. In addition as a result of the extreme complexity of the investigated subject study not one of these concepts is universal and exhaustive at the present time. Further systematic analysis of these problems is necessary.

The explanation of the quantitative characteristics of oxidizing processes, which take place at the tissue, cellular and molecular levels of the different functional systems providing for the gas exchange of the whole organism, continues to remain a particularly weak link. /33

The concept of regulating oxygen exchange originated at the same time as discoveries of the energy significance of the oxidizing processes necessary for the activity of the animal organism (Bert, 1878; I. M. Sechenov, 1880). From that time on, respiration began to be considered as essentially as oxidation process with the basic task of regulating the organism's oxygen supply and removing carbon dioxide (Haldane, 1922).

In 1884, P. M. Al'bitskiy wrote in his doctoral dissertation: "We see in the animal organism a whole series of very complex mechanisms able to compensate for the harmful influence of the external environment, but these mechanisms prove to be effective only while in quite narrow limits and cannot provide for an invariable internal environment of and organism under extreme conditions" (p. 114).

The presence of a strictly specialized reflex mechanism of respiratory regulation for hypoxic conditions testifies to the important role of the nervous system in adapting the organism to conditions of a changed gas environment.

According to contemporary concepts respiratory regulation is performed by two means: reflexively and by means of humoral action upon the respiratory center.

In the opinion of several authors, there are various cells, in the area of the respiratory center, some of which react to intracellular changes in CO_2 and others to reflex impulses (Banus, et al., 1944).

Alongside the previously discovered baroreceptors, providing for regulation of blood pressure in the wall of the aortic arch and in the region of the bifurcation of the carotid artery, that is, at the "turn" of the arterial system, there were discovered chemoreceptors, capable of sensing the chemical composition of the blood. The existence of chemoreceptors in the organism was predicted by I. P. Pavlov thirty years before their discovery.

In 1894, I. V. Pavlov, in a report to the fifth congress of the Society of Russian Physicians in memory of M. I. Pirogov, noting the importance of the study of the effect of different substances on the peripheral endings of the centripetal nerves, /34
said; "These endings must be extremely diverse and specific, similar to the nerve endings of sensory organs, each adapted to its own unique stimulus whether this be mechanical, physical, or chemically produced".[1]

The presence of chemoreceptors in the region — of the aortic arch was convincingly proven in the experiment by the Heymans father-son team (1927), and in 1930 C. Heymans (the son) and colleagues discovered chemoreceptors in the region of the carotid sinuses possessing extremely high sensitivity and adapted to sensing the chemical composition of the blood.

In the reflex mechanism humoral factors — oxygen, carbon dioxide gas and H-ions — have foremost significance as adequate stimuli of the chemoreceptors. Loeschcke and colleagues (1958) show that a change in the pH in the zone of the respiratory center does not directly influence respiration, acting on the center, but indirectly, through the chemoreceptors, located in the recessus lateralias of the fourth ventricle.

The chemoreceptors of the carotid sinus and the aortic arch have foremost significance in the regulation of the oxygen regime of the organism.

Even in the case of normal oxygen pressure in the blood the chemoreceptors are constantly in a state of "hypoxic" excitation which disappears with an increase in the arterial pO_2 to 170 ml of mercury (Deyours, 1958, and others). High oxygen concentrations seem to produce "physiological denervation" of the chemoreceptors (Drips, Comroe, 1947).

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1 I. P. Pavlov: Poln. Sobr. Soch. (Complete Collected Works, volume 1, Moscow, 1951, page 525.

The discovery of the most important regulator of respiration and circulation—the chemoreceptors of the sino-carotid and aortal sinuses,—achievements in the study of chemoreception as a whole and the discovery of chemoreceptors of the venous channel and of tissue chemoreceptors solidly confirm the concept of the participation of chemical agents in the regulation of respiration and circulation. (Ye A. Moiseyev, 1927; Heymans, 1927; Hering, 1927; M. N. Anichkov, 1929; and others). It has now been quite convincingly proven that chemoreceptors participate significantly in regulation of the chemical properties of the internal environment of the organism and in maintaining its chemical stability. Possessing high sensitivity to threshold fluctuations of arterial pressure of oxygen, carbon dioxide and the concentration of hydrogen ions, the arterial chemoreceptors are the first indicators of these fluctuations and provide for emergency adaptation of the respiratory system. The respiratory center itself and the respiratory formations in the walls of the ventricles of the brain, being a more steady and inert regulatory mechanism come into action later. /35

In studying the influence of different pharmacological substances on the carotid balls, the basic method is the method of isolating the carotid sinus, developed by Ye A. Moiseyev (1926). precisely, with the help of this method, in experiments on dogs Ye. A. Moiseyev discovered reflexes from the carotid pressure receptors on respiration. The Moiseyev method with a small modification was used by the Heymans for perfusing the isolated dog sinus.

The role of the peripheral chemoreceptors has not been studied up to the present time. In the opinion of M. V. Sergiyevskiy (1961) the peripheral chemoreceptors participate mainly in the regulation of local processes.

At the present time, a great amount of experimental material on physiological mechanisms of the adaptation of man and animals to oxygen insufficiency has accumulated in the literature. Analysis of this problem was begun in Russia with the studies of I. M. Sechenov and his closest students and followers—V. V. Pashutin (1881), P. M. Al'bitskiy (1884), and others, and abroad with the works of Bert.

However, despite the fact that the hypoxic state has long held attention of various investigators, many aspects of this problem have not yet been studied. At the present time we do not have at our disposal sufficient materials revealing the intimate mechanism lying at the basis of adaptation to oxygen insufficiency.

In the most general form two types of adaptive reactions of the organism to hypoxia are considered in the literature. The first type is that of extra-cellular compensatory reactions (respiratory, hemodynamic and humoral) providing for a normal oxygen supply to the cells; their effect is realized through the agency of the nervous system or by the neuro-humoral route. The second type is that of tissue /36 cellular adaptive reactions determining the metabolism in correspondence with the oxygen supply.

Adaptive reactions of the first type compensate for oxygen deficiencies in the blood by means of deepening breathing and increasing the frequency of breathing movements, increasing the minute volume of the heart, increasing the oxygen capacity of the lungs, redistributing the blood among the organs with varying sensitivity to oxygen deficiency and also by means by increasing the alkalinity of the blood, which increases as a result of hyperventilation.

Oxidizing enzymes of the tissues also fight for oxygen together with extra-cellular compensatory reactions.

The possibility of physical-chemical changes in the tissues and the adaptation of the tissues themselves to a hypoxic environment was mentioned by F. Bert (1878), V. V. Pashutin (1881), P. M. Al'bitiskiy (1884), Holden (1927) and later - by N. M. Sirotinin (1931), Ye. M. Kreps (1945), V. V. Strel'tsov, I. M. Khazen, (1946) and others.

The study in the laboratories of M. N. Sirotinin and G. Ye. Valdimirov on the dynamics of changes in the acid-base balance of the blood, which may influence the course of chemical processes in the tissues and cause changes in the respiratory function of the blood also had important significance. Detailed information on this problem is given in the monograph by I. M. Dedyulin (1941) Z. I. Barbashova (1970) greatly contributed to the study of the biochemical basis of the changes in the general resistance of the organism and adaptive changes of the tissue chemism in the process of acclimatization to hypoxia.

The studies of L. L. Shik (1947) established that under the influence of decreased oxygen pressure the level of exchange may drop below the level of the basal metabolism. The author assumes that the basic cause of the decrease in oxygen consumption in conditions of hypoxia is the decrease in the intensity of the oxidizing processes. Lowering the body temperature is a secondary process. In the opinion of K. P. Ivanov (1968) oxygen deficiencies in the inhaled air leads to the suppression of chemical thermoregulation.

In conditions of hypoxia the very mechanisms of tissue respira-

tion change qualitatively. A. V. Palladin (1954) established /37
that maintaining stability in the total absorption of oxygen by the tissues takes place against a background of significant changes in the very mechanism performing tissue respiration since in this case the basic process of tissue respiration is disturbed--the process of cleavage of hydrogen from the substrate.

The investigation of Ye. M. Kreps and colleagues (1956) shows that in conditions of hypoxia there is first of all observed a compensatory increase in the activity of several enzymes (cytochromoxidases and carboanhydrases), owing to which a sufficient level of tissue respiration is ensured.

As N. A. Arkahangel'skaya (1946) indicates, the adaptive changes to hypoxia take place in the cell itself and most probably in the nuclear apparatus regulating the cellular metabolism.

According to the data of Kamakura (1955), hypoxia primarily acts on the membrane permeability. The use of certain pharmacalogical substances (ethyl carbamate) prevents a decrease in human erythocytes of the potassium content and an increase of the sodium content. Ethyl carbamate in subnarcotic doses significantly extends the life of rats at an altitude of 12,000 m (145 mm of mercury) and doubles the life expectancy of a frog heart in a nitrogen atmosphere.

In Hurtado's study (1963), data are given on a study of the activity of enzymes in the tissues of animals and men acclimatized to high-mountain conditions. The materials obtained testified to the increased activity of the mitochondrial oxidation system in natives of high-mountain conditions. Reynafarje (1962) considers these changes to be mechanisms providing for a higher degree of utilization of oxygen through enzymes.

It must be assumed that the numerous compensatory reactions participating in the process of adaptation are of different significance in the various periods of the development of oxygen starvation.

Depending on the degree of hypoxia or other factors these sometimes act conveniently and sometimes sequentially. However, they are always directed towards the most perfect adaptation of the organism to the effect of the external environment and to the preservation of life in the most varied conditions of existence.
The metabolism of the brain in normal and pathological conditions is of great interest. Experimental data on the biochemistry of /38
the brain during dying and revivication of the organism are presented in the monograph of M. S. Gayeveskaya (1963).

A great number of works have been published on the study of the physiological mechanisms of adaptation to hypoxia. It is sufficient to mention the monographs of J. Barcroft (1925), J. Holden (1927), P. I. Yegorov (1936), E. Von Lier (1947), A. M. Charnyy (1947, 1961), I. R. Petrov (1949, 1967), G. Armstrong (1954), Z. I. Barbarshova (1960), A. Z. Kolchinskaya (1964), N. A. Agadzhanyan and M. M. Mirrakhimov (1970) Y. E. Kovalenko, I. M. Chernyiakyov (1972) and others.

Large groups of scientists in our country have scientific conferences to systematically discuss the results of their investigations in studying the influence of hypoxic states on the organism.

The true organizer and inspirer of scientific symposia is N. M. Sirotinin. It was under his guidance, in 1949 at the conference on hypoxia in Kiev, that the most contemporary and scientifically well-founded classification of hypoxia was developed. According to this classification, we can distinguish: 1) hypoxic hypoxia, developing: a) from a decrease in inhaled pO; b) as a result of a blockage of the permeation of oxygen into the blood through the respiratory tract; c) due to disturbance of extrernal respiration; 2) hemic hypoxia: a) of the anemic type and b) hypoxia with inactivation of the hemoglobin; 3) the circulatory type of oxygen starvation, having: a) a congested form and b) an ischemic form; 4) tissue hypoxia in which the tissues are deprived of the possibility of normal utilization of oxygen as a result of a disturbance in oxidizing processes in them.

Although the basis of this classification is the single pathogenic principle of the development of hypoxic states, its basic shortcoming is the absence of the most commonly occurring combination type of hypoxia.

A further improvement of the classification of hypoxic states, with consideration of data obtained in recent years with the use of contemporary methods of investigation, is dictated by the requirements of many branches of biomedical science in an era of unforeseen scientific and technical progress. In the past decade a new field /39
of knowledge has developed — molecular biology — which interprets the most important manifestations of life activity as a result of the structure and properties of molecules and molecular interactions. It is now possible to no longer speak of cellular, but of molecular pathology and to explain the nature of certain diseases by changes in the structure of a specific type of protein molecule in the tissues of the organism (V. A. Englehardt, 1959).

"Respiration," writes V. A. Englehardt, stands before us as a physiological phenomenon, of primary importance wholly and completely resting on the interaction and participation of several types of molecules — oxygen and carbon dioxide, on the one hand, and respiratory pigments on the other" (1967).

A further study of the mechanism of the appearance of all the above enumerated forms of compensatory reactions will make it possible to control these reactions, to discover the nature of many pathological states, to uncover the possibility for broad regulation of energy exchange in the organism, and consequently, to find means of increasing the resistance of the organism to oxygen deficiency and other extreme effects, and to determine the limits of permissible oxygen concentration in air-tight compartments in oxygen therapy.

CHAPTER II

THE INFLUENCE OF OXYGEN DEFICIENCY ON THE ORGANISM

It is known that the influence of any factor of the external environment on the organism has minimum and maximum limits. Life is possible only within these limits and severe functional disturbances which may lead to the death of the organism begin beyond their bounds. Within these limits there are most favorable, optimal conditions and less favorable but permissible conditions. /40

A complex of unfavorable factors influencing the human organism, even in insignificant quantities in the case of prolonged action, be the cause of of a substantial shift in the state of health. Therefore the problem of maintaining a man's efficiency in the case of a prolonged stay in air-tight compartments acquires important theoretical and practical significance at the present time and in essence becomes new, independent bio-medical problem.

Habitability is the sum of many factors: the barometric pressure, gas, chemical and ion composition of the atmosphere, the temperature, humidity and motion speed of the air, the noise level, ionizing radiation, light conditions, personnel accommodations, water, food and clothing supply and etc.

One of the basic requirements imposed upon a medium of habitation is that the gas environment be safe for human health and not go beyond the bounds of the physiologically permissible limits.

1. DECOMPRESSION RATE AND ABILITY TO WITHSTAND ACUTE HYPOXIA

During flight modern flight vehicles come under conditions approximating a complete vacuum, in a medium not compatible with the concept of life. In the case of a rupture in pressurization and a rapid critical drop in the cabin pressure, the crew of the craft will be subjected to the danger of a rapid onset of acute oxygen starvation, possible damage to the lungs, the inevitable development of aeroembolism and the phenomena of boiling and vapor formation in the organs and tissues of the organism. In the combined /41 effects of these factors acute oxygen deficiency presents the greatest danger. Very small oxygen reserves completely satisfy the physiological requirements of man and animals under condition of constant replenishment of this supply from the atmospheric air. With a rupture in the pressurization of an aircraft cabin at high altitudes (more than 10,000 meters) and loss of the vitally important properties of the atmosphere a man without protective devices very quickly loses consciousness; since the oxygen reserves in the human organism are extremely small they can last only a very insignificant time - minutes and even seconds. Moreover, unconsciousness and other threatening symptoms begin in man long before complete exhaustion of the oxygen reserves in the organism. Tables 6 and 7 present data for time to unconsciousness for a man breathing atmosspheric air at an altitude of 7500 meters and breathing pure oxygen at altitudes of 13,000 to 17,000 meters.[1]

It is necessary to note that the time to unconsciousness for a man breathing atmospheric air at critical altitudes (more than 10,000 meters) and breathing pure oxygen at altitudes of more than 15,000 meters, is approximately identical and equals 15-30 seconds. This fact becomes understandable if we consider for approximately this same time (for 8-12 seconds) the oxygen from the lungs which is circulating in the blood enters the heart and brain.

Such a high speed of development of acute hypoxia at high altitudes is explained not only by the decrease in the partial pressure of oxygen in the inhaled air, but also by the phenomena of the degasing (deoxygenation) of the organism characteristic for these conditions. In the case of extreme degrees of rarefaction of the atmosphere the organism looses oxygen and other gases from the blood through the lungs just as blood outside the organism looses these gases, being placed in conditions close to a total vacuum. The /42
phenomenon of degasification of the organism is already observed at altitudes on the order 12,000 meters and becomes clearly pronounced at altitudes greater than 15,000 meters where the partial pressure of oxygen in the alveolar air is physiologically equal to zero, although physically there is still oxygen in the atmosphere. It is precisely on this basis that certain foreign authors consider an altitude of 15,000 meters, in relation to the oxygen supply, to be an altitude equivalent to the conditons of outer space (Strughold, 1954).

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[1]The term time to unconsciousness is understood to mean that segment of time during which a man retains sufficient capacity for work and consciousness when breathing in conditions of extreme degrees of atmospheric rarefaction.

TABLE 6. TIME TO UNCONSCIOUSNESS OF A MAN AT AN ALTITUDE OF 7500 METERS IN AN ALTITUDE CHAMBER ACCORDING TO THE DATA OF SEVERAL AUTHORS

Author		Time to unconciousness		
		minimum	maximum	average
A.P.Apollonov et al		1 min 30 sec.	3 min. 48 sec.	2 min. 18 sec.
G.Armstrong		2 " –	4 "	3 "
K.H. Shtrukhgol'd		–	4 "	– –
V.K. Bondarenko et al		3 min 14 sec.	4 " 49 sec.	4 min.
V.A. Skrypin		4 min	14 " 37 sec.	7 min. 07 sec.
G.V. Altuktov, V.B. Malkin		4 " 31 sec.	15 " 49 sec.	7 min. 25 sec.
G. Dirinsgofen		35 sec.	22 " 30 sec.	
N.A. Agadzhanyan, G. A. Davydov[1]	I	3 min. 45 sec. / 9 min. 30 sec.	9 min. 45 sec. / 86 min. 10 sec.	6 min. 45 sec. / 52 min. 30 sec.
	II	3 min. 45 sec. / 3 min.	35 min. / 89 min. 07 sec.	23 min. / 53 min.

[1] I - subjects, exposed for this first time to under high-mountain conditions: II - mountain climbers. In the numerator are presented data obtained before acclimatization to the mountain climate; in the denominator, after 45 days of acclimatization.

The use in aviation and astronautics of air-tight cabins with excess pressure in relation to the external atmosphere makes it possible to fly at high altitudes, protecting the crew from the fatal effect of these altitudes. However, in real flight conditions the possibility of decompression is not excluded - loss of excess pressure, which may be relatively slow or rapid. The influence of slow decompression does not cause significant changes in the organism, while with rapid (explosive) decompression profound functional disturbances appear. There is no single opinion as regards the boundary between explosives and slow decompression. G. Armstrong (1954) considers decompression to be explosive if the rate of pressure drop exceeds the rate of drop observed in rising by 1500 meters per minute. F. Violette (1961) determined decompression to be explosive, if the coefficient of leakage (the ratio of the area of the opening to the volume of the cabin) exceeds 1:100 m^2/m^3 and the ratio of the initial pressure to the final pressure is more than 2.3. /43

TABLE 7. TIME TO UNCONSCIOUSNESS OF A MAN BREATHING PURE OXYGEN AT ALTITUDES OF 13,500 - 17,000 M

Altitude, m	Data of T.Bentsinger	Time (data of V.A.Skkrypin) minimum	maximum	average
13 500	—	6 min 07 sec	30 sec	—
14 000	50 sec	47 "	4 min 45 "	2 min 45 sec
14 500	25 "	30 "	3 " 40 "	1 " 04 "
15 000	15 "	19 "	1 " 22 "	34 "
15 500	10 "	17 "	27 "	21 "
16 000	9 "	15 "	21 "	18 "
17 000	9 "			

Such an interpretation, in our opinion, is one-sided. In evaluating the different parameters of decompression it is necessary to consider not only the degree of change in the absolute values of physical factors of the medium, but also the nature and the degree of reaction of the different functional systems, the individual peculiarities of the organism, the presence of protective equipment and etc.

The physical characteristics of any pressure drop are determined by the duration of the drop, its magnitude and rate. The greater the time of a drop, the less will be its speed and consequently the more easily the decompression will be withstood by the organism and the less danger it will offer it.

The magnitude of a drop is determined by the pressure difference in an air tight cabin before the beginning of decompression and after its completion. The rate of a pressure drop expresses the ratio of the pressure in the cabin before the moment of depressurization to the pressure after decompression. Ignoring even /44
one of the above mentioned parameters leads to an incorrect concept of the nature of decompression. The parameters of the drop are determined in turn by those conditions under which decompression in the cabin takes place, in particular by the altitude and flight speed, the original pressure and gas composition in the cabin, the volume and degree of damage to the cabin.

Thus, from the point of view of physiology modern flight vehicles, equipped with air-tight cabins, seemingly, and completely solve the problem of flight in outer space, However, in real conditions it is impossible not to consider the possibility of air leakage from the cabin. Therefore the study of the time a man can retain the ability to work at different rates of cabin decompression acquires important significance. It is established that the time from the beginning of decompression to the appearance of pronounced functional disorders in man (disturbances in writing, dimness in the eyes, appearance of local cramps, disturbance of respiration rhythm, bradycardia etc.) in the case of a rate of climb of 2m/sec was on the average 58 minutes, and the altitude "ceiling" was 6527 meters. In the case of rising at a rate of 0.1 meters per second these values were, respectively, 13 hours 21 minutes and 5101 meters (N. A. Agadzhanyan et al. 1965).

Investigation of conditioned reflex activity, writing characteristics and movement coordination dictates that the degree of expression of disturbances in the analytic-synthetic activity of the higher sections of the brain depends both on the degree of oxygen starvation and also on the duration of its action upon the organism.

The state of the cardiovascular system was evaluated according to the nature of change in the electrocardiogram, the arterial pressure and the characteristics of vascular reactions. According to the degree of altitude climb, the EKG registered decreases in the R-R interval, a decrease in the P, R and T spikes, and in individual experiments - a decrease in the QRS interval with a simultaneous shift to the left of the electrical axis of the heart. All this indicates the presence of quite pronounced hypoxia and overstraining of myocardium. These changes were more pronounced in experiments with a rate of climb of 0.1 meters per second.

The development of hypoxia was accompanied by a change in the blood inflation level and tome of the vessels. In the case of a rate of climb of 2 m/sec, the subjects displayed an increase in the blood inflation of the brain vessels and a significant decrease in the inflation of the vessels of the lower extremities, as well as a decrease in the vascular tone. /45
A different picture was observed in the case of climbing to "altitude" at a rate of 1.0 m/sec. In these conditions there was a decrease in the blood inflation of the vessels of the brain and the extremities.

Experimental data show that a change in the rate of fall of barometric pressure in the environment has a significant influence in the formation of the response reactions of the organism.

Having established under two decompression regimes that, for humans the change in the high-altitude "ceiling" and the time to unconsciousness is a function of the rate of decompression, in the case of two decompression regimes, we decided to expand our investigation to experiments on animals. In doing this, in addition to regimes of 2 and 0.1 m/sec we also used other rates of decompression (25, 75, 150, 300 and 500 m/sec). The results obtained are shown in Table 8, in which the dependence of the altitude "ceiling" and time to unconsciousness upon the rate of decompression is clearly seen.

TABLE 8. CHANGE OF THE ALTITUDE CEILING AND SURVIVAL TIME OF WHITE RATS AT AN ALTITUDE OF 12,000 METERS AS A FUNCTION OF THE RATE OF "CLIMB" IN AN ALTITUDE CHAMBER (ACCORDING TO N. A. AGADZHANYAN AND A. V. SERGIYENKO)

Decompression regime, m/sec	No. of experiments	Altitude "ceiling", m			Survival time		
		minimum	maximum	average	minimum	maximum	average
2	26	11 700	14 700	13 370	105 min 35 sec	131 min 42 sec	121 min 32 sec
25	30	13 050	14 325	13 618	8 " 42 "	9 " 33 "	9 " 08 "
75	22	14 150	16 750	16 088	3 " 08 "	3 " 51 "	3 " 32 "
150	38	17 050	18 900	18 286	115 "	130 "	123 "
300	30	20 000	22 800	21 495	67 "	76 "	72 "
500	40	24 000	27 200	25 445	48 "	55 "	52 "

Note: In all series of experiments P is less than 0.05

The lower the rate of climb, the lower the altitude "ceiling," and vice versa. However, if we consider the time to unconsciousness, an inverse dependence is observed - the slower the climb is performed, the greater is the time to unconsciousness. The results of investigations of the physiological reactions of the organism showed that during rapid climbs a greater load falls upon the central nervous system, while during slow climbs, on the cardiovascular system. /46

2. CHANGES IN THE PARTIAL PRESSURE OF GASES IN THE ALVEOLAR AIR IN RAREFIED ATMOSPHERE CONDITIONS

In order to understand the physiological mechanisms of hypoxic disorders and to develop prophylactic measures aimed at providing for the safety of high-altitude flights, it is first of all necessary to study the characteristics of gas exchange under extreme degrees of atmospheric rarefaction. This is necessary because the fundamental condition for a normal oxygen supply to the organism amounts in effect to the maintenance of a sufficient pO_2 in the alveolar air which is the true gas medium for the organism.

Table 9 shows the relationship between the partial pressure of oxygen in the inhaled and alveolar air at different altitudes.

As is seen from Table 9, during breathing atmospheric air at sea level the partial pressure of oxygen in the inhaled atmospheric air is 159 mm of mercury, and in the alveolar air, 102 - 107 mm of mercury, i.e., 52 - 57 mm of mercury lower.

Studies by domestic and foreign authors have shown that, with a decrease in the atmospheric pressure, the partial pressure of oxygen in the alveolar air drops more slowly than in the surrounding air. Thus, M. Ye. Marshak (1948, 1961) showed that if the partial pressure of oxygen in the surrounding air decreases by 24 mm of mercury during a climb from 4000 to 6000 meters, in the alveolar air it drops only by 13 mm of mercury.

At an altitude of 4500 meters the partial pressure of oxygen in the inhaled air equals 91 mm of mercury. In the absence of compensatory-adaptive reactions the alveolar oxygen pressure at this /47 altitude would be (according to theoretical data) 41 mm of mercury, but in fact, owing to intensified breathing, it decreases only to 53 mm of mercury. Likewise an altitude of 8000 meters the partial presure of oxygen in the alveolar air is not 6 mm, but 26 mm of mercury.

TABLE 9. RELATIONSHIP BETWEEN THE PARTIAL PRESSURE OF OXYGEN IN INHALED AND ALVEOLAR AIR AT DIFFERENT ALTITUDES

Altitude, m	Atmospheric pressure mm Hg	Partial pressure of Oxygen, mm Hg: in inhaled dry air	in inhaled wet air	in alveolar air: experimental data	in the absence of compensatory changes and PCO_2 -40 (calculated data)
0	760	159	149	102-107	109
1 000	674	141	131	—	91
1 500	634	133	123	82	83
2 000	596	125	115	75	75
3 000	526	110	100	69	60
4 000	462	97	87		47
4 500	433	91	81	53	41
5 000	405	85	75	47	35
6 000	354	74	64	40	24
7 000	308	65	55	34	15
7 500	287	60	50	30	10
8 000	267	56	46	26	6
9 000	230	48	38	21	0
10 000	198	41	31	17	—
11 000	169	35	25	13	—
12 000	145	30	20		—

At the present time there are different opinions expressed in the literature concerning the minimum amount of oxygen required to be present in the alveolar air in order to sustain life. Some authors (I. M. Sechenov) cite a value equal to 25 mm Hg, which corresponds to an altitude of 8000 meters, while others (K. E. Schaefer) consider the critical value to be 33 mm Hg (7000 meters).

In calculating pO_2 in the alveolar air it was assumed that pCO_2 and the water vapor pressure in the alveolar air remain unchanged at high altitudes, making up a total of 87 mm Hg (pCO_2 40 mm Hg and pH_2O 47 mm Hg).

The experimental data gathered here and abroad indicates that it is necessary to define more precisely such a concept. Indeed, if the saturation of air with water vapor at body temperature (plus 37°) may be assume to be equal to 47 mm of mercury for all altitudes, then with a rise in altitude, when pulmonary ventilation increases, the process of discharging carbon dioxide from the organism is changed. /48

The dynamic study of gas exchange under high levels of atmospheric rarefaction, conducted by I. M. Dedyulin (1941), established that carbon dioxide is washed out of the alveoli during an extended stay at the same altitude. Thus, for example, during a one-day stay in an altitude chamber at an "altitude" of 4500 - 5000 meters, the pCO_2 of the alveolar air decreased from 38 to 26.3 mm of mercury.

In P. K. Isakov's investigations (1947), it was revealed that an increase in the $p_A O_2$ and a decrease in the $p_A CO_2$ were observed in the case of repeated "ascents" to an altitude of 5000 meters (in the course of an hour) (Table 10).

TABLE 10. THE INFLUENCE OF REPEATED ALTITUDE CHAMBER ASCENTS ON THE PARTIAL PRESSURE OF OXYGEN AND CARBON DIOXIDE GAS IN THE ALVEOLAR AIR
(mm Hg.)

	Ascent						
	1st	2nd	3rd	4th	5th	6th	7th
Oxygen	37.4	45.3	41.3	47.8	47.1	51.4	55.0
Carbon dioxide gas	33.6	28.8	30.3	26.5	27.1	24.1	21.5

In altitude chamber ascent by mountain climbers also showed that their pCO_2 decreased from 34-38 mm hg at sea level to 18-28 mm hg at altitudes of 7,000 - 9,000 m (N. A. Agadzhanyn, G. A. Davydov, 1967).

As is known, in conditions of normal atmospheric pressure the values p_AO_2 and p_ACO_2 vary in mutually opposite directions. A decrease in p_AO_2 is accompanied by an increase in $p_A CO_2$ (hypoventilation of the lungs), and an increase in p_AO_2, by a decrease in p_ACO_2 (hyperventilation).

This characteristic of the variation of p_AO_2 and p_ACO_2 was noted in 1875 by I. M. Schenov. In theoretical calculations of the composition of alveolar air he made the assumption that the partial pressure of nitrogen in the alveoli is constant. Hence it followed that the total of p_AO_2 and p_ACO_2 is also an invariable value. Further experimental investigations showed that this assumption is true only for an organism existing in a state of stable equilibrium with the surrounding environment. In various kinds of "transition" states, the p_AN_2 and the total of /49

p_AO_2 and p_ACO_2 vary in relation to the nature of pulmonary ventilation. The value of the p_AN_2 decreases during hyperventilation and increase during hypoventilation in comparision with the p_AN_2 during quiet breathing (N. A. Kurshakov, N. A. Troitskiy, 1951).

TABLE 11. PARTIAL PRESSURE OF GASES IN THE ALVEOLAR AIR (mm Hg) AND THE RESPIRATORY COEFFICIENT (r) FOR DETERMINING THE TIME TO UNCONSCIOUSNESS OF A MAN AT AN ALTITUDE OF 7500 m (287 mm Hg)

Subjects	Gas and resp. coefficient	At ground conditions before ascent	Time of taking samples at an altitude (minutes) 3	17	60
B-ov	Oxygen	116,2	40,8	37,9	34,3
E-ov		111,2	40,8	34,4	33,0
G-ov		117,3	36,0	28,7	31,1
$\bar{X} \pm m$		114,9±1,9	39,2±1,5	33,7±2,7	32,8±0,9
Value of f				$t_3=1,78$	$t_3=3,59$
" " P				>0,05	<0,05
B-ov	Carbon dioxide gas	25,7	15,1	15,2	13,2
E-ov		32,8	14,1	10,5	10,3
G-ov		30,0	13,9	13,2	12,7
$\bar{X} \pm m$		29,5±2,1	14,4±0,4	13,0±1,4	12,1±0,9
Value of f				$t_3=0,96$	$t_3=2,34$
" " P				>0,05	<0,05
B-ov	Nitrogen	571,1	184,1	186,9	192,5
E-ov		568,9	185,1	195,1	196,7
G-ov		565,7	190,1	198,1	196,2
$\bar{X} \pm m$		568,6±1,6	186,4±1,9	193,4±3,4	195,1±1,4
Value of f				$t_3=1,80$	$t_3=3,69$
" " B				>0,50	<0,05
B-ov	Respiratory coefficient	0,746	2,040	1,380	0,810
G-ov		0,830	1,860	0,625	0,550
$\bar{X} \pm m$		0,936	1,010	0,570	0,620
Value of f		0,837±0,06	1,640±0,32	0,858±0,27	0,660±0,08
" " P				$t_3=1,87$	$t_3=2,97$
				>0,05	<0,05

The experimental studies conducted in our laboratory (N. A. Agadzhanyan, G. A. Davydov, 1967), showed that changes in the partial pressure of gases at the same altitude depend not only on the adaptation of the organism to hypoxia during repeated ascents, but also on the decompression rate and the time the alveolar air is taken at any altitude, i. e., the time spent under conditions of f rarefied atmosphere (Table 11). /50

As is seen from the data in Table 11, the time of spent at a certain altitude has independent biological significance of its own and causes a regular dynamic decrease both of the pCO_2 and of the pO_2 in the alveolar air. This phenomenon was analyzed in more detail by G. A. Davydov and V. P. Nikolayev (1972).

In determining the "time to unconsciousness" at an altitude of 7500 meters the experiment is broken down into three stages. The first stage consists of breathing pure oxygen and ascending to an altitude of 7500 meters. The second stage begins from the moment the oxygen mask is removed at 7500 meters and ends after approximately 30 seconds, when the p_AO_2 value decreases to the norm (100 mm Hg). In the third stage the p_AO_2 of the alveolar air has already become hypoxic (pO_2 less than 100 mm Hg).

Table 11 shows the values of p_AO_2, p_ACO_2 and p_AN_2 during an extended stay of a man at 7500 meters. The values of p_AN_2 were calculated according to the following formula:

$$p_AN_2 = (B - 47) - p_AO_2 - p_ACO_2 , \qquad (1)$$

where B is the total pressure at an altitude of 7500 meters, equal to 287 mm of mercury. The values of the respiratory coefficient (R) are also entered in the table.

The dynamics of the changes in the composition of the alveolar air during the course of the entire experiment are graphically illustrated in Figure 5. The initial points of p_AO_2 and p_AN_2 correspond to the average initial composition of the alveolar air, which was determined in the subjects before beginning the experiment. After removing the mask (from the moment t = 3 minutes), the curves of p_AO_2, p_ACO_2 and p_AN_2 are plotted according to the data in Table 11. The curve of the oxygen saturation of the subjects' blood is also shown in Figure 5.

In plotting the curves of p_AO_2, p_ACO_2 and p_AN_2 in the interval of time from t equal to 10 minutes to 0 minutes, we assumed that: 1) inflow of air under the mask is completely excluded; 2) the pressure in the chamber changed uniformly during the ascent; 3) the value of /51
p_ACO_2 remained constant.

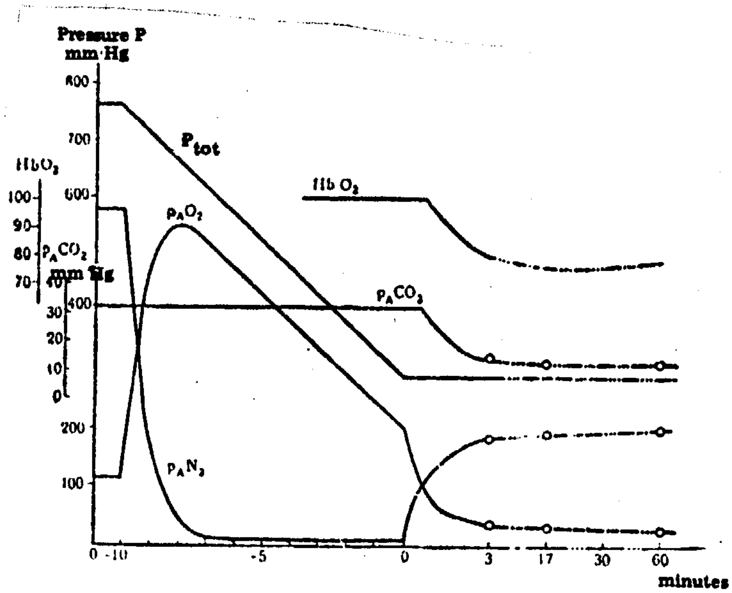

Fig. 5 Dynamics of the Composition of Alveolar Air in a Man in Experiments to Determine the Time to Unconsciousness at an Altitude of 7500 Meters p_{tot}. Pressure Change in the Altitude Chamber During the Experiment; p_AO_2, p_ACO_2, p_AN_2 - the Partial Pressure of the Oxygen, Carbon Dioxide Gas and Nitrogen in the Alveolar Air; HbO_2 - the Oxygen Saturation of the Arterial Blood

The process of the "gradual" washing of nitrogen out of the lungs after conversion to breathing pure oxygen with a constant external pressure is characterized by the equation (Fowler et al. 1952, Edelman et al. 1968):

$$[(p_AN_2) = (p_AN_2)_0 \left[\frac{V_{FRC}}{V_{FRC} + V_T - V_D}\right]^n \qquad (2)$$

where (p_AN_2) is the partial pressure of nitrogen in the alveolar air after the n-th inhalation of pure oxygen (mm Hg); $(p_AN_2)_0$ is the initial partial pressure of nitrogen in the alveolar air (nm Hg); P_{FRC} is the functional residual capacity of the lungs (ml); V_T is the respiratory volume (ml); V_D is the volume of anatomical dead space (ml).

Equation (2) characterizes the process of an ideal mixing of gases in the lungs. The actual process of the washing of nitrogen from the lungs differs somewhat from the ideal due to the nonuniformity of ventilation of particular parts of the lungs, (which occurs even in healthy persons) and the discharge of nitrogen from the blood and tissues into the lungs (Darling et al. 1940; Fowler et al. 1952; J. Comroe et al. 1961; Edelman et al 1968). The p_AN_2 curve (see Fig. 5) corresponds to ideal washing of nitrogen from the lungs of a healthy man, in whom $V_{FRC} = 3000$ ml in the sitting position, $V_T = 500$ ml, $V_D = 150$ ml with a respiration rate of 12 per minute (J. Comroe et al, 1961). During an ascent the actual p_AN_2 curve in our experiments differs little from the ideal. /52

With the conversion to breathing atmospheric air at an altitude of 7500 meters the process of the replacement of oxygen in the lungs by nitrogen is characterized by the same regularities as is the process of the substitution of nitrogen by oxygen during the conversion to breathing pure oxygen. Therefore the relative rates of increase of the p_AN_2 curve and decrease of the p_AO_2 curve from the moment $t = 0$ are approximately identical with the initial rate of decrease of the p_AN_2 curve.

However as is known, one of the first reactions of an organism in conditions of hypoxia is hyperventilation of the lungs, whereby the lungs are filled with nitrogen at more rapid rates. Moreover, from this moment due to hyperventilation the partial pressure of carbon dioxide gas in the alveolar air began to decrease and the rate of decrease of the p_AO_2 curve is diminished somewhat.

In agreement with the p_AN_2 curve the partial pressure of oxygen in the alveolar decreased to 100 mm Hg approximately $t = 30$ seconds after the conversion to breathing air. In Fig. 5 it is also seen that the hemoglobin oxygenation curve (according to oxyhemometric data) begins to decrease significantly 45 seconds after removing the mask. As is known, the blood, having passed through the lungs, flows to the helix of the ear, where the oxyhemometric sensor was attached, after approximately 13 - 15 seconds (Darling et al. 1940).

Thus, in these experiments a clear correlation appears between the dynamics of the changes in alveolar air composition and the dynamics of the change in arterial blood oxygenation.

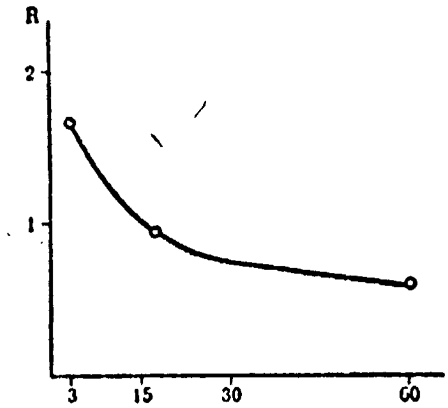

Fig. 6 Change in the Respiratory Coefficient R in Experiments to Determine the Time to Unconsciousness at an Altutide of 7500 Meters

In conditions of a changed gas medium, (as with rarefaction of the atmosphere) a new gas equilibrium between the alveolar air and the surrounding medium, and consequently, a stable condition of gas exchange is gradually extablished. The duration of this process is determined by the degree of hypoxia. /53

In order to determine the stable alveolar air composition at an altitude of 7500 meters it is necessary that the man stay for an extended period of time at this altitude, i.e., possess increased resistance to hypoxia. As we have already mentioned at altitudes greater than 7000 meters unconsciousness develops after only 5 to 10 minutes (and sometimes even earlier) due to acute oxygen starvation. The subjects who participated in our experiments had increased resistance to oxygen starvation after preliminary mountain acclimatization and in the majority of cases the time to unconsciousness at an altitude of 7500 meters was more than 60 minutes.

Results of an analysis of alveolar air samples indicate that even a stay of an hour at an altitude of 7500 meters is insufficient for establishing a stable state of gas exchange.

The instability of gas exchange in experiments to determine the "time to unconsciousness" at high altitude is more graphically manifested by dynamics of the change in the respiratory coefficient

(R) of the subject (fig. 6). As is known it is possible to characterize each portion of the inhaled air by its own particular value. If p_AO_2 and p_ACO_2 are known the value of R may be calculated by /54
J. Comroe's equation:

$$R = \frac{(1 - F_1O_2) \cdot p_ACO_2}{p_1O_2 - p_AO_2 - F_1O_2 \cdot p_ACO_2} \qquad (3)$$

where F_1O_2 and p_1O_2 are respectively the fraction concentration and partial pressure of oxygen in moist inhaled air at body temperature.

Bargeton uses another form of this equation:

$$R = \frac{p_ACO_2}{\frac{p_AN_2}{p_1N_2} \cdot p_1O_2 - p_AO_2} \qquad (4)$$

where p_AN_2 and p_1N_2 are, respectively, the partial pressure of nitrogen in the alveolar and moist inhaled air.

Bargeton (1967) showed that with an exhalation volume amounting to 58% of the total exhalation volume the value of R becomes equal to the mean value of R for all exhaled air. When exhalation is retarded by holding the breath and compressing of the lungs in proportion to the degree of exhalation the oxygen absorption by the blood greatly exceeds the discharge of carbon dioxide. Therefore the value of R significantly decreases in the final portions of the exhaled air. For example given a duration of exhalation equal to 10 seconds, R decreases to 0.2 (Kim et al, 1966).

On the other hand, during forced exhalation the values of pO_2, pCO_2 and R become very close to their mean values (Bargeton, 1967).

Thus, the value of R, calculated according to the parameters of the alveolar gas, depends on the volume and rate of exhalation, and also on the moment the sample of alveolar air is taken.

In the experiments we analyzed, the air sample was taken at the end of forced breathing and the participation of the subjects in this procedure was strictly uniform. Therefore, the observed changes in the composition of the alveolar air samples in proportion to the time the subjects spent at high altitude can only be due to the specific effects of acute hypoxia on the gas exchange.

In our experiments the values $p_1N_2 = (B - 47) \times F_1N_2$ and $p_1O_2 = (B - 47) \times F_1O_2$ were respectively 190 and 50 mm of mercury. The dynamics of the variation of R in time are graphically shown in Fig. 6. The curve of R is plotted according to the average values of the respiratory coefficient for all subjects. /55

Calculations of the values of R according to equation (4) were absolutely correct only for the case where the amount of nitrogen entering the lungs during inhalation is equal to the amount of nitrogen expelled from them during exhalation. In the experiments under consideration the process of filling the lungs with nitrogen had still not been completed after 3 minutes. Therefore, calculation of the values of R for this moment of time gives somewhat exaggerated results. However this overestimation is insignificant in comparison with the increase in R as a result of the increased washing of carbon dioxide of the organism.

In the first minutes of the action of acute hypoxia on the organism the respiratory coefficient increases and may exceed the initial value by more than two times. Its value significantly decreases in proportion to the stay at an altitude of 7500 meters.

The dynamics of the change in the alveolar air composition at high altitudes are conditioned by two factors: 1) the change in the gas composition of the inhaled air and 2) the reaction of the organism to hypoxia.

A comparatively high value of p_AO_2, recorded at an altitude of 7500 meters 2-5 minutes after removing the oxygen mask, is caused by a number of factors. In this stage of the experiment, some oxygen remained in the lungs. The high value of p_AO_2, evidently, was also maintained due to the entry of oxygen into the alveoli from the blood and tissues, since an organism possesses several oxygen reserves (A. M. Charnyy, 1961; P. A. Korzhuyev, 1966; A. A. Vishnevskiy et al. 1967). Moreover, in the case of hyperventilation the level of alveolar oxygen increases as a result of the intensified flow of atmospheric oxygen in the inhaled mixture.

The lowering of p_ACO_2 in the course of the experiment is caused by the hyperventilation of the lungs in response to acute hypoxia. The process of lowering p_ACO_2 is extended in time in connection with the presence of comparatively large reserves of carbon dioxide gas in the blood and tissues (Farhy, Rahn, 1960).

Further investigations to establish the correlations between changes in the function of respiration and blood circulation make it possible to reveal more intimate and physiological mechanisms of the disturbances which arise in the conditions of a significantly altered gas medium, and to develop corrective measures. /56

3. THE INFLUENCE OF HYPOXIA ON THE FUNCTION OF BLOOD CIRCULATION AND BLOOD OXYGENATION

Adaptation to oxygen deficiency is a very complex and multifaceted process, in which practically all organs and systems of the organism participate.

Oxygenation of the arterial blood is the resultant function of respiration and blood circulation. The oxygen pressure in the tissues, and consequently, the normal course of oxidizing processes, to a great degree depends on the degree of oxygenation of the arterial blood.

As is known, the oxygen in the blood occurs in two forms: in a free, physically dissolved stall (in the plasma) and in the bound state (combined into oxyhemoglobin). Oxygen freely dissolved in blood is subject to the laws of gases dissolved in liquids. Its content is directly proportional to its pressure and depends upon the solubility of oxygen in plasma (the absorption coefficient) and on the temperature. The absorption coefficient for oxygen (a) in human plasma at a temperature of 37° and a pressure of 760 mm Hg. is equal to 0.023. The pressure of the oxygen dissolved in the plasma is determined by the partial pressure or the oxygen pressure in the surrounding medium, with which the blood strives to enter gas equilibrium. The pressure of the oxygen, dissolved in the arterial blood leaving the lungs, approaches the pO_2 of the alveolar air, although it is somewhat lower than the latter due to the comparatively slowed diffusion of oxygen through the alveolar walls and the capillary endothelium.

The oxygen pressure in the blood flowing from the tissues depends upon the partial pressure of oxygen in the tissues fluids, and the latter in turn is determined by the intensity of the tissue respiration in the various tissues.

The higher the pressure of the free oxygen, the more it occurs in the chemically bound form, i.e., the more the hemoglobin combines with the oxygen and turns into oxyhemoglobin. According to Hüfner's data (1894), one gram of hemoglobin can combine with 1.34 - 1.36 ml of oxygen. /57

The amount of oxygen (in ml) which can be bound by 100 ml of blood with complete conversion of all hemoglobin into oxyhemoglobin, is called the oxygen capacity of the blood.

The oxygen capacity of blood is determined by the amount of active hemoglobin contained in it. It decreases during various anemias and poisonings by certain poisons, for example, carbon monoxide, nitrites, and aniline, which deprive the hemoglobin of the ability to combine with oxygen and to form easily dissociating oxyhemoglobin. In the case of carbon monoxide poisoning, the hemoglobin turns into carboxyhemoglobin, and in the case of poisoning with nitrites and aniline, methhemoglobin is formed.

The oxygenation of the blood expresses the ratio of the amount of bound oxygen to the oxygen capacity of the blood:

$$HbO_2 = \frac{\text{bound } O_2}{\text{oxygen capacity}} \times 100.$$

Thus the oxygenation of the blood is understood to mean the percentage of oxyhemoglobin in relation to the hemoglobin available in the blood.

At sea level the hemoglobin of the arterial blood is not completely saturated with oxygen but amounts to approximately 95-97%.

The underoxygenation of the arterial blood results from the uneven ventilation of the alveolar air in different parts of the lungs and the conditions of blood circulation in the minor circulatory cycle (Haldane, 1922; N. N. Savitskiy, 1940; N. Ye Marshak, 1961, 1969; V. V. Parin, F. Z. Meyerson, 1965).

The ability to withstand hypoxia also greatly depends on the functional state of the cardiovascular system, since for normal oxygenation of the arterial blood it is necessary to have a specific correlation between the air exchange and blood supply of the lungs. Disturbing the normal correlation between the alveolar ventilation and the blood supply of the lungs in conditions of a rarefied atmosphere leads to a worsening of the oxygenation of the blood and the development of oxygen insufficiency. The alveolar ventilation (AV) in a healthy man at rest equals approximately /58
4 liters per minute, and the pulmonary blood supply (PS) is 5 liters per minute. The degree of oxygenation of the blood depends chiefly on the ratio $\frac{AV}{PS}$. Experimental studies showed that the ratio $\frac{AV}{PS}$ is influenced not only by the nature of the air exchange in the different sections of the lung and the rate of oxygen diffusion,

but also by the characteristics of the variation of the minute volume of the blood, the level of arterial pressure, the tone of the vessels of the minor cycle and the functional state of the cardiovascular system of the organism as a whole.

A study of the vascular reactions in conditions of hypoxia can have a certain significance in an examination to reveal the causes producing a lower individual resistance of a man to oxygen starvation.

Low resistance to hypoxic hypoxia is due to a functional deficiency in the regulation of the cardiovascular system. A. P. Apollonov (1953) and M. D. Vyadro (1958), having studied individual resistance to hypoxia in the case of ascent to an altitude of 5000 meters without oxygen, established that patients with hypertonic disease withstand oxygen diffenciency satisfactorily, and patients with vegetative dystonia withstand it poorly in the majority of cases. At the same time other authors established that, in the process of altitude chamber training, changes on the part of the cardiovascular system are also smoothed over simultaneously with an increase in the altitude resistance (M. Ye Vasilenko, O. G. Gazenko et al. 1958).

V. N. Alinfanov (1968) and L. M. Lemensheva (1969), having used combined functional loads, arrived at the conclusion that a vectorometric analysis of the electrocardiogram in the frontal plane is a valuable addition to a quantitative evaluation of the changes in the myocardium, arising in conditions of oxygen deficiency.

It was important to conduct a complex investigation of the physiological reactions of the organism for a more complete study of the mechanism of hypoxic damage to the cardiovascular system. Analysis of the experimental material showed that in conditions of oxygen starvation (at altitudes of 3000-5000 m) the systolic and diastolic arterial pressure increases somewhat in the majority of sub- /59
jects. In the majority of cases, the increase in the maximum pressure is expressed to a greater degree than that in the minimum pressure, which also causes an increase in the pulse pressure.

It is interesting to note (that in contrast to healthy persons) in subjects with hypertension, the increase in pulse pressure during oxygen deficiency took place not as a result of the systolic pressure, but rather as a result of a lowering of the diastolic pressure.

In experiments on animals (dogs and cats) it has been shown that in the case of hypoxic hypoxia, the pressure in the minor cycle increases due to a narrowing of pulmonary vessels, and there is also an increase in minute volume of the heart (M.Ye.Marshak, 1961; N. V. Sanotskaya, 1961, 1962; S. A. Bernshteyn, 1966, et al.).

Denervation of the carotid and aortic reflexogenic zones prevents an increase in pressure in the pulmonary artery in the case of hypoxia. Together with an increase in arterial pressure, in conditions of hypoxia the pulse quickens, the frequency and depth of respiratory movements are increased, the pulse wave propagation speed rises, the elasticity of the vessels increases and the peripheral vascular resistance decreases. We consider these functional changes to be one of the adaptive reactions of organisms, having great significance for maintaining the partial pressure of oxygen in the tissues at the optimum level.

The results of our earlier experiments and the data in the literature indicate the independent nature of the reaction of the organs of respiration and the cardiovascular system to oxygen deficiency. This is expressed both in the unequal quickening of the pulse and respiration, and also in the different nature of the changes in the arterial pressure and electrocardiograms. Thus, in an EKG taken during the development of hypoxia, the flattening of the T spike in all recordings, as a rule, was more pronounced in subjects with sinus tachycardia. Individual differences in variation of pulse, respiration and arterial pressure proved to be more pronounced at an altitude of 6000 meters (N. A. Agadzhanyan, M. I. Vakar et al. 1960).

It was also important to show the dependence of the reactions of the cardiovascular system on the oxygenation of the arterial /60 blood, i.e., on the degree of hypoxia. Table 12 shows the results of observations of the change in blood oxygenation of subjects at different altitudes (before the altitude chamber "ascent" the blood oxygenation of the subjects was 94-96%).

TABLE 12. CHANGES OF THE SATURATION OF THE BLOOD BY OXYGEN AT VARIOUS ALTITUDES
(Data of N. A. Agadzhanyan, M. I. Vakar et al., 1960).

Subject	Oxygen content of blood (%) at altitude			Subject	Oxygen content of blood (%) at altitude		
	3000 м	5000 м	6000 м		3000 м	5000 м	6000 м
K-ov	89—90	77—83	70—72	G-ov	87—89	70—72	—
K-ov	78—80	70—72	—	Ch-ev	91—92	70—71	—
R-ov	80—83	68—74	—	R-ov	88—90	68—72	—
A-n	88—90	80—82	58—70	N-ov	89—90	72—78	—
K-ov	76—78	66—68	58—68	V-ov	90—92	75—83	62—75
B-n	89—90	76—83	62—76	Kh-ov	75—82	60—64	48—52
S-ov	90—92	82—87	66—74	Kh-ov	85—87	58—62	—
A-n	77—78	68—78	—	Kh-ov	90—92	60—68	—
S-ov	90—92	62—70	—	Kh-ov	84—86	66—70	—

From Table 12 it is obvious that the degree of oxygenation of the blood decreases in all subjects during an altitude chamber ascent to 3000, 5000 and 6000 meters, the decrease being the greater, the higher the altitude. An increase in hypoxic changes on the EKG and more pronounced shifts in the arterial pressure together with the progressive decrease in blood oxygenation are noted. The development of compensatory reactions on the part of the cardiovascular system and respiration is already observed, with a decrease in blood oxygenation by 3-5%. However the amount of blood oxygenation in the subjects fluctuates over a wide range at the same altitude. At altitudes of 5000-6000 meters the lowest value of blood oxygenation was noted in subject Kh-ov, who possessed low resistance to hypoxia. During ascents to altitudes of 5000-6000 meters the general condition of this subject sharply deteriorated which was manifested in heavy perspiration, paleness, slowed reactions and etc. This makes it possible to conclude that subject Kh-ov's low resistance to oxygen starvation was the result of an insufficient development of compensatory reactions. However, it is /61
necessary to bear in mind that in certain persons pronounced manifestations of hypoxia may develop at an altitude of 5000 meters even with a sufficiently high level of oxygenation of the arterial blood.

The latter, probably, is connnected with a high individual sensitivity to oxygen starvation. In experiments simulating a loss of cabin pressure, it was shown that the first symptoms of disorders in psychic activity appear with a decrease in the oxygenation of the arterial blood to 64%, on the average, and unconsciousness begins with a blood saturation equal to 56-62% (Hemingway, 1944; Hoffman, Clark, Brown, 1946).

In the case of acute hypoxia, a dependence between blood oxygenation, EEG changes and behavioral reactions were also established (N. A. Agadzhanyan, I. Dvorzhak et al. 1971).

Likewise with an identical degree of blood oxygenation, changes in electrocardiograms and shifts in the arterial pressure are expressed to the same degree neither in different subjects nor in the same subject during different periods of his stay at a specific altitude. Individual fluctuations in the levels of blood oxygenation during hypoxia evidently result from the fact that the respiratory and cardiovascular compensatory reactions of the organism are expressed unequally in the subject. In the case of determinations of the time to unconsciousness at an altitude of 7500 meters the blood oxygenation fluctuated over the range from 76-82 to 58-70% (N. A. Agadzhanyan, G. A. Davydov, 1967).

The fluctuations in blood oxygenation in one in the same subject during different periods of his stay at high altitudes, which were discovered in our investigations, can probably be explained by the fact that in the first minutes spent at high altitude a sufficiently high blood oxygenation is provided for a certain time as a result of compensatory readjustment of respiration and circulation. Later, the percentage of oxygen in the blood, which is stabilized according to the degree of adaptation, is gradually decreased according to the degree of suppression of compensatory mechanisms.

In experiments with conversion to breathing pure oxygen at altitudes of 5000, 6000 and 7500 meters it is noted that the blood oxygenation in these conditions increases to the original values. /62
In this case normalization of the functions of respiration and the cardiovascular system is always observed. Only by analyzing the EKG is it possible to discern deviations from the norm: deflection of the electric axis of the heart to the left by 5-8 degrees as a result of development of altitude meteorism, leading to a change in the anatomical position of the heart.

It is necessary to take into account the fact that hypoxia, depending on the functional state of the central regulatory mechanisms, in some cases causes a reflex contraction of the peripheral vessels, and in other cases, as a result of the decreased oxygen pressure in the tissues, causes vascular expansion. Under rarefied atmospheric conditions elevated blood pressure as well as intensified breathing and increased frequency of cardiac contractions set in as a result of an elevated tone of the respiratory and vascular motor centers and are aimed at adapting the organism to oxygen starvation. However, it must be assumed that the tone of the vascular motor and respiratory centers cannot remain elevated for an extended period of time with oxygen deficiency, and in persons with a low resistance to hypoxia, disturbances of the regulatory mechanism may arise, which are correspondingly reflected on the respiration and functioning of the cardiovascular system.

Different means of protecting the organism are used in order to prevent the above-mentioned disturbances. At altitudes not exceeding 12,000 meters, a satisfactor solution of the problem of combating oxygen starvation is provided by the use of devices with a continuous oxygen supply, and also by the use of devices of the "demand oxygen apparatus" type. With the increase in the altitude tolerance of aircraft it became necessary to development other methods, in particular the combined use of air tight cabins, full pressure suits and oxygen equipment, providing oxygen for breathing at high pressure.

The problem of the blood oxygenation of a man staying in conditions of a rarefied atmosphere has been dealt with quite extensively in domestic and foreign literature. The majority of these studies were conducted at altitudes of 3000-12,000 m with the subject breathing air or oxygen at the pressure of the surrounding atmosphere.

The results of the investigations enabled the authors to compile special tables of the percentage of oxygen in the blood at different altitudes (G.G. Gazenko, Ye.Ya. Shepelev, 1953; G. Altukhov et al., 1954). There is little information on the change in blood oxygenation in high-altitude conditions in the case of pressure breathing. /63

We conducted a special series of investigations for the purpose of studying blood oxygenation with the use of high-altitude clothing and with pressure breathing. The initial value of blood oxygenation was taken to be 100%, since the subject breathed pure oxygen during the entire experiment. Moreover in addition, variation in the frequency in amplitude of respiratory movements and chest circumference, the pressure, exerted on the body by the pressurized suit in the region of the middle and lower part of the chest and the lung ventilation were determined. In all, 42 investigations at altitudes up to 30,000 meters were conducted with the use of ordinary and improved models of high-altitude special equipment.

The values of the blood oxygenation at different altitudes with the use of commercial and experimental pressure suits are given in Table 13.

The basic factor influencing the degree of blood oxygenation is the height of ascent. However, the oxygen content in the blood most noticibly decreased in the case of an ascent to altitudes from 12000-15000 meters, since it is precisely at these altitudes that switching from breathing under the pressure of the surrounding atmosphere to breathing under increased pressure in the lungs takes place. A further increase in altitude with the total pressure under the helmet kept at 145 mm Hg is reflected much less in the level of blood oxygenation.

At an altitude of 15000 meters the oxygen content in the blood is, on the average, 90%, and at an altitude of 20000 meters and more it fluctuates at around 89%.

The data on the oxygen content in the blood at altitudes of 20000 meters higher and with the use of commercial pressure suits are close to the data obtained by A. G. Kuzetsov (1959) et al. The results of the investigation showed that the level of blood oxygenation is determined by, in addition to altitude, individual pecularities of the subje.. and the characteristics of the pressure suit. With the /64 use of ordinary pressure suits at altitudes of 15000-20000 meters and more this value fluctuates between 84-80%, decreasing to 71-74% in isolated cases, while with the use of improved pressure suits at the same altitudes the oxygen content is 90-89% and only decreases to 82-81% in certain cases.

It is known that the most essential and urgent reaction of the organism to hypoxia is intensification of lung ventilation, which is provided by intensifying the impulse activity of the inspiratory neurons of the respiratory center and by a corresponding /65 influence on the muscles (A. M. Kulik, 1967). Intensification of pulmonary ventilation is already observed at an altitude of 1000-1200 meters, i.e., with a decrease in the p_AO_2 90-93 mm hg. The maximum increase in the respiratory minute volume takes place at an altidue of 7000 m (Gray, 1950; A. V. Beregovkin et al, 1963). A number of other auxiliary reactions of the organism to aerohypoxia are aimed at increasing the oxygen supply to the tissues as a result of increasing the frequency of cardiac contractions, the systolic volume, the linear speed of blood flow, change in the vascular tone and blood oxygenation (Haldane, Priestly, 1935; A. P. Apollonov, 1953; Z. I. Barbashova, 1960; N. A. Agadzhanyn, 1968 et al).

TABLE 13. CHANGES IN THE OXYGEN CONTENT OF THE BLOOD DURING BREATHING OF OXYGEN UNDER INCREASED PRESSURE AT ALTITUDES 15000, 20000, and 30000 m (data of N. A. Agadzhanyan, M. I. Vakar et al., 1959).

Subject	"Earth" before ascent	The volume of oxyhemoglobin in blood (in %) by altitude: 15000 м, Experimental press. suit	15000 м, commercial press. suit	20000 м, Experimental press. suit	20000 м, commercial press. suit	30000 м, Experimental press. suit	30000 м, commercial press. suit	"Earth" after descent
K-ov	100	95	—	95	86	94	—	97
"	100	—	82	84	—	84	—	94
A-n	100	87	80	85	75	81	74	90
"	100	9[illegible]	82	89	80	95	75	97
"	100	92	83	88	80	87	74	96
R-ov	100	88	82	87	82	80	78	94
M-ov	100	92	82	88	80	86	84	100
"	100	94	87	92	84	97	87	100
"	100	92	85	88	82	90	84	100
K-ov	100	94	90	94	92	92	84	—
"	100	85	81	84	78	90	89	94
A-n	100	86	80	83	79	86	76	84
"	100	85	80	92	80	97	82	100
R-ov	100	92	81	92	84	92	86	99
M-ov	100	95	86	95	87	95	89	—
"	100	—	88	90	85	91	80	100
K-ev	100	97	90	95	90	—	—	100
"	100	—	90	87	81	87	68	—
"	100	—	84	—	77	88	71	95
"	100	92	86	91	81	88	74	100
G-ov	100	84	79	—	—	82	76	—
	100	90	84	89	82,1	89.1	80	

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Data are available concerning the mechanisms of hypoxic changes in body temperature (K. P. Ivanov, 1968), and in oxygen pressure in the brain (Ye A. Kovalenko, 1966) the skeletal muscle (N. V. Sanotskaya, 1961) and other tissues of the organism.

We conducted a complex investigation of a number of functions in intact and narcotized animals under the effect of increasing hypoxia and a study of the correlation ratios (N. A. Agadzhanyan, Yu. V. Shevchenko, 1970).

The experiments were conducted on white rats weighing 180-250 grams each in a 250-liter altitude chamber. Decompression in the chamber was performed at a rate of 25 m/sec to an altitude of 12000 m. The survival time was the criterion of endurance to acute hypoxia.

We recorded the respiration and pulse rates, the rectal temperature and the relative oxygen content in the muscles of the rear extremities of the rats by the polarographic method.

Two series of experiments were conducted on 286 animals. The experiments of the first series were conducted on intact animals, and of the second series - on animals, narcotized with Nembutal. In each series of experiments there were animals with their extremities fixed to a special stand and animals with freely moving extremities.

Table 14 and Fig. 7 show data on the survival of rats in altitude of 12000 meters under the effect of increasing hypoxia.

In the first series of experiments the survival of the fixed animals was two times less than that of the free animals, which, evidently, is connected with the condition of increased muscular tension, under which the oxygen consumption of the organism is /66
significantly increased (H. McIlwain, 1962). Moreover, it is also impossible to ignore the negative influence of the pain factor on survival.

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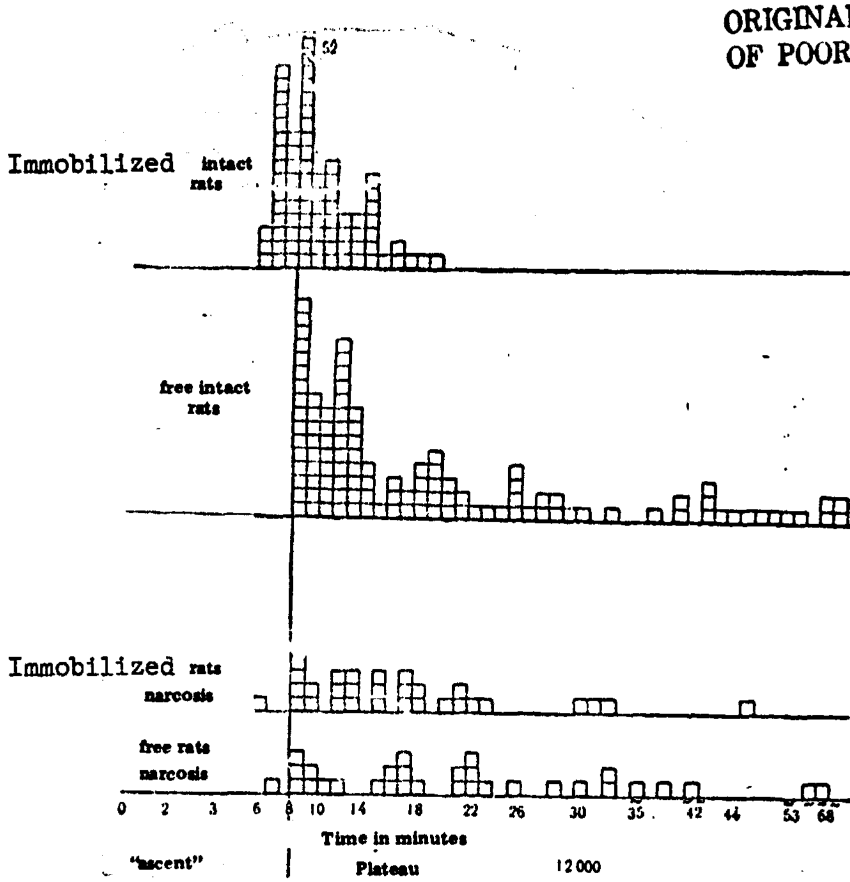

Fig. 7 Histogram of the Survival of White Rats with Increasing Hypoxia

Narcosis, excluding motor activity and pain stimulation, significantly increased the altitude resistance in immobilized animals (17.2 ± 1.4 minutes), not reaching, however, the survival time of free animals. This, possibly, is explained by the disturbance of the blood flow and hampering of breathing with fixation.

The dynamics of the function were recorded for the immobilized intact and narcotized animals. Fig. 8 shows the results obtained in one of the experiments on an intact animal. A two-phase amplification of the respiration and pulse rate (A and B) was noted in the experiment with a subsequent reduction of these indicators and a lowering of the rectal temperature. The oxygen content in the muscle begins to decrease at an altitude of 1000 meters.

As follows from Fig. 8, the beginning of the lowering of the rectal temperature, and the peaks A and B of the respiration and pulse rates are observed during the development of the first phase of changes in the pO_2 in the muscle. Peak A of the respiration and pulse rates (altitude 2800-3700 m) most probably was caused by neuro-reflex influences, caused by the high sensitivity of the chemoreceptors of the sino-carotid and aortic regions to the effect of oxygen deficiency. This hypothesis is confirmed by experiments in which hyperventilation in narcotized rats, which reached 135% of the original level, was already observed after 4 respiratory volumes of a mixture containing 10% oxygen. After cutting the carotid bodies the rats did not react to hypoxia (Colinet-Lagncaux et al. 1967). The decrease in the pO_2 in the muscular tissue at this stage is evidently caused by the redistribution of the blood flow for the purpose of centralizing the circulation, which is achieved by vasoconstriction in the muscles and vasodilation in the brain and cardiac muscle. /67

TABLE 14. SURVIVABILITY OF WHITE RATS UNDER INCREASING HYPOXIA

SERIES OF EXPERIMENTS	CONDITIONS OF EXPERIMENT	SURVIVABILITY MINUTES	NO. OF ANIMALS
I. Intact rats	Immobilized	10,2±0,4	110
	Free	21,2±1,[illegible]	109
II. Narcotized Rats	Immobilized	17,2±1,4	30
	Free	22,7±2,3	31

The secondary amplification of respiration and pulse (Peak B at altitudes of 6300-8000 m) is probably connected with the direct influence of oxygen deficiency in the blood on the tissues of the brain together with continuing neuro-reflex influences. An atmospheric rarefaction corresponding to an altitude of 8000 m is evidently critical, since subsequent decompression causes a progressive decrease in the respiration rate, cardiac contractions and pO_2 in the muscles. The mechanism of the development of this phase remains unclear, but, possibly, it is connected with a decrease in the oxygen requirement of the brain, which is observed with a decrease in the pO_2 in the venous blood to 24-26 mm Hg (N. K. Kalinina, Yu. S. Alyukhin, 1969).

Hypothermy in rats in the case of hypoxia is a characteristic reaction and arises as a result of the increased heat exchange of the organism and the suppression of chemical temperature regulation (K. P. Ivanov, 1968).

In addition to the explanations given it is also impossible to exclude other intimate physiological mechanisms, in particular the role of neuro-humoral-stress reactions, participating in the formation of adaptive reactions to oxygen deficiency (I. R. Petrov, 1967).

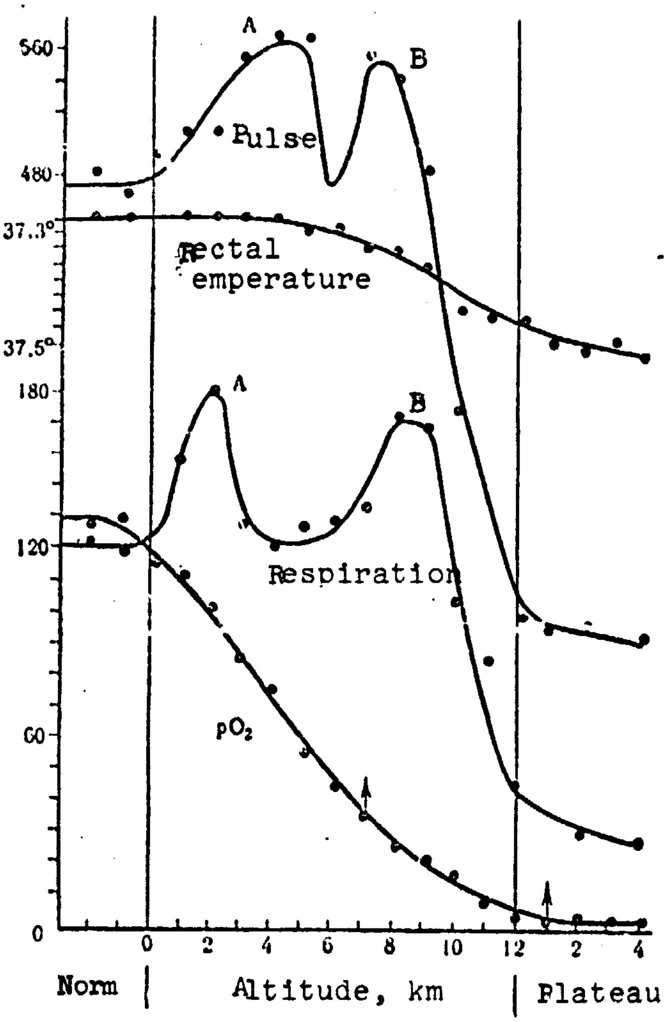

Figure 8. The character of changes in the respiratory frequency, pulse, rectal temperature (in absolute values) and pO_2 of mice (in relative values) for increasing hypoxia.

Thus, the results of the investigations made it possible to establish qualitative characteristics in the case of the action of acute hypoxia and the correlation between physiological reactions during different functional states.

As we have already indicated, after the discovery of the chemoreceptors, located in the carotid and aortic reflexogenic zones, there appear a great number of experimental data testifying to their specialized reaction to variation in the partial pressure of oxygen. This specialized functional property of the sino-carotid sinuses is also the result of their specific structural features, in particular, the very abundant blood supply of the chemoreceptor cells.

The experimental studies by Daly and colleagues (1954) indicated that the level of the oxygen requirement of the carotid body is approximately 4 times greater than the oxygen requirement of the upper cervical ganglion and two times greater than the brain tissue (Kety, Schmidt, 1945). The thick interweaving of vessels in the carotid body forms an "extraordinary network" of arterial venous anastomoses. Direct determination of the bulk speed of the blood flow and the oxygen requirement of the carotid tissue made it possible to reveal the distinguishing features of its oxygen supply in comparison with other structures of the organism.

The bulk speed of the blood through the bodies is 2000 ml per 100 g per minute; through the brain, through the heart muscle, 64 - 151 ml; through the thyroid gland, 560 ml. The oxygen requirement of the carotid body tissue in the cat, according to the data of Daly and colleagues, is 9 ml per 100 g per minute. In this case, on the average, 38 mm^3 of blood flows through the carotid body in a course of a minute. The exceptionally high rates of oxygen demand by the carotid body obtained by these authors (9 ml per minute per 100 g of tissue) were later subjected to a careful experimental verification with the use of more modern and still more sensitive methods of investigation.

Perfusing the carotid bodies of cats through the common carotid artery, Fay (1970) showed that the oxygen requirement of the body is only 1.5 ml per minute per 100 g of tissue, i.e., 20% of the value obtained by Daly and colleagues (Table 15). From the data given in Table 15 it is obvious that the values of the oxygen requirement of the cat carotid body in vitro, obtained by Fay (1970) and Leitner and Lianbet (1971) are very close (respectively, 0.030 and 0.027 microliters per minute), but significantly less than those obtained by Daly and colleagues (1954) and by Purves (1970).

TABLE 15. THE OXYGEN REQUIREMENTS FOR CAROTID BODY OF OF CAT IN VITRO (ACCORDING TO DATA FROM VARIOUS AUTHORS)

	Daly, Lambertsen, Schweitzer (1954)	Purves (1970)	Fay (1970)	Leitner, Lianbet (1971)
Dry weight of carotid body, μg.	400		nearly 400	44
pO_2, mm Hg.	90	95-103	140-200	680
Oxygen requirement (VO_2 in μl per min).	0.18	0.128	0.030	0.27

Further studies were aimed at investigating the intimate physiological mechanisms of the effects of oxygen insufficiency on the chemoreceptors. It was shown that in the case of hypoxia both the carotid and the aortic reflexogenic zones participate in the compensatory respiratory reaction, but the significance of the carotid sinuses is especially great (L. I. Ardashnikova, L. L. Shik, 1948; Grant, 1951). Although there is a specific connection between the oxygen pressure in the arterial blood and oxygen content in it, which is expressed in the oxyhemoglobin dissociation curve, the question of what is the stimulus of the above-mentioned chemoreceptors - change in the oxygen content or pressure in the arterial blood - remained open for a long time.

It is known that the oxygen content and pressure in the arterial blood vary differently with different forms of hypoxia. In the case of hypoxic hypoxia there is a decrease in both the partial pressure and in the oxygen content in the arterial blood; in the case of anemic hypoxia, and also in the case of poisoning with toxic substances, (for example, carbon monoxide) the oxygen content in the arterial blood decreases, despite a normal oxygen pressure /71
in the alveolar air.

The excitation of the chemoreceptors of the carotid zones observed in conditions of hypoxic hypoxia is caused by a drop in the partial pressure of the oxygen in the arterial blood. In the opinion of M. Ye. Marshak (1961), a change in the oxygen content in the arterial blood does not influence the chemoreceptors of the carotid zones. These results contradict the data of Landgren and Neil (1951).

The investigations of numerous authors have established that the sensitivity of the chemoreceptors to changes in the oxygen pressure in the arterial blood is very great.

In the experiments of Alvarez-Buya (1953), it .s shown that even with an insignificant change in the oxygen pressure in the arterial blood, causing a decrease in the hemoglobin saturation of only 1-2%, an intensification of electrical activity in the sinus nerve is observed.

In the opinion of A. N. Kulik (1967), the threshold stimulation of the respiratory center is not identical in different persons. Stimulation of the chemoreceptors in conditions of a rarefied atmosphere elicits a reflex increase in the pulmonary ventilation, which in turn p' motes an excess washing of carbon dioxide from the organism, and counters the intensification of the breathing.

It is known that the intensification of pulmonary ventilation in the case of hypoxia is mainly the result of a reflex from the sino-carotid and cardioaortic chemoreceptors in response to a drop in the oxygen pressure in the arterial blood. The carotid gland is of prime significance here. By cutting out (denervating) the sino-carotid zones the ventilator reaction to hypoxia either completely disappears or is delayed and exists at a lower level. It is shown that the nature of respiration depends on the type of animal and the duration of the effects of hypoxia (L. I. Ardashnikova, 1952, 1959). Experiments on rabbits with the carotid bodies removed established the absence of a ventilator reaction in them in the case of a gradual decrease in the pO_2 in the air. In denervated dogs acute hypoxia (inhalation of nitrogen) also did not cause reflex intensification of respiration; however, in contrast to the reaction of the rabbits with a slow increase in hypoxia, dogs with denervated sino-carotid chemoreceptors experienced an increase in pulmonary ventilation, although it was less pronounced than that of intact animals. /72

The author comes to the conclusion that the single mechanism, providing for the rapidly beginning compensatory increase in pulmonary ventilation during a decrease in the partial pressute of oxygen is the chemoreceptors. Conditioned-reflex connections, producing a respiratory and circulatory reaction for adaptation to and compensation for oxygen deficiency in the inhaled air, are not established after the operation.

Without dealing with the different theories put forward to explain the mechanism of the excitation of chemoreceptors under the influence of changes in the pO_2, pCO_2 and pH of the blood, we will mention only the very important fact that the receptor cells of the carotid body are excited when the decomposition of ATP in its tissue predominates over its resynthesis. In this light, impulsation from the chemoreceptors acquires the meaning of a signal giving warning of threatened overexpenditure of the energy resources of the tissues. Although the carotid chemoreceptors possess exceptionally high sensitivity, the carotid bodies are far from being the only carriers of internal chemical reception in the organism. The network of peripheral vessels is rich in chemoreceptors which are greatly similar to the carotid and aortic chemoreceptors; however, in connection with their great latent period and low excitability these peripheral chemoreceptors, probably, participate in the regulation of primarily local processes. The peripheral chemoreceptor mechanism, evidently, is the more ancient and represents a homologue of the "gas analyzer" of the environment in aquatic animals, although, in the opinion of S. V. Anichkov and M. L. Belen'kiy (1962), the high sensitivity of the carotid bodies of mammals in comparison with the homologues of amphibia, for example seemingly contradicts the theory of the ancient origin of the chemoreceptors of the carotid zone.

A large number of studies, performed on denervated animals, is dedicated to the investigation of the role of the sino-carotid receptors in the reactions of individual physiological systems of the organism, primarily the respiratory system. We established a correlation between changes in the different functional systems during both the brief and prolonged action of oxygen deficiency /73 upon the organism of animals with denervated sino-carotid chemoreceptors. Several series of experiments were conducted for this purpose.

The first series of experiments were performed on white rats. Bilateral disconnection of the sino-carotid zones was performed under Nembutal narcosis by means of a careful treatment of the region of the bifurcation of the carotid artery with a 10% phenol solution (E. A. Konza, 1970). Intact animals were subjected to operative intervention with the exposure of the carotid arteries, without treating with phenol.

Hypoxic hypoxia was produced by raising the animals in a low pressure chamber to an altitude of 12000 m at a rate of 25 m/sec. During the entire ascent of the fixed animals a complex recording was made of the cardiac activity (EKG), respiration, rectal temperature and oxygen pressure in the femoral muscle. The results obtained were analyzed by means of variation statistics.

In these investigations (N. A. Agadzhanyan, N. A. Usakova, 1970) it is shown that during an ascent to an altitude of 12000 meters the frequency of respiration quite significantly increases both in intact and in denervated rats, which agrees with the data of other authors. Differences in the reaction of the respiratory system of intact and denervated rats were observed in the zones of slight and moderate hypoxia. under extreme degrees of atmospheric rarefaction (at altitudes greater than 8000 m) the role of reflex regulation of the physiological functions, probably, disappears. This is confirmed by the identical degree of suppression of respiration in denervated and intact rats. The general nature of the change in the frequency of cardiac contractions was analogous to the nature of the changes in respiration. These data correlate with the result of an investigation of oxygen pressure in the femoral muscle. The decrease in the pO_2 in the muscle in denervated rats took place more rapidly than in the intact animals.

Thus, it was shown, that with a rapid decrease in the oxygen content in the inhaled air in the case of rats with denervated sino-carotid chemoreceptors, the reaction of the respiratory system is delayed and exists at a lower level than in the case of intact animals. This leads to a more pronounced hypoxia of the tissues. The chemoreceptors of the sino-carptid zone do not significantly participate in the regulation of the reactions of the cardiovascular system to rapidly increasing hypoxia.

The rectal temperature, which was 0.60° and 0.43° less at an altitude of 12000 meters, gradually decreased in proportion to the increase in hypoxia of the intact and denervated animals. This agrees with the data of L. L. Shik (1948), Ye. V. Gubler, (1952), N. A. Agadzhanyan (1968), K. P. Ivanov (1968). It is known that the temperature control center, located in the hypothalanus, possesses high sensitivity to hypoxia, as a result of which oxygen deficiency in the inhaled air leads to the suppression of chemical temperature regulation. In the opinion of N. N. Sirotinin (1941) et al. in the case of rats, hypothermia may be a protective reaction of the organism to a low oxygen content in the inhaled air. Insufficient study has been given to the problem of the role of the receptors of the sino-carotid zone in the regulation o. the heat exchange of the animal organism. G. N. Veselkin and Ye. S. Zykina-Garmenitskaya (1957), in experiments on rabbits with the carotid bodies removed, established that the sino-carotid zones play a significant role in the reflex mechanism of the development of a fever reaction with the introduction of a pyrogenic substance into the organism. /74

In order to expose the role of the sino-carotid zones in animals with different levels of acclimatization to hypoxia and to obtain comparitive data in second series were conducted in high-mountain conditions (the Tuya-Ashu Pass, altitude 3200 m) on rabbits and rats, brought from Moscow (sea level) and marmots (native to the mountains).

The operation of glomectomy was performed under the stereomiscroscope. It consisted of the simultaneous bilateral removal of the carotid body and its surrounding adventitia from the region of bifurcation of the common carotid artery (A. I. Yelfimov, 1971).

The survival time at an altitude of 12000 meters (with an altitude chamber ascent at a rate of 25 m/sec) was determined as a test characterizing the dynamics of the acclimatization of different types of animals to a high mountain climate.

Investigations were conducted on 30 rabbits, 120 rats and 29 marmots. In all, 179 animals were subjected to 201 tests.

Data on the altitude resistance of intact and denervated rats on different days of mountain acclimatization are presented in Table 16 and Fig. 9.

From Table 16 it is obvious that a reliable increase in the altitude resistance of intact and denervated rats began only after 30-40 days of mountain acclimatization. It is necessary to note that the survival time in the altitude chamber at 12000 meters on all the indicated days of acclimatization was statistically higher (P less than 0.05) in the case of intact rats than in the case of rats with the sino-carotid bodies removed. /75

Fig. 9 Altitude resistance (survival time in minutes at 12000 meters) of intact (1) and denervated (2) rats at various days of mountain acclimatization. Confidence interval calculated for P=0.05.

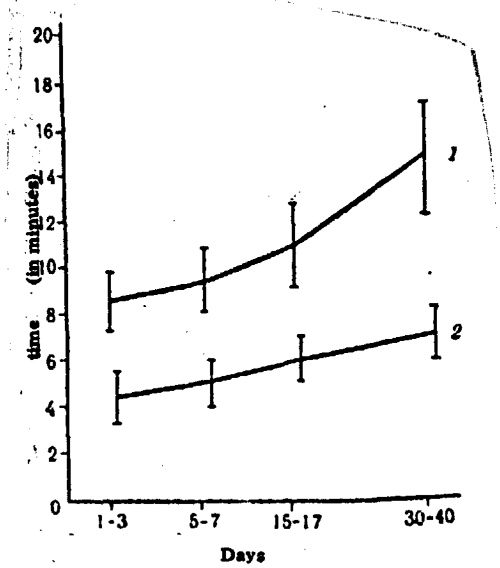

TABLE 16. SURVIVAL TIME (in seconds) OF ANIMALS AT AN ALTITUDE OF 12,000 m FOR VARIOUS DAYS OF ACCLIMATIZATION IN THE MOUNTAINS
(Experiments of A. I. Yelfimov)

Statistical Indicator	Intact rats				Denervated rats			
	Days of acclimatization							
	1—3	5—7	15—17	30	1—3	5—7	15—17	30—40
n	9	43	17	12	10	27	27	6
M	530	582	673	820	266	311	367	435
±m	±31	±30	±70	±78	±38	±36	±26	±41
P[1]	—	>0,05	>0,05	<0,01	—	>0,05	<0,05	<0,01

[1] The reliability P is calculated in relation to the data for the 1 - 3 days

Analogous data are obtained in experiments on rabbits (Table 17).

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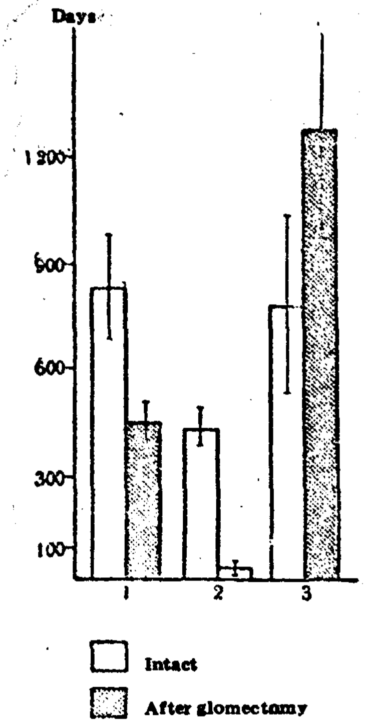

Fig. 10 Altitude resistance (in seconds) of rats (1), rabbits (2) and marmots (3) on the 25th day of mountain acclimatization

From the data given it is obvious that a reliable (P less than 0.05) increase in altitude resistance is noted for intact rabbits toward the thirtieth day of mountain acclimatization. In the animals which have been operated on the survival time sharply decreases on the 15-30th days. The altitude resistance of intact rabbits in the acclimatization periods mentioned is significantly increased (P less than 0.5) in comparison with the animals which have been operated on.

Different results are obtained in experiments on marmots (Marmota caudata) which constantly inhabit the given mountain region (the Tuya-Ashu Pass). It was established that if the survival time of intact marmots in the case of an ascent to an altitude of 12000 m was 780 seconds, then on the 25th day after glomectomy it increased to 1280 seconds (Fig. 10).

These results, in the first place, indicate that in the case of mountain natives (marmots) the altitude resistance is higher than that of animals brought from sea level (rabbits, rats), and, in the second place, the removal of the sino-carotid bodies causes opposite changes in these animals. Thus, if the altitude resistance of rabbits and rats after denervation of sino-carotid chemoreceptors is decreased, then, as we have already mentioned, in marmots, it on the contrary is increased.

In order to explain certain intimate mechanisms of the adaptation of different types of animals to a high mountain climate the dynamics of the change in certain factors in the blood were investiagated in addition to the determination of the altitude resistance.

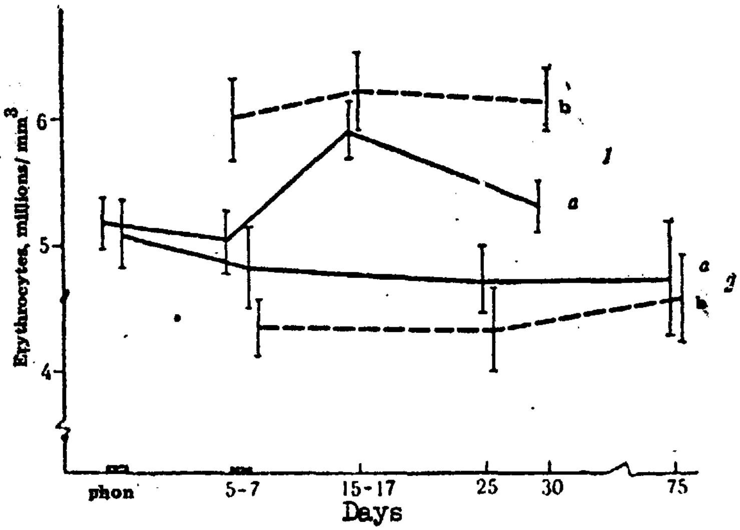

Fig. 11 Nature of the change in the number of erythrocytes in rabbits (1) and marmots (2) on different days of mountain acclimatization (Tuya-Ashu Pass, altitude 3200 m).
a - intact animals; b - after glomectomy

Figure 11 shows the dynamics of the change in the number of erythrocytes in rabbits and marmots on different days of mountain acclimatization (experiments of A. I. Yelfimov and Ye. M. Bebinov).

TABLE 17. HIGH-ALTITUDE RESISTANCE (TIME OF SURVIVAL IN SECONDS AT AN ALTITUDE OF 12,000 m) IN RABBITS IN DIFFERENT PERIODS OF MOUNTAIN ACCLIMATIZATION.

Statistical indicator	Background	Control		Glomectomy	
		15–17 days	30 days	15–17 days	30 days
n	15	10	11	8	6
M	220	313	418	30	39
±m	±20	±22	±50	+3	±6
P	—	>0,05	<0,05	<0,05	<0,05

From the data given it is obvious that as in the case of the investigation of the altitude resistance, changes on the part of the erythrocytes of denervated rabbits and marmots are in opposite directions, i.e. the number of erythrocytes after glomectomy in rabbits significantly increases (more than in the case of intact animals) and, on the other hand, in the case of marmots it decreases. /78

The experimental data obtained reveal several characteristics of the adaptation to hypoxia of different species of animals. The further study of the physiological mechanisms of the adaptation of an organism to oxygen deficiency provides the possibility of controlling compensatory reactions, and consequently, of finding ways to increase the resistance of the organism to hypoxia.

4. THE INFLUENCE OF HYPOXIA ON CONDITIONED REFLEXES AND THE BIOELECTRIC ACTIVITY OF THE BRAIN

Although a large number of fundamental investigations have been dedicated to the study of the influence of oxygen insufficiency on the organism, our knowledge about this problem is far from complete. Thus, while the adaptive reactions, directed toward maintaining constant partial pressure of gases in the blood and towards increasing the oxygen utilization by the tissues have been well studied, we know little about the complex readjustment, arising under the affects of hypoxia, of the activity of the different functional systems of the organism and the mechanisms of their disturbances, expecially of the functions of the higher sections of the brain.

It has been shown that the higher sections of the central nervous system are particularly sensitive to oxygen deficiency and endure complete absence of oxygen only a few minutes (V. V. Strel'tsov, 1939, L. A. Orbeli, 1940, I. R. Petrov, 1949).

The numerous investigations of domestic and foreign authors which have been conducted in recent years have significantly broadened our understanding of the changes in the activity of the central nervous system under the effects of hypoxia.

The conditioned reflex method was used for studying the influence of oxygen starvation on the higher nervous activity of animals. The first changes in conditioned feeding reflexes were observed at altitudes of 1000-3000 m (shortening of the latent /79
period, increase in the magnitude of conditioned reflexes and unconditioned salivation), and, as a rule, phase states were noted in the animals at higher elevations (4000-6000 m) and, finally at altitudes of 6000-7000 m conditioned reflex feeding reactions completely disappeared (A. V. Lifshits, 1949; V. N. Zvorykin, 1951; M. P. Brestkin, 1952; Malmejac, Plane, 1952; V. A. Isabayava, 1954; G. V. Altukhov, 1955, et al.) The authors explained these changes in conditioned reflex activity by the disturbance of the processes of internal inhibition at the beginning, and subsequently, by the development of threshold inhibition.

We studied the higher nervous activity in conditions of a rarefied atmosphere by means of conditioned motor (defense) reflexes.

Considering the enormous biological role of the conditioned reflex in the "most precise and delicate" adaptations of the organism to environmental conditions and knowing that the speed of developing and strengthening a conditioned reflex is an important indicator of the adaptability of an animal to specific conditions, we not only studied the systematic operation of the cerebral hemispheres and the condition of the different types of internal inhibition in conditions of a rarefied atmosphere, but also directly studied the characteristics of the formation of temporary connections with the action of oxygen deficiency on the organism.

In order to solve the problems put forth in this section of the study we used a method allowing for simultaneous recording of the conditioned reflexes, respiration and cardiac activity under altitude chamber conditions in experiments on dogs, and also for an electroencephalogram to be taken in experiments on rabbits.

The altitude chamber was equipped with the necessary apparatus for conditioned motor and secretory reflex tests. Conditioned stimuli were placed inside the chamber and were turned on from a control panel located outside the altitude chamber. Figure 12 shows a diagram of the setup for testing reflexes and the control panel.

The investigations were conducted on six dogs both under terrestrial conditions, and at different altitudes (2000-10000 m). The ascent rate in all experiments was 15 m/sec. The conditions of performing the tests in a rarefied atmosphere make impossible the use of the pneumatic and mechanical systems of recording conditioned motor reflexes which were used by V. P. Protopopov, E. A. Asratyan, G. P. Konradi et al. in their experiments in conditions of normal barometric pressure. /80

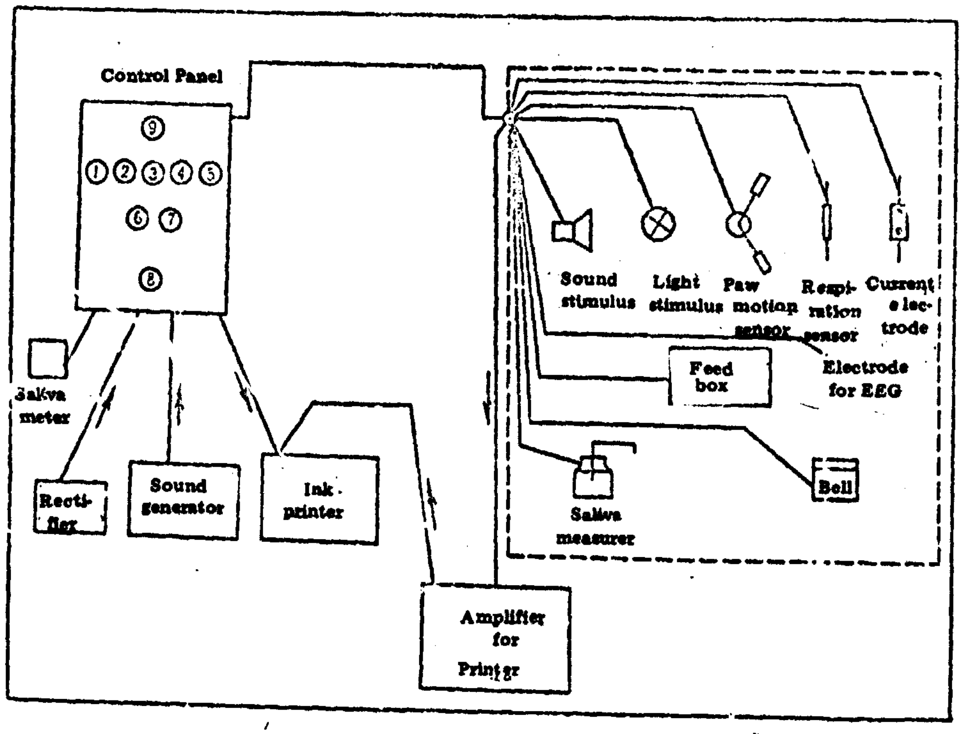

Figure 12. General scheme of the setup for investigating conditioned reflexes.

We used a variable resistance with a system of levers as a sensor receiving the paw moments produced by the animal in response to conditioned and unconditioned stimuli. The sensor was attached to the right rear paw so that the axis or rotation of the rheostat slider was at the same level as the knee joint. /81

We determined the amount of response motor reaction and the force of the electric current according to the readings of the measuring instruments and the data registered on an oscillograph.

Motor electrical-defense, conditioned reflexes were developed according to a specific stereotype to stimuli of varying intensity (bell, a tone of varying frequency and light).

In order to obtain audio frequencies, an audio oscillator was used which made it possible to establish both the pitch and the intensity of the tones presented in precise quantitative units.

The electrocardiagram and respiration were recorded simultaneously with the investigation of the conditioned motor reflexes.

In all, six dogs were subjected to 419 tests, of which 93 tests were at various altitudes (Table 18).

TABLE 18. RESULTS OF EXPERIMENTS CARRIED OUT FOR THE STUDY OF THE HIGHER NERVE ACTIVITY OF DOGS AT VARIOUS ALTITUDES

Name of Dog	Type of Nervous System	Altitude, m: earth before ascent	2 000–5 000	6 000	7 000	8 000	9 000	10 000
Pirate	Strong with a predominance of stimulatory processes	173	4	17	4	7	6	1
Chestnut	Same	74	2	11	—	3	4	4
Beetle	Strong with a predominance of inhibiting processes	45	5	8	1	1	3	1
Blossom	Strong, balanced	23	1	2	—	1	—	—
Marquise	Same	7	—	4	—	—	—	—
Little Bear	Weak type	4	—	3	—	—	—	—
	Total	326	12	45	5	12	13	6

As a result of the investigations it was established that at altitudes of 2000-5000 m there is noted a certain shortening of the latent period, an increase in the magnitude of the conditioned reflexes to all stimuli and - in individual cases - even loss of differentiation.

In one dog (Beetle) at an altitude of 5000 m there was observed in the first half of the experiment a lengthening of the latent period and disturbance of the force relationships according to the compensating hypnotic phase pattern. The different picture of the changes in the conditioned motor reflexes of the various dogs with all conditions being equal indicates, in the first place, the significance of the typological characteristics of the nervous system of animals in development of oxygen starvation; in the seond place it indicates that an altitude of 5000 m is the boundary altitude, at which the organism is on the line between the physiological and pathophysiological states. /82

These experiments show that a 45 minute stay of the animals at altitudes of 2000-5000 m does not cause severe damage to the higher nervous activity, which must be connected with the development in these conditions of sufficiently effective compensatory reactions, above all on the part of the respiration and cardiovascular system, enabling the animals to adapt to these altitudes.

As far as the equilibrium of the basic cortical processes at altitudes of 2000-5000 m is concerned, it changes toward a relative intensification of the excitation process.

The results of experiments conducted at an altitude of 6000 m indicate that in all dogs at this altitude there is already suppression of the conditioned reflex activity, expressed in a prolongation of the latent period, absence of reaction to specific stimuli (light) and distortion of force relationships (according to the type of the compensating and paradoxical hypnotic phases).

With a comparison of the results obtained in our laboratory by the secretory conditioned reflex method (G. V. Altukhov, 1955) and data obtained on the same dogs by the conditioned motor reflex method, it is possible to observe that in the case of an investigation of the feeding reflexes, differentiation is, as a rule, lost at an altitude of 6000 m, while during the test of a motor stereotype at this altitude it is almost always preserved.

The difference observed in identical conditions of oxygen starvation can, evidently, be explained by the biological characteristics of the motor and secretory reactions.

Conditioned motor defense reflexes are more resistant to oxygen deficiency than are feeding reflexes.

The typological characteristics of the nervous system of the subject animals show up clearly at an altitude of 7000 and particularly 8000 m. At this altitude we also noted prolongation of the latent period, an absence of reaction to specific stimuli of the stereotype and a distortion of force relationships. In addition the above mentioned disturbances were more pronounced in dogs with predominance of the inhibiting process. The unconditioned reaction was preserved at an altitude of 8000 m; however, it was somewhat weakened and lagged behind the moment of application of the electrical stimulus. /83

The retention of differentiation at high altitudes, evidently, can be explained not by the increase in the tonus of internal inhibition, but by the development of protective inhibition at these altitudes.

I. P. Pavlov considers the deep inhibition which develops under the influence of unfavorable influences to be the normal physiological defense mechanism of the organism with a pathogenic origin, protecting the brain cells from depletion and functional destruction.

Such inhibition, threshold in nature and protective in value, was observed in dogs at altitudes of 8000 to 10000 m. The conditioned reflexes to individual stimuli were sharply suppressed up to their complete disappearance. Unconditioned reflexes were also disturbed.

At the same time that we studied the hypoxic disturbances of the developed dynamic stereotype of conditioned motor reflexes we also conducted investigations of extinction inhibition in the same conditions.

I. P. Pavlov attributed great significance to the study of extinction inhibition. He considered it to be a biologically necessary adaptation for the economy of energy expenditure of the nervous system. "Thanks to the inhibition which appears," wrote I. P. Pavlov, "the conditioned stimulus as a signal conforms to the detailed conditions of its physiological role, not giving rise to useless work." [1]

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[1] I. P. Pavlov: Poln. Sobr. Soch (Complete collected works) Volume 3, Book II, Moscow, 1951, page 390.

The data obtained indicate that oxygen deficiency at an altitude of 6000 m, while still not having significant influence on the stimulatory process, weakens the process of active inhibition, which was expressed in the chaotic and undulating nature of the extinction of reflexes.

The nature and speed of extinction of a conditioned motor reflex at an altitude of 8000 m depended on the stress of the protective inhibition, whereby the more intensive was the latter the more rapidly the conditioned reaction to the stimulus being extinguished disappeared.

If we analyze the material obtained without considering the conditions in which the organism of the animal is found, then at first glance the impression may be created that at an altitude of 8000 m active inhibition is intensified and becomes more complete. However, this is indeed not so. The rapid extinction of a conditioned motor reaction at an altitude of 8000 m is not produced by an increase in the tone of active (extinction) inhibition, but by the development, as we have already noted, of threshold protective inhibition, which caused the weakening of both cortical processes. Analyzing materials on the problem of inhibitory stimuli, I. P. Pavlov indicated the double functional role of the inhibitory process, which is manifested on the one hand in the most delicate adaptation of the organism to the environment, and on the other in the protection of the cortical cells from further destruction and exhaustion. "In the case of intense inhibitory tonus of the cortex it deepens the inhibition, as if supplementing the inhibition at hand. /84

In the process of formation of conditioned reflexes we find very complex manifestations of synthetic and analytic activity of the higher sections of the brain, since the physiological role of the cortex of the cerebral hemispheres is, on the one hand, switching (in mechanism) and on the other, signalizing (in value). Therefore, it is of great interest to obtain data on the possibility of analyzing conditioned reflexes directly in conditons of oxygen starvation (at an altitude of 6000 m).

We determined that it is, in principal, impossible to form temporary connections to audio signals in conditions of acute oxygen deficiency. However, it was shown that the rate at which conditioned reflexes are formed on the ground and at an altitude of 6000 m is different (Table 19).

The process of the formation of conditioned connections at the indicated altitude proceeded more slowly and with fluctuations.

A clear relationship between the rate of development of conditioned reflexes and the typological characteristic of the nervous system of the subject animals was noted here.

The difficulty of the formation of temporary connections in conditions of oxygen starvation undoubtedly indicates a lowering of the functional level of the cerebral cortex of the brain. Moreover, temporary connections developed in conditions of oxygen deficiency are distinguished by their instability and easy inhibition.

TABLE 19. RATE OF DEVELOPMENT IN DOGS OF CONDITIONED ELECTRO-DEFENSE REFLEXES

Name of Dog	Type of nervous system	On what connection the conditioned reflex developed (1) and became fixed (2)			
		On Earth		At 6000 m	
		1	2	1	2
Pirate	Strong, balanced	4	4	9	20
Marquise	Same	3	5	8	14
Beetle	Strong, inhibited	2	4	12	22
Chestnut	Uninhibited	4	6	10	24
Little Bean	Weak	8	12	Conditioned reflex did not develop.	

G. T. Sakhiulina (1949) also observed a sharp disturbance of the switching function of the cerebral cortex after prolonged periods of anemization of the central nervous system. Thus, our experiments not only established the fact of the weakening of earlier developed and fixed conditioned connections, but also of the disruption of the switching function - the development of new temporary connections in conditions of oxygen starvation.

It was also shown that a conditioned reaction on the part of respiration and cardiac activity, as a rule, appeared with a significantly smaller number of combinations of conditioned and unconditioned stimuli, than a motor defense reaction. In other words, in development of conditioned reflexed come gradually to the forefront in agreement with general biological rules. In addition, changes in respiration and cardiac activity occur in direct relation to the initial functional conditions of the respiratory and vascular motor center. Thus, if a conditioned stimulus was given against a background of infrequent breathing, then the changes, as a rule, expressed themselves in an increase in the frequency of respiratory movements, and visa versa. Already in 1899 N. Ye. Vvedenskiy directed attention to this fact when he stimulated the vagus nerve with an electric current.

Very often, especially in experiments with the extinction of a conditioned reflex, the vegetative reaction continued to be preserved while local conditioned and unconditioned motor reactions were absent. This is probably the result of the varying biological significance and typographical localization of the structural elements of the cortex providing for and regulating a given reaction of the organism, but it also depends on the functional mobility of the cortical processes developed in the process of phylo-and ontogenesis for a more perfect adaptation of the organism to changing environmental conditions. /86

At altitudes of 6000 - 8000 m conditioned reflexes of the organs of respiration and the cardiac activity almost completely disappear, and at altitudes of 10000 m and more there begin to be severe disturbances of the vitally important functions of the organisms, expressed in the appearance of periodic breathing, arrhythmia of the pulse and indicating the exhaustion of the compensatory capacities of the organism.

The possible use of electrophysiological methods of investigation, in particular the method of electroencephalography, is also of great interest. It has been established that the dynamics of the change in the bioelectric activity of the brain under the effects of hypoxia pass through three stages: predominance of exitation rhythms at moderate altitudes; dominance of slow wave activity from an altitude of 8000 m and suppression of electric activity up to complete "silencing" from an altitude of 11000 m (O. I. Parfenova, M. N. Livanov, 1945; V. B. Malkin, A. N. Razumeyev, G. V. Izosimov, 1963; Motobayashi, Mitarai, Ando, 1963). However, in the works of the authors, just mentioned the bioelectrical activity of the brain in conditions of decreased barometric pressure was investigated with the animal in a fixed position which did not allow the relationship between changes in biopotentials and behavorial reactions of the animals to be determined.

The correlation between changes in the EEG and the behavior of animals in conditions of increasing hypoxia was traced in our laborato y (L. V. Kalyuzhnyy, N. A. Agadzhanyan, I. N. Zakharova, 1967).

In order to explain the physiological role of the different formations of the brain in the performance of protective compensatory reactions of the organism it is important to study the intercenter relationships, the regularity and sequence of development /87
of changes in the biological activity of the cortex and subcortical formations and to reveal the features which are specific for each structure. For this we chose the structures of the brain directly

participating in the formation of specific reflex behavioral acts.

The experiments were performed on rabbits with nichrome electrodes permanently implanted in the following structures: the visual zone of the cortex, the dorsal hippocampus, the lateral margin of the hypothalamus and the reticular formation of the midbrain. Electrodes 20-25 μm thick for subcortical recording and 300 μm thick for cortical recording were implanted bipolarly with a distance of 1-2 mm between the electrodes.

In all rabbits with a developed, conditioned food-acquiring reflex, the background bioelectrical activity was characterized by regular oscillations of the biopotentials at a frequency of 4-5 oscillations per second and an amplitude of 80-100 microvolts. In response to a rhythmic light signal there were observed on the EEG bursts of synchronized oscillation of potentials with a frequency of 8-10 per second in all recordings studied as well as a reaction of simulating the rhythm of light flashes in the visual zone of the cortex and the lateral margin of the hypothalamus. At altitudes of 2000-3000 m the level of excitation in the structures of the brain increases, which is expressed by an increase in the number of intersignal food-gaining reactions, loss of differentiation, a decrease in the energy of delta waves on the EEG (up to 85±7%) and the predominance of the theta rhythm in all recordings investigated, equal to 5-7 oscillations per second and an amplitude of 70-100 microvolts, and sometimes with individual bursts to 8-9 oscillations per second. At this period, the behavioral reactions of "raising up the ears" were observed in the rabbits mainly. Moreover, a pronounced preliminary motor behavior reaction was constantly recorded at these elevations. It is characteristic that it is precisely at this period that the integrator indicates a distinct drop in energy of delta wave activity and the presence of intersignal EEG reactions of "imposition" in the lateral margins of the hypothalamus (L. V. Kalyuzhnyy, N. A. Agadzhanyan, I. N. Zakharova, 1967). The above-mentioned changes indicate the predominance at altitudes up to 4000 m of the excitation of the parasympathetic subcortical sections of the brain as a result of an increase flow /88
of impulses from the chemo- and baroreceptors.

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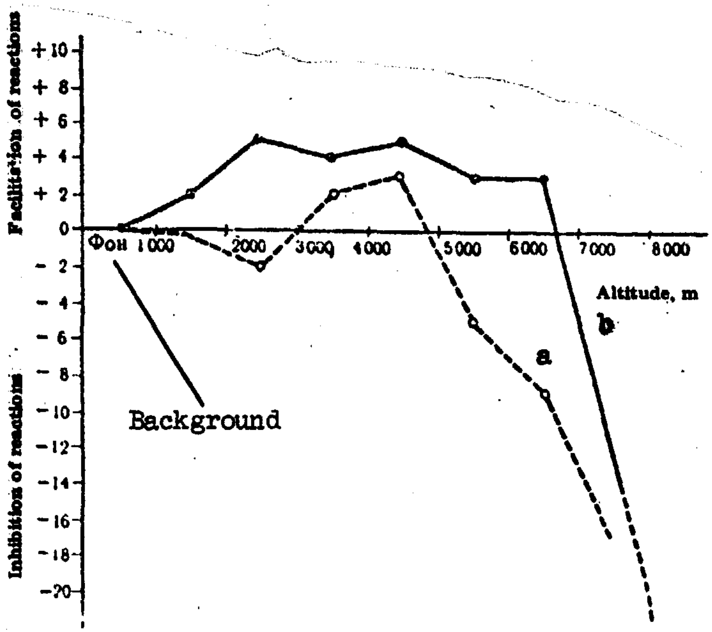

Fig. 13. Change in the reaction of "self stimulation" (a) and "avoidance" (b) under the effects of increasing hypoxia.

Experimental investigations, conducted in our laboratory by G. P. Goroyan, indicate that in conditions of a rarefied atmosphere, corresponding to altitudes of 3000-4000 m, a reliable (P less than 0.05) increase in the "self-stimulation" reaction and a certain facilitation of the "avoidance" reaction (Fig. 13) are observed. In these conditions, facilitation of the "self-stimulation" reaction was blocked by a cholinolytic substance - scopolamine but was not blocked by aminazine, while the "avoidance" reaction was only inhibited to a certain degree by aminazine and not blocked by scopolamine (N. A. Agadzhanyan, G. P. Goroyan, L. V. Kalyuzhnyy et al. 1968). The above-mentioned changes become understandable if we consider that the lateral hypothalamus is the unconditioned subcortical feeding center with a cholinergic nature of excitation.

These results provide a basis for assuming that at moderate altitudes a biologically positive motivation condition arises in animals as a result of the dominance of excitation from forward-lateral sections of the hypothalamus and cholinergic activation mechanisms. It is necessary to note that in human beings at altitudes of approximately 3000-4000 m, as a rule, a state of euphoria /89 and exaltation appears.

In proportion to the further increase in hypoxia at altitudes of 5000-7000 m, a second increase in the excitation level in the structures of the brain is noted, which is characterized by a decrease in the energy of delta waves on the EEG, a generalization of the reaction assimilating the rhythm of stimulation over all recording structures of the brain and an absence of the conditioned food-acquiring reflex. This is produced by the increased excitation of the subcortical non-specific activating system of the brain. At altitudes of 5000-7000 m, there is observed an inhibition of the "self-stimulation" reaction and a significant facilitation of the "avoidance" reaction which was blocked by aminazine and not blocked by scopolamine.

An analysis of the experimental data presented indicates that the biologically positive motivation state observed in animals in conditions of moderate hypoxia (at altitudes of 3000-4000 m) at is replaced at altitudes of 5000-7000 by a biologically negative motivation state as the result of the predominance of excitation of the adrenergic structures of the subcortex - the reticular formation of the midbrain and the rear-medial sections of the hypothalamus. It should be noted that in our early investigation it was established that it is impossible to extinguish a conditioned defense reaction in dogs at an altitude of 6000 m (N. A. Agadzhanyan, 1956). In our laboratory, studies by L. V. Kalyuzhnyy showed that the hypothalamus, being functionally and "chemically" a heterogenic formation, determines the differentiation of the biological significance of a stimulus and directly participates in the formation of the response reaction of the organism in extreme conditions, in particular with increasing hypoxia.

Finally, at altitudes greater than 7000 m, threshold inhibition develops in the structures of the brain, being expressed in the disappearance of conditioned reflexes, and the development of slow wave activity, which is first recorded in the cortex and then in the subcortical structures. At altitudes greater than 8000 m both the /90
"self-stimulation" reaction and the "avoidance" reaction disappear.

It is very characteristic that in the case of the creation of a "plateau" on the EEG at an altitude of 7000 m the slow waves of the cortex may, for a certain period of time, be again replaced by the theta rhythm, i.e. by the same activity which is observed in the subcortical formation. Beginning with an altitude of 8000 m a slow wave rhythm of high amplitude appeared even in the subcortical recordings and above of all in recordings of the hypothalamus. In other cases, the delta activity was recorded simultaneously in recordings of the hypothalamus and hippocampus, while in the reticular formation of the midbrain, rapid activity in the form of irregular oscillations of 4-6 cycles per second and an amplitude of 40-60 microvolts was observed.

Probably, specific paths of impulsation passage are less disturbed by the effects of hypoxia.

At the time when slow waves were observed in the hypothalamus, the rabbits, as a rule, were completely immobile and lay prone on the floor of the chamber. At altitudes of 8000-9000 m the energy of the delta waves increased to 204 ± 38% (data from the biopotential integrator).

With an ascent to higher altitudes (11000-12000 m) EEG recordings from the cortex, hypothalamus and hippocampus registered still slower frequencies of biopotential oscillations, which also became less regular, while in recordings from the reticular formation of the midbrain, an abrupt flattening of the bioelectrical curve to 20-30 microvolts was recorded. Individual oscillations of biopotentials, which corresponded to single terminal respiratory movements of the animal, were observed on the EEG against this background. Generalized clonic spasms as a rule developed after these and a rapid "descent" was produced. At ground atmospheric pressure, normal rhythms of respiration and EEG were soon reestablished.

Several sequential stages were also observed in the case of the reestablishment of conditioned reflex activity and normal electrical activity after having endured acute hypoxia. Immediately after the "descent" as a result of the blockage of afferent impulsation the EEG "imposition" reaction was not established in any of the structures investigated and the conditioned reflex was absent.

Later, the reaction of the "imposition" of the rhythm of the signal presented appeared in proportion to the reconstruction of the conditioned reflex activity in the visual region of the cortex and the lateral margin of the hypothalamus. Consequently, the picture of functional changes in the brain in conditions of oxygen deficiency may be divided into a series of sequentially developing stages. Disturbance of brain activity began from the cortical formations, then the intermediate brain was damaged and finally - the midbrain. /91

A study of certain neuro-chemical mechanisms of brain reactions showed that in conditions of increased oxygen insufficiency there is observed an initial predominance of excitation of a cholinergic nature of the forward-lateral sections of the hypothalamus, and at altitudes of greater than 5000 m, excitation of an adrenergic nature of the rear-medial sections of the hypothalamus and the reticular formation of the midbrain, which leads to the dominance of a biologically negative motivation state and the suppression of conditioned feeding reflexes.

Having revealed the presence of the correlation between changes in the EEG and behavioral reactions in experiments on animals, we undertook the test of determining in experiments of human beings the depth and sequence of the changes observed under the effects of acute hypoxia. A special series of experiments was conducted for this purpose (N. A. Agadzhanyan et al. 1971). The subjects were healthy men, 20-30 years in age, who passed the flight-medical board and were suited for altitude chamber experiments without limitations.

The nature of the change of the physiological reactions of an organism in breathing pure nitrogen or helium was studies in the subjects.

Complex recording of the following physiological factors was performed in the experiments: EEG (8 recordings), skin-galvanic reflex, motor reactions in solving arithmetical problems (writing sample), EKG, frequency and volume of breathing and oxygenation of blood. Motor reactions in solving arithmetical problems (counting from 1 to 1000) were recorded with the use of an electric contact pencil. In all, 45 subjects were subjected to more than 200 tests.

It is known that adaptation to hypoxia is a very complex and multifaceted process in which practically all the organs in the system of the organism are involved. As we have already noted, the resulting function, characterizing the effectiveness of compensatory-adaptative reactions of the organism, is the level of oxygenation of the arterial blood. The oxygen pressure in the tissues, and, therefore, also the normal course of oxidizing processes, greatly depend on the degree of oxygenation of the arterial blood. /92

It must be mentioned that not only the degree but also the rate of growth of oxygen starvation influence the degree of oxygenation of the blood. In our experiments it is shown that, depending on the rate of growth of hypoxia, the degree of oxygenation of the blood at a given altitude fluctuates within wide limits (from 48 to 76%). Individual differences are particularly clearly manifested in the case of slow rates of growth of hypoxia and, visa versa, the more rapidly oxygen starvation appears, the more these differences level out.

The time from the beginning of breathing pure nitrogen or helium to the appearance of severe functional disorders was, on the average, around 2 minutes in our experiments. Individual fluctuations varied within the limits of 5-8 seconds.

The investigations showed that the first signs of disturbance of the higher nervous activity appear in man at the 50-55th second of breathing nitrogen and helium with a blood oxygenation equal to 75-80% (Fig. 14). This coincides with the appearance of theta waves on the EEG. The subject, as a rule, does not perceive the indifferent signals used at this time.

In proportion to the increase in hypoxia, and in particular with a blood oxygenation equal to approximately 70% (75-80 seconds of breathing nitrogen or helium), delta waves appear on the EEG (at first isolated, and then in groups, and finally in the case of severe hypoxia the delta waves become predominant. The appearance of delta waves is accompanied by regular changes in the motor reaction and memory, namely errors in completing simple arithmetical problems; perseveration phenomena are noted. In our opinion, these phenomena express the presence of functional disassociation between the cortex and subcortical (thalamic) regions. The "automatism"

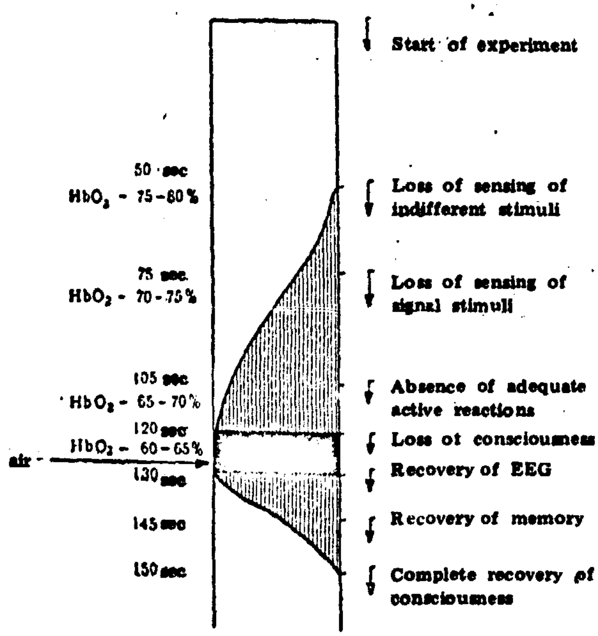

Fig. 14 Change of behavioral reaction of a man in conditions of acute oxygen starvation.
[See explanation on following page]

KEY TO FIGURE 14.

On the left - time from the moment of breathing pure nitrogen or helium and percentage of blood oxygenation (oxyhemometry data); on the right - symptoms of functional disturbances; crosshatched area - degree of expression and rate of growth of disturbances.

phenomena characteristic of high altitude hypoxia very often appear with the predominance of delta waves on the EEG. For example, the subject performs writing motions but does not produce a graphic inscription. Subsequently with a blood oxygenation equal to approximately 65% and below (115-125 seconds of breathing nitrogen or helium), loss of unconsciousness begins.

Consciousness as a structural phenomenon undergoes a number of successive and complex changes under the effects of acute oxygen starvation. First, the ability to perceive indifferent signals, /94 which do not have great biological and social significance, is disturbed. In proportion to the increase in hypoxia the subject loses the ability to perceive his surroundings as a whole with all their fine details and indifferent stimuli and it is as if all attention or active consciousness is concentrated on fulfilling and perceiving the basic task of the experiment. Subsequently, with deep hypoxia even this ability and also the feeling of danger are lost, the memory retains only traces in the form of the perception of proprioceptive signal from the muscles of the whole body. Then, (after approximately 120 seconds) loss of consciousness begins. In this period the structures of the brain, performing active information activity, are completely inhibited and only those sections function which regulate the activity of vitally important organs and systems (respiration, cardiac activity).

After returning to breathing atmospheric air, the ability to adequately react to external signals and to perform coordinated psychomotor activity returns after 30 seconds, and the EEG picture begins to be restored even earlier, after 15 seconds.

A complex study of the different functional systems shows that repeated exposure to high altitude factors produces a gradual adaptation of the organism to sharply changing conditions of the surrounding gas medium (to a lesser degree, pulmonary ventilation changes and tachycardia decreases).

The explanation of the physiological mechanisms of hypoxic disturbances and the establishment of a correlation between the degree of blood oxygenation, EEG changes and behavorial reactions make it possible to predict the degree of disturbances of brain functions and to develop concrete prophylactic measures for different levels of oxygen starvation. This may find practical application in the establishment of medical monitoring to evaluae the adequateness of spacecraft crew responses to different signals.

CHAPTER III

ARTIFICIAL ATMOSPHERE AND ITS INFLUENCE ON THE ORGANISM

In order to maintain the normal working capacity and health /95
of a man located in an airtight cabin it is necessary to maintain a sufficient total pressure and optimal partial pressure of oxygen, carbon dioxide and other gases in it.

In order to solve this problem it was necessary to conduct a broad range of investigations, aimed at studying the influence on a man of an extended stay in small, sealed compartments in conditions of an artificial atmosphere.

Experiments involving men staying in airtight cabins with an atmosphere, close to normal terrestrial atmosphere, have already been conducted in the Soviet Union. However, interest is seeking broad technical and biological possibilities for supporting human life in extreme conditions and the necessity of using an attired environment for clinical purposes posed the problem of studying different variants of an artifical gas medium. In addition, with regard to the physiological capacities of man as a biological creature, the limits of the permissible variations of the parameters of this medium must be determined primarily by the length of time spent in it. The requirements of the gas medium will become increasingly strict in proportion to the increase in the time spent in such an environment and to an ever greater degree it will become necessary to consider not only the direct influences of the environment on the organism, but also the reverse influences of the organism on the gas medium surrounding it.

As applied to an extended stay in airtight compartments, the problem of the permissible limits of variation of the total barometric pressure, the physiological basis of the permissible concentrations of oxygen and carbon dioxide, the ion composition of the air and so forth require further analysis.

If in biological experiments on animals and with the /96
participation of men it is shown that it is possible for an organism to remain for an extended period of time without harm in conditions of significant fluctuations of the most important components of the gas medium in sealed compartments, then physicians and biologists will acquire broader possibilities

for the formulations and selection of the artificial atmosphere used in airtight compartments.

It is particularly important to explain the biological role of atmospheric pressure and inert gases in order to derive the physiological basis of the oxygen regime and to create a scientifically well-founded general theory of the formation of an artificial atmosphere in sealed inhabited systems.

For many years now, the question of the possibility of using a gas medium, consisting only of oxygen in inhabited cabins has been considered in the literature. In particular, until recently many physiologists in the USA considered that in spacecraft it is expedient to create and maintain a gas medium, consisting of a "monogas"--oxygen (Schaefer, 1964, et al.) However, such a conclusion was made in the absence of a general theory and sufficiently complete analysis of the problem.

The rapid tempo of the development of astronautics and the clear prospects of increasing the distance and duration of spacecraft flights are stimulating medical and biological studies, expanding and putting forth new problems for space medicine. All these investigations are directed toward providing for the safety of man in outer space and for creating the conditions necessary for maintaining normal activity and efficiency.

The problem of maintaining efficiency during an extended stay in conditions of an artificial atmosphere, with relatively limited motor activity and incoming external information, has acquired important significance at the present time, especially in connection with the increse in the duration of space flights. In order to solve this problem it has become necessary to conduct a broad range of medical and biological investigations at home and abroad (Welch et al. 1961, 1963; N. A. Agadzhanyan, A. G. Kuznetsov, 1962; D. I. Ivanov et al. 1963; A. M. Genin, 1964; A. V. Lebedinskiy, S. V. Levinskiy, Yu. G. Nefedov, 1964; A. G. Kuznetsov, et al. 1964 and others).

Great attention is given to the orthostatic hypotension which appears in astronauts after flights (Berry et al. 1962) and after experiments with extended stay in conditions of hypokinesis (Miller et al. 1964; A. L. Myasnikov, et al. 1965, and others) or in a water medium (Graybiel, Clark, 1961; David, 1961; Graveline, 1962; Yu. V. Vanyushina, 1963; Vogt, 1965, and others). /97

One of the primary factors acting on the organism of a man in airtight compartments is the limitation of motor activity. It is sufficient to say that the oxygen consumption and the exhalation of carbon dioxide in subjects progressively decreased not only during prolonged bed rest, but also in sealed chambers of small volume (Welch, et al, 1961; D. I. Ivanov et al. 1963; A. G. Kuznetsov, I. A. Agadzhanyan et al. 1963). At the same time, there is noted an increased discharge from the organism in the urine of such elements such as sodium, calcium, potassium, nitrogen, sulfur and phosphorus.

The influence of hypodynamia on the organism may be arbitrarily divided into two basic groups: the influence leading to changes in the organism immediately during a prolonged limitation of muscular activity, and the influence of the consequences of hypodynamia on the different functions of the organism. To the first group belong atrophy of the muscles, as well as of the bones, difficulty in moving the joints, changes in brain circulation, vascular tone, etc. The second group of disturbances includes, for example, the lowering of the organism's resistance to orthostatic effects, acceleration, acute hypoxia, heavy physical loads, and so forth.

Under measured physical loads, after the termiantion of hypodynamia, a sharp rise in the pulse rate and an increase in arterial pressure are recorded (A. V. Korobkov, 1961; A. G. Kuznetsov, N. A. Agadzhanyan et al. 1963).

Taylor (1949), Miller et al.(1964), and Lamb et al. (1965) indicate a decrease in the capacity of the respiratory and cardiovascular system to rapidly supply the working tissues with oxygen and a significant increase in the amount of lactic acid in the organism during muscular work after hypodynamia.

A number of authors have established that variation in the level of energy expenditure directly depends on the dimensions of an airtight chamber. During a seven-day stay by three subjects in a spacecraft cabin simulator, 5.7 cubic meters in volume, the energy expenditure was, on the average, 32 kilocalories per kilogram of body weight per day (2300 kilocalories per day for a man weighing 70 kilograms) with an oxygen consumption of 473 liters and exhalation of 403 liters of carbon dioxide. With a four-day stay /98
by two subjects in a mock-up of a spacecraft, 18.2 sq. meters in area, the energy expenditures were, on the average, 40 kilocalories per kilogram body weight per day (2800 kilograms per day) with a consumption of 581 liters of oxygen and the exhalation of 494 liters of carbon dioxide (Celentano et al. 1963).

On the basis of the data obtained, the authors concludé that

C-2

there was approximately a 30% increase in motor activity in the larger chamber.

With the aid of physical training and the use of an "active" gas medium in a cabin, it is possible to decrease or even completely eliminate the deficit of muscular activity and in this way to prevent the development of orthostatic instability.

In Soviet and foreign literature there are a limited number of studies dealing with the influence of hypodynamia on human energy expenditure during the performance of physical work. Taylor et al. (1949) did not find that there subjects had an increased oxygen consumption during physical work after extended bed rest. A. V. Lebedinskiy, S. V. Levinskiy and Yu. G. Nefedov (1964) in studies with subjects staying for an extended period of time (from 10 to 120 days) in sealed compartments of small volume obtained the opposite results. With a measured physical load the oxygen requirement increased to a greater degree than before the beginning of the experiments. The processes of the liquidation of the oxygen debt were also significantly slowed down.

The basic cause of the disturbance of the organism's oxygen regime during work after many days of bed rest is the limitation of muscular activity. Variation of the hydrostatic factor of the organism's fluid medium, caused by staying in a horizontal position, in the opinion of B. S. Katkovskiy (1966), is of secondary importance.

Analysis of published data shows that in the case of a man undergoing an extended stay in compartments of limited volume there is, in the first place, disturbance of the physiological mechanism which control the organism's oxygen requirement, leading to increasing energy expenditure during the performance of physical work. Upon transition through ordinary conditions of motor /99
activity, restoration proceeds in a reverse order.

With an increased carbon dioxide content in the inhaled air (pCO_2 more than 8 mm Hg), functional changes in the organism appeared earlier and proved to be more pronounced (I. R. Kalinichenko, 1966 et al.)

Increased pulmonary ventilation, contraction of blood vessels and retardation of circulation are specific for increased carbon dioxide concentrations. The given circumstance must be considered when developing the principles of the formation of an artificial atmosphere for flight vehicle cabins, since capillary contraction slows saturation of the organism with nitrogen. This process does not depend on pulmonary ventilation or breathing rhythm. It is also known that carbon dioxide slows desaturation of the organism by nitrogen.

In recent years experiments have been conducted to look into possibility of a man staying for an extended (up to 15-30 days) period in an atmosphere of practically pure oxygen (90-94%) under a total pressure corresponding to altitudes of 7,000-10,000 m (308-198 mm Hg) (A. N. Genin et al. 1967).

The subjects' ability to perform mental and physical work does not change significantly in these conditions. The oxygen requirement was on the average 19.2 l/h, the carbon dioxide exhaled --16.1 l/h, energy expenditure--2304 Kcal/day.

In the authors' opinion, the gas medium under consideration does not make significant demands on the organism's adaptive capabilities. In addition, data are given on decompression disorders observed in the experiment, depending on the duration of desaturation of the organism.

Long-term (up to 14 days) investigations conducted at ground pressure showed that with an increase in the oxygen concentration in the inhaled air to 40%, no significant changes in the physiological reactions of the organism are observed, while an atmosphere containing 53% oxygen causes regular changes in the coagulative and anticoagulative systems of the blood, in the immunological properties of the organism as well as a lowering of altitude resistance (N. A. Agadzhanyan, et al. 1968).

In the case of an extended stay at an altitude of 3050 m with /100
an oxygen concentration equal to 55%, Hanno and Gaito (1960) observed toward the end of the experiment a decrease in working ability and the phenomenon of asthenia. These changes might also depend on the primitiveness and monotony of the tasks performed. Therefore, in order to maintain working ability in the indicated conditions the authors recommend posing complex and varied tasks, which might creatively stimulate a man.

The results of an experiment with two pilots staying for 17 days in an altitude chamber at a pressure equal to 250 mm Hg and in a pure oxygen atmosphere are of interest (Heather, 1961). The duration of the experiment (17 days) was determined by the period required for a flight around the moon. The use of a pure oxygen atmosphere was connected with the fact that from the technical point of view, in the author's opinion, it is much more difficult to maintain a constant ratio of different gases than of oxygen alone in a craft's cabin.

In this experiment the subjects manifested the phenomena of irritation of the pulmonary tissue and respiratory passages, and also a weight loss of 2.7 kg in one of the subjects and 1.4 kg in the other. In the experiment of Haustom and Riley (1947) subjects were submitted to slow acclimatization in an altitude chamber by means of a gradual ascent (in the course of three weeks) to an altitude of 6100 m and a stay at the indicated altitude for 10 days.

The work of D. I. Ivanov et al (1963) deserves particular attention here. The authons studied the ability of a man to stay for an extended period (to 30 days) in conditions of reduced barometric pressure, corresponding to altitudes of 3,000-7,000 m with a partial oxygen pressure in the inhaled air of from 150-200 mm Hg. It was shown that a month-long stay in the above mentioned conditions is completely possible with quite a high degree of retention of working ability. In the author's opinion the rarefaction factor does not have independent biological significance within the range of the values investigated.

Interesting psychophysiological investigations were also conducted abroad in 30-and 17-day experiments (Welch, Morgan et al. 1961; Welch, 1963). In a 30-day experiment the air was rarefied, corresponding to an altitude of 5486 m. The subjects breathed /101 a gas mixture (oxygen-40%, nitrogen-60%). In the 17-day experiment the rarefaction was equal to 10,200 m and the subjects breathed pure oxygen.

In these investigations the authors noted a drop in diastolic pressure toward the end of the investigation, some lowering of the vital capacity of the lungs, an increase in the restoration time of the cardiac rhythm after orthostatic testing and an increase in the atrio-ventricular conductivity and lability of the T spike on an EKG. Restoration of functions occurred two months after the end of the experiment. It was also noted that the subjects lost weight (2.8-3.6 kg in the 30-day experiment and 2 kg in the 17-day one) with a decrease in the water content in the body, and a decrease in the total volume of plasma and blood. The total water requirement in the 30-day experiment was 1686-1999 ml, in the 17-day experiment, 2220-2238 ml per day. The total water excretion was respectively 970-1114 and 1008-1374 ml per day.

In the authors' opinion, the shifts in the water balance in the 17-day experiment are primarily caused by the extracellular water content; in the 30-day experiment changes also developed in the cell content. Despite the weight loss, the fat content in the organism increased.

Along with scientific analysis of the parameters of the microclimate of spacecraft cabins, the attention of scientists in recent years has also been drawn to the question of replacing the nitrogen in the cabin air with inert gases. The expedience of such a substitution derives from an examination of the fundamental physical and chemical properties of inert gases and the results of physiological-hygienic and technical investigations which indicated the advantages of certain inert gases, in particular, helium (M. I. Yakobson, 1950; Bowman, Dingman, 1960; A. G. Dianov, A. G. Kuznetsov, 1963).

It is known that the solubility coefficient of helium in fats (0.0148) is significantly less than that of nitrogen (0.0667), and the rate of diffusion (1202 m/sec at 0°C and 760 mm Hg.) is greater than in the case of nitrogen (453 m/sec). The heat conductivity of helium is much greater than that of nitrogen: the coefficient of heat conductivity of the latter is 5.68, and that of helium is 33.6, and in addition the specific heat of helium (1.25) greatly exceeds that of nitrogen (0.251). On the strength /102 of these factors an atmosphere containing helium is more preferable when it is necessary to eliminate excess heat from the organism.

In recent years both at home and abroad physiological studies have been conducted on the ability of a man to endure a multiday stay in a gas medium where the nitrogen of the air has been replaced by helium with normal total pressure (A. G. Dianov, A. G. Kuznetsov, 1963) and with a pressure of 258 mm Hg (Bortek et al. 1966). A. G. Dianov, A. G. Kuznetsov et al. conducted two long-term studies on men in an airtight chamber five cubic meters in volume at ground barometric pressure. As a result, it was established that it is possible for a man to stay up to 25 days in an airtight chamber where the nitrogen of the air has been replaced by helium.

The investigations showed that the most significant functional changes which appear in the human and animal organism under the influence of a helium-oxygen atmosphere are caused by the physical properties of helium--high heat conductivity and low density.

The further the technology of hermetically sealed cabins has improved, the more pronounced have become the impurities contaminating the air. The sources of contamination may be defects in the equipment used in the cabins, coverings and polymer material, the operation of electronic equipment and, perhaps most of all, man himself as a biological object. It is sufficient to note that chromatographic analysis of human excretions reveals up to 400 compounds belonging to 22 chemical groups.

The complexity of revealing the range of transferability of traces of toxic substances within a sealed compartment is greatly increased by the fact that the interaction of different compounds may lead to the formation of new toxic products. In the case of an extended stay in a helium-oxygen medium 68 second-stage components are found: alcohols, aldehydes, hydrocarbons, ketones, sulfur compounds, etc. (Adams et al. 1966).

Complex clinico-physiological and hygienic investigations were conducted in order to make a physiological evaluation of the favorability of the above-mentioned gas medium for future manned space flights. It was shown that oxygen absorption and carbon dioxide exhalation increased in a helium-oxygen medium. In the authors' opinion, this is connected with the increased water loss in the case of reduced pressure. The diffusion capacity of /103
carbon dioxide did not change. The vital capacity of the lungs in the first period of the experiment decreased and then gradually returned to the original level (Robertson et al. 1966).

As a result of the decreased density of the gas medium the respiratory volume increased by approximately 40%. The authors did not observe changes indicating any harmful influence of the atmosphere under investigation upon the functioning of the lungs.

Despite the experimental studies which have been conducted here and abroad during the past ten years, up to the present time the basic physiological criteria for choosing the total pressure and oxygen regime in manned spacecraft cabins have not been decisively established; also, no sufficient bases have been established with respect to the use of a specific gas diluent. Comparative studies with helium-oxygen and nitrogen-oxygen gas mixtures show very small and very dubious advantages for both mixtures.

According to theoretical calculations helium has certain advantages in comparison with nitrogen: it is much more rapidly released from the organism upon transition from the two gas atmosphere of an airtight cabin into the purely oxygen medium of a spacesuit. Helium, as the gas with the smallest coefficient of absorption, is theoretically more preferable also from the point of view of the preventive treatment of atelectasis.

On the basis of theoretical calculations the opinion also existed that in a helium-oxygen medium the danger of decompression disorders is decreased since helium has a lower solubility in the connective and fatty tissues in comparison with nitrogen and it is more rapidly eliminated from the organism.

Studies performed on human beings did not reveal any significant difference between helium and nitrogen both from the point of view of the frequency of appearance of altitude pains and the gravity of decompression sickness symptoms (Roth, 1966). Moreover it was discovered that under identical desaturation conditions a helium bubble is formed in the capillaries at the initial stages and grows more rapidly and attains a size exceeding that of a nitrogen bubble by 1.8 times (Neswald, 1967).

In the opinion of Neswald (1967), with identical partial pressure of inert gases and oxygen in a manned cabin a neon-oxygen mixture, from the physiological point of view, should be somewhat better than a helium-oxygen or a nitrogen-oxygen mixture. However, the question of the biological role of inert gases /104
still needs further experimental verification and refinement.

In evaluating the above-mentioned gas mixtures it is also necessary to take account of the fact that the rate of combustion in a helium-oxygen medium is 4-5 times greater than in a nitrogen-oxygen medium (depending on the type of liquid fuel).

In order to determine decisively the efficiency of a given or artificial atmosphere for a manned cabin it is necessary to make further long-range studies on human subjects. The time factor has especially important significance for establishing the influence of an artificial atmosphere on the different physiological systems of the organism.

A specific artificial atmosphere for a spacecraft cabin can be recommended as the most rational only in the case where the duration of laboratory experiments conducted with the participation of a sufficient number of subjects exceeds the duration of a real flight.

In addition to the question dealing with the physiological basis of an artificial atmosphere, great attention has been given to the study of the influence on the organism of the conditions of an extended space flight: the limitations in movement, isolation, monotony, and the constant threat of external dangers, all of which influence the interrelationship between two members.

In the opinion of Monroe, Cramera and others with respect to space flights, from the psychological point of view a two-man crew is not desirable. The authors come to this conclusion not only on the basis of their own 30-day experiment but also on the basis of observations of polar explorers who have spent many months in the Central Arctic. "There comes a moment," one of them writes, "when there is no longer anything to say to the other person, when even a man's hidden thoughts become open and the way in which the other person blows out the lamp or throws his shoes on the floor or eats causes a flood of irritation. This can happen between the best of friends."

On the other hand, a three-man crew is also unstable, since it is possible for two men to conspire against the third. Then, /105 instead of "maintaining harmony of temperament" the collective efforts of the entire group may be destroyed.

As a result of a relatively small number of experiments, valuable factual material has been obtained on human efficiency during an extended stay in a small, sealed space, making it possible to develop some principles for setting up an artificial environment in a sealed cabin (A. M. Genin, 1964; Schaefer, 1964; N. A. Agadzhanyan, 1969).

With respect to spacecraft cabins this problem has unique features resulting, on the one hand, from the specific conditions of space flights, and on the other, from the existence of a certain compromise between the desire for creating optimal comfort conditions for the crew members and the technical facilities for providing them.

In connection with the rapid development of aviation, and particularly, of rocket technology, aviation and space medicine together with biological sciences as a while, is faced with the most important task of studying the role and physiological characteristics of the individual compensatory and adaptive protective reactions of the organism to external influences and to develop measures to increase its resistance.

In connection with the decreased pressure in manned flight vehicle cabins, particularly in the case of manned space flight, a number of questions having important practical significance arise. How probable is the danger of the appearance of decompression sickness in space flight? What ways are there to prevent decompression disorders? Does the atmosphere need to contain nitrogen? Is it worthwhile to replace the nitrogen of the air with other inert gases? Does the very factor of the length of time spent in an altered gas medium, etc. have independent biological significance? Numerous investigations have been conducted in recent years in order to solve all these scientifically practical questions and to protect the organism from adverse flight factors.

The choice of gas medium and the amount of pressure to be used in the spacecraft cabin are the subject of lively argument between engineers and physiologists. Thus, for example, experiments are being conducted in the USA to determine the relationship between cabin weight and pressure. These experiments have indicated that an increase in pressure will require thickening of the cabin skin. For a space station designed for eight men and operating with solar battery power, increasing the cabin pressure from 300 to 760 mm Hg will increase the weight of the cabin skin by more than 4 times (Parker, Ekberg, 1963). /106

Table 20 gives data on gas leakage (through openings of different diameters) in the case of different barometric pressures in a manned cabin (Konecci, 1964). The decisive factor for determining the requirements of a life support sytem is the duration of the space flight.

TABLE 20* GAS LEAKAGE FROM SPACECRAFT (DATA FROM KONECCI, 1964)

Cabin pressure mm. Hg	Gas Leakage (in kg) during a flight of x days				
	1	10	30	100	1000
		Orifice	$6\cdot10^{-3}$ cm²		
760	24,7	247	740,6	2 469	24 689
517	18,4	184	552,4	1 812	18 420
414	15,6	156	470,2	1 567	15 670
258	11,7	117	352,8	1 176	11 760
		Orifice	$6\cdot10^{-4}$ cm²		
760	2,47	24,7	73,8	247	2 469
517	1,84	18,4	55,2	184	1 842
414	1,56	15,6	47,1	156	1 567
258	1,17	11,7	35,3	117	1 176
		Orifice	$6\cdot10^{-5}$ cm²		
760	0,247	2,47	7,25	24,7	247
517	0,183	1,84	5,44	18,4	184
414	0,156	1,56	4,53	15,6	156
258	0,127	1,17	3,53	11,7	117
		Orifice	$6\cdot10^{-6}$ cm²		
760	0,024	0,24	0,72	2,47	24,7
517	0,018	0,18	0,54	1,84	18,4
414	0,016	[illegible]	[illegible]	1,56	15,6
258	0,012	0,12	0,35	1,17	11,7

*Translator's Note: commas represent decimal points.

Among USA physiologists the opinion is widespread that in spacecraft to be flown for periods up to 2 weeks it is expedient to create and maintain a gas medium consisting of pure oxygen (Schaefer, 1964). The recommendations have been carried out in the spacecraft "Mercury," "Gemini," and "Apollo." In spacecraft of the "Apollo" type the life support system permits three astronauts to inhabit an airtight cabin, 7.65 cubic meters in volume (the volume of the "Gemini" cabin--2.265 cubic meters, and of the "Mercury"--1.42 cubic meters) for a 14-day flight in a pure oxygen atmosphere at a pressure of 258 mm Hg both in ordinary clothes and in space suits. It was initially proposed that a two-gas mixture (oxygen and nitrogen) be used, but weight limitations, the wish to simplify the gas medium control system and reduce air leakage from the cabin, and the biomedical data led to the conclusion that pure oxygen at low pressure is the most rational solution. The high-pressure oxygen system present in the "Apollo" spacecraft provides for a of oxygen into the cabin, compensating for gas leakage and the oxygen consumption. The maximum gas leakage is 91 grams per In the case of damage to the cabin skin for a hole 12.5 mm in diameter the pressure is automatically maintained at 188 mm Hg for five minutes. American experts consider that this time is completely sufficient for the astronauts to be able to put on their space suits. /107

In addition to maintaining oxygen pressure in the space suits and cabin, the high-pressure oxygen system provides the necessary pressure in the water and water-glycol mixture tanks, and also operates the cyclic water accumulator. In connection with the tragic death of the American astronauts, experts in the USA again returned to an examination of the problem of the choice of parameters of the gas medium in spacecraft and began to develop a two-gas life support system for fuure spacecraft.

However, despite the available information, problems of the physiological basis of the oxygen regime in manned spacecraft cabins have still not been sufficiently studied and it is not yet possible to draw definitive conclusions and make recommendations, particularly with respect to extended space flights.

In the opinion of the experts, at the contemporary stage of development of astronautics the range of permissible fluctuations of the parameters of an artificial medium must be determined with regard to the structure of an actual spacecraft and flight program. In addition, it is necessary to consider that an increase in space flight duration along requires a more strict approach to the determination of gas medium parameters and a more precise analysis of the changes introduced into the artificial medium by the astronaut himself. It is also necessary /108 to bear in mind that in a space flight, particularly in a long one, compromise at the expense of the crew is impossible.

It is impossible not to agree with the opinion of G. Armstrong, that medical and biological studies dealing with physiological criteria ought to be concluded 5-10 years before a planned spacecraft is first launched. In this connection doctors and biologists have already before them the problem of finding the optimal physiological-hygienic criteria for normalizing an artificial habitable environment and developing an appropriate work and rest regime for space flights of different durations, mainly, with respect to determining the range of the permissible partial pressure of oxygen and carbon dioxide, determining the biological role of inert gases, the permissible range of temperature, humidity, barometric pressure and so forth.

1. ORGANIZATION OF LONG-TERM STUDIES AND THEIR PHYSIOLOGICAL-HYGIENIC CHARACTERISTICS

As we have already indicated, in recent years both in the USSR and abroad long term experiments have been conducted in hermetically sealed compartments of limited volume both at normal pressure and at decreased barometric pressure.
These studies have shown that the more perfect the life-support systems are, the less the environment of a hermetically sealed compartment differs from an ordinary environment and, consequently, the less it influences the human organism and its working ability.

The problem of habitation under the artificial atmospheric conditions of airtight compartments has acquired in recent years real significance in a number of areas of human activity.
Further analysis of this problem requires the close and daily cooperation of engineers, biologists, doctors, mathematicians and many other specialists. The end goal of the medical and biological investigations conducted under laboratory conditions in the Soviet Union is to obtain specific data for performing extended flights and conquering outer space for peaceful purposes. /109

Medical and biological studies should be directed not only toward providing the optimal gas medium conditions, but also toward developing measures for organizing efficient work and rest periods for the crew members, and toward seeking effective means of ensuring the safe conduct of long-term experiments in airtight compartments of limited volume. Materials on the organization and maintenance of extended altitude chamber investigations at normal and low pressure and the results of physiological and hygienic studies are set forth below.

Information on arranging the subjects' day, their food ration, clothing used, microbic contamination of the compartment and so forth is necessary for subsequent evaluation of the physiological data.

A large group of collaborators participated in the organization and medical and technological maintenance of these investigations.

In order to study the effect of an extended stay within an artificial atmosphere on the human organism, two extended experiments in a sealed compartment of limited volume were conducted with four subjects participating: a 60-day experiment at ground level pressure and a 62-day experiment at a total pressure corresponding to an altitude of 7,000 meters.

A wide range of physiological and hygienic investigations was performed during each experiment. The hygienic investigations included studying the microclimate, gas and ion composition of the air, the dynamics of the bacterial flora in the chamber and qualitative changes in its composition. Complex investigations of the functions of different systems of the organism--higher nervous activity, external respiration, pulmonary gas exchange, cardiovascular system, morphololological composition of the peripheral blood and so forth--were performed in order to reveal physiological shifts. The physiological reactions were recorded each three to four hours on an "Al'var" oscillograph. The daily period of /110 the organisms' physiological reaction was investigated on particular days of the experiment. At the same time there was continuous observation of the general condition and behavior of the subjects, and the regular radio reports of there state of being were also considered. In addition to performing general clinical analyses the phagocytic activity of neutrophiles, the absolute number of eosinophiles in the blood and 17-corticosteroids in the urine were also determined. The ionization level in the chamber was periodically measured and the microbic contamination of the air investigated, and various portions of the skin were washed for bacteriological investigations. The subjects' day was arranged so that 8-10 hours were spent in physiological studies and physical exercise with the remaining time divided into rest, nighttime sleep, reading literature, cleaning the compartment, preparing and eating food, etc. Radio communication between the experimenters and the subjects was kept to a minimum and performed during the period of physiological studies provided by the program.

After the end of the long-term experiment, the researchers determined the altitude resistance of the organism, the resistance to acceleration on a centrifuge and the resistance to great physical loads (on a "running track" stand), and also performed X-ray kymography of the organs of the chest cavity. Functional tests, consisting of a strictly measured complex of special physical exercises developed specifically for compartments of limited size and weightless conditions, were used for the purpose of a dynamic study of the functional state of the cardio-vascular system and respiration and compensation for the lack of motor activity during the course of the experiment (M. A. Cherepakhin, 1961).

Before and after the long-term experiment, clinical-physiological studies were conducted and also functional changes in the auditory, vestibular and motor analyzers were studied.

In comparing the data obtained in the ground (control) experiment with the data from the high altitude experiment it may be noted that in the latter case the total microbe count was significantly lower (Figure 15).

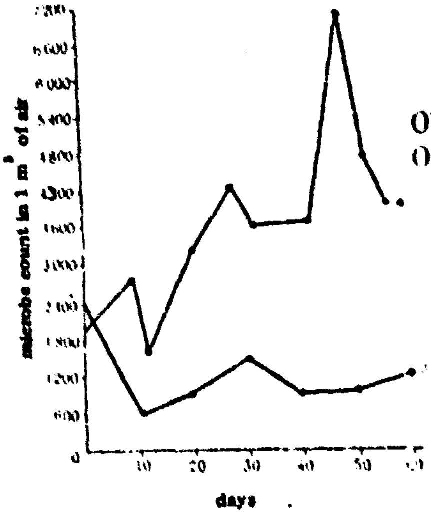

Figure 15. Microbe count in the ground (a) and high altitude (b) experiment.

The overall microtopography of the skin was recorded for comparison of the microflora of individual sections of the skin before and after the long-term experiments. Before the experiment the subject took a hygienic shower and bath, after which culture-print with agar and tampon washings were taken from the skin of the chest, back, both palms and soles of the feet for subsequent laboratory study of the microflora. The number of colonies grown on the prints was calculated for one square centimer of skin. The results obtained in the ground experiment are shown in Table 21. /111

The data in Table 21 indicate a significant quantitative growth of microbe flora from all untreated sections of skin while on the treated right foot no progressive increase in the number of microbe cells is noted.

The microbe flora on the prints represents basically coccus species: staphylococcus, sarcine, streptococcus, tetracoccus, and also bacilli. Around 5% of the staphyloccus possessed pathogenic properties (hemolytic activity).

Investigations of bacteriological contamination of the air of a chamber conducted by N. N. Sitnikova showed that during isolation the number of microbes in the air increased by two times. The bacteria count of the air of the chamber increased /112
mainly due to the rapid multiplication of microbes on the subjects' skin with their subsequent transition to an air environment. The significant increase in the number of microbe cells on the untreated portions of the skin took place, evidently, due to a lowering of the bactericidal properties of the skin.

TABLE 21

NUMBER OF LIVING MICROBE CELLS PER CM^2 SKIN

Subject	Portion Studied	Date of Culture (All 1962)						
		1/19	1/25	11/1	11/15	3/1	3/15	3/20
		Day of Experiment						
		1st	7th	14th	28th	42nd	56th	60th
N-	Left foot	10	63	82	176	179	171	180
	Right foot	11	19	53	20	16	11	23
	Chest	9	18	--	--	34	46	49
	Back	11	14	--	--	25	40	65
Ts-ko	Left foot	5	28	66	175	201	178	More than 200
	Right foot	6	20	9.5	26	22	25	27
	Chest	2	5	--	--	28	79	94
	Back	5	7	--	--	48	90	91

V. V. Borshchenko, I. G. Popov, and F. K. Savinich made an evaluation of the degree of contamination of the skin and clothing by means of comparing the results of analyses of water washings from the skin and part of the clothing for chlorides (Mohr's method) and acidity (Kubel's method) before and after the experiment. In addition to an investigation of whole parts of the clothing, pieces of tissue sewn onto the cloth were subjected to analysis for the purposes of studying the processes of the penetration of skin excretions through layers of clothing. It was established that around 95% of the chlorides and 91-92% of organic substances, that is, the bulk of skin and other excretions, are retained by the cloth.

As the experiment of Ya. Kuno (1961) indicated, the intensity of perspiration and the concentration of chlorides and organic substances in the perspiration fluid vary significantly in different people.

The specific living conditions of crew members during a flight--the small volume of the living quarters of the ship, the limitation of water consumption for toilet needs, the absence of earth gravitation and so forth--lead to the necessity of seeking special means of cleaning the skin with a minimum water consumption. Moreover, during an extended stay under the above-mentioned conditions a man's skin will undoubtedly require supplementary feeding, vitamins and additional means of protection from ultraviolet and other rays. All these components may easily be included in the so-called waterless skin cleaning facilities which provide for normal functioning of the skin under flight conditions. /113

V. V. Ogleznev and A. M. Finogenov together with their colleagues at the Institue of Medical Cosmetics proposed physiologically inert cleansing agents, which do not contain aromatic or volatile substances capable of creating significant vapor concentrations in the cabin atmosphere, for performing the daily cleaning of exposed portions of the body (face, neck, hands) and feet.

On long space flights it is important to have a rational feeding schedule for the astronauts, and therefore we also gave great attention to the organization of subjects nutrition in conducting extended experiments.

V. P. Bychkov designed a food ration (several menus), quantitatively and qualitatively full-valued with regard to the conditions of a long-term experiment in a closed chamber of limited volume. The ration contained: water 1664-1698 g, protein 123-128 g, fat 116-125 g, hydrocarbons 483-448 g with a calorie count of 3573-3545 Kcal. The ratio of proteins, fats and hydrocarbons in the experiments was optimal (1:1:4), so that the daily calorie intake consisted of approximately 14.4-15% protein, 30.4-33.3% fat and 51.7-55.2% hydrocarbons. According to the data of the Institute of Nutrition, Academy of Medical Sciences, USSR, these are the most efficient ratios. The food allowance contained fruits and multiple vitamin pills.

It is necessary to note that although in both long-term experiments the subjects had approximately the same food allowance and the studies were conducted in the same chamber, their actual food requirements differed. Thus, in the high- /114
altitude experiments, the subjects' appetite was good for almost the entire period of time spent at an altitude of 7,000 meters. Toward the end of the experiment subject Ch-v's weight increased by 9.3 kg, and subject A-v's weight--by 4.2 kg. An entirely different picture was observed in the 60-day ground experiment. Subject's M-ov and Ts-ao, beginning with the second half of the experiment, did not completely eat the food offered and their appetite sharply decreased. In the long-term ground experiment the subjects' weight showed practically no change.

For comparison, Table 22 presents data on the actual consumption by the subjects of the mean daily food allowance in the two different experiments.

TABLE 22

ACTUAL CONSUMPTION OF WATER AND FOOD IN GROUND AND HIGH-ALTITUDE EXPERIMENTS

Conditions of Experiment and Name of Subjects	Amount of Water, g	Content, g			
		Proteins	Fats	Hydro-carbons	Calorie Value Kcal
Altitude 7,000m A-ov and Ch-v	1887	131.6	115.4	494.0	3638.6
"Ground" N-ov and Pa-ko	1688.5	120.8	100.7	489.2	3438.0

In spite of the good organoleptic qualities of the food and the wide variety of the products included in the food ration A daily average of 165 grams of food and water, containing 20.5 grams protein, 18.5 grams fat and 36.5 grams hydrocarbon, was left uneaten by subjects M-ov and Ts-ko.

From Table 22 it is possible to conclude that the food ration, designed for conditions connected with a long-term stay in a closed compartment of small volume, proved to be excessive. The absence of equipment in the pressure chamber for heating the food worsens its flavor qualities, lowers uptake assimilability and leads to a rapid dislike of the food. From this same table it is obvious that the mean daily water consumption in the high-altitude experiment is approximately 200 grams greater than in the ground experiment. In our opinion this is explained by the characteristics of the water-salt exchange under decreased barometric pressure, in particular by the increased release of water by the organism.

2. THE METHOD OF FORMING AN ARTIFICIAL ATMOSPHERE IN AN AIRTIGHT CHAMBER /115

Conducting long-term biological investigations in airtight chambers of limited volume requires, first of all, special scientific analysis of the problems connected with the realization of an effective system for regulating the given parameters of the microclimate in the cabin, with maintaining optimal sanitary-hygienic conditions and with providing continuous medical control and the necessary safety measures.

A man under these conditions for an extended period of time is subject to the effect of a number of unique environmental factors, characterizing the habitability, which to a significant degree differ from an ordinary terrestrial environment. In the studies by A. V. Lebedinskiy, Yu. G. Nefedov, et al. (1964), N. A. Agadzhanyan, A. G. Kuznetsov, et al. (1964) and Schaefer (1964) it was emphasized that this unique environment is to a great degree formed by the living organism itself. The whole importance of a deep and comprehensive study of the properties of the gas medium in manned airtight cabins results from this specific characteristic.

It is necessary to show and differentiate what changes in the physiological reactions of the organism are caused by the influence of individual factors of the medium and what are the results of the long-term life activity of living organisms in airtight compartments.

In setting experiments in which the object of investigation is man it is necessary to be particularly careful and precise in controlling the conditions under which the experiment is conducted and the state of health of the subjects.

Long-term experiments were conducted in a specially equipped type SBK-48 pressure chamber. The total net volume of this chamber with the air lock is 9.8 m^3, and the total airtight volume equals approximately 15 m^3.

In preparing the pressure chamber for conducting long-term high altitude investigations it was necessary to introduce a number of changes and additions to the construction of the chamber and several of its constituent units. The purpose of these changes was to increase the hermeticity of the chamber, to provide additional engineering and fire safety measures, and to create satisfactory sanitary living conditions for the subjects.

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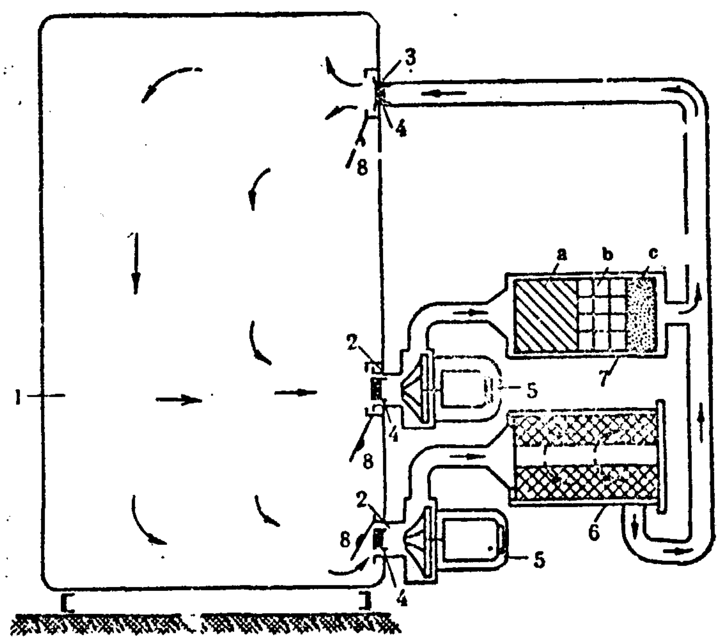

Figure 16. Schematic diagram of an air purification system. **1--altitude** chamber; 2--entry pipes; 3--exit pipe; 4--dust filter; 5--air injection fan units; 6--filter, filled with chemical absorbent; 7--filter, filled with silica gel (a), activated charcoal (b), hopcalite (c); 8-covers.

The first altitude chambers used were equipped with external life-support systems, enabling a given gas composition, temperature and humidity of the air in an airtight chamber to be maintained for several months. An external life support system was developed by B. A. Miloslavov, G. I. Badikov and A. V. Chashchin.

In order to provide for the possibility of an extended human stay, the altitude chamber was equipped with a folding table and bed, a soft armchair, additional shelves for storing food supplies, a wash basin, sanitary facilities, etc. The altitude chamber was thermally insulated. Along with a commerical aircraft intercom type communication device, the chamber was equipped with a duplex communications sytem designed for continuous operation for three months. /117

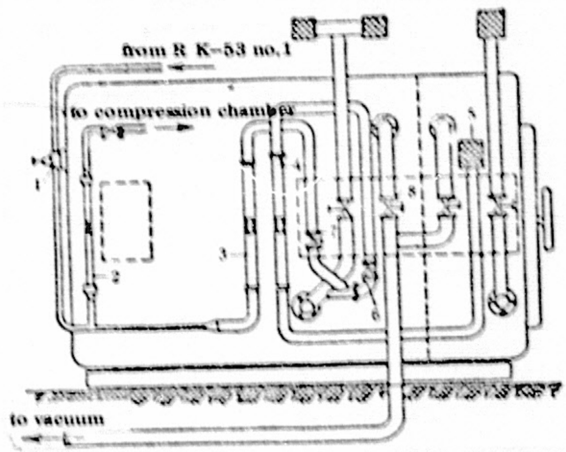

Figure 17. Assembly diagram of a rotameter setup for measured feeding of oxygen and air into an altitude chamber. 1--RK-53 No. 2 oxygen reduced; 2--RS-3 rotameter; 3--RS-5 rotameter; 4--RS-7 rotameter; 5--air filter; 6--7--sylphon valves; 8--vacuum valve.

Lime chemical absorbent, consisting of 97% calcium hydroxide and 3% sodium hydroxide, was used as the basic chemical absorbent.

The air purification system consists of two airtight cartridges with filters filled with chemical absorbent. The cartridges are placed outside the chamber (Fig. 16).

Type "DV-2" fans driven by commutatorless capacitor motors inject the chamber air through the filters. If the fans driving the air through the chemical should cease to operate, the concentration of the harmful impurities given off by a man begin to increase in a manned airtight cabin. According to the conditions of the experiment a brief increase in the partial pressure of carbon dioxide to 7.6 mm Hg was allowed.

According to the calculations made, the maximal permissible carbon dioxide concentration (7.6 mm hg) will be reached after approximately 2 hours.

Air was removed from the altitude chamber through two pipes screwed into the chamber, and the purified air was supplied through a common pipe located in the upper part of the chamber. This arrangement of pipes provided for uniform distribution of the purified air throughout the chamber. The mean motion speed of the air in the chamber was 0.2-0.3 m/sec.

The air pipes are provided with folding hermetically closing covers, used for cutting the system off from the altitude chamber while replacing filters and performing repair work.

The use of such a system together with a measured oxygen supply system makes it possible to ventilate the altitude chamber with an atmospheric oxygen mixture with a given oxygen concentration periodically during an extended experiment (with the aid of the RS-7 and RS-5 rotameters) (Fig. 17).

A cooling system with automatic temperature control, a schematic diagram of which is shown in Fig. 18, was used for maintaining a constant air temperature in the chamber. /118

In order to preserve a constant air temperature in the chamber it is necessary that the power of the cooling unit correspond to the thermal load, that is, to the heat flows in the chamber.

The amount of heat given off by one man into the environment fluctuates from 90 Kcal/hour at rest to 250 Kcal/hour during intense physical work. The limited mobility of subjects in a chamber of small volume and the absence of intense physical load make it possible to assume the heat-evolution of one man to be equal to approximately 100 Kcal/hour and for two subjects--correspondingly, 200 Kcal/hour.

The heat evolution of the electrical devices (electric lights, fan motors) is: 16 10-watt lights--137 Kcal/hour (q_{ill}) and fan motors--138 Kcal/hour (q_m). The heat evolution from the

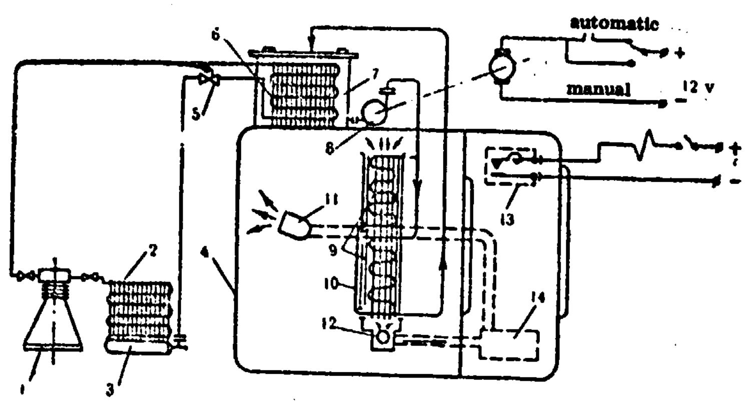

Figure 18. Schematic diagram of automatic temperature control system. 1--FAK-07 U compressor; 2--condensor; 3--receiver; 4--SBK-48 K low pressure chamber, 5--TM-2 F type thermoregulating valve; 6--evaporator F=4.8 m^2; 7--brine tank V=0.1 m^3; 8--Gear-driven centrifugal regulator pump; 9--cooling radiators, two; 10--radiator casings; 11--cold air reflector; 12--air intake connection; 13--thermostat; 14--fan unit.

condensation of vapor entering the chamber from human respiration--q_{cond}. Vapor condensation takes place on the cooling surfaces of the radiator:

$$q_{cond} = r(G_{H_2O}) \text{ man} \cdot \text{Kcal/hour},$$

where r is the latent evaporation heat: for water r = 539 Kcal/kg; G_{H_2O} = 120 g/hour is the weight amount of water vapor given off by two subjects;

$$q_{cond} \cdot r \cdot (G_{H_2O}) \text{ man} = 539 \cdot 0.12 = 64.8 \text{ Kcal/hour}$$ /119

During the reaction of the absorption of CO_2 by the lime chemical absorbent q_{react}, heat is also evolved:

$$Ca(OH)_2 + CO_2 \; CaCO_3 + H_2O + 19.9 \text{ cal.}$$

The molecular weight of carbon dioxide equals 44, consequently, 19.9 cal is evolved upon the absorption of 44 g of carbon dioxide. Two investigators exhaled 50 liters (an hour equals 87 g/hour CO_2). Therefore, the heat evolution during reaction is:

$$q_{react} = \frac{19.9 \cdot 87}{44} = 39.3 \text{ cal/hour.}$$

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Consequently, the total amount of heat entering the chamber is

$$Q_{(cham)} = \Sigma gn = qr + Q_{ill} + q_m + q_{cond} + q_{react} = 200 + 137 + 138 + 64.8 + 0.04 = 540 \text{ Kcal/day}.$$

The cooling unit can be selected according to the amount of heat load in the chamber $Q_{cham.}$ It is known that the cooling effect of a unit depends on the evaporation temperature of the coolant.

We shall determine the required air flow through the radiator (W_a), if the heat flow in the chamber = 540 Kcal/hour, the air temperature in the chamber is +21° and the barometric pressures are respectively 760 and 308 mm Hg.

The unit weight of air at 760 mm Hg is 1.29 kg/m^3. The output temperature from the radiator, according to the results of measurements made during the experiment, was 6°. This is the minimum possible temperature since the temperature of the brine and the cooling surfaces of the radiator must not be below 0° lest the surface of the radiator freeze because of moisture from the air. If there is a higher temperature at the radiator output then it is necessary to significantly increase the air injection.

Thus, at a pressure of 760 mm Hg W_a is:

$$\frac{540}{1.29 \cdot 0.24(21-6)} = 116 \text{ m}^3/\text{h},$$

and with a pressure of 308 mm Hg in the chamber the required air flow is increased and is:

$$W_a^1 = 116 \cdot \frac{760}{308} = 286 \text{ m}^3/\text{h}.$$

Elements of the cooling unit already described were used for drying the air in the chamber. A schematic diagram of this system is shown in Figure 19. This air drying system provided for maintaining a relative humidity in the chamber of between 45 and 60% during the long-term experiments.

The system described above provided for reliable and high quality purification of the air in the chamber, and also for keeping the temperature, humidity and oxygen percentage in the chamber within the given limits during the entire experiment.

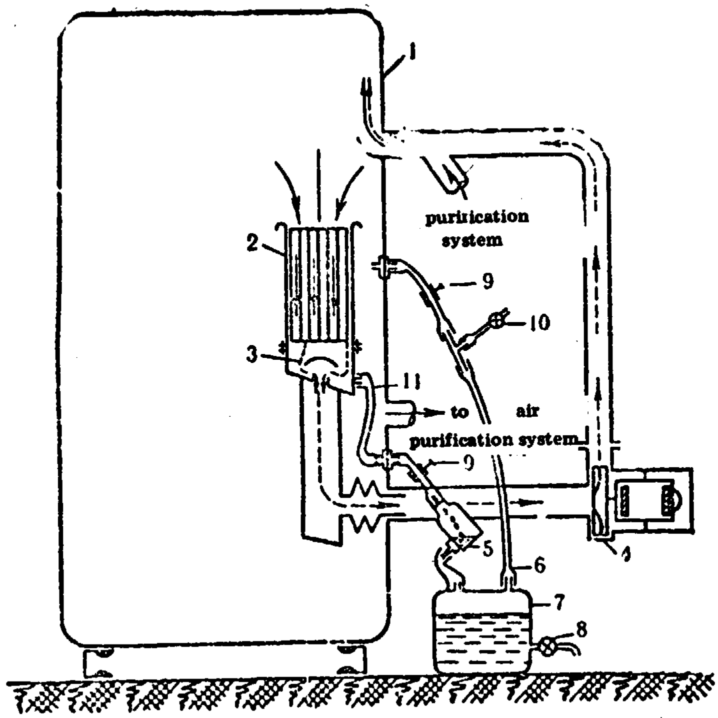

Figure 19. Schematic diagram of air drying system. 1--altitude chamber; 2--radiator-dryer; 3--baffle plate; 4--fan; 5--control tank; 6--vacuum pipe; 7--condensate tank; 8--valve; 9--pinchcock; 10--valve; 11--pipes.

From graphs of the variation of the microclimate parameters in the altitude chamber during the 62-day experiment, conducted at an altitude of 7,000 m (308 mm Hg), it is obvious that (Fig. 20) the carbon dioxide concentration in the air did not exceed 1.5 mm Hg (0.5%). Only before replacement of the chemical absorbent cartridges (approximately only every 2-1/2 days) did its concentration increase briefly to 2.2-2.8 mm Hg. The oxygen concentration in the air was maintained for the entire experiment within the range 56.4-58.5%, that is, it deviated from the given value by not more than 1%.

The temperature and humidity control systems were also distinguished by their high accuracy. /121

Thus, the relative humidity remained within the predetermined range during the entire experiment and varied between 52 and 65%. The temperature in the chamber varied within the limits from +21 to +23 degrees (the deviation from the predetermined temperature did not exceed ±1°).

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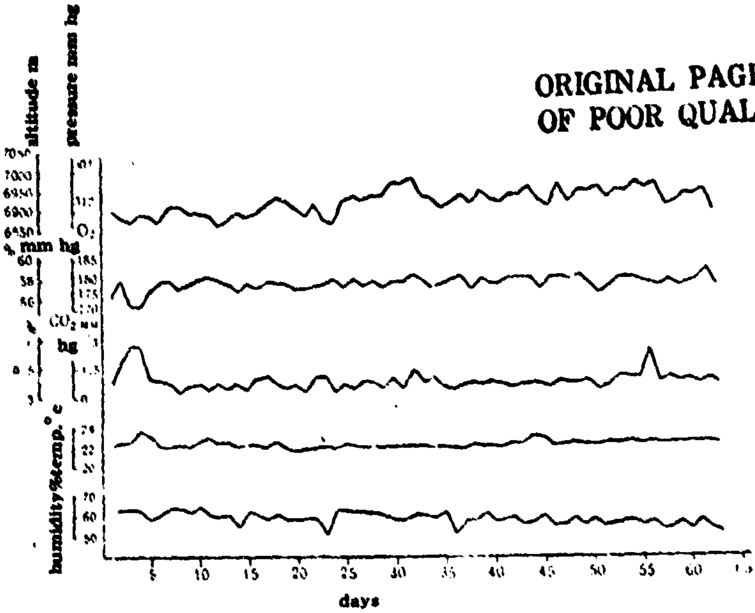

Figure 20 Nature of variation of microclimate parameters in altitude chamber.

Analysis of the accuracy of maintaining the parameters of the gas medium showed that even with the introduction of two additional experimenters into the chamber (for taking blood, air samples and washing the skin for bacterial investigations) the life-support systems did not vary greatly from the given parameters.

Periodically (at least once a week) conducted analyses of the gas medium for the content of harmful impurities in the air of the altitude chamber (for carbon monoxide, ammonia, aldehydes, hydrocarbons, and nitrogen oxides, mercaptanes and hydrogen sulfide) did not reveal the presence in the chamber air of ammonia and aldehydes, which were dissolved in the condensate removed from the chamber. The concentration of the remaining noxious impurities, as a rule, were significantly below the maximum permissible values.

These data show the high operating stability of the life support system. /122

Analysis of the chamber air for the oxygen and carbon dioxide content was performed continuously on automatic gas analyzers of the types OA-2209, UAV-1 and UKV-1. In addition, every two to three hours controlled analyses were made on an Orsat-Fischer type gas analyzer.

A special system (Fig. 21) was used for taking samples of the

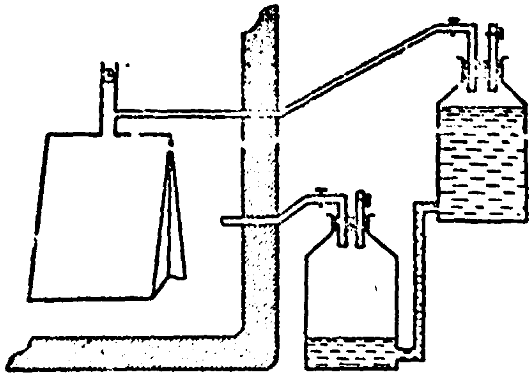

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Figure 21. System for taking samples of inhaled and exhaled air from an altitude chamber in high-altitude experiments.

inhaled and exhaled air in the "high-altitude" experiments.

Thus, the equipment used for regulating the microclimate in the airtight chambers made it possible to conduct investigations on the influence on man and animals of low barometric pressure with an increased oxygen content in experiments lasting up to 100 days.

The engineering level and accumulated experience already make it possible to use such equipment in experiments of greater duration.

For conducting investigations in an atmosphere with an increased oxygen content it is necesary to have further analysis of a number questions with regard to ensuring fire safety and, above all, to designing clothing and bedding which do not absorb oxygen. It is necessary to further perfect the equipment of chambers designed for conducting long-term experiments in artificial atmospheric conditions. The principal solution to /123 the problem is the creation of climatic altitude chambers for conducting complex long-term investigations with maximum approximation to space flight conditions: audial and visual isolation from the external environment, special illumination automatically and precisely controlled barometric pressure, gas and ion composition of the air, and so forth.

The rapid rate of development of rocket construction and the promise of the application of oxygenation for climatic purposes stimulate medical and biological investigations and bring forth new problems, in particular, with respect to the study of the operating characteristics and efficiency of lifesupport systems, and the creation of corresponding devices providing for the physiological control of the state of a man and his working capacity in unusual conditions.

3. RESULTS OF PHYSIOLOGICAL INVESTIGATIONS

As we have already indicated, the physiological reactions of the organism during an extended stay in a limited space have been studied by many Soviet and foreign authors. It was established that under hypodynamia serious functional shifts arise which are expressed, in particular, in a progressive loss of muscular strength, a significant shortening of the duration of sleep, changes on the part of the cardiovascular system, disturbance of psychomotor activity, worsening of working ability and so forth. In this regard it is of great theoretical and practical interest to study the functions of the higher sections of the brain. In addition, there is great significance in a dynamic investigation of the bioelectric activity of the brain as an indicator reflecting the general tone of the human cortex during an extended stay in artifical atmospheric conditions.

Modern achievements in the use of the conditioned reflex method in combination with the EEG open new possibilities for studying the mechanisms of the formation, reinforcement and extension of temporary connections, permitting direct observation of the nature of changes in cortical neurodynamics during the course of the investigation.

EEG AND CONDITIONED REFLEX ACTIVITY DATA /124

At present a small number of studies have been conducted under prolonged adynamia and isolation, in which, together with other physiological indicators, the electroencephalogram was also studied (F. D. Gorbov et al., 1968; D. I. Ivanov et al., 1963).

For recording the biopotentials of the brain in long-term experiments we used a bipolar (frontal-occipital) pickup. The first 10 days the electrodes for picking up the bio-currents of the brain were attached by means of special helmets which were kept on the head of the subjects night and day. On the following days the electrodes were attached by means of special collars placed on the head only during the time of recording. The EEG investigations during the long-term experiments were made jointly with Ye. A. Il'in, and the conditioned reflex activity investigations--jointly with G. P. Doronin.

The bioelectric activity of the brain was recorded daily at 0900, 1300, 1700 and 0300 hours. In addition, on particular days the EEGs were recorded every 4-5 hours for studying the nature of the daily periodicity of the bioelectric activity of the brain.

The EEG analysis showed that during a two-month stay in an airtight chamber the subjects maintained a prominent alpha rhythm of sinusoidal form. The frequency of this rhythm was 9-10 Hz. Alpha wave amplitude fluctuations were significant and underwent regular changes during the course of the experiment. The maximum alpha rhythm amplitude of 25-30 μv before the beginning of the experiment increased toward the end of the first month in the chamber on the average up to 77-80 μv, and toward the 60th day--to 87-93 μv.

Changes in the alpha index, that is the percentage ratio of alpha waves to other EEG waves, are of great interest. On the EEG of subject M this index on the first days of the experiment increased on the average from 40-49%, and after which it gradually decreased to 27%. The alpha index on the EEG of subject Ts. increased up to the 40th day in the chamber to 53%, and then gradually decreased and toward the end of the experiment it reached, on the average, 27%.

The β rhythm was well pronounced in both subjects during the entire experiment. Its frequency in N fluctuated between 16 and 24 Hz, and in Ts.--16-20 Hz.

Analysis of the dynamics of the appearance of slow waves revealed a significant difference between the subjects. Thus, before the experiment the EEG of subject M. displayed only solitary slow waves of a frequency of 4-6 Hz. Subsequently these waves began to appear at first in isolated groups, and then in a greater number, and toward the 50th day in the chamber slow waves became predominant. In subject Ts. waves of a frequency of 4-6 Hz. appeared in a small amount only before the beginning of the experiment and after the 50th day in the chamber. During the entire experiment both subjects had slow waves of a frequency from 0.5 to 2 Hz. In addition, the EEG of subject Ts. revealed hypersynchronic discharges. /125

Recently the attention of doctors and biologists has turned to the question of the rhythms of physiological processes. In analyzing the obtained data we also turned our attention to the daily periodicity of changes in the bioelectric activity of the cerebral cortex on different days of the experiment. It was established that during the first month subject N. had an alpha rhythm frequency of 10 Hz at 0900 hours and at 1700 hours and at 0300 hours the alpha rhythm decreased to 9 Hz. During the second month in the chamber the alpha rhythm frequency at 1700 hours remained the same, as also at 0900 hours, and at 0300 hours it again decreased to 9 Hz. Finally, on the last days of the experiment the alpha rhythm frequency remained constant during the day and was equal to 10 Hz.

These clear daily variations in alpha rhythm frequency were not observed on the EEG of subject Ts.

The fact of a significant decrease in the alpha index from the morning hours to the night hours is also interesting. The subjects retained this regularity only during the first month. Thus, if the mean value of the alpha index of N. at 0900 hours during the first month was 61%, then at 1300 hours it decreased to 47%, and from 1700 hours to 0300 hours it reached 30%, that is, it became half that of the morning hours.

The alpha index of subject Ts. at 0900 hours during the first month was, on the average, 52%. At 1300 hours it decreased to 34%, and at 1700 hours increased to 38%, still remaining 14% lower than the alpha index during the morning.

In the second month of the experiment the alpha index of subject N., on the other hand, increased during the evening and nighttime. At 0900 hours it was, on the average, 21%, at 1300 hours--30%, at 1700 hours--32%, and at 0300 hours--31%, that is, higher by 10% than in the morning. /120

During the second month in the chamber the alpha index of subject Ts. did not change significantly at any time of day. Its mean value at 0900 and 1300 hours was 36%, and at 1700 hours decreased to 35%.

A regular variation also was revealed in the daily fluctuations of alpha rhythm amplitude. Thus, in the case of N. at 0900 hours the alpha rhythm amplitude on the average equaled 74/18 μv, at 1300 hours--77/17μv, and 1700 hours --89/23μv and, finally, at 0300 hours--87/23, that is, during the night it always increased. In the case of Ts. the alpha rhythm amplitude, on the other hand, always decreased during the evening hours.

We shall see that typological characteristics of the nervous system are also manifested in the nature of the daily periodicity of the bioelectric activity of the brain. In our subjects the alpha rhythm amplitude during the time spent in the chamber not only did not decrease, but, on the other hand, increased in comparison with the original level. In the opinion of M. N. Livanov (1960), such an increase is either a reflection of synchronization of the electrical activity of nerve cells located at separated parts of the cortex (forehead-occiput), or is connected with the influence of the reticular substance on the cortex. The degree of synchronization of the electric potentials of cortical cells reflect the level of activation of the cortex by the reticular substance. While playing an important role in the process of the formation of a conditioned reflex, the upper sections of the brain cannot fulfill their role without the agency of subcortical formations which perform transmission and distribution of signals, and also regulation of basic nerve processes. With a low level of cortical activation by the subcortical nonspecific ascending system in a state of rest the cortical neurons are easily drawn into coordinated synchronized activity, which leads to an increase in the amplitude of EEG fluctuations with the cortical neurons in an inactive condition. M. N. Livanov considers synchronization to be a condition of the cortex in which irradiation both of the exciting and the inhibiting process is facilitated.

In order to study the functional state of the cortex we also used an electroenphaloscope instrument constructed by M. N. Livanov and V. M. Anan'yev for multipoint recording (more than 50 pickups) of bioelectric potentials.[1] /127

The use of this instrument and the application of computer technology for analyzing the data made it possible to study the influence on the functional state of the brain of a 62-day stay at an altitude of 7,000 meters in artificial atmospheric conditions.

The biopotentials repeatedly before the experiment and again after it ended, were simultaneously recorded from 50 sections of the cerebral cortex. To this end 50 needle electrodes were arranged uniformly

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[1]We performed electroencephalography of the subjects before and after the 62-day high altitude experiment in the laboratory of M. N. Livanov with the participation of N. A. Gavrilova. The data were processed on a computer.

on the head with a neutral electrode on the chin. After suitable amplification the bioelectric potentials were displayed on a kinescope screen.

The stronger the negativity under an electrode was, the brighter the illumination of the corresponding point on the screen was. The brightness, and consequently, the degree of negativity or positivity were judged according to changes in the amplitude of 50 vertical columns, each of which corresponded to a specific luminous point on the screen. The mosaic of bioelectric activity appearing on the screen was recorded on motion picture film.

As the investigations of M. N. Livanov (1960) indicated, in the case of conditioned reflex activity there appears synchronization in the operation of individual sections of the cerebral cortex. This signifies that a functional interconnection or correlation is established between them. Hence the task was posed of explaining what correlations occur in the cerebral cortex in a state of rest under the influence of sound and light stimuli, and also during a change in the functional condition of the organism in the course of a 62-day stay in artificial atmospheric conditions at an altitude of 7,000 meters.

Four groups with varying degrees of synchronization (inter- /128
correlations in the operation of sections of the brain, where synchronization is understood to mean unidirectionality of changes of biopotentials in time, were isolated on the basis of a theoretical Gaussian distribution. The first is the group of negative interaction, when the sections of the brain entered into inter-correlation lasting from 0 to 22% of the time in question (1-1/2 seconds was taken as the unit of time in question). The second is the group of independently operating sections of the brain with inter-correlation limits from 22 to 44% of the time in question. The third is the group of low synchronization with inter-correlations from 45 to 75% of the time in question. And, finally, the fourth is the group of high synchronization, where agreement in operation of different sections of the cortex exceeded 75% of the time in question.

Studying the nature of the bioelectric activity of the subjects' brains before the long-term experiment made it possible to establish the presence of a living diffuse-focal mosaic. Against a background of approximately identical amplitude oscillations (80-95 µv) there periodically appeared strictly low potentials, the amplitude of which exceeded the remaining oscillations by 2 to 4 times. These centers of increased electrical activity were distinguished by great variability both with respect to localization and to duration.

A comparison of the data on the functional interrelationships of different sections of the cortex with the topographical characteristics of the conducting paths of the mosaic, made jointly with our colleague from the Brain Institute, S. B. Dzugayeva, permitted us to hypothesize that the high level of synchronized activity of the cerebral cortex takes place because of short association fibers and callous body fibers. Evidently, in addition to these formations of the brain, long association fibers also participate in establishing low-level synchronous activity.

Supplying sound and light stimuli led to a change in the inter-correlations not only in the auditory and visual apparatus, but also in the cerebral cortex.

After the subjects left the altitude chamber, where they spent 52 days in artificial atmospheric conditions at an altitude of 7,000 meters, new observations were made. Visual analysis of the electroencephalograph data obtained indicate that during an extended stay in a closed chamber of small volume there occurs a weakening of the excitation process and a shift in the interrelation of basic nervous processes in the direction of inhibitions. This is indicated by the decreased mobility of the bioelectric /129 mosaic, disappearance of centers of increased activity and appearance of a special form of bioelectric activity--"overflows."

The latter are characterized by the fact that the negativity or positivity arising at a given moment in a more or less extensive zone is accompanied by a process of the reverse sign in adjacent zones. In the following moment the negativity and positivity seemingly change places. "Overflows" are the result of a spatial change of amplitudes and phases of the predominant oscillations. The reticular formation probably also participates in their appearance. The sound and light stimuli used after the end of the experiment produced an extremely weak reaction in the cerebral cortex of the subject and contributed to an intensification of "overflows."

Thus, the results of EEG analysis indicate that conditions of prolonged limitation of mobility and a certain decrease in sensory stimuli lead to a lowering of cortical tone, and that all the above-mentioned changes, including disturbance of the daily periodicity of bioelectric activity, basically belong to the second month spent in the chamber.

We propose that the described method of recording biopotentials and analyzing them with the aid of a computer may be successfully used for analyzing actual problems of aviation and space medicine, since it opens great possibilities for studying the activity of such a complex system of interconnected nervous elements as the brain. Studying the bioelectric activity of the cerebral cortex of a man in an airtight chamber makes it possible at each moment to determine the function of the higher sections of the central nervous system and thus to introduce qualified medical control over its condition.

In addition to studying the bioelectric activity of the brain the conditioned reflex activity was investigated in order to make a more in-depth study of the higher nervous activity and the level of working ability.

In developing a method for investigating higher nervous activity we proceeded from the fact that, for a man undergoing a prolonged stay in an airtight chamber of limited volume under conditions of an artificial atmosphere, hypokinesia and isolation, the working ability is determined first of all, by the ability to rapidly and errorlessly differentiate and solve mental problems of different complexity with the retention of a high level of coordination of motion while performing goal-directed activities. /130

For studying conditioned reflex activity, we used a method, which in essence required that the subject respond to different conditioned signals, according to a preliminary verbal instruction, with a motor reaction, connected in the one case with solving specific arithmetical problems and in the other with tracing different geometrical figures. The stimulus stereotype was composed of direct light signals (red, white, yellow, green)and verbal signals: "white light," "red light," "blue light."

In each investigation a three digit number was given which was the starting point for the subsequent solution of the problems. The content of a problem was determined by the conditioned signal.

With the white light switched on the subject had to write under the given three-digit number the first two digits and perform subtraction, for example 732 - 73. Addition of a three digit number and its two final digits, for example 732 + 32, was performed to the verbal stimulus "white light." To yellow light the subject had to multiply the same three-digit number by a two-digit number consisting of its extreme digits, that is, 732 x 72. With the red light switched on the subject traced with an electrocontact pencil a figure, consisting of two circles connected by a broken line, to the green light the subject drew the outlines of a small square in blue ink, and to the verbal signal "blue light"--the outline of a large green square.

An evaluation of the conditioned reflex reactions connected with tracing figures makes it possible at the same time to consider the state of differentiation inhibition, the speed of response reactions (according to the time taken in drawing the outlines of a figure) and the accuracy of reproducing a line, that is, fine movement coordination.

In addition, at the second and sixth point in the stereotype the inhibiting verbal stimulus "red light" was given, which was not to be accompanied by any motor reactions of the subject.

The motor reactions in solving arithmetical problems and tracing figures were recorded on an ink oscillographic unit with the aid of a special electrocontact pencil.

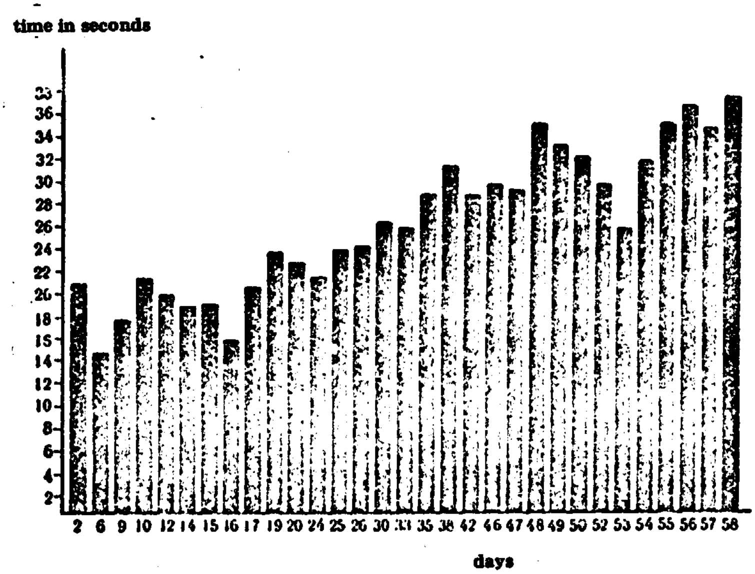

Figure 22. Time of conditioned motor reaction of subject M-Ov to red light.

In two long-term (60 day) experiments with four subjects /131
226 studies were made according to a previously developed and reinforced stereotype. In addition, during the course of the experiment a changed stimulus stereotype was presented 36 times.

The changes in conditioned reflex activity observed in the case of an extended stay under relative adynamia and isolation were characterized, first of all, by a wavelike nature and a certain phasing in reactions (in different periods of the investigation). This is manifested particularly clearly in the solution of arithmetical problems.

During the course of the investigation the most pronounced and clear changes in the nature of conditiondd reflex activity were observed in the subjects in the case of the conditioned motor reaction to red light, connected with tracing a geometrical figure. From figures 22 and 23 it is obvious that the time taken for tracing a geometrical figure increased from day to day. In this case the coordination accuracy did not change significantly. If on the first days the time taken for tracing a figure was 15-20 seconds, after 30 days it was up to 25-28 seconds for the same figure, and toward the end of the investigation (50-60 days) it reached 35-37 seconds.

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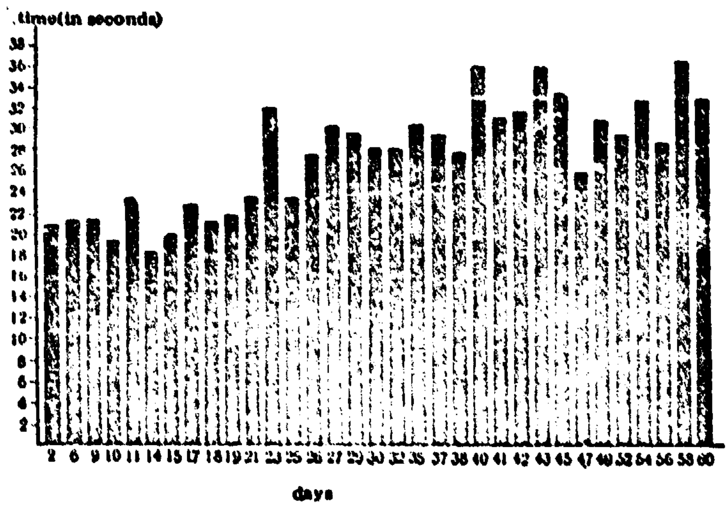


Fig. 23. Time of conditioned motor reaction of subject Ts-ko to red light.

Under low barometric pressure the time required for tracing also increased toward the end of the first month of the experiment, however subsequently a decrease in this index was observed.

It is interesting that in the ground experiment the coordination quality did not improve with an increase in the time required for tracing figures, but at an altitude with a rarefaction equal to 308 mm Hg, a decrease in the time required for reproducing the contours of figures was accompanied by a certain worsening of coordination at the end of the experiment. This may possibly explain the decrease in the time required for tracing geometrical figures upon receiving different stereotype stimuli, which was observed in the second month of the high altitude experiment. It is interesting that in this period significantly more errors in calculation are admitted. It is characteristic that most errors (from 60-100%) were observed in performing the most complex task which was the multiplication of two numbers (response reaction to yellow light).

One of the indicators of conditioned reflex activity is the total time spent by a subject in performing all the response reactions determined by the stimulus stereotype. The stability of the total time spent in performing a task characterizes the end of the process of forming a dynamic stereotype. Analysis of this indicator made it possible to reveal quite clearly in the high altitude experiment the individual differences in the time taken in performing a task for all stimuli of the stereotype (Table 23). /133

TABLE 23

MEAN TIME OF PERFORMING MOTOR REACTIONS TO STIMULUS STEREOTYPE AND DEVIATIONS FROM THE MEAN (SECONDS)

Subject	Mean time of performing task	Deviation from the mean on different days: Minimum	Maximum	Difference between minimum and maximum value
A-ov	72.4	-24.0	+24.9	48.9
Ch-ov	55.4	-11.3	+ 8.7	20.0

In the ground experiment with N-ov and Ps-ko these differences were less pronounced and basically related to the speed of solving arithmetical problems.

Both in the experiment at normal barometric pressure, and in the case of the 62-day experiment in artificial atmospheric conditions at an altitude of 7,000 meters (308 mm hg), the direction of changes in the time taken for tracing geometrical figures is identical, especially during the first month; that is, the time of performing fine, coordinated response reactions increases.

Some decrease in the time of response motor reactions toward the end of the experiment (especially in the case of the high-altitude experiment), in our opinion, occurs because the very fact of the end of a long-term experiment is a powerful second-signal stimulus, mobilizing reserve compensatory-adaptive mechanisms for maintaining the tone of the higher sections of the cerebral cortex. In conducting long-term investigations it is noted that even the moment of transition to the second half of the experiment, irrespective of its total duration, is accompanied by significant changes in the neuro-psychic cone and behavior of the subject. This was manifested particularly graphically in the high-altitude experiment. /134

In addition to the change in the motor function indicators, the accuracy of solving arithmetical problems was also significantly disturbed at this period. The majority of calculation errors were received in the second half of the ground experiment (in eight of nine for subject N-ov and in 18 of 27 for subject Ts-Ko In the high-altitude experiment errors were observed primarily at the end of the first month.

The periods of the greatest inhibition of cortical processes were observed at the end of the first month in the high-altitude experiment and on the 40-50th day in the ground experiment. In addition to an increase in the time taken for tracing figures this period manifested an increase in the number of calculation errors and significant changes in the behavior of the subjects. Characteristic features of this period were: emotional instability, irritability, decreased motor activity, loss of interest in the studies being conducted (sometimes to complete indifference), decreased mental efficiency and memory of material read, weakening of self-criticism, and sometimes even the appearance of a lack of discipline. In the daytime the subjects were sleepy, and at night--suffered from insomnia. During the first month of the experiment both subjects exhibited a quite restful and deep sleep. On an actogram during the course of the night (primarily during the period of falling to sleep) only solitary motor reactions were noted. During the high altitude experiment the subjects complained of dryness of the mucous membranes of the lips and eyes, which stopped after two weeks. From the beginning of the third week there were increasing complaints of a "stuffy feeling which appeared periodically" in the altitude chamber, especially at the time of physical exercises.

Toward the end of the first month changes in behavior become more pronounced: motor activity significantly decreases, sluggishness and slow reaction lasts a long time in the morning; sometimes the

subjects doze while recording physiological functions, and make errors in switching the pickups. As a rule, they take a long time in falling asleep and often wake up during the night. During the day their mood changes often--periods of sluggishness and indifference alternate with euphoria. Interest in reading fiction and specialized literature significantly decreases and the subjects begin to get bored with the monotony of the experimental setup. The subjects /135
do not always carry out precisely the schedule of the day and do not show interest in prompt and accurate fulfillment of the research program. The following remarks appear in the diaries: "The day has no meaning for us--whether it's Sunday or a weekday. It's all the same. The research program has become boring" (Subject Ch-ov) "We don't do the physical exercises because we like them, but, you understand, because they are necessary" (Subject Ts-ko). Appetite noticeably decreased toward the beginning of the second month and the subjects systematically returned certain foods (fatty canned meats, cheese, and others).

In the opinion of the subjects, during an extended stay in a altitude chamber the weather has a significant influence on mood: during sunny weather and on holidays the mood gets worse, during bad weather--it improves. Such a seemingly paradoxical effect is connected with the fact that the subjects connect good weather and holidays with thoughts of amusements, positive emotions, of which they are deprived, spending a long time in a closed chamber of limited volume.

Increasingly the subjects write about the monotony of the experimental setup. For example, subject M-ov remarks: "Everything proceeds monotonously. Every day is like every other day even more than two drops of water; time passes slowly. I have little interest in anything and no desires. Boredom has begun." The monotony of the experimental conditions depresses the subjects and an attempt to introduce variety and to restructure the established stereotype causes dissatisfaction. It is characteristic that the subjects even become bored with music. Repetition of the same musical recordings during the day causes irritation. The time sense is lost and sometimes the subjects lose track not only of the date and the month but also the day of the week.

Toward the end of the second month there appear in the journals complaints of fatigue, rapid exhaustion after performing physical exercise, and problems in coping with mental strain (even in reading fiction).

At the end of the experiment, even though there were cases of the dissatisfaction of the subjects with one another, this was not significantly reflected in their friendly relationships. Diary entries are indicative in this regard: "The time passes twice /136
as fast if you can feel your comrade's elbow." (Subject M-ov),

"I always cheered up Slava when he got upset or depressed; we became very friendly during the experiment." (Subject Ch-ov).

On the 50th day of the high altitude experiment A. complained of an unpleasant sensation in the muscles and joints: "Gnawing pains in the joints, like rheumatism, appeared, which intensified toward evening... after physical exercise these pains disappear. To a somewhat lesser degree Subject Ch. experienced similar phenomena.

It also should be noted that the subjects frequently noted the negative influence of the constant temperature in the chamber on general well-being. From the 40-50th day they often began to ask that the temperature be decreased to 17-18°, at which point their mood and sleep improved.

For several days before the end of the experiment the subjects became more mobile and happy, they showed a tendency to make jokes, showed interest in the research and a desire to communicate with the crew on watch.

The theme of the end of the experiment predominates in the diaries and the subjects summarize their impressions.

Thus, the data from observing the subjects also confirm the conclusions of phasing and cyclicity not only in the physiological reactions of the organism, but also in behavior.

The results of investigating the higher nervous activity in the two long-term (multiday) experiments lead to the conclusion that an extended (two-month) stay both at ground level, and at low to 308 mm Hg pressure under conditions of relative isolation and hypodynamia lead to a lowering of the excitability of the central nervous system. The greatest changes in cortical functions are noted in the second half of the experiment and are characterized by a wavelike nature and cyclicity. Observations of the subjects behavior, and also the results of an investigation of conditioned reflex activity and the bioelectric activity of the brain testify to the individual typological characteristics of higher nervous activity and the ability to withstand prolonged isolation in airtight chambers of small volume.

INVESTIGATION OF THE FUNCTIONAL STATE OF THE ACOUSTIC, VISUAL AND VESTIBULUS ANALYZERS /137

As a result of steadying auditory adaptation it was shown that during an extended stay in a new acoustic environment there occurs a certain lowering of the threshold of audibility in proportion to the duration of the stay. This physiological phenomenon, in the opinion of G. V. Gershuni (1949), reflects the general adaptation of the organism to the new conditions.

The total noise level in our experiments was 60-65 decibels. The spectral composition of the noise, recorded on ferromagnetic film, was subsequently analyzed on a spectrograph. The auditory sensitivity in the experiments was studied by Yu. V. Krylov.

The studies showed that basically high-frequency noise, the maximum amplitude of which occurs in the range from 800 to 2500 cycles per second, is generated in the operation of the life-support system. No significant differences are observed in the amplitude and frequency characteristic of the noise in the control and high altitude experiments, which makes it possible to relate the changes observed in the functional systemsof the organism, in particular, the acoustic analyzer, to the influence of other factors (low barometric pressure, different gas ratio in the surrounding autosphere, hypodynamia of relative isolation, etc.).

As a result of an investigation conducted in the 60-day ground experiment it is established that the hearing threshold increases by different frequencies in the different subjects. The highest increase in the threshold takes place at frequencies of 500 and 3000 cycles per second.

Against a background of a spread in the hearing thresholds, during the second half of the experiment in both subjects there was noted a relative lowering of the hearing thresholds by 5-15 db in relation to their highest values.

The dynamics of auditory excitability during the course of the entire experiment are characterized by a definite wavelike nature.

In the high altitude experiment the dynamics of auditory excitability do not significantly differ from the data obtained inthe ground experiment: There is noted a wavelike nature of changes in auditory excitability, and a tendency toward a lowering of the hearing threshold in subject Ch. by 7.5-10 db at all frequencies investigated and in subject A. by 5-7.5 db.

The sharp transition from ordinary life to conditions of a prolonged stay in a closed airtight chamber of small volume was accompanied by a restructuring of many previously former ingrained habits. In studying the processes of auditory adaptation under conditions of the short-term effect of noise on man, G. V. Gershuni (1949) came to the conclusion that under the influence of this factor complex restructuring takes place in the organ of hearing, encompassing all units of the analyzer. Evidently, by increasing the time of noise exposure in the auditory apparatus, complex adaptation processes develop, which during the first days of the continuous action of noise are manifested in a raising of the threshold of /138 hearing and, subsequently, in a lowering of the threshold of hearing. This phenomenon may be taken as the outcome of the processes of the organism's adaptation to a new, unusual environment.

The results of investigations of the visual analyzer, conducted by Yu. V. Kamen'shikov, are given in Tables 24 and 25.

TABLE 24

STATE OF VISUAL FUNCTIONS IN SUBJECTS BEFORE AND AFTER THE 60-DAY GROUND EXPERIMENT

	Subject			
	Ts-ko		N-ov	
	Before Experiment	After Experiment	Before Experiment	After Experiment
Acuteness of vision	1.8	1.8	2.0	2.0
Critical frequency of coalescence of flickering	33.6	33.3	35.0	34.0
Binocular vision		Stable		
Nearest point of accommodation, cm	13.0	9.0	12.0	9.5
Nearest point of convergence, cm	14.5	12.0	7.5	7.0
Fusion reserves	8.0	7.7	8.3	8.3
Night vision, sec	25	23	20	21
Optic base		Norm		

From Table 24 it is obvious that the conditions of the experiment did not have any influence on the majority of investigations of visual functions. Only the nearest point of accomodation in both subjects at the end of the experiment came closer by 3-4 cm, which was 70-79% of the original value. The nearest point of convergence also came nearer by 2.5 cm in the case of subject Ts-ko and by 0.5 cm--in the case of subject M-ov (83 and 97% of the original value). It is very probable that this was the result of the prolonged stay in a compartment of limited volume, where the subjects could not completely weaken their accommodation with emmetropic refraction. /139

TABLE 25

STATE OF VISUAL FUNCTIONS IN SUBJECTS BEFORE AND AFTER THE 62-DAY HIGH ALTITUDE EXPERIMENT

	Subjects			
	Ch-ov		A-ov	
	Before Experiment	After Experiment	Before Experiment	After Experiment
Visual acuity	1.28	1.05	1.28	1.13
Critical frequency of coalescence of flickering	36.8	32.8	36.6	34.0
Binocular vision	Stable			
Nearest point of accommodation, cm	10.0	10.5	8.5	10.0
Nearest point of convergence, cm	7.5	9.0	7.5	8.5
Speed of visual perception	0.13	0.17	0.09	0.11
Color thresholds[1]				
1	3.0	4.7	3.0	5.0
11	11.7	12.3	8.0	12.7
111	13.7	16.6	10.0	18.3
Optic base	Norm			

[1]Light threshold of the experiment on the AN-56 anamoloscope; I, II, III--color receivers of the differential system of the eye.

Ten days after the end of the experiment the indicated functional changes completely disappeared.

As is seen from Table 25, after the "high-altitude" experiment there was an insignificant lowering of all visual functions investigated which did not exceed the norms established for a flight-surgeon's examination.

The binocular vision was stable. Inspection and photography of the optic base did not reveal significant changes. In investigating the optic base after rotation on a centrifuge both before /140 and after the multiday experiment, there was observed a small expansion of the veins of the reticular membrane; the size of the artery did not change.

Analysis of the results obtained showed that an extended stay in artificial atmospheric conditions with a normal partial pressure of oxygen in the surrounding air does not have an unfavorable influence on the effectiveness of the visual analyzer.

Similar results are also obtained in our experiments with respect to the vestibular analyzer (V. I. Kopanev). It was shown that, although as a whole resistance to vestibular stimulations did not significantly decrease, nonetheless, vegetative reactions to them proved to be significant. The pronounced vestibular-sensoral and vestibular-somatic reactions, observed during a prolonged stay in an airtight chamber, testified to an increase in the excitability of the vestibular analyzer.

In addition to data from illusiometry and the duration of postrotatory nystagmus, the most sensitive indicators characterizing the functional state of the vestibular analyzer during stimulation are vegetative shifts.

Experimental investigations conducted earlier showed that a proper program of motor activity promotes stabilization of the physiological reactions of the organism (G. V. Altukhov, N. A. Agadzhinyan, 1961, et al.).

The regular use of a special set of controlled physical exercises can to a certain degree compensate for the unfavorable effects of prolonged hypodynamia and isolation. A system of goal-directed muscular efforts, fulfilling the natural requirement for motor activity will maintain the general tone of the cortex and have a favorable influence on the condition of the different functional systems of the organism. In turn, stabilization of the physiological indicators will promote the maintenance of a sufficiently high physical and mental efficiency. The personal interest of the subjects, a sense of patriotic duty, and high moral responsibility for the quality of work performed, may also have great significance. The last factor is particularly important in the case of extended space flights.

RESULTS OF AN INVESTIGATION OF THE FUNCTION OF THE CARDIOVASCULAR SYSTEM AND EXTERNAL RESPIRATION [1] /141

As is well known, the working capacity of the human organism is most often limited by the functional capacities of circulation

[1] The research was conducted together with our colleagues Yu. B. Bizin, M. M. Osipova and I. R. Kalinochenko.

and respiration. The circulation and respiration functions are important indicators in studying the influence on the organism of an extended stay in sealed chamber of small volume under conditions of a changed gas medium and low barometric pressure. The purpose of our investigations was to make a comparative study of the influence on functional conditions of the cardiovascular system and respiration of an extended stay in an airtight chamber under ground and low barometric pressure conditions (308 mm Hg).

These investigations showed that a multiday stay by humans under normal barometric pressure conditions does not cause significant disturbances in the activity of the cardiovascular system. Only some functional changes were observed on the part of the pulse, blood pressure, and respiration (Tables 26 and 27).

TABLE 26

CHANGE IN PULSE AND RESPIRATION OF SUBJECTS N-OV AND TS-KO IN THE 60-DAY CONTROLLED EXPERIMENT (AVERAGE DATA FOR EACH TEN DAYS)

Day of Experiment	Pulse (beats per minute) of subjects		Respiration (per minute) of Subjects	
	N-ov	Ts-ko	N-ov	Ts-ko
10th	49	66	15	10
20th	49	61	15	10
30th	56	69	12	9
40th	55	65	10	8
50th	55	73	10	10
60th	59	74	9	8

In the case of both subjects there occurred a quickening of the pulse toward the end of the experiment, a decrease in the maximum and minimum pressure and a decrease in the frequency of respiration. These changes were of a cyclic nature. Usually this wavelike nature was repeated every 10 to 15 days and was more pronounced in the first 30 days of the experiment.

Prolonged absence or insufficiency of movement not only lowers the physical condition of a man, but also may entail a complicated symptom complex of disorders, called "hypokinetic sickness" (Kraus, Raab, 1961).

TABLE 27

/142

CHANGE OF MAXIMUM, MINIMUM AND PULSE PRESSURE OF SUBJECTS AVERAGE VALUE FOR EVERY 10 DAYS OF THE EXPERIMENT (mm. Hg)

Day of Experiment	"Earth"						Altitude 7,000 m					
	N-ov			Ts-ko			A-ov			Ch-ov		
	maximal	minimal	pulse	maximal	minimal	pulse	maximal	minimal	pulse	maximal	minimal	pulse
Before Experiment	120	60	60	121	61	61	120	60	60	130	70	60
10th	113	53	60	115	60	55	118	61	57	116	60	56
20th	110	50	60	109	53	56	109	56	53	117	61	66
30th	109	47	62	110	50	60	105	52	46	118	58	60
40th	104	50	54	110	51	59	106	60	46	120	67	58
50th	105	48	57	109	51	58	104	55	49	119	66	53
60th	107	48	59	105	51	54	104	55	46	117	65	52

A characteristic example of such disorders is given in the study by Taylor et al.(1949) who, in studying healthy, well-conditioned young people after a three-week stay in bed, discovered an increase in the oxygen dept, a lowering of "breathing efficiency" and "heart endurance" (extreme tachycardia) in response to a standard physical load.

The increased pulse frequency under conditions of relative adynamia may also to some degree be explained by disturbance of the cholnergic action of the vagus nerve, which is observed in the absence of necessary physical activity. The predominance in this case of the adrenergic action of the sympathetic nerve leads to a volume change in the vessels and tissues.

Kh. S. Koshtoyants (1954) also referred to the existence of a connection between the action of chemical factors of nervous excitation and the metabolism of an innervated organ.

Evidently,this also explains the lowering of blood pressure observed in our experiments. Table 27 presents data on the change in blood pressure in the control and high-altitude experiments. /143

As a consequence of the disturbance of the ratio of minimum and maximum pressure,the pulse pressure also changed, becoming more significant in the high-altitude experiment. Thus, the difference between the initial and final values of the pulse pressure in subject A-ov was 14 mm hg.

In the investigations of Welch et al (1961) with subjects staying for 30 days at an altitude of 5490 m, a lowering of the diastolic pressure with simultaneous disturbance of the excitability of the cardiac muscle was also observed. The majority of authors explain regular changes in blood pressure, both in the direction of a decrease and of an increase, by a predominant raising or lowering of vascular tone, in the first place, the tone of the precapillaries. The size of the pulse and minute volume of the heart plays a significant role in the change in blood pressure. In our opinion, changes in the interrelationship between the activity of the heart and the state of vascular tone, arising as a result of a deficiency in motor activity in a small-volume chamber, lie at the base of the changes in blood pressure observed in long-term experiments.

TABLE 28

CHANGE IN PULSE FREQUENCY IN SUBJECTS N-OV AND TS-KO AFTER PHYSICAL LOAD (IN PERCENT) IN RELATION TO CHANGES IN PULSE DURING THE GIVEN TEST BEFORE THE EXPERIMENT, TAKEN AS 100%

Day of Experiment	Time of Measurement After Physical Load (in minutes)					
	1		5		10	
	TS-ko	N-ov	Ts-ko	N-ov	Ts-ko	N-ov
8-11th	127	155	94	133	94	101
20-21st	143	156	100	140	--	120
30-33rd	141	130	132	133	122	133
41-47th	136	156	120	137	109	130
57-60th	134	136	122	142	121	131

We did not discover significant changes on the EKG either /144
in the control experiment nor under conditions of an altitude of 7,000 meters.

Basically, the amplitude of spikes and the duration of intervals on EKGs taken in a state of rest do not go beyond the limits of physiologically permissible values. It is necessary to note only a certain decrease in the maximum value of the P spike under the influence of altitude. If in the ground experiment the maximum aplitude of the P-spike reached 3 mm, then in the high altitude experiment it did not exceed 2 mm.

Wavelike changes in the EGK spikes (P, R, T) were revealed during the course of the long-term experiment with stability of their time components (PQ, QRS).

For the purpose of revealing elements of deconditioning, the functional capability of the organism in response to physical load was determined, and orthostatic and Val'sal'va tests were also taken.

The data obtained indicate that the degree of change in the pulse after physical load depends on the duration of the experiment. As a rule, toward the end of the experiment there was observed a significant quickening of the pulse in response to a measured load in comparison with the data obtained on the first days. At the same time, the time taken for the restoration of the pulse to the original values increased.

TABLE 29

CHANGE IN BLOOD PRESSURE OF SUBJECTS (IN mm hg) AFTER PHYSICAL LOAD IN THE 7,000 m ALTITUDE EXPERIMENT

Day of experiment	subject A-ov				
	before load	after load (minutes)			
		1st	5th	10th	15th
5-ii	120/60	125/60	115/65	110/55	—
10-ii	117/55	125/65	115/60	110/60	112/50
15-ii	110/50	102/50	105/50	105/55	100/50
20-ii	110/57	110/60	105/55	100/50	100/50
25-ii	100/50	110/50	110/45	105/55	—
30-ii	1[illegible]/50	125/60	120/60	110/55	—
35-ii	110/55	115/65	115/65	110/65	—
40-ii	110/60	110/60	105/55	112/60	—
45-ii	105/60	100/55	100/55	—	—
50-ii	105/55	125/70	120/70	120/70	—
55-ii	100/50	90/50	95/50	108/55	—

Subject Ch-ov

Before Load	After Load (minutes)			
	1st	5th	10th	15th
120/65	125/65	125/65	120/60	—
110/65	125/65	118/65	120/60	118/60
100/50	130/65	125/60	115/50	—
125/65	130/65	120/65	118/60	—
118/50	115/55	125/65	—	—
120/70	120/70	118/70	120/70	—
140/80	133/80	140/80	130/75	—
120/70	120/65	110/62	110/60	—
110/60	125/78	125/70	115/65	—
130/70	115/66	100/50	100/55	—
120/70	125/73	120/75	120/75	—

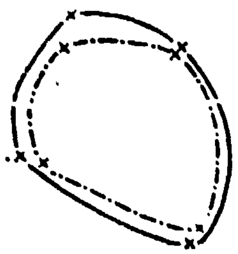
Table 28 presents the results of the change in pulse frequency after physical load obtained in the control experiment. /145

As is seen from Table 28, the pulse frequency increased after physical load in proportion to the duration of the experiment. Thus, in the case of subject Ts-ko, on the 11th day the pulse frequency increased by 27% and on the 20th day by 43% in comparison with the initial values. Subsequently, the pulse frequency after physical load remained at the same level.

The general tendency for the pulse frequency to change after physical load was the same in the high altitude experiment as in the control experiment.

The individual EKG component did not undergo significant changes. The blood pressure did not significantly change after physical load. Data on the change in blood pressure after physical load in the high altitude experiment are given in Table 29.

As is seen from the data in Table 29, the blood pressure after physical load increased insignificantly only on the first 10 to 15 days of the experiment. Subsequently it was maintained at a lower level than before load. The "negative phase" observed after physical load is an indicator of fatigue of the cardiovascular system and weak conditioning of the cardiac muscle due to an insufficiency of motor activity of the subjects in a chamber of small volume.



/146

T—14.7 cм . . . . 13.2 cм
L—15.2 cм . . . . 14.5 cм
F—14.8 cм² . . . . 138 cм²

Before experiment	After experiment

Figure 24. Diagram of X-ray picture of subject N-ov's heart in front right projection before experiment (solid line) and after experiment (dotted line). T--diameter; L--length; F--Area.

The X-ray studies of the chest and heart, made by P. M. Ivanov and A. R. Mansurov before the beginning of the long-term experiment did not reveal fresh focal or infiltration changes in the lungs. The heart was of normal configuration, its contracting function did not have significant deviations from the norm. A second X-ray study taken immediately after the end of the long-term experiment showed that, both in the ground and high-altitude experiments, no significant changes occurred in the lungs;

TABLE 30

RESULTS OF X-RAY STUDIES OF THE SIZE OF THE HEART SHADOW

Subject	moment of study in relation to experiment	Basic diastolic dimensions of the heart picture cm				Certain zones of the cardiac-vascular contour, cm								area cm^2	
						left ventricle		left auricle		left artery		right auricle		during systole	during diastole
		Mr	Mc	T	L	duration	amplitude	duration	amplitude	duration	amplitude	duration	amplitude		
Ground (control) experiment															
N-ov	Before	5.7	9.0	14,7	15,2	8.1	0.2—0.6	14	0.1	3.1	0.15—0.25	7.8	0.2—0.5	140	148
	After	4.7	8.5	13,2	14,5	8,0	0,2—0,6	1.3	0,1—0.15	3,6	0.2—0,25	7.3	0.2—0,5	129	138
	15 days later	4,4	10,0	14,4	15,3	9,0	0,3—0.6	1,9	0,1—0,2	3,6	0,2—0,25	6.4	0,1—0,5	149	154
Ts-ko	Before	5.1	9.0	14.1	15.3	9.3	0,25—0.6	1.2	0.2	3.8	0.2—0.3	6.8	0.15—0.5	144	155
	After	4.5	8.5	13.0	14.5	8.4	0.2—0.6	1.6	0.1—0.15	3.7	0.2—0.35	6.0	0.2—0.5	132	141
	15 days later	4.6	9,0	13.6	14,7	8.7	0.2—0.6	1.4	0.1—0.15	2.6	0,2—0,3	6.3	0,2—0,4	133	142
High Altitude Experiment															
A-ov	before	5.9	7.7	13,6	14,9	11.2	0,2—0,7	1.3	0.1—0.15	4.0	0.2—0.3	7.4	0.2—0.4	140	150
	after	6,0	7,9	13.9	15,8	11,2	0.2—0,7	1,5	0,1—0.15	3,0	0.2—0.3	7,8	0,2—0,5	145	156
Ch-ov	before	4.4	10.4	14.8	16.5	12.1	0,15—0.7	2,2	0.1	3.1	0.2—0.3	7,7	0.15—0.5	160	172
	after	4.6	10,9	15.5	16.5	12,2	0,15—0,7	1,9	0.1—0.15	3,2	0,2—0,3	7.6	0,2—0,4	164	175

the depth of inhalation did not significantly change. In analyzing the X-rays attention is drawn to the significant change in the dimensions of the shadow of the heart (Table 30).

It proved to be the case that in the ground experiment the size of the shadow of the heart in both subjects became significantly smaller than before the experiment, both in the systolic state and in the diastolic state. The diameter of the heart was smaller by 15 mm in subject N-ov, and by 11 mm in subject Ts-ko. From Table 30 it is obvious that in both cases the amplitude of heart contraction did not undergo significant changes.

According to measurement data of the right and left halves of the diameter of the heart it is possible to note that there was a somewhat greater decrease on the part of the right half. Figure 24 shows a diagram of an X-ray picture of subject N-ov's heart before and after the 60-day ground experiment. X-ray studies conducted 15 days after the end of the experiment showed a practically complete restoration of the functional shifts mentioned above: the diameter of the heart both in systole and in diastole /148 approximated the original, however the frequency of cardiac contractions in both subjects still remained quite high.

Considering the increased frequency of cardiac contractions and the amplitude of pulsation immediately after the end of the experiment, the decrease in the dimensions of the heart was the result of changes which developed in the myocardium itself. These changes obviously can be connected with hypokinesis and, consequently, they may be viewed as a phenomenon of partial functional atrophy.

While the phenomenon of functional atrophy of the skeletal musculature is well studied, with regard to the heart of a healthy man there is very little information in the literature. It is interesting to note that the X-ray observations of persons subjected to analogous influences in an experiment lasting 30 days conducted by P. N. Ivanov and A. R. Mansurov (D. I. Ivanov, et al., 1963) did not in any case show the presence of signs of functional atrophy in the form of a significant decrease in the dimensions of the heart. It is possible that these phenomena begin to develop and become significant only after more than 30 days.

However, as is seen from Table 30, in the 62-day high altitude experiment these phenomena could not be observed, which, partially is explained by the more regulary performed physical exericse of these subjects.

Dynamic observation of the degree and nature of the development of and recovery from functional atrophy of the cardiac muscle has important significance for the conducting of investigations connected with prolonged stays under conditions of adynamia and isolation.

The presence of these materials may lead to the organization and correct evaluation of work and rest periods and prophylaxis of the observed functional changes.

It is known that the change in gas exchange during and after the performance of measured work may serve as an index of the working capacity not only of the respiratory, but also of the cardiovascular system.

We investigated the influence of an extended stay in an airtight chamber on the function of external respiration and gas exchange. The respiratory minute volume (RMV) was measured with a dry gas counter. The pulmonary gas exchange was investigated by the combined Douglas-Holden method. /149

In the airtight chamber the subjects breathed gas mixtures fed into an altitude chamber; in the ground experiment the mixture did not differ from normal atmospheric air, while in the high altitude experiment it consisted of 57% oxygen and 43% nitrogen. The composition of the inhaled, exhaled and alveolar air was analyzed on a Holden apparatus. A special system, consisting of two tanks connected with each other and with an altitude chamber, was used for taking air samples. Samples of the alveolar air were taken with a Holden tube fed into vacuumized gas pipettes.

For calculating the amount of absorbed oxygen, liberated carbon dioxide and energy consumption with the aid of the tables we developed (see Table 4), we reduced the RMV to standard conditions (0 degrees, 760 mm Hg dry state), and in all remaining cases used the actual RMV value.

The investigations showed that a gradual decrease in the respiration rate is observed during an extended stay in an altitude chamber.

The respiratory volume minute decreased from 6.7-8.8 liters during the control period to 5.4-5.6 liters during the time the subject spent in the altitude chamber. Also, in the second half of the experiment the RMV decreased more than in the first. Thus, during the first month the RMV decreased by 20.3% and during the second by 24.8%.

Table 31 presents data on the change in the index of pulmonary gas exchange. In the control period the oxygen absorption was 222-302 ml/min. While the subjects were in the altitude chamber the oxygen absorption decreased, and the maximum decrease in oxygen absorption was observed in the second half of the experiment. As a whole, during the entire time spent in the chamber the

TABLE 31. INDICES OF GAS EXCHANGE AND BASIC EXCHANGE FOR AN EXTENDED STAY OF SUBJECTS IN AN ALTITUDE CHAMBER.

Conditions of experiment	Subject	Indices of gas exchange	control period	Day		of stay in chamber					Period of after effect (days)		
				6th	18th	29th	33rd	41st	48th	55th	1st	3rd	
Ground	N-ov	Oxygen absorption, ml/min	302	150	195	198	240	200	260	290	290	300	
		Carbon dioxide ex-haled, ml/min	230	140	100	200	250	150	230	225	240	235	
		Respiratory co-efficient	0.76	0.93	0.82	1.0	1.02	0.75	0.88	0.78	0.83	0.78	
		Basic exchange kcal/ day	1 434	744	941	999	1 211	948	1 274	1 305	1 403	1 433	
				6th	11th	16th	23rd	37th	47th	54th	1st	2nd	
	Ts-ko	Oxygen absorption, ml/min	270	158	180	210	210	230	155	160	200	267	
		Carbon di-oxide ex-haled, ml/min	250	150	100	158	155	200	200	157	180	224	
		Respiratory co-efficient	0.93	1.0	0.89	0.75	0.74	0.87	1.29	0.98	0.90	0.84	
		Basic exchange kcal/day	1 339	778	884	995	897	1 124	782	803	986	1 205	
				12th	20th	28th	36th	47th	60th		2nd	8th	22nd
Rarified atmosphere with normal PO_2	A-ov	Oxygen absorption, ml/min	222	296	156	175	155	120	150		223	227	251
		Carbon dioxide exhaled, ml/min	182	164	112	169	143	125	124		235	200	187
		Respiratory co-efficient	0.82	0.55	0.72	0.97	0.93	1.04	0.83		1.05	0.88	0.74
		Basic exchange kcal/day	1 541	1 965	0 055	1 256	1 100	873	1 043		1 622	1 598	1 708
				13th	23rd	29th	37th	46th	59th		2nd	8th	22nd
	Ch-ov	Oxygen absorption, ml/min	274	248	240	191	164	183	193		228	293	274
		Carbon dioxide exhaled, ml/min	186	160	202	175	156	197	173		205	221	235
		Respiratory co-efficient	0.68	0.64	0.84	0.91	0.95	1.08	0.90		0.90	0.75	0.85
		Basic exchange kcal/day	1 836	1 650	1 670	1 355	1 182	1 330	1 368		1 613	2 000	1 901

basic volume decreased in the case of subject A-ov by 21.1%, in the case of Ch-ov by 22.1% (high altitude experiment), in the case of N-ov by 26.1%, and in the case of Ts-ko by 33.2% (ground experiment).

The decrease in the indices of gas exchange and energy exchange in persons remaining for a long time in a state of hypodynamia is also mentioned by D. I. Ivanov et al. (1963), Welch et al. (1961) and others. In particular, D. I. Ivanov et al. (1963) in a 30-day experiment with rarefaction of the air in an altitude chamber corresponding to an altitude of 7000 meters, and a normal oxygen supply to the organism, discovered a decrease in the basic exchange by 15-20 percent on the average as compared with the initial level. /152

Thus, in all subjects during an extended stay in a chamber of small volume both under conditions of normal, and low (to 308 mm Hg) barometric pressure, there was noted slowing of the rhythm and a decrease in the respiratory minute volume, oxygen consumption, carbon dioxide exhalation and basic exchange. In addition, all the above numerated indices of the function of external respiration and pulmonary gas exchange decreased more in the second month of the experiment than in the first. Hence it follows that the amount of basic exchange directly depends on the length of time spent in a chamber of small volume.

The decrease in the oxygen consumption of the organism, resulting from hypodynamia, is evidently a cause of the smaller gas exchange indices. The decreased oxygen consumption of the organism, in turn, led to a slower respiration rate and a lower respiratory minute volume.

The long-term (62-day stay) at an altitude of 7,000 meters did not have any specific influence on the state of the cardiovascular system and respiration in comparison with the data obtained in the 60-day ground experiment. The observed functional shifts are connected with the general asthenization of the organism and the lower vascular cone primarily caused by the lack of motor activity and lower nervous impulsation.

RESULT OF HEMOTOLOGICAL INVESTIGATIONS AND CORTICOSTEROIDS

In selecting the atmospheric parameters of the airtight chambers it was also important to explain the effect on blood formation of an extended stay under conditions of a changes gas medium and lower barometric pressure.

The blood system is extremely unstable and reflects the effects of different factors of the external and internal environment on the human organism. /153

Hematological studies were performed by N. I. Yezepchuk by the usual method in the course of the long-term experiments (high-altitude and ground). In addition, the phagocytic activity of the neutrophiles was studied.

The investigation showed that in the 60-day ground experiment in the case of both subjects the number of erythrocytes, the hemoglobin content, the color index, and the sedimentation rate did not vary significantly. In the first seven days from the beginning of the experiment the number of reticulocytes somewhat decreased: in subject Ts-ko by 5%, in subject N-ov by 6%. However, this decrease did not go beyond bounds of permissible physiological variation. On the 14th and 28th day the number of reticulocytes increased to 10-12% in the case of subject Ts-ko and to 14-15% in subject N-ov. Subsequently, an insigificant reticulocytosis was maintained in both subjects up to the end of the experiment. During the first week of the day there was also an insignificant anisocytosis of erythrocytes and an increase in the number of thrombocytes (from 267,300 to 418,000) per cubic mm of blood in subject Ts-ko and from 239,000 to 488,400 in subject N-ov. By the 35th day and before the end of the experiment, the number of thrombocytes returned to normal.

In the high-altitude experiment during the first 30 days the number of erythrocytes in the subjects remained within the limits of the initial values and only on the 38-41th day was there noted a small increase in the number of erythrocytes, which was accompanied by an increase in hemoglobin content from 12-15 to 15.2-15.8 g%. In subject A-ov, reticulocytosis up to 11-13% also took place. The number of thrombocytes did not change during the entire experiment.

The total number of leucocytes fluctuated within normal limits. At the same time the ratio of formal elements of the blood was somewhat disturbed. Thus, in subject N-ov, lymphocytosis up to 44% was noted (absolute amount 3220 with an original of 2500) and the number of rod-nucleus neutrophiles increased to 6.5% on the 7th day and to 9% on the 60th day of the experiment. The relative and absolute number of lymphocytes also increased somewhat in the case of subject Ts-ko during experiments with a simultaneous increase in the number of rod-nuclear cells to 7%.

In studying the leucocytic formula, initially, no significant changes in the number of eosinophiles were revealed while in the second half of the experiment (from the 34th to the 35th day) the number of eosinophiles increased, which specifically testifies to the additional strain of the organism. /154

The data on the phagocytic activity of neutrophiles are of interest. According to the information available in the literature, in healthy males not subject to any outside influences phagocytosis varies from 31-38%, the phagocytic number from 4 to 5 and the phagocytic index from 1.3 to 2.

In the ground experiment from the 13th to the 27th day, activation of the phagocytic activity of neutrophiles was noted. Thus, if in the case of subject N-ov on the 13th day of the experiment phagocytosis was 60%, the phagocytic number 3.7 and the phagocytic index 1.86, then on the 20th day they were respectively 89, 9.7 and 8.7 (Table 32), whereby these changes depended on the increase in the percent of phagocytized neutrophiles and primarily on the increase in the phagocytic number, since each neutrophile captured more microbes than under normal conditions. At the very end of the experiment there was observed a second wave of activity of the phagocytic reaction. The percentage of phagocytizing neutrophiles sharply increased.

TABLE 32

CHANGE IN THE PHAGOCYTIC INDEX IN SUBJECTS DURING THE GROUND EXPERIMENT

Day of experiment	Phagocytic index of subject		Day of experiment	Phagocytic index of subject	
	N-ov	Ts-ko		N-ov	Ts-ko
13th	1.86	3.89	9th	1.44	1.10
20th	8.70	2.96	0th	3.03	5.20
27th	6.40	--	1st day of aftereffect.	1.67	1.52
35th	1.89	0.62			
42nd	0.76	0.53	2nd day of aftereffect	0.62	0.70

The wavelike changes in the phagocytic reaction were not of /155
a pathological nature since these indices rapidly returned to the norm. However, this test, evidently, also indicates the functional strain of the organism.

In the experiment with decreased barometric pressure there were also observed, from the 21st day in the case of subject A-ov and from the 31st day in the case of subject Ch-ov, changes in the phagocytic activity of the neutrophiles (Table 33). In addition, it was found that the number of phagocytized neutrophiles decreased somewhat, although each of them captured considerably more microbes than under normal conditions, that is, the phagocytic number and phagocytic index increased. A phase of suppression preceded the increase in the phagocytic activity of the neutrophiles.

TABLE 33

CHANGE IN THE INDICATORS OF PHAGOCYTIC ACTIVITY OF NEUTROPHILES IN THE HIGH-ALTITUDE EXPERIMENT

Moment of Observation		Indicators for Subjects					
		A-ov			Ch-ov		
		Phagocytosis %	Phagocytic number	Phagocytic index	Phagocytosis %	Phagocytic number	Phagocytic index
Before Experiment	I	82	3.06	3.01	79	5.0	3.94
	II	67	6.02	4.19	78	3.7	2.9
	III	64	7.02	4.99	70	3.8	2.71
Day of Experiment	21st	63	10.6	10.14	47	2.6	1.23
	31st	57	10.5	8.43	61	10.4	8.5

In order to show directly the effects of prolonged adynamia, decreased barometric pressure and relative hypodynamia and isolation on the hereditary structure of the organism, a comparative investigation of the chromosomes in a culture of the peripheral blood was conducted before and after the experiment. The frequency of deviation in chromosome number before and after the high-altitude experiment was determined in the leukocytes.[1] No significant changes were observed here.

But, a prolonged stay at a low barometric pressure causes temporary fluctuation of specific indices of the peripheral blood: the number of erythrocytes and the hemoglobin content increases, which may be considered the result of thickening of the blood due to an increase in moisture losses, and, correspondingly, the number of reticulocytes increases, testifying to the activation of bone marrow blood formation. /156

A wavelike fluctuation of the phagocytic reaction was observed. However, the rapid restoration to the norm indicates that these

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[1]These studies were conducted in the laboratory by A. A. Prokof'yeva-Bel'govskaya

changes were not of a pathological nature.

In analyzing the resultsof hematological investigations it is extremely important to establish the dependence of these changes not only on the amount of the total pressure in the airtight chamber and the composition of the atmosphere, but also on the nature of the bacterial contamination of the chamber and the neuro-humoral rearrangement appearing under these conditions.

It is known that under extreme conditions there occurs a reorganization of the operation of the endocring glands producing a change in the exchange processes corresponding to the new conditions. A more pronounced rearrangement may be observed in the cortical matter of the adrenal gland, in which connection this gland is most often the object of investigation.

Activation of the function of the adrenal gland, as is known, is observed under the effects of many stimuli, including some not having a pronounced biologically negative value.

As G. Sel'ye (1960) noted, the excess development of cortical steroid hormones may cause "adaptation sickness," entailing the necessity of establishing the limits within which hyperfunction of the cortex of the adrenal gland is useful for the organism.

The question of the role of the reactivity of the organism is viewed one-sidedly in Sel'ye's conception. In his opinion, the sickness "may be acquired with equal regularity through the general effect of different pathogenic factors, that is, as the result of nonspecific stress." Sel'ye considers "stress" or "the general adaptation syndrome," to be a stereotypical protective physiological reaction of the organism to "conditioning factors" of exogenic and endogenic nature, in which the hormones of the adrenal gland cortex and the front part of the pituitary gland participate.

There is no doubt that the level of functioning of the /157
cortex of the adrenal gland will in each concrete case depend not only on the nature and amount of extreme outside influences, but also on the individual characteristics of the organism.

It seems to us that one of the deficiencies of Sel've's conception is the absoluteness of his concept of the nonspecificity of different stress factors. Stress effects, although they cause a standard reaction ofthe adrenal gland cortex, probably perform this by means of different afferent paths and not through some single "stress mediator," as Sel'ye, advancing the establishment of the nature of this mediator as a basic problem, believes.

It is difficult to assume that the influence on the adrenal gland cortex of such factors as pain, oxygen starvation, hypoglycemia or hypological shock, is manifested along the same paths. In this connection it was extremely interesting to evaluate the functional state of the human organism by studying the output of 17-oxycorticosteroids in the long-term experiments and comparing the data obtained with the diuresis values.[1]

The amount of corticosteroids in the urine was determined by reaction with phenylhydrasine proposed by Zalber and Porter.

Usually, the amount of 17-oxycorticosteroids eliminated from healthy persons, according to the data of N. A. Yudayev, is 4 mg per day. It is also considered that during the night time the elimination of steroids is lower than in the daytime. According to the data of I. F. Balakhovskiy (1962), the average elimination of 17-OH oxycorticosteroids in eleven soldiers on special duty was 3.7 mg per day, and in the period when they performed parachute jumps, it was 5-8 mg per day.

The results of our investigations showed that both in the 60-day ground (control) and in the 62-day high-altitude experiments the elimination of corticosteroids was within the limits of the upper boundary of the norm, namely: in subjects N-ov and A-ov, during eight days the amount of eliminated steroid hormones was less than 5 mg per day only three times, and in subjects Ts-ko and Ch-ov it did not once drop below 5 mg per day.

In analyzing the dynamics of changes in the activity of the adrenal gland cortex we established that the subjects experienced no significant differences in the elimination of 17-oxycorticosteroids in the long-term experiments. /158

In the case of subjects A-ov and Ch-ov, in addition to the total amount of eliminated corticosteroids, their elimination by fractions during the day was investigated: the urine was collected every four hours during the day, and every eight hours at night. In all days investigated the amount of hormones eliminated at night was less than during the day. The daily rhythm of eliminating 17-oxycorticosteroids was the normal one characteristic for healthy individuals. No significant difference was observed in the elimination of 17-oxycorticosteroids in the subjects who spent an extended period in the altitude chamber in normal atmosphere conditions and in low barometric pressure conditions (7,000 meters).

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[1]The investigation of corticosteroid hormones was conducted in the laboratory of I. F. Balakhovskiy.

During an extended stay in a closed chamber of small volume in conditions of hypodynamia and relative isolation, significant changes appear in the functional state of different physiological systems of the organism. The application of maximum outside influences creates conditions under which the requirements for the smooth functioning of the systems which provide for the support of the organism and the appearance of protective and adaptive reactions, are sharply increased.

In studying the reactivity of the organism before and immediately after the experiment we performed functional tests on the resistance to radial acceleration, oxygen deficiency and intensive physical exercise. The level of the compensatory capabilities of the organism decreased in all subjects after an extended stay in a chamber of small volume. Therefore, a special complex of measures was developed which was directed toward maintaining the efficiency level of the subjects with the inclusion of physical exercises and regulation of the parameters of the gas medium in the cabin (periodic lowering of pO_2 and raising of pCO_2).

CHAPTER IV /159

THE INFLUENCE OF HIGH OXYGEN CONCENTRATIONS ON THE ORGANISM

Interest in the problem of hyperoxia has significantly increased in connection with the use of pure oxygen for medical purposes in clinical practice and for breathing by pilots and divers.

There has been an especially extensive development of hyperbaric oxygen therapy, which has essentially become an independent division of medical science. The contemporary understanding of the oxygen regime of the organism and its regulation have made it possible to use oxygen (at normal and, especially, high pressure) for curing diseases and, in particular, in performing operations where the ordinary means of supplying the tissues with oxygen are excluded.

The high degree of effectiveness of elevated oxygen pressure in the case of hemic forms of hypoxia was experimentally proven in the classic experiment of Haldane, where animals, suffering from carbon monoxide poisoning, survived in a medium with high oxygen pressure because of the transfer of oxygen in the dissolved form to the tissues by the blood plasma. However, in clinical practice oxygen under high pressure has begun to be used only recently, for example, in the case of different types of ischemic hypoxic conditions (disturbances of the cerebral and coronary circulation, in the case of anaerobic infections and so forth), and also for improving the results of radiation therapy of malignant neoplasms and attenuating general radiation reactions. The use of oxygen therapy after irradiation decreases to a significant tissue hypoxia, improving reduction and oxidation processes.

What are the physiological grounds for oxygen and hyperbaric oxygen therapy? The oxygen reserves in the human organism are extremely small. It has been experimentally established that the /160 organism contains around 2-2.5 liters of oxygen. As we have already indicated, the small reserves of oxygen in the organism completely satisfy the physiological requirement of man and animals when these reserves are constantly renewed from the surrounding atmospheric air. Threatening symptoms, indicating severe disturbances of vitally important functions of the organism, begin in man long before the disappearance of all the oxygen reserves in the organism.

The literature contains information on the great effectiveness of oxygenation of the organism and the possibility of prolonged periods of stoppage of respiration and circulation. However, in the majority of cases these conclusions are made by means of simple calculations and are not based on sufficient experimental material and in depth analysis from the vantage point of contemporary knowledge concerning the oxygen regime of the whole organism or of isolated organs or tissues.

By breathing oxygen, particularly under elevated pressure, the oxygen reserves in the organism may be increased. Thus, for example, theoretical data, which were subsequently verified and confirmed experimentally, indicatethat at a pressure of 3 atmospheres the amount of oxygen contained in the lungs increases by almost 18 times (by 6 times due to the fact that almost the entire volume of the lungs is filled with oxygen, and by 3 times because of the gas density). If this volume is reduced to standard conditions (STPD), then it turns out that in this case the oxygen content in the lungs is 9 liters, that is sufficient "reserves" to supply the requirements of the organism for 30-45 minutes.

In addition, different ratios occur in the blood. When breathing atmospheric air, the arterial blood contains 18-20 ml of oxygen in the bound form (oxyhemoglobin) per 100 ml of blood. The dissolved oxygen contained in the plasma is, in toto, 0.3 ml per 100 ml of arterial blood.

It is known that even in ordinary conditions almost the entire oxygen capacity of the hemoglobin (95-97%) is used. Breathing pure oxygen, even at high pressure (3 atmospheres), leads to an increase of the pO_2 in the alveolar air from 100 to 2200 mm Hg (in breathing pure oxygen in atmospheric conditions p_AO_2 increases to 675 mm Hg). In addition, the gradient between pO_2 in the alveoli and the alterial blood sharply increases and instead of the usual 5-10 mm it is around 200 mm. However, the significant increase /161 in pO_2 in the arterial blood observed here leads only to a small increase in oxygen content (3-5%) due to additional bonding of hemoglobin and, in agreement with the Henry-Dalton law, to an increase in the oxygen absorbed in the plasma from 18-20 to 25-27% by volume), providing for the oxygen requirement of the organism for only several minutes. Consequently, it is much more difficult to create significant oxygen "reserves" in the blood and in the tissues, than in the lungs.

As a result of experimental studies with the use of the polarographic method it has been established that by raising the pO_2 in the inhaled air by five times in different tissues of animals (rats) there was observed a comparatively small (30-40%) increase in oxygen pressure (A. A. Vishnevskiy et al, 1967). The use of high oxygen pressure for breathing in some experiments led to the appearance of oxygen convulsions. The authors showed that a significant effect of oxygenation under pressure is observed when breathing is stopped and circulation retained and a very moderate effect when circulation is stopped, since a small oxygen reserve is created in the tissues. In striving to increase these "reserves" one must not forget that breathing pure oxygen even at ordinary ground pressure has a pronounced toxic effect. An unreasonable attempt to obtain an "infinite" increase in the oxygen content in the blood and tissues may lead to the opposite result, since in breathing pure oxygen, even under ordinary pressure, "hyperoxic hypoxia" develops in the human and animal organism and dangerous symptoms of oxygen poisoning appear.

Experimental investigations of the influence of an increased partial pressure of oxygen on the organism of animals were begun in the last century. However, even now it is still not possible to explain sufficiently the pathological effect of high oxygen concentrations and the resultant physiological shift.

In the opinion of a number of scientists, in breathing pure oxygen its influence during the first hours may lead to disturbance of the Bohr effect. Gesell (1925) first turned attention to the /162 disturbance of carbon dioxide transfer in the case of high degrees of oxygen saturation of the blood. When breathing pure oxygen the hemoglobin of the blood is almost completely oxygen saturated and is reduced by a small amount. Moreover there is a large amount of dissolved oxygen in the plasma. Therefore, the tissues, in consuming oxygen, do not decrease its content in the blood to the usual level. Since hemoglobin in normal conditions bonds more carbon dioxide, than does oxyhemoglobin, in a hyperoxic medium the venous blood is richer in oxyhemoglobin than usual, and, consequently, incorporates less carbon dioxide. The transport of carbon dioxide by the blood is hindered. All this leads to an accumulation of carbon dioxide in the tissues and the development of acidosis, which in turn causes amplified ventilation. In confirmation of this thesis Gesell mentions that during physical exercises or upon the inhalation of gas mixtures with a high carbon dioxide content hyperoxic convulsive attacks are intensified. Recent experimental data have shown that the process described above does not play a leading role in the pathogenesis of oxygen poisoning. In the light of this conception the different toxic effects of oxygen with different partial pressures and the development of toxic edema of the lungs remain incomprehensible. **Superfluous argument against** Gesell's conception is that some organisms are more sensitive to oxygen than to carbondioxide. There are also other hypotheses.

Thus, according to the data of Lemann (1935) and Massart (1936), in raising the partial pressure of oxygen, enzyme activity is disturbed due to blocking and conversion to an oxidized form. Disturbance of the activity of these enzymes in turn leads to the cessation of the function as catalysts of the reduction, and also to an increase in the content of organic acids in the blood. There are grounds to assume that an increased oxygen content causes not only inhibition of the activity of some enzymes, but also of their dysfunction, in particular, selective damage to sulfhydryl enzymes. Haugaard (1946) considers that during the period before the beginning of a hyperoxic convulsive attack there occurs inactivation of an enzyme containing a sulfydral group, with the exception of cholinestase. In his opinion, the chemical mechanism of this activity is connected with the oxidation of the SH group to the inactive S-S group.

The inhibition of enzymatic mechanisms is confirmed by the data of Stadie et al.(1944) who determined in vitro a 30% decrease in cellular oxidation in the lung of a dog placed for two days in an atmosphere of pure oxygen at a pressure of 760 mm Hg. /163

Breathing oxygen promotes more rapid oxidation of incompletely oxidized metabolic products (lactic acid, acetone bodies etc.).

I. M. Dedyulin (1941) carried out considerable research on the influence of hyperoxia on the biochemical factors of the blood. The observed changes, in the author's opinion, basically result from a shift in the acid-base equilibrium.

In a number of investigations it is shown that in the process of breathing pure oxygen, the histamine content in the pulmonary tissue increases (Groduot, Chome, 1965). Evidently this may also explain the increased toxicity of oxygen upon the introduction of adrenocorticotrophic hormones and cortisones.

Oxygen may act on oxidation processes both directly and indirectly, influencing the enzyme system.

Ye. M. Kreps (1945) mentions a change in the activity of carbon anhydrase in human blood in conditons of hyperoxia. According to his data, the fluctuations in the activity of this enzyme are performed with the participation of the sympathetic nervous system and are of an adaptive nature.

At the present time there exist numerous theories concerning the significance of the peroxidation of fats in the manifestation of oxygen toxicity (Mendel et al.1964, and others). As is known, peroxidation leads to the breakdown of polyunsaturated fatty acids. These compounds make up the bulk of the membranes necessary for normal cell functioning.

Disturbances in the activity of the endocrine system play an important role in the genesis of the toxic effect of oxygen (Campbell, 1938; Bean, 1945). An increase in the arterial oxygen pressure leads to a narrowing of the vessels, which in turn decreases the amount of oxygen used by the brain cells, while an increase in the venous and tissue carbon dioxide pressure, in Bean's opinion (1945), on the other hand, produces a vessel-expanding effect in the tissues of the brain and an increase in oxygen pressure at the brain cell level. Lambertsen et al.(1953) /164 observed in these conditions a decrease in the amount of blood flowing to the brain. Because of the harmful effects of pure oxygen, scientists for a long time could not bring themselves to conduct experiments on human beings. Moreover, some authors even warned against the therapeutic use of pure oxygen for more than two hours (Plesser, 1937).

At the present time the reaction of the organism to short-term moving of pure oxygen has been quite well studied, not only in experiments on animals, but in physiological studies on human beings. The existing long-term observations in the areas of clinical practice and aeronautics testify to the absence of significant disturbances arising during the brief use of pure oxygen in conditions of normal or lowered atmospheric pressure. All this indicates, on the one hand, the important significance of the time factor in the pathogenesis of oxygen poisoning, and on the other, the complete functional reversibility of the changes which develop in the first hours of breathing pure oxygen.

In 1939 the first experiment was conducted in which people breathed 90% oxygen at normal pressure (760 mm Hg) for three days (Becker-Freyseng, Clamann, 1942).

In beginning their investigations on human beings, the authors, on the basis of a comparative analysis of the literary data, proceeded from the working hypothesis that the survival rate of animals breathing high concentations of oxygen should increase in proportion to an increase in the size and total surface of the body with its corresponding decrease in relative metabolic intensity, and consequently, the harmful effects should decrease. From this point of view,especially favorable conditions, in the author's opinion, are created for man.

It is established that when breathing pure oxygen in normal atmospheric conditions, mice and rats, as a rule,die after approximately 45-80 hours, guinea pigs and rabbits after 90-100 hours, dogs and cats after 60-150 hours and monkeys after 150-216 hours. The simplest animals and arthropods do not die in these conditions. Evidently, cold- /165 blooded animals possess high resistance to oxygen because of the relatively low body temperature. Turtles and frogs survived in an oxygen atmosphere at room temperature for an indefinitely long time. However, at a pressure on the order of several atmospheres, pure oxygen - even if breathed for a brief period - proved to be fatal for all animals, first attacking the nervous system.

Data on the influence on the organism of breathing pure oxygen at pressures above 1 atmosphere are presented in detail in the monographs of G. L. Zal'tsman (1951) and A. G. Zhironkin et al (1965).

In the experiment of Becker-Fraysing and Clamann (1942) their initial hypothesis of the very great human tolerance of high oxygen concentration was not proven. Already on the second day their subjects exhibited a significant decrease in the vital capacity of the lungs, an increase in body temperature and an increase in pulse rate. In addition, in the peripheral blood there was observed a moderate decrease in the hemoglobin content, and an increase in the number of erythrocytes and leucocytes. At approximately the same time in both subjects paresthesia appeared, initially on the fingertips and then the toes (itching and numbing); at times pains arose in the knee joints. The blood pressure here remained practically unchanged. The alveolar carbon dioxide pressure decreased significantly in both subjects (to 28-30 mm Hg). These phenomena continued to intensify and after approximately 60 hours nausea began, there was continuous vomiting of mucous and the experiment was quickly stopped.

Later, Bean (1945) conducted similar studies on volunteers who for 65 hours continuously breathed 90% oxygen at normal atmospheric pressure. This experiment also had to be stopped due to significant disturbance of breathing.

The histopathological-anatomical studies conducted by Gable and Townsend (1962) on casualties of aviation disasters (50 people) showed that a thickening of the alveolar membrane in the form of capillar platelets was noted in jet pilots.

Comroe et al. (1945) obtained interesting data on a great amount of experimental material. Having studied 90 persons, the authors established that upon inhaling oxygen at normal pressure the subjects complained of chest pains (in 82%), on the average appearing 14 hours from the beginning of the experiment, coughing (in 50%), painful sensations in the throat (in 32%), pains in the ears (in 28%), fatigue (in 25%). In individual /166
cases there are pains in the joints and muscles, occasional pains in the extremities, nausea and dizziness (in 7 subjects).

The authors explained the chest pains by the development of tracheobronchitis and damage to the pulmonary parenchyma. According to the opinion of N. N. Sirotinin (1952), an inflammatory reaction of the pulmonary tissue becomes distinct in animals after approximately two days in an oxygen atmosphere. Pathological changes are noted not only in the lungs but also in the liver, heart, spleen, kidneys, and intestines. Plethera, congestion and degeneration of the cardiac muscle fibers were revealed. A number of authors consider the changes in the myocardium to be secondary, arising due to the hypoxia which develops as a result of severe pulmonary damage (Kaunitz, 1942, et al.).

Dickens(1946) indicates a gradual and irreversible disturbance of cerebral tissue restoration under the influence of oxygen, whereby different tissues possess different resistances to oxygen. The author determined the following order of tissue sensitivity to oxygen: cerebral cortex (homogenates) greater than cerebral cortex (pieces) greater than spinal cord greater than liver greater than testicles greater than kidneys greater than lungs greater than muscles.

In connection with the wide use of oxygen in medical practice and aeronautics in recent years investigations were conducted to explain the pathogenic effect of pure oxygen on the organism and to develop preventative measures aimed at providing for safety when breathing high oxygen concentrations. These studies made use of a wide arsenal of physiological, pathomorphological and clinical methods of investigations.

An analysis of the data in the literature shows that increasing the oxygen pressure in the blood produces a complex effect on the organism. The nature and degree of the changes occurring in the activity of different systems and organs depends on the partial pressure of oxygen in the inhaled air and the duration of its influence.

However, despite the great number of fundamental studies /167
on the influence of the toxic effects of oxygen on the organism, many aspects of this problem have not yet been sufficiently studied. There is little information about the permissible level of the partial pressure of oxygen in the atmosphere of manned airtight cabins, and of the influence on the human organism of different oxygen concentrations in the inhaled air during an extended (multiday) stay in conditions of normal and low barometric pressure.

PERMISSIBLE pO_2 LEVELS IN INHALED AIR

Until recently the majority of authors have considered that the maximum pO_2 level which a man can endure is on the order of 425 mm Hg

(Becker-Freysing, Clamann, 1942; Welch et al., 1961, and others). In our opinion there exists a direct connection between the maximal permissible oxygen level and the breathing time. With prolonged breathing even smaller amounts of oxygen may have a toxic effect, while even higher oxygen pressures do not cause pathological disturbances with brief breathing. If the pO_2 is significantly increased, then changes in the lungs begin after several hours. Contradictory information is given in the literature concerning the threshold and permissible pO_2 levels in the inhaled air. In rats that had spent time in a pure oxygen environment at a pressure of about 450 mm Hg, disturbances of the pulmonary function, and in some cases, death were observed (Dickerson, 1964, et al.). Campbell (1938) in experiments lasting 33 days did not establish in various animals any harmful effects of pure oxygen at a pressure of 433 mm Hg. According to the data of Brooksby et al. (1966), the threshold level at which oxygen causes functional disturbances in mice and rats lies between 550 and 650 mm Hg.

Interesting data were obtained by Robinson et al. (1966) in experiments on monkeys (Macaca Mulatta) that spent seventeen days in an atmosphere with a high oxygen content--96-98% at pressures of 600, 650, 690, 725 and 760 mm Hg.

Thirty-seven monkeys took part in the experiment, 25 of them experimental and 12 control. As in earlier experiments by other scientists, the authors noted breathing disorders. After 5-7 days the monkeys suffered from progressive depression, they bunched up, became completely inactive and remained in this position until death. The lungs of the monkeys that died were bloodless, reddish-brown or orange in color, with a completely dry surface and hard structure (tunnels in formalin). While in the 12 control monkeys the weight of the lungs did not exceed 1% of the body weight, in the animals which died the lungs weighed from 2.23 to 3.39% of the body weight. In the first 48 hours fatal forms of intercurrent pneumonia were observed. Fluid transudate filled most of the centrally located alveoli. The authors note that during this period death may occur from anoxia. Beginning with the fifth day the alveola boundary cells became significantly larger and young fibroblasts appeared. At a pressure of 600 mm Hg not one monkey died. However, insignificant focal proliferative changes were also observed in these animals. /168

Similar changes in the organs and tissues of different animals were observed by other investigators (Bean, 1945; I. S. Balakhovskiy et al., 1962, and others).

Schaefer (1964) presents somewhat different data in his study. In his opinion, at ground level pressure a 50% mixture of oxygen and nitrogen (which corresponds to a pO_2 in the inhaled air of 360 mm Hg and in the alveolar of 300 mm Hg) is the maximal permissible concentration, after which cardio-pulmonary disorders appear. It is shown that even a single day spent in such a mixture causes a decrease in the vital capacity of the lungs and a gradual slowing of the cardiac rhythm. According to Bert, an oxygen concentration in the arterial blood equal to 30-35% is a fatal concentration.

The limit of unrestricted oxygen tolerance is 100% at an altitude of 3750 m and 60% at ground level (Becker-Freysing, Clamann, 1942).

Berry and Smythe (1962) noted an increase in the nitrogen discharge in the uring of mice that spent 3-4 weeks in a pure oxygen environment at a pressure of 226 and 187 mm Hg. Dejours et al.(1958) established that the intensification of breathing, observed due to impulses passing from the chemoreceptors, as a rule, disappeared with a p_AO_2 above 170 mm Hg, which corresponds to 230 mm Hg pO_2 in the inhaled air.

Another oxygen limit may be established by means of a comparative study of respiration sensitivity to carbon dioxide and oxygen. The experiments with respiration retardation conducted by Hesser (1962) showed that a decrease in the alveolar oxygen pressure below 300 mm Hg increases the sensitivity to carbon dioxide. These data also provided grounds for Schaefer to consider /169 the maximum value of p_AO_2 to be 300 mm Hg.

All this must be considered in analyzing the changes in the physiological reactions of the organism observed under the prolonged influence of oxygen.

As a result of investigations carried out in recent years it has been established that it is possible for man and animals to spend an extensive period of time at a pressure below 425 mm Hg in a pure oxygen atmosphere or an oxygen-nitrogen mixture (Welch, et al.,1961; N. A. Agadzhanyan, A. G. Kuznetsov, 1962; Roth, 1964; A. M. Genin et al., 1967, and others).

A number of authors did not discover any changes in animals that breathed pure oxygen at a pressure of 197 mm Hg for 24 and 51 days (Dines, Hiatt, 1964).

Brooksby et al.(1966) conducted investigations on the influence of the continuous effect of 100% oxygen at a pressure of 450 mm Hg for 64 days on rats (temperature of medium 25°, CO_2 0.3-1%).

The authors determined the weight and growth rate and the amount of food and water taken. After the experiment the heart was punctured and 5-6 cm^2 of blood was removed in order to determine the hematocrit, glutathion and other studies. All animals survived and were killed upon completion of the 64-day experiment.

Tissue sections of the brain, lungs, liver, kidneys, heart, adrenal glands, thymus gland and the gasto-intestinal tract were taken for histological studies; the bone marrow was also analyzed.

The authors note that in the course of the 64-day experiment the animals did not show signs of fatigue, paralysis or dyspnea.

The histological and hematological studies did not reveal any significant differences in the change in reticulocytosis and hemopoiesis in the bone marrow in the control and experimental animals. The glycogen distribution in the cerebrum and cerebellum of the animals, which is an indicator of disturbances in the central nervous system, was normal.

On the basis of these data the authors conclude that a 64-day stay in a pure oxygen atmosphere at a pressure of 450 mm Hg does not have a harmful influence on the organism of rats. In their opinion, a pO_2 level, equal to 450 mm Hg, lies below the peripheral value at which pathological changes arise in rats. The authors /170 also recommend raising the permissible pressure limits to 550 mm Hg.

These materials contradict the data of many authors who in these conditions observed acute pulmonary illness accompanied by hemmorhaging, atelectasis and severe emphysema in different animals (A. G. Zhironkin et al., 1965, Weir et al., 1965, and others).

It seems to us that it is necessary to observe maximum care in selecting an atmosphere for a manned airtight cabin. Therefore, the materials of Brooksby et al. need further careful experimental verification, particularly if we consider that this experiment was conducted on a limited number of animals (in all, 11 rats). These data do not allow one to proceed without risk in similar experments on human beings, much less make practical recommendations with respect to maximal permissible oxygen concentrations.

The life expectancy of animals depends not only on the oxygen content in the gas mixture inhaled, but also on the individual and specie resistance of different members of the animal world to the toxic effects of oxygen. In a gas medium containing 80-90% oxygen, guinea pigs die on the third to fifth day, white rabbits on the third to fourth day, gray rabbits on the fifth to seventh day, rats and dogs on the seventh day, and frogs on the eighth to thirteenth day (G. N. Zilov, 1956, et al.).

In Kaplan's opinion (1967), during an extended stay in a pure oxygen atmosphere in a spacecraft cabin with a total pressure equal to 258 mm Hg there occurs a decrease in the erythrocyte mass in the circulating blood and a gradual development of hemolysis. Interesting data on the permissible oxygen content in the air of airtight cabins are revealed in the experiment of I. S. Balakhovskiy et al. (1962). This study compares data obtained with different partial pressures of oxygen, but identical barometric pressures. At an altitude of 2,000 meters the barometric pressure was 600 mm Hg, therefore rats breathing pure oxygen in these conditions breated it at the same partial pressure as did rats breathing 80% oxygen at "ground level."

The life expectancy of rats breathing pure oxygen with a partial pressure of 600 mm Hg did not exceed one week, while with the same partial pressure of oxygen, but with the addition of 20-30% nitrogen, most rats lived around a month without visible functional disturbances.

It is only possible to explain the results obtained by assuming that nitrogen possesses the ability to protect the organism from the toxic effects of oxygen. The mechanism of this protection, in all probability, consists in increasing lung ventilation during an increase in the partial pressure of oxygen. Since the oxygen consumption remains the same, the alveolar air is deprived of it, and enriched in nitrogen; in this case the partial pressure of oxygen decreases sharply. It is easily seen that in an atmosphere of pure oxygen or in gas mixtures in which the oxygen content is quite high, such a protective mechanism is impossible. /171

Irrespective of the mechanism conjectured, the observed fact of the protective effect of nitrogen in the case of the development of oxygen poisoning has great practical significance.

Although the most pronounced changes in breathing pure oxygen occur in the lungs, other organs are also involved in the pathological process. Here it is important to establish whether the changes in them are secondary, caused by the disturbances in the function of the lungs, or whether oxygen directly acts upon a number of tissues.

Another problem also arises--why does the principal damage occur to the lungs: is it due to the fact that the lungs are subjected first and to the greatest degree to the influence of oxygen, or because they are most vulnerable to this influence? Indicative in this regard are experiments on frogs, in which the respiratory surface is distributed between the lung tissue and the skin. In frogs, both of these tissues are damaged by the action of pure oxygen, from which it follows that the principal damage occurs to the lungs because of their greater contact with the oxygen.

Despite the large number of works dedicated to the study of the influence of high oxygen concentrations on the organism, many problems remain unexplained. Little study has been given to problems dealing with the physiological mechanism of the toxic effect of oxygen and the role of the higher sections of the brain. Information on the threshold levels of the partial pressure of pure oxygen, causing the toxic effect, is insufficient. There /172 is still no single opinion with respect to the maximal permissible oxygen concentration in the air of manned airtight cabins under different barometric pressures, the "safe" periods of stay in such an environment with respect to oxygen poisoning have not been established, and so forth. In the literature available to us we have not been able to find information on the prolonged (more than 30-day) action on the organism of a pure oxygen atmosphere at low barometric pressure. Hence, we conducted research on the effect on the organism of prolonged breathing of high oxygen concentrations in conditions of normal and low atmospheric pressure, in particular, we studied the effect on the organism of animals of a prolonged (100-day) stay in a pure oxygen atmosphere in conditions of low barometric pressure (198 mm Hg, corresponding to an altitude of 10,000 meters).

1. THE NATURE OF THE CHANGE IN THE GAS EXCHANGE DURING AN EXTENDED STAY IN A HYPEROXIC MEDIUM

Since in the case of breathing in an atmosphere with a high oxygen content the greatest changes are observed on the part of the lung tissue, it was important to study the gas exchange dynamics in conditions of a high partial pressure of oxygen. The solution of this problem is important not only for the practical application of oxygen in biology and medicine, but, first of all, for understanding the mechanism of the effect of this factor on the animal and human organism. In spite of the reality of this problem, until recently the literature has contained contradictory information, which to some degree may be the result of the experimental conditions and the methodological approaches used.

Some studies have convincingly proven the reliability of the Douglas-Holden method for correctly evaluating gas exchange during oxygen respiration (N. N. Savitskiy, 1940; A. G. Denbo, Ye. M. Kreps, 1959). A comparative study of the Douglas-Holden method and Krogh methods by means of alternating them in one experiment made it possible to establish that the oxygen consumption determined by the first method was approximately two times greater than that determined according to the second method. Further investigations showed that this difference depends not only on correction for nitrogen, but also on the nitrogen washed out of the tissues of the organism (A. P. Brestkin, A. G. Zhironkin, 1959; A. G. Zhironkin et al., 1965), and also on the nitrogen penetrating through the skin layers into the organism and exhaled by the lungs. /173

The fact of nitrogen diffusion through the human skin during the breathing of oxygen finds substantiation in the investigations of N. M. Petrun' (1960), who discovered an increase in carbon dioxide liberation and oxygen absorption through the skin, especially at high temperature, in the case of persons dressed in rubber suits. The Krogh method is more accurate in these conditions with the exception of the initial period (first 20 to 30 minutes of breathing oxygen), which is characterized by a small increase in the level of oxygen consumption, depending on the additional physical dissolving of oxygen in the blood and tissues and the establishment of equilibrium with intestinal gases (Stadie et al., 1944).

As the investigations of Campbell and Poulton showed (1938), the solubility of oxygen and plasma is more than two times greater than that of nitrogen. Approximately the same relationship is maintained for adipose tissue.

A. G. Zhironkin et al. (1965) did not reveal any significant shifts in the amount of oxygen absorption in people who breathed oxygen for four hours. The partial pressure of carbon dioxide in the alveolar air in this case decreased from 45.2 to 38.7 mm Hg, which, evidently, reflects a weakening of the exchange processes and disturbance of the respiratory function of the blood. A decrease in the vital capacity of the lungs plays a definite role here. Ohlsson (1947) connects the lower vital capacity with expansion of the vessels of the lungs, and also with the sweating of fluid from the capillaries into the lung tissue.

Some authors have found an increase in oxygen absorption in conditions of hyperoxia (Ye. M. Berkovich, L. G. Okhnyanskay, 1952, and others), others a decrease in the gas exchange (G. N. Zilov, 1956, and others). Many investigators have found no changes in the level of oxygen consumption.

There is also contradictory data concerning the nature of changes in the indicators of external respiration (Respiratory Minute Volume (RMV) and its components).

Bert (1878) in experiments on animals first established the /174
dependence of the intensity of gas exchange and the amount of oxygen

contained in an inhaled gas mixture. According to his data, the maximum increase in gas exchange under normal barometric pressure is observed with a 45-48% oxygen content in the inhaled air. In the case of a higher oxygen content the gas exchange and body temperature decrease as a result of the suppression of exchange processes. The data of G. N. Zilov (1956) and others agree with this.

It seems to us that an essential problem of many investigations was the insufficient consideration given to the dynamics of the gas exchange at different stages of a stay by living organisms in conditions of an increased partial pressure of oxygen. In the investigations of A. G. Zhironkin et al. (1965) it is shown that during an extended stay of white mice in a medium with 60 or 90% oxygen content the gas exchange most often is established at levels somewhat exceeding the usual level, and in addition, in the first period of the effect of a hyperoxic medium, the oxygen consumption significantly increased and later somewhat decreased, usually still remaining higher than the original level. Evidently, such dynamics reflect a restructuring of the reduction and oxidation processes which occurs in correspondence with a sharp change in the partial pressure of oxygen in the surrounding medium. As is known, as a result of the effects of hyperoxia there is an increase in the excitability of the respiratory center, in pulmonary ventilation and in the intensity of the reduction and oxidation processes in the tissues.

However, while in the first moment of the effects of hyperoxia pulmonary respiration is stimulated, in the next moment it is inhibited to a certain degree. There is also a retardation of the rate of circulation and a contraction of the peripheral vessels. These reflex-humoral reactions are aimed at limiting the entrance of oxygen into the tissues and at equalizing its pressure in the thorax of the organism. Moreover, hyperoxia suppresses the functioning of the enzyme system. The readjustment of exchange processes which arises under the influence of hyperoxia is also manifested at the moment when animals return to air of normal composition, when a decrease in the oxygen consumption level is noted, followed by a return to the original level. Oxidation processes and the 175
physiological functions connected with them, evidently, are already again restored to the normal level in connection with the decreased partial pressure of oxygen in the surrounding atmosphere.

Transferring animals from an environment with an elevated oxygen content into a normal air environment is analogous in its effect to a transfer from air into the conditions of a hypoxic medium (A. D. Zhironkin et al., 1965; N. A. Agadzhanyan, 1968).

The effects of hypoxia after an extended stay in conditions of an increased partial pressure of oxygen may be looked at as a unique methodological approach making it possible to reveal the fine disturbances in the regulation of exchange processes which cannot be revealed in other conditions.

With the aid of an hypoxic test it is also possible to reveal the early pathology developing during a stay in a hyperoxic medium, that is, to determine the minimum periods in which a decrease in altitude resistance and other functional disturbances are observed without visible pathological changes. The oxygen consumption in animals (rats) in an atmosphere with a high content of this gas (96%) was determined in the investigations of Fabre et al.(1965). The author showed that the oxygen consumption during the first two days of the experiment was significantly greater than in an experiment with a normal atmosphere. On the third day the oxygen consumption decreased. This phenomenon may be connected with several factors, first of all with the fact that motor activity increases in a hyperoxic medium. It has been established that rats are more mobile during the first two days of the effects of pure oxygen than in the same period spent in normal atmospheric conditions. It is assumed that cellular oxidation increases; however, this has still not been proven since the mechanism of enzyme inhibition is as yet insufficiently known and it is difficult to explain the toxicity of oxygen by it.

Thus, from an analysis of the data and the literature it follows that at the present time it has still not been conclusively established what oxygen concentrations in the inhaled air caused an increased level of gas exchange in animals and man and what concentrations act in the opposite way. In addition to the oxygen concentration,the time factor also has independent biological significance. A further more in-depth study of this important /176
physiological factor in the dynamics of spending an extended period of time in conditions of an elevated partial pressure of oxygen will make it possible to more fully reveal the objective picture of the influence of this factor on the oxidation processes in the organism.

In long-term (multiday) experiments on animals it was shown that high oxygen concentrations (89-95%) with a total pressure of 760 mm Hg already by the third day caused a decrease in the oxygen consumption and a lowering of the oxidation and phosphorylization ability of the brain tissue. In addition to the disturbance of the metabolic processes,changes were noted in the immunological properties of the organism, in particular, an abrupt suppression of the biosynthesis of antibodies and of nonspecific resistance to endotoxin. Electrophysiological studies showed that the EEG is dominated by excitation rhythms and that slow high amplitude oscillations are recorded which are similar to epileptoid discharges, characterizing an extreme degree of excitation of the structures of the brain (M. A. Agadzhanyan et al., 1968).

This section of the book presents the results of a study of the function of external respiration, the composition of the alveolar air and the diffusion capacity of the lungs obtained during a long (up to 14 days) stay of subjects in an atmosphere with a high oxygen content at ground level pressure (N. A. Agadzhanyan et al, 1970).

The experiments were conducted in a GBK-63 altitude chamber having a volume of 7.8 cubic meters and specially equipped for extended human occupation. The presence of an external air regeneration system in the chamber made it possible to continuously remove the carbon dioxide and harmful impurities given off by the organism, and also to maintain stably the predetermined parameters of the microclimate. The oxygen feed into the chamber and lock was performed with the aid of rotameters.

Table 34 presents data on the microclimate and gas composition of the atmosphere of the airtight chamber at different periods of the experiment.

The indices of external respiration were studies on an AOOZ-M apparatus, the gas exchange was studied according to Holden's method and alveolar air samples were taken according to Holden's method with subsequent analysis on a VTI-2 apparatus.

The DL index, representing the number of milliliters of gas, passing through the alveolar-capillar membrane per minute with a difference in the partial pressure of gas on both sides of the membrane of 1 mm Hg, is used at the present time for characterizing diffusion conditions. The quantity D_L reflects the total of a /177 number of factors, which together determine the diffusion conditions.

DL_{CO} was measured with the aid of Hobart's diffusion test. The instrument is equipped with a spirograph recording the weight and volume of respiration, an infrared CO-analyzer callibrated for two ranges (0-0.05and 0-0.05% CO),and a Ran and Otis sampler for alveolar air. The subsequent calculation, in addition to the respiration rate and respiratory minute volume, made it possible to determine: the percentage of carbon dioxide absorption, the lung diffusivity DL_{CO} (in ml/min/mm Hg), the CO in the alveolar air, the lung conductance CL_{CO} (in ml/min/mm Hg), and the CO in the inhaled air. At the moment of testing the subjects continued to breathe the same hyperoxic gas mixture, but with the addition of 0.05% CO.

As a result of these investigations it was established that on the second day after the replacement of the usual gas medium by a hyperoxic one (53.8% oxygen),both subjects had the sensation of a lump and slight pain in the chest after deep breathing. On the third day these phenomena ceased.

TABLE 34

MICROCLIMATE IN GAS COMPOSITION OF THE AIR IN THE ALTITUDE CHAMBER DURING DIFFERENT PERIODS OF THE EXPERIMENT (AVERAGE DATA)

Indicators	Experiment No. 1			Experiment No. 2		
	Outset	Period of influence of oxygen	Residual effect	Outset	Period of influence of oxygen	Residual effect
Temperature, °C	23.8	23.4	24.5	24.0	24.0	25.0
Relative humidity,%	70.0	78.3	59.5	58.0	80.0	65.0
Oxygen content, %	20.9	53.8	20.9	20.9	40.2	20.9
Partial pressure of oxygen, mm Hg	159	400	159	150	298	159
Carbon dioxide, %	0.1	0.3	0.1	0.1	0.1	0.1

From Table 35 it is obvious that under the influence of high oxygen concentrations both subjects experienced an increase in the RMV, in the oxygen consumption (the former in the initial stage of below the proper norms) and in the exhalation of carbon dioxide and a decrease in the exhalation reserve volume.

We observed the increase in the oxygen consumption in the first week (N. A. Agadzhanyan et al., 1968) and, in the case of animals, during an extended period (21 days) in a gas medium with a partial pressure of oxygen equal to 400 mm Hg (53% in ground level conditions and 98% at an altitude of 5,000 m). The increase in the gas exchange in these conditions is explained by the increase in the level of oxidation processes. However, this increase, according to the data of many authors, is observed only in the case of oxygen concentrations not exceeding 60% (460 mm Hg). /178

In our investigation the p_AO_2 during the effects of hyperoxia reached 300-345 mm Hg, while the alveolar pCO_2 did not exceed

TABLE 35

THE NATURE OF THE VARIATION IN EXTERNAL RESPIRATION DURING THE TIME OF OBSERVATION (AVERAGE DATA)

Index	Subject M-ov			Subject N-ov		
	period					
	Initial	Hyperoxia	Residual effect	Initial	Hyper-oxia	Residual effect
Respiration rate ,min.	11	9	11	7	9	8
RMV: actually, l/min.	5,05	7,08	5,3	4,2	5,9	5,2
% of proper	71,0	99,5	75,5	70,1	99.5	83,0
Oxygen consumption						
actually ml/min	243	279	238	215	260	215
% of proper	85,4	98	84,8	90,5	109,5	91,5
Carbon dioxide exhaled ml/min	178	231	197	166	217	177
Vital capacity actual ml	4 600	4 338	4 413	5 250	4 750	5012
% of proper	102	97	99	121	112	119
Exhalation reserve volume ml	1 050	865	1 010	1 880	1220	1 390
Maximum pulmonary ventilation:actual l	103	97,5	97,0	112	91,5	111
% of proper	115	112	112	152	124	150

the limits of the background variations.

The data from an investigation of the pulmonary diffusivity are given in Table 36. As is seen from these data, on the fourth day in a hyperoxic gas medium the pulmonary diffusivity of both subjects somewhat decreased in comparison with the initial values, which were somewhat higher than the norm (17/30 ml/min/mm Hg). Toward the end of the period spent in a hyperoxid gas medium the subjects' pulmonary diffusivity tended toward normalization. /179

TABLE 36

PULMONARY DIFFUSIVITY, PERCENTAGE OF CO ABSORPTION, PULMONARY CONDUCTANCE BEFORE, DURING AND AFTER TIME SPENT IN A HYPEROXIC GAS MEDIUM

Subject	Initial Period	Period of Oxygen Influence, Days						After Effect Period, Days		
		1st	3rd	4th	6th	8th	Average	7th	8th	9th
		Preliminary Diffusivity, ml/min/mm Hg								
M-ov	39.2 36.8	34	39.0	32.9	27.2	40.5	34.7±2.5	30.1	28.6	25.9
N-ov	44.1 42.1	52.0	48.2	28.2	36.3	27.6	38.5±4.7	47.8	53.5	42.4
		Absorption, CO %								
M-ov	61.0 58.8	51.2	57.1	50.0	52.8	57.1	53.6±1.4	57.3	51.2	53.8
N-ov	68.0 58.4	66.7	61.7	55.0	56.8	52.6	58.6±2.7	64.9	61.9	60.0
		Pulmonary Conductance ml/min/mm Hg								
M-ov	7.2 8.4	7.4	6.5	5.4	5.3	6.5	6.2±0.4	6.3	7.0	6.0
N-ov	9.0 6.3	8.4	6.0	10.9	6.7	6.7	7.7±0.9	7.5	7.1	8.2

It is necessary to note that changes in the lungs during prolonged breathing in an atmosphere containing high oxygen concentration are mentioned by many authors. Ernsting (1961) discovered a decrease in the pulmonary diffusivity of subjects even after three hours of inhaling pure oxygen at sea level. Helvey (1964) did not establish any decrease in the DL in subjects who spent 14 days at altitudes of 5500, 8200 and 11,100 meters in a pure oxygen atmosphere with a pO_2 equal respectively to 379, 260 and 167 mm Hg. The latter, evidently, was the result of the lower value of pO_2 in the inhaled air. In our experiment the pO_2 was 400 mm Hg. The decrease in DL observed in specific cases was irregular and small in value. The most probable cause of the decrease in DL in the case of breathing high oxygen concentrations consists in the fact that the hemoglobin blocked by oxygen, despite its great affinity for carbon monoxide, cannot combine with it. Therefore, the absorption and diffusivity of the lungs are /180 decreased with respect to CO. Hence, a method of separately determining the true diffusivity of the pulmonary membrane and the volume of blood in the pulmonary capillaries has recently been used.

Thus, complex experimental investigations have shown that an extended stay in a hyperoxic gas medium (pO_2 = 400 mm Hg) leads to a certain increase in the RMV, the oxygen consumption, carbon dioxide exhaled and an increase in the partial pressure of oxygen in the alveolar air. It has been established that a multiday stay by a man in atmosphere containing 53% oxygen pO_2 = 400 mm Hg) causes a shift on the part of the respiratory system. In an atmosphere containing 40% oxygen (pO_2 = 290 mm Hg), even in the case of a prolonged (up to 14 day) stay, no significant changes in the gas exchange and external respiration appear. Thus, these materials show that an atmosphere containing 40% oxygen (pO_2 up to 300 mm Hg) may be used (up to 14 days) in manned airtight compartments, and also in the practice of deep-sea, altitude and clinical medicine.

2. THE INFLUENCE OF HYPEROXIA ON THE BLOOD COAGULATING SYSTEM AND SOME INDICES OF THE IMMUNOREACTIVE CONDITION OF THE ORGANISM

The literature contains only isolated information about the influence of hyperoxia on the blood coagulating system and also on the antibody formation and phagocyte activity of leucocytes (G. S. Kolot, 1965; M. A. Agadzhanyan et al., 1968; L. A. Palosh, 1954, 1970, and others).

The aim of our investigations was to study the coagulating and anticoagulating properties of the blood in the case of an extended stay by a man in hyperoxic conditions. For this we conducted two long-term (up to 25-day) experiments on four subjects and 20 short-term (up to 24-hour) experiments on 20 subjects.

In the first long-term experiment the subjects spent 24 days /181 in an altitude chamber, 10 days of which were spent in an atmosphere containing 54% oxygen (pO_2 = 400 mm Hg). In a second experiment lasting 20 days the subjects spent 14 days breathing a gas mixture containing 40% oxygen (pO_2 = 300 mm Hg). Short term experiments were conducted to determine the threshold oxygen concentration and the time of the onset of changes in the blood coagulating activity in hyperoxic conditions. The subjects spent 24 hours in an atmosphere containing 60 and 94% oxygen (10 experiments each with a pO_2 of 453 and 715 mm Hg respectively). In order to study the influence of hyperoxia on the subjects' blood coagulation processes at different periods of a stay in atmosphere with a high oxygen content the following indices were determined: blood coagulation according to the Mas and Magrot method, blood circulation time according to Duke's method, fibrinogen concentration according to Rutberg's method, the fibrinolytic activity according to Koval'skiy's method, plasma recalcification according to Howell's method, change in the blood coagulation processes according to thromboelastographic data and tabulation of the formal elements of the peripheral blood.

The phagocytic activity of leucocytes was determined with a one-billionth suspension of a daily agar inert culture of golden staphylococcus, strain number 209. The phagocytosis process was evaluated according to the following criteria: number of active phagocytic cells, phagocytic index (average number of absorbed microbodies per phagocyted leukocyte) and the phagocytic capacity of leukocytes (the product of the value of the phagocytic index and the number of leukocytes per cubic millimeter of blood).

The studies showed that under the long-term effects of high oxygen concentration,blood coagulation undergoes regular changes (N. A. Agadzhanyan, B. K. Rybakov, 1971). The nature and degree of these changes depend on the duration of the effect and the partial pressure of oxygen.

Table 37 presents data from a thromboelastographic investigation of blood coagulation processes of subjects under the influence of a gas medium containing 54% oxygen (100 mm Hg).

From these data it is obvious that an increase in the index r, a decrease in the maximum amplitude and a decrease in the elasticity of a blood clot were noted in both subjects on the fifth day in a gas medium containing 54% oxygen. On the tenth day spent in the hyperoxic medium the relaxation time (r) lengthens still more, and the maximum amplitude and blood clot elasticity increase somewhat in comparison with the preceeding investigation, remaining, however, low in comparison with the original levels. The changes in the thromboelastogram, observed in hyperoxic conditions, are shown in Figure 25.

As is known, the maximum amplitude and blood clot elasticity /182 are in direct dependence on the fibrogen concentration in the blood, and also on the number and functional condition of thrombocytes. The number of thrombocytes and their functional activity also influence the formation of thromblastin and thrombin; that is, they change the reaction time (r) on the thromboelastogram (B.A. Kudryashov, 1960). According to our data, the number of thrombocytes on the fifth day in a hyperoxic medium decreased by 47% in the case of subject M-ov and by 44% in the case of N-ov. On the ninth day the number of thrombocytes decreased still more in the case of subject N-ov, and somewhat increased in the case of subject M-ov, but still remained significantly lower in comparison with the initial levels (Table 38).

TABLE 37

THROMBOELASTOGRAM DATA FROM SUBJECTS SPENDING AN EXTENDED PERIOD OF TIME IN AN ATMOSPHERE WITH A HIGH OXYGEN CONCENTRATION (54%)

Subjects	Index	Initial Da a	Period of Influence of Oxygen, Days		Period of Residual Effect, Days		
			5th	10th	2nd	10th	30th
N-ov	r (Reaction time),min.	6.0	8.5	10.5	3.5	9.5	6.5
	K (3rd phase of blood coagulation (min)	4.0	3.5	4.0	1.0	3.5	2.0
	MA (Maximum amplitude)	69.0	45.5	62.5	65.0	55.5	50.0
	E(Blood clot elasticity)	222	83	167	186	125	100
M-ov	r (Reaction time), min.	4.0	6.0	9.5	2.5	11.0	6.5
	K (3rd phase of blood coagulation), min	2.0	2.0	4.5	0.5	3.5	2.0
	MA (Maximum amplitude)	67.0	45.0	57.0	68.0	51.5	51.0
M-ov	E (Blood clot elasticity)	203	82	133	212	106	104

The bleeding time and coagulability, determined before /183
the experiment and after a ten-day stay in a hyperoxic medium, also testify to a decrease in the coagulating activity of the blood. While in the blank test the bleeding time in both subjects was one munute, after a ten-day stay in a gas medium containing 54% oxygen it increased to three minutes. The blood coagulation time increased from nine minutes fifty seconds to fourteen minutes thirty seconds in the case of subject M-ov and from eleven minutes forty seconds to fifteen minutes in subject N-ov.

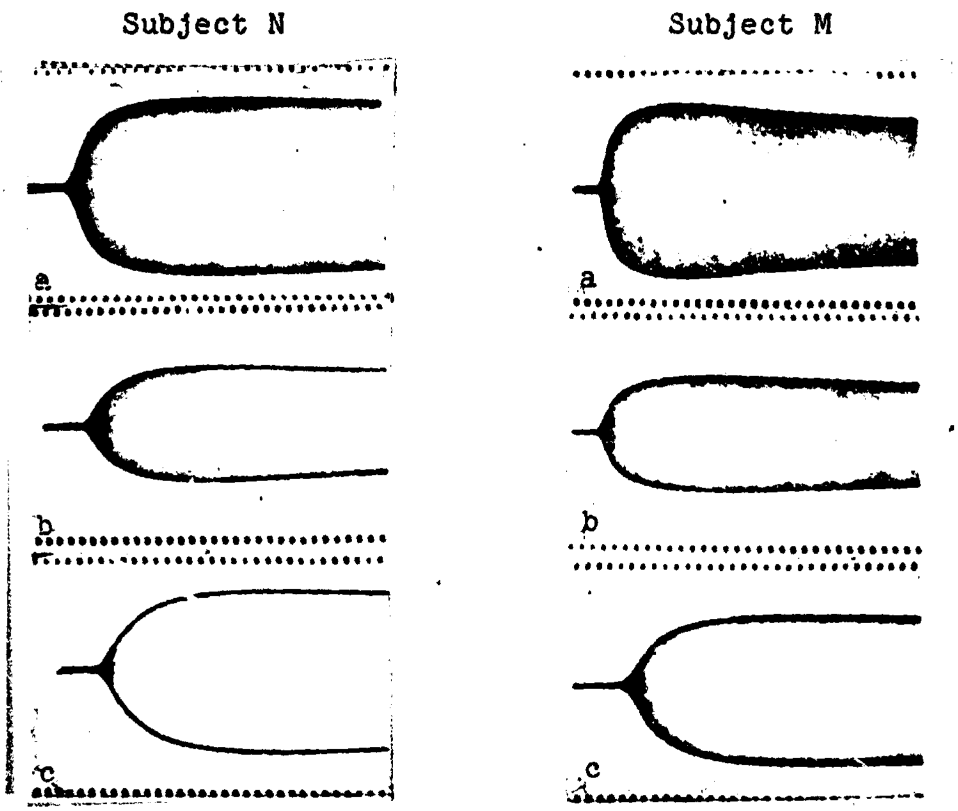

Figure 25. Thromboelastograms of Subjects M-ov and N-ov: a--initial data; b--fifth day in hyperoxic conditions; c--ninth day in hyperoxic conditions.

TABLE 38 /184

NUMBER OF THROMBOCYTES IN THE PERIPHERAL BLOOD OF SUBJECTS IN HYPEROXIC CONDITIONS (54% OXYGEN)

Subjects	Initial Data	Period of Influence of Oxygen, Days		Residual Effect Period, Days			
		5th	9th	2nd	6th	10th	30th
M-y	245,340	130,240	133,240	245,100	262,300	299,880	259,080
N-ov	369,600	206,420	140,360	182,400	279,990	237,220	265,650

The fibrogen concentration and fibrenolitic activity of the blood did not significantly change during the course of the experiment.

TABLE 39

THROMBOELASTOGRAM DATA FROM SUBJECTS DURING AN EXTENDED STAY IN AN ATMOSPHERE WITH A HIGH OXYGEN CONCENTRATION (40%)

Subjects	Index	Initial Data	Period of Influence of Oxygen Days			Period of Residual Effect, Days	
			4th	7th	11th	3rd	16th
N-ov	r (reaction time), min.	7.0	7.5	9.0	2.0	10.0	12.0
	K (third phase of blood coagulation), min	4.0	3.0	5.0	1.5	5.5	7.0
	MA(Maximum amplitude)	56.5	61.0	56.0	72.0	52.0	54.0
	E (Blood clot elasticity)	130	156	127	257	108	117
R-ov	r (reaction time), min.	7.5	8.0	8.5	2.5	7.0	6.5
	K (third phase of blood coagulation), min	4.0	5.0	5.0	2.0	5.0	5.0
	MA (Maximum amplitude)	55,0	46.0	48.0	65.0	54.0	48.0
	E (Blood clot elasticity)	122	85	92	186	119	120

As far as the morphological composition of the peripheral blood is concerned, it is necessary to note a significant decrease in the number of reticulocytes. On the 9th day spent in a hyperoxic medium reticulocytes almost completely disappeared from the peripheral blood. The number of reticulocytes was restored only on the /185
sixth day after the medium with high oxygen concentration was replaced by a normal atmosphere.

Somewhat different data are obtained in the second long-term experiment (Table 39).

As is seen from Table 39, changes in the thromboelastogram indices in the case of both subjects are greatly similar to the changes observed in the preceding experiment. The basic difference is in the degree of the changes. The indices (r) and K increase in proportion to the time spent by the subjects in a hyperoxic medium, which points to the hypocoagulation effect of hyperoxia. The maximum amplitude and blood clot elasticity remained at the initial level in the case of subject N-ov, and in the case of subject R-ov, decreased somewhat.

The changes produced on the eleventh day in the hyperoxic medium are of interest. At this moment, according to the thromboelastogram data, a sharp increase is noted in the coagulation capacity of the blood. The reaction time (r) and the index K decreased in both subjects. The maximum amplitude and blood clot elasticity significantly rose. In the opinion of L. A. Palosh (1970), such changes are caused by "overcompensating" reaction, leading to deviations toward the positive side.

Changes, analogous to those obtained in the preceeding experiment, may also be observed in the examination of the dynamics of the thrombocyte number under the influence of a prolonged stay in a gas medium containing 40% oxygen (Table 40).

TABLE 40

NUMBER OF THROMBOCYTES OF SUBJECTS IN A GAS MEDIUM CONTAINING 40% OXYGEN

Subjects	Initial Data	Period of Influence of Oxygen, Days			Residual Effect Days
		4th	7th	11th	
N-ov	268,800	289,800	228,800	244,480	224,400
R-ov	239,680	222,870	189,980	209,100	221,200

On the seventh day, that is, at the moment of the most pronounced thromboelastographic changes, the number of thrombocytes decreased by 15% in the case of subject N-ov and by 21% in the case of R-ov. /186

It is characteristic that on the eleventh day in a hyperoxic medium, when, according to thromboelastographic data, a clear rise in the blood clotting ability is noted, the number of thrombocytes also rose in both subjects.

The blood circulation time, fibrogen concentration and fibrenolytic activity did not significantly change during the time spent in the chamber.

The blood clotting ability in both subjects was somewhat lower during the entire period spent in the hyperoxic medium and for three days after the transition to a normal atmosphere.

It was extremely important to reveal the nature of the change in the blood clotting activity in the case of relatively brief breathing of higher oxygen concentrations.

Investigations of the blood clotting activity, conducted before and after a one day stay in an atmosphere with a pO_2 of 715 mm Hg, (94% oxygen) showed that a slowing of the coagulation processes is observed in these conditions (Table 41)

TABLE 41

AVERAGE INDICES OF THE COAGULATING AND FIBRENOLYTIC ACTIVITY OF THE BLOOD BEFORE AND AFTER THE EFFECTS OF HYPEROXIA (94% OXYGEN)

Indices	Before Hyperoxia	After Hyperoxia	P
Fibrenogyn concentration, mg%	300	260	<0.001
Plasma reclassification, sec.	120	128	<0.05
Fibrenolytic activity of the blood, min.	173	188	<0.1
Blood circulation time, sec.	150	176	<0.02
Blood coagulation time, min.	9.7	10.8	<0.02
Number of thrombocytes, thousand	333	267	<0.001

The changes in the indices characterizing the speed of coagulating processes, although they do not go beyond the limits of normal physiological fluctuations, are, however, clear, unidirectional and statistically reliable, with the exception of the retardation of the fibrenolytic activity of the blood.

A study of the influence of short-term (24-hour) hyperoxia (60% oxygen) on the coagulating activity of the blood showed that a one-day stay in such an atmosphere does not lead to significant changes in the coagulation processes. /187

The results of investigation of the phagocytic activity of leukocytes testified to a decrease in the phagocytic activity in hyperoxic condition. In comparison with the reference period on the fifth day of a stay in a gas medium containing 54% oxygen it was discovered that all indices and particularly the number of cells capable of phagocytosis decreased. Only on the tenth day of the aftereffect period was there observed a gradual rise in the phagocytic index. Analogous, but less pronounced, changes occurred in an atmosphere containing 40% oxygen (M. V. Markaryan).

Investigation of the content of sialic acids in the blood serum of the subjects revealed that they had increased on the seventh and eleventh days of the action of an atmosphere with a high oxygen content on the organism. In the aftereffect period the sialic acids' concentration in the blood serum decreased almost to the initial value. In addition there was an inverse relationship between the degree of phagocytic activity of leucocytes and the sialic acids' content.

Apparently, an increase in the sialic acids' content in the blood serum against a background of suppression of the phagocytic process can be viewed as a compensatory mechanism intended to fulfill the function of the biological protection of the organism.

Thus, the results of the experiments show that during an extended stay in a hyperoxic gas medium the coagulability of the blood is changed in the direction of hypocoagulation. The degree of change of the coagulating activity of the blood and of the immunoreactive state of the organism depends not only on the pO_2 value, but also on the time spent in a hyperoxic gas medium. The experimental data obtained in our experiments may be used for the scientifically based application of oxygen in clinical practice and for formulating the gas medium to be used in manned airtight compartments.

3. THE INFLUENCE ON THE ORGANISM OF ANIMALS OF A PROLONGED STAY (UP TO 100 DAYS) AT AN ALTITUDE OF 10,000 METERS IN A PURE OXYGEN ATMOSPHERE /188

The creation of an atmosphere containing practically pure oxygen at a low total pressure in a cabin produces significant technical advantages, but runs into serious objections because of the danger of fire, the appearance of decompression disorders, atelectasis of the lungs, irritation of the mucous membranes of the upper respiratory passages and eyes, possible disturbances of the water-salt exchange, blood circulation, etc.

The basic task of this section is to reveal the direct causes of the above-mentioned disorders and to determine the capability of the organism to adapt to an existence in a pure oxygen atmosphere with a low total pressure.

In order to study the functional and structural disturbances which arise during a prolonged stay in a pure oxygen atmosphere, chain motor conditioned reflexes and the composition of the peripheral blood were investigated and the DNA contained in the nuclei of liver cells, the transaminase activity and amount of sugar in the blood were determined. In addition, we conducted X-ray studies of the organs of the chest cavity of experimental animals and observed the dynamics of the salt-water exchange, the weight variation, blood composition and general behavior of the animals.

Several hygenic and bacteriological studies, were also conducted in the course of a 100-day stay in a pure oxygen atmosphere and in particular the dynamics of the change of the basic parameters of the microclimate was continuously monitored and the contamination of the cabin air was determined.

The experiments were conducted on rats in an SBK-48M altitude chamber specially equipped for conducting long-term studies in conditions of low barometric pressure, corresponding to an altitude of 10,000 meters (198 mm Hg).

In order to avoid decompression disorders and to create a high level of partial oxygen pressure in the chamber the animals were gradually raised to the given altitude while the chamber was ventilated with pure oxygen.

The temperature, humidity, oxygen and carbon dioxide content in the chamber during the course of the experiment did not exceed the predetermined variations (pO_2 = 190-195 mm Hg; pCO_2 = 0.1-0.4%; temperature 21±2°; relative humidity 60-70%). The operating principle of the life-support system is described in Chapter III . The feed and water regime was identical for all animals. /189

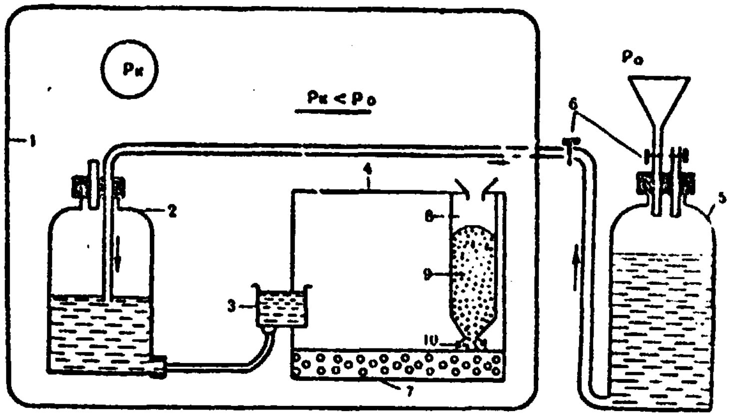

Fig. 26. Diagram of Water and Food Supply. 1 - Altitude Chamber; 2 - Receiving-Distributing Bottle; 3 - Drinking Dish; 4 - Cage; 5 - Water Tank; 6 - Control Valves; 7 - Silica Gel; 8 - Food Hopper; 9 - Food; 10 - Food Trough.

The rats were given feed consisting of two-thirds wheat and one-third oats. Once every five-seven days the animals received bread, meat and multiple-vitamins.

The cages were equipped with external tanks for water connected with a drinking dish inside the cage. Water was added in proportion to consumption from a tank located outside the chamber. The water was conserved by the addition of silver nitrate in the amount of 0.05 mg per liter. A diagram of the system for providing the animals with water and food is shown in Fig. 26.

In all, 203 white rats were observed, of which 148 were subjected to the effects of pure oxygen at an altitude of 10,000 meters and 55 rats were kept at normal atmospheric pressure and served as the standard.

Results of an Investigation of Higher Nervous Activity

Numerous investigations previously had shown that in conditions of a rarefied atmosphere the basic controlling factor causing disturbance of higher nervous activity is oxygen deficiency.

We did not find any articles in which the selective effect on the central nervous system of the same factor of rarefaction with sufficient provision

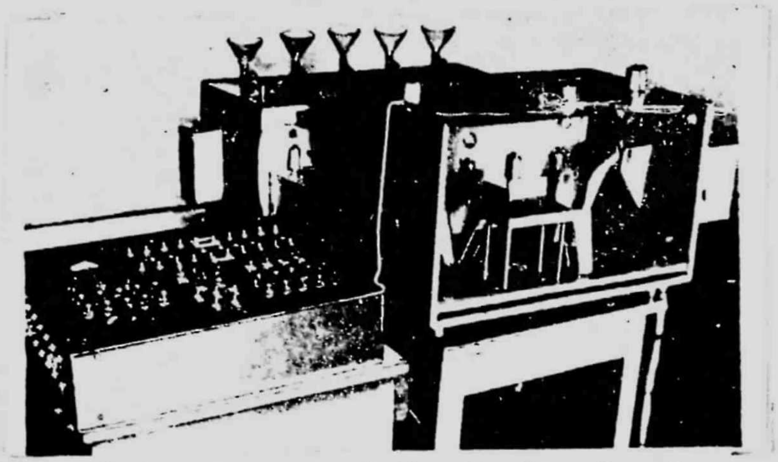

Fig. 27. General Appearance of the Device for Investigating Chain Conditioned Motor Reflexes.

of the organism with oxygen, particularly with regard to longterm effect, had been investigated.

The method of chain conditioned motor reflexes, developed in the laboratory of L. G. Voronin, was used for studying the higher nervous activity of rats. An automatic electrical device was developed and prepared to suit the characteristics of an investigation in conditions of a rarefied and changed gas medium (G.P. Doronin, B.A. Miloslavov).

The basic units of the device (Fig. 27) are a working chamber, a compartment for keeping the animals separately, which consists of five boxes, a control panel, and a recording device for registering the motor response reactions of the animals. Light stimulators and contact areas are located within the chamber. A system of contacts operates when the rats move onto a contact area, which switches on conditioned stimuli in a specific sequence.

On the side wall of the chamber there is an automatic feeding trough which operates when the animals correctly perform a sequence of conditioned reflex motions.

The working chamber communicates through a system of holes with the five boxes in which the rats are held during the entire experiment, obtaining water and a controlled amount of food. /191
Remote control from a movable portable panel made it possible to use the device in long-term experiments not only in ground conditions, but also at low barometric pressure (at altitudes of 3000-10,000 meters).

The conditioned reflex activity was evaluated according to the latent period and the rate of response reactions to stimuli, and also according to the time the animals stayed on the contact areas.

After development and reinforcement of conditioned reflexes a background was established at normal atmospheric pressure. Each experiment used a stereotype, composed of 18 positive chain stimuli and 6 conditioned inhibiting stimuli.

During the long-time experiment, each animal was given from 671 to 776 chain stimuli, and in 98-99.5% of the cases a clear reaction was noted, representing a chain of food-procuring conditioned motor reflexes.

During the first days spent at an altitude of 10,000 meters the rats displayed a certain intensification of the orientation reaction, an increase in general motor activity and an increase in the number of intersignal reactions.

Most of the applications of a chain stimulus were accompanied by a clear chain motor reflex.

Loss of individual links of the chain reflex during the course of the first month of the experiment was noted in 24 cases, during the second month -- in 13 cases, and during the third month -- in 10 cases. Only isolated cases of the loss of reactions to the second stimulus of the chain occurred in the animals. The third link of the chain was preserved in 100% of the cases.

The results obtained show that during a long term (100-day) stay at an altitude of 10,000 meters and normal oxygen supply the time taken for performing all links of the chain and the entire chain motor reflex did not significantly change. The first link of the chain, in response to the first "triggering" stimulus, is performed especially accurately.

The constancy in performing the chain motor reflex during the entire experiment indicates that the analysis and synthesis of a chain of food-procuring motions are not disturbed in a pure oxygen atmosphere with a rarefaction corresponding to an altitude of 10,000 meters. In studying conditioned disinhibition in specific cases, inadequate reactions were observed when the signal value of an additional component of the conditioned inhibition was not perceived and the animal performed a motion corresponding to the positive chain. Sometimes switching on a conditioned inhibition lead to a state usually observed with the action of a differentiation stimulus. The animal in these cases remained /192 in the original pose or moved away from the stimulus.

Thus, the results of an investigation of chain conditioned motor reflexes showed that in the case of an extended stay in conditions of low barometric pressure corresponding to an altitude of 10,000 meters in a pure oxygen atmosphere chain, conditioned motor reflexes completely preserved their structure and the time characteristics of individual links of the chain. Conditioned disinhibition proved to be the weakest link. The increase in the number of inadequate and negative reactions in the first period of the experiment is the consequence of the relative weakening of the process of internal inhibition.

The nature of response reactions to the use of a conditioned inhibiting stimulus normalizes in proportion to the time spent by the animals in a pure oxygen atmosphere under a total pressure of 198 mm Hg. This shows that in the process of adaptation to the effects of low barometric pressure, a normal relationship of the basic nervous processes is restored.

STUDY OF CERTAIN INDICES OF THE WATER-SALT EXCHANGE, PERIPHERAL BLOOD COMPOSITION AND DNA DISTRIBUTION IN LIVER CELL NUCLEII

As is known, all the physical-chemical processes in the organism take place with the participation of water. Metabolism, heat regulation, maintenance of a constant osmotic pressure and acid-base equilibrium -- all these physiological reactions take place with the active participation of water and salts.

Water constitutes up to 60-70% of body weight, approximately 50-70% of the water is found within the cells, extracellular water comprises 16-20% and up to 15% of the water occurs in the intertissue fluid.

The amount of water entering and leaving the organism may fluctuate quite significantly and depends on the temperature of the environment, the partial pressure of gases in the air, the humidity, barometric pressure, etc.

We determined the hydrophilic nature of the tissues and the blood hydration of the weight method. The tissue and blood sample taken were dried to a constant weight at a temperature of 100-115°. /193

The chloride content of the urine was determined by direct titration according to Mohr's method. The blood chlorides, after their extraction with 92% alcohol, were titrated with a 0.1 N solution of silver nitrate.

Changes in the weight of the experimental and control rats may be judged according to the data in Tables 42 and 43.

TABLE 42

WEIGHT CHANGE OF CONTROL RATS

No. of rat	Wt. before experiment, g	Wt. of rat during experiment, g											
		15th day		40th day		54th day		64th day		85th day		98th day	
		Wt.	Wt. balance	Wt.	Wt. balance	Wt.	Wt. balance	Wt.	Wt. balance	Wt.	Wt. balance	Wt.	Wt. balance
97	261	265	+4	275	+14	270	+9	272	+11	290	+29	303	+42
98	246	258	+12	270	+24	270	+24	265	+19	290	+44	307	+51
99	185	193	+8	205	+20	220	+35	230	+45	—	—	—	—
100	243	220	—23	214	+29	215	—28	242	—1	—	—	—	—
101	225	237	+12	249	+24	250	+25	255	+30	275	+50	289	+64
102	245	250	+5	275	+30	270	+25	265	+20	267	+22	281	+36
103	248	254	+6	260	+12	267	+19	270	+22	—	—	—	—
104	258	270	+12	280	+22	285	+27	292	+34	—	—	—	—
Mean for group	239	243	+4	253	+14	256	+17	262	+23	280	+41	295	+56

The data presented show that a significant weight loss was observed in the experimental rats. By the fifteenth day spent at high altitude in six of ten rats the body weight balance was negative; it was positive in three, and in one remained unchanged. By the end of the first month, in all ten experimental rats the weight balance was negative. Later, some increase in weight was noted in nine animals, not reaching however; the initial level by the 55th day, and in only one rat (No. 43) was the balance positive. By the 85th day the weight balance in all rats became positive.

The weight loss might be explained by a protein deficiency in the food and the increase in water losses by the effects of staying at high altitude. However, in our experiments in the con- /194 trol animals which also received the same food ration, the weight balance during the entire period of investigation was positive. Consequently, the negative weight balance is not caused by protein deficiency, but by the increase in water losses by the tissues of the organism, caused by the influence of the rarefied air of the altitude chamber.

TABLE 43

WEIGHT CHANGE OF EXPERIMENTAL RATS

No. of rat	Wt. before experiment, g	Wt. of rats during experiment, g											
		15 th day		27th day		55th day		62nd day		85th day		98th day	
		Wt.	Wt. balance	Wt.	Wt. balance	Wt.	Wt. balance	Wt.	Wt. balance	Wt.	Wt. balance	Wt.	Wt. balance
41	215	160	−55	162	−53	182	−33	210	−5	278	+63	288	+73
42	230	223	−7	175	−55	187	−43	180	−50	228	−2	238	+8
43	160	155	−5	110	−50	187	+27	223	+63	268	+108	283	+123
44	200	207	+7	153	−47	162	−38	—	—	—	—	—	—
45	195	197	+2	140	−55	145	−50	—	—	—	—	—	—
46	220	220	0	171	−49	192	−28	230	+10	305	+85	315	+95
47	193	190	−3	145	−48	167	−26	—	—	—	—	—	—
48	215	191	−21	131	−84	174	−41	215	0	281	+66	268	+53
48	194	202	+8	141	−53	180	−14	207	+13	278	+84	275	+81
50	178	176	−2	116	−62	137	−41	—	—	—	—	—	—
Mean for group	200	192	−8	141	−55	172	−30	211	+5	275	+66	278	+72

In the experiment by Swann and Collings (1943) conducted on rats in an altitude chamber at an altitude of 5400 m in conditions of oxygen deficiency, a significant weight loss in proportion to the time spent at high altitude was also noted. The authors connected the decrease in weight of the experimental rats with an increase in the water loss through the lungs (due to hyperventilation) and skin at high altitude.

Observation of the weight change of the experimental and control rats also made it possible for us to note two other facts we feel are interesting. Intensive weight loss was observed only during the first 30-40 days the animals spent at high altitudes. By the 55th day the weight begins to increase, although its balance still remains negative. Later, in the second half of the experiment, the weight increase of the experimental rats becomes more pronounced in comparison with the control rats and, if we take into consideration that the increase in the weight /195
of the experimental rats basically takes place during the last 30 to 35 days of the experiment, the difference in the weight increase of the experimental and control rats becomes still more significant.

We believe that adaptation of the organism to the new conditions occurs during the first stage (30-40 days) of the stay in conditions of low barometric pressure and that when it begins, physiological functions are relatively normalized. The data obtained by X-ray study of the organs of the chest cavity also testified to this. /195

X-ray analysis showed that a number of reversible functional and morphological changes in the organs of the chest cavity appear when breathing pure oxygen at an altitude of 10,000 meters: the dimensions of the chest cavity decrease, the transparency of the pulmonary margins is lowered, the pulmonary figure and solitary or multiple focal darkenings in the lungs are intensified and the dimensions of the heart shadow increase. All this points to the development of atelectases in the lungs and stagnation phenomena in the vessels of pulmonary circulation. No significant deviations appeared in the functional activity of the diaphragm. The indicated changes were of a reversible functional nature and were more pronounced in the first two days spent at an altitude of 10,000 meters.

These data agree with the results of pathomorphological investigations. After the animals spent two days at an altitude of 10,000 meters in a pure oxygen atmosphere the parenchyma of the lungs in the rhizosphere proved to be partially collapsed. A thickening of the interalveolar septa was also noted. The lungs of rats, subjected to the experiment for more than two months, appeared the same as the lungs of the control animals.

A study of the structure of the blood and lymphatic vessels, the elastic body of collagen fibers and the argyrophilic membranes of the lungs of the experimental animals did not reveal any serious damage. All this leads us to consider that the collapse of pulmonary tissue in the conditions of our experiment is of a reversible nature and does not lead to an insufficiency of blood oxygenation. Probably, the pulmonary parenchyma gradually adjusts in proportion to the time spent in a pure oxygen atmosphere at a total pressure of 198 mm Hg and in proportion to the adaptation to these conditions.

The possibility is not excluded that the hormonal regulation of the metabolism, in particular of the protein metabolism, is disturbed at the end of the experiment, as a consequence of which a more intensive increase in weight is observed in the experimental rats in comparison with the control rats. If the weight loss is attributed to moisture losses, then it may be assumed that this should be reflected in the water content in the tissues. /196

TABLE 44

WATER CONTENT IN THE TISSUES OF EXPERIMENTAL AND CONTROL RATS (IN %) DURING DIFFERENT PERIODS OF THE EXPERIMENT

Day of Investigation	Brain		Liver		Kidneys		Lungs		Muscles		Skin		Blood
	Experiment	Control	Experiment	Control	Experiment	Control	Experiment	Control	Experiment	Control	Experiment	Control	Experiment
2nd	77.5	79,2	76,4	71,3	77,8	74.8	78.2	80,8	74.7	76.7	61.2	63.2	84.5
8-th	78,4	79,1	76,9	72,8	77,3	71,8	80.5	77,3	74.6	74.8	56,0	61.3	86,2
15-th	79,4	82,2	75,5	72.9	73.8	75,1	79.5	77,3	71.7	74,5	37.1	66.6	85.5
30-th	86.6	83.7	73,6	71.1	78,0	76,2	78.4	77,9	76.2	73,1	64.9	64.9	80.0
45-th	85,8	84,7	75,5	76,8	77,3	74,3	77.8	81,3	76.5	76,1	63,9	64,5	80.1
60-th	82.7	81.6	75,1	75,7	76,1	75.1	78.8	80.1	75.3	74,3	66.8	65.7	85,1

Van Lier's study (1947) indicates some tissue dehydration during a stay in conditions of low barometric pressure. In the first place it is possible to expect water loss by such tissues as the skin, muscles, and liver, usually considered to be a reservoir of fluid in the organism.

The research conducted showed that the decrease in the water content of the skin of experimental animals coincided in time with the decrease in body weight of the animals. These changes were most clearly pronounced toward the 15th day of the experiment, when the water content decreases almost by half (Table 44).

The water loss by the blood was insignificant and was most clearly manifested on the 30th day of the experiment. The number of erythrocytes, a change in which may influence the amount of dry residue in the blood, remains practically at the same level. /197

As was already mentioned, the water exchange depends on many factors determining the state and distribution of water in the organism. Salts, particularly sodium chloride, are one of these factors which enable water to be bound with tissue colloids and blood to be enriched with water. The relation between salt exchange and water exchange is so intimate that the water-salt exchange is usually considered as a unit.

In the blood and tissue fluids sodium chloride occurs in the dissociated state in the form of sodium and chlorine ions.

In case of an increase of the content of sodium ions the ability of colloids to swell is increased and the amount of bone marrow increases several times.

We examined the chloride content in the 66 rats not subjected to the effects of low barometric pressure (control experiments). Data from a statistical analysis are given in Table 45.

TABLE 45

CHLORIDE CONTENT IN THE BLOOD OF RATS (IN MG %)

Statistical index	Before experiment	During experiment (days)			
		2nd	15th	43rd	85th
M	542	483	513	501	497
±m	±3.5	±9.6	±11.6	±9.1	±5.8
n	66	8	10	9	5
P[1]		<0.01	<0.01	<0.01	<0.01

[1]Reliability (P) is calculated in relation to data obtained before the experiment.

A certain wavelike nature of variations in the chloride content of the blood was noted during the process of the experiment, although a general tendency to decrease was quite distinctly manifested.

During the first 15 days, in 7 of the 10 experimental rats the chloride content of the blood decreased and only in three animals did the chloride content either not change or even increase somewhat.

As a rule, a decrease in the chloride content was also observed in the following periods. /198

An additional series of experiments during which the chloride content in the blood and urine was studied simultaneously on five rats, was set up in order to make more precise the data on the change in chloride content for an extended stay at high altitudes. The data obtained from this group of animals is given in Table 46.

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TABLE 46

THE CHLORIDE CONTENT IN THE BLOOD AND EXCRETION WITH THE URINE IN TEST RATS

No. of rat	Day of experiment	Amt. of urine, ml	Amt. of NaCl		
			In daily urine mg	In ml urine, mg%	In blood mg%
172	2-nd	0,5	2,2	872	485,0[1]
	9-th	0,2	—	—	467,0
	15-th	1,2	5,5	585	546,8
	30-th	1,5	11,4	1 521	—
173	2-nd	3,0	8,4	559	514,8
	9-th	6,5	25,7	790	492,7[1]
	15-th	7,6	45,1	1 211	493,2[1]
	30-th	0,5	2,3	1 872	421,2[1]
174	2-nd	2,0	9,8	977	479,7[1]
	9-th	2,0	9,9	989	461,4[1]
	15-th	3,5	19,5	1 112	521,9
	30-th	9,5	29,7	[illegible]	491,4[1]
175	2-nd	0,1	—	—	479,2
	9-th	0,3	—	—	481,1[1]
	15-th	1,2	5,5	585	499,0
	30-th	6,5	23,0	707	476,7[1]
176	2-th	[illegible]	10,6	1 416	491,4
	9-th	0,2	—	—	459,0[1]
	15-th	2,0	13,5	1 346	560,0
	30-th	6,0	26,9	896	468,0

[1] Statistically reliable decrease of chlorides in blood ($P<0.05$)

It is obvious from Table 46 that together with a decrease in the chloride content in the blood there is an increase in chloride elimination with the urine. Not only did the daily amount of chlorides eliminated rise, but also their concentration in the urine increased. The daily diuresis of the rats (after decreasing in the first half of the experiment) gradually increased in proportion to the time spent at high altitude. /199

Most authors connect the disturbance of the water balance at high altitudes with losses of moisture through the lungs. However, this situation could only occur in the case of hypoxia, when pulmonary ventilation increased. In the given experiment the oxygen supply was sufficient and the organism was influenced only by the factor of atmospheric rarefaction. Therefore, the disturbance in the water-salt exchange in these conditions, evidently, was caused by other mechanisms.

It may be assumed that with decreasing barometric pressure the total loss of moisture from the body surface will increase due to imperceptible perspiration (Ya. Kuno, 1961).

We did not find in the literature any direct data on the influence of low barometric pressure on an increase in fluid loss by the organism. However, it is well known that under such conditions evaporation increases as a result of a decrease in collisions between evaporating molecules and molecules of a gas whose concentration is reduced due to rarefaction. The direct measurements of vapor evaporation, which were made by A.I. Shaposhnikov and B.S. Perepletchikova in our experiment, showed that the total amount of fluid evaporated from one and the same surface in the case of normal and low barometric pressure is different (Table 47).

TABLE 47

EVAPORATION OF LIQUID (in g) IN CONDITIONS OF NORMAL AND REDUCED BAROMETRIC PRESSURE

Index	"Earth"	10,000 m altitude
Temperature ,C	20—23	20—25
Humidity , %	45—65	42—60
Amount of liquid evaporated ,g	1 125	2 150
Evaporability ,g/cm^3	2.3	4.4

The problem of chloride loss by the organism is very interesting. Is it the result of a disturbance of the reabsorption properties of the renal canal apparatus or is it the consequence of moisture lost by the organism? We are inclined to consider chloride loss as an attempt by the organism to establish electrolytic and salt equilibrium of body fluids. Further special investigations are necessary for a conclusive solution of this problem, in particular, for revealing the intimate mechanism controlling the water-salt exchange of the organism in conditions of low barometric pressure. /200

In our experiments we also conducted hematological investigations with an extended stay by animals in conditions of low barometric pressure and a normal oxygen content in the inhaled air (Yu. P. Bizin).

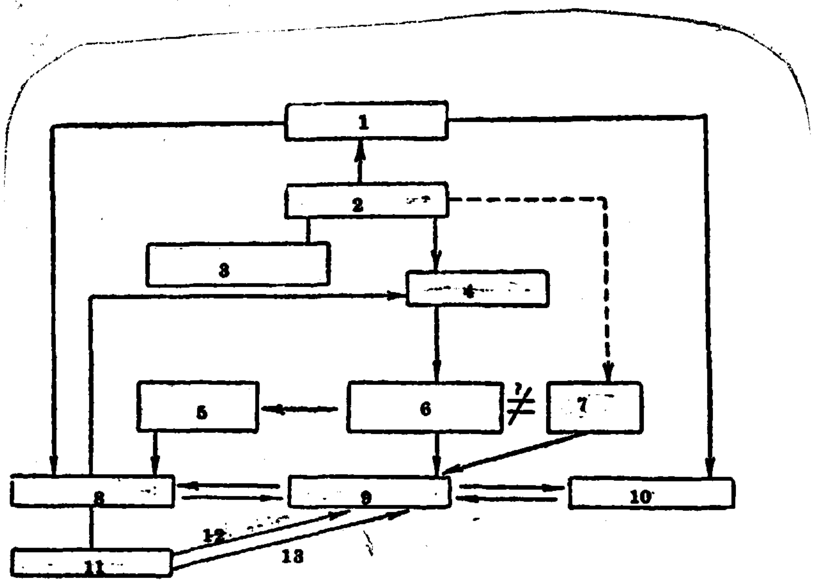
Two periods of high altitude polycyphemia are usually considered: (1) the appearance in a large quantity of only mature forms of erythrocytes and (2) the increased appearance of young erythrocytes from the bone marrow.

Until recently the opinion was widely held in physiology and hematology that hypoxia causes stimulation of erythropoiesis in the bone marrow. The degree of oxygen saturation of the bone marrow was recognized as the universal factor controlling erythropoiesis.

Experimental data recently accumulated indicate that the bone marrow is not stimulated by hypoxia, for example after blood loss or in conditions of a rarified atmosphere, but on the contrary, it is suppressed. More precisely, hypoxia does not stimulate erythropoiesis directly, but through an intermediate link--erythopoietins (Ya. G. Uzhanskiy, 1968; V. I. Voytkevich, 1968, 1969). Erythropoietins are found in various organs, but the removal of these organs does not deprive the organism of the ability to form them.

The physiological mechanism of the influence of erythropoietins upon erythropoiesis has been sufficiently studied in the laboratory of Ya. G. Uzhanskiy (1968). It has been established that as a result of hypoxia not only the function of blood circulation and respiration but also of erythropoiesis changes in reflex fashion (Fig. 28). The increase in the erythropoietic activity of the blood serum observed here, in the opinion of Ya. G. Uzhanskiy, may depend on the increase in the amount both of erythropoietins in the blood, and also of the biologically active products of the decay of erythrocytes or other metabolic products.

C-3



Key: 1 - Central nervous system; 2 - Hypoxia; 3 - Catabolic metabolic products; 4 - Erythrodiuresis; 5 - Angeal tenzenase; 6 - Products of erythro decay; 7 - Erythro poeitins; 8 - Circulation; 9 - Erythropoeises 10 - Respiration; 11 - Blood reservoir; 12 - Erythropoeises; 13 - Products of erythro decay.

Fig. 28. Diagram of erythropoieses regulation (according to Ya. G. Uzhanskiy).

Two groups of animals were investigated in order to explain the influence on the blood system of an extended stay in a pure oxygen atmosphere at low barometric pressure: one group for 100 days was kept at an "altitude" of 10,000 m (pressure 193 mm Hg, oxygen content 98%); the second group was kept in conditions of normal barometric pressure.

Before the experiment no significant deviations from the norm in the blood picture were observed in any rat. During the period of the experiment the most significant changes occurred on the part of the red blood. Already on the third day after the ascent to "high altitude," in two of the experimental rats the amount of hemoglobin increased by 2.3 g%. The number of erythrocytes increased insignificantly. These factors began to increase particularly noticeably from the fourteenth day of the experiment. Thus, the amount of hemoglobin increased on the average by 3.4 g%, which corresponded to 120% of the initial level. The amount of erythrocytes increased on the average by 2,200,000, or by 134% in comparison with the initial level.

The erythrocyte and hemoglobin content of the blood of the experimental rat remained elevated up to the fortieth day and only in the second half of the experiment did a tendency toward normalization of these factors appear. Complete restoration set in on the 58th day. Later toward the end of the experiment the amount of erythrocytes and hemoglobin remained at the initial level. /202

Simultaneously with an increase in the amount of hemoglobin and erythrocytes in all experimental rats the amount of reticulocytes in the peripheral blood increased. On the third day of the experiment it increased on the average of from 3% to 5%. The maximum increase in the number of reticulocytes to 6% was noted on the fourteenth day of the experiment and coincided with the erythrocytosis observed in the rats. Subsequently the number of reticulocytes somewhat decreased.

In the second half of the experiment the number of reticulocytes again increased to 6% in the experimental rat, and this level was preserved until the end of the experiment. The increased content of reticulocytes in the blood was maintained even after the end of the experiment and exceeded the initial level by 1.8-2%. In the control rat during the entire period of observation the reiticulocyte content did not significantly change.

The reticulocyte content in the blood is an indicator of the intensity of medullary hemopoiesis, more precisely, of red cell hemopoiesis. Therefore, reticulocytosis in the rats during the experiment indicate stimulation of medullary hemopoiesis. This is also indicated by the a earance of immature forms of erythrocytes--polychromatophiles and normoblasts in the peripheral blood of the rats. Thus, a prolonged stay in conditions of low barometric pressure leads to activation of the erythropoietic function of the blood marrow.

The erythrocytosis and reticulocytosis observed and the appearance of polychromatophiles normoblasts in the blood confirm to some degree the hypothesis of the presence of two periods of "high-altitude" polycythemia.

The amount of thrombocytes increased insignificantly on the fourteenthday of the experiment (from 450,000 to 580,000). Later it decreased to the initial values and remainedat this level during the entire experiment. In the control rat the amount of thrombocytes during the entire period of observation was within the limits of the physiological norm.

Changes on the part of white blood cells were less pronounced. /203
In the experimental rats the amount of leukocytes and eosinophiles

increased slightly in comparison with the initial data. After the experiment the indices rapidly normalized.

In all experimental and control rats the relative amount of lymphocytes before the experiment was approximately 54-60%, and of neutrophiles--30-38%. Since rats have a lymphocytic type of blood formation, this ratio is normal.

During the experiment a relative lymphcytosis was observed in the test animals which exceeded the limits of the initial level and fluctuated from 65-85%. In the remaining periods of the investigation absolute lymphocytosis also took place, which was accompanied by relative neutropenia (to 15-25%).

As far as cytological changes in the blood are concerned, it is possible to note only an insignificant plasmatizationof mononuclears in the experimental rat during different periods of the experiment. In the control rats no significant deviations were noted in the leukocytic formula.

Thus, the investigations showed that the changes on the part of most hematological factors are reversible and disappear after the end of the experiment.

Data from an investigation of the DNA content in liver cell nuclei are also of interest. As is known, the DNA content in an individual cell is an integral indicator of its functional state. By studying the DNA distribution in a sufficiently large number of cells we obtain the possibility of evaluating the general state of the organ or tissue.

Here we limited our investigation to a determination of the DNA in specific parenchymatous cells--hepatocytes, which are the basic anatomical and functional population of the tissue elements of this organ.

The distribution of the DNA content in the nuclei of the cells under consideration was studied in our experiments by Ye. Ye. Simonov on the basis of photometric changes in contact preparations stained according to Fel'gen's method. Photometry was performed on a device especially assembled for these purposes with photoelectric recording of absorption. The DNA content in the parenchymatous liver cell was calculated by means of comparing the data from photometric measurement of "standard" nuclei and the nuclei of small lymphocytes, the average DNA content in which is 6 pg. (pigment granules).

Cytophotometric investigation of the parenchymatous cells of the control animals showed that the DNA content in individual nuclei of this cellular population fluctuates within the range 4-5 to 48 pg and higher, on the average amounting to 17.8 pg per "average" nucleus (cell). As a result of an analysis of variation curves of the amount of DNA in individual nuclei of the cells investigated (2200) it was established that most of them (73%) were produced by nuclei with a DNA content exceeding 14 pg, while nuclei with a content of 10-14 and less than 10 pg DNA, total around 27% (22.9% and 4.1% respectively). /204

An analysis of the DNA distribution in the nuclei of the parenchymatous liver cells of the experimental animals (6,000 cells were studied) revealed that even in this case there is observed approximately the same scattering of values of the DNA content, as in the control (Table 48); however in the experimental animals the quantitative relationships of the groups of cells with a DNA content of more than 14 pg, 10-14 pg and less than 10 pg proved to be somewhat different, oust as, on the other hand, the average DNA content calculated per "average" cell (nucleus) was also somewhat different.

TABLE 48

QUANTITATIVE RELATIONSHIPS OF CELLS WITH VARIOUS DNA CONTENT AND THE LIVER OF CONTROL AND EXPERIMENTAL ANIMALS

Conditions	Average DNA content in nucleus, pg	Percent of cells with DNA content		
		Up to 10 pg	10-14 pg	More than 14 pg
Control	17.8	4.1	22.9	73.0
Experiment	16.6	8.0	34.0	58.0

From Table 48 it is obvious that the change in the quantitative relationship of the indicated groups of cells is of a dual nature and is expressed by an increase in the number of cells with a DNA content of less than 14 pg and a decrease in the number of cells with a DNA content of more than 14 pg.

If we bear in mind that in the case of normal adult rats /205
the growth of liver tissue is primarily performed by increasing the mass of individual cells (the endomitotic type of growth, in which cell division does not occur), then the data we obtained

(increase in the number of cells with lower DNA content) may be considered to be an indication of a certain suppression of this process.

A study of the inclusion of thymidine-C^{14} in the liver tissue showed that this suppression is temporary, since after the end of the experiment the nature of the inclusion of thymidine -C^{14} in the liver of the experimental rats practically did not differ from that in the case of the control rats. Data on the activity of aminotransferases are interesting in this connection. These enzymes perform the transfer of amino groups from amino acids to keto acids, as a result of which new amino acids are formed. An increase in the activity of aspartates and alanine aminotransferases may indicate the development of destructive processes in the tissues and, in particular, liver damage.

The aminotransferase activity was determined in two groups of animals, of which one was kept at an altitude of 10,000 m for 5 days, and the other--98 days (Table 49).

TABLE 49

TRANSAMINASE ACTIVITY IN EXPERIMENTAL RATS (UNITS)

No. of rats	5-day experiment			No. of rats	98-day experiment		
	AGT*	ALT**	AGT/ALT		AGT	ALT	ACT/ALT
1	182	49	3.7	7	169	48	3.5
2	182	65	2.8	8	143	42	3.4
3	240	72	3.3	9	195	81	2.4
4	227	68	3.3	10	213	126	1.8
5	159	51	3.1	11	124	42	2.9
6	218	82	2.6	12	169	62	2.7
Average	201	63	3.2		166	66	2.5

A comparison of the data in Table 49 and the results of determinations of transaminase activity in control animals (transaminase activity in their blood fluctuating within the range: AGT--from 124 to 209 units, ALT--from 42 to 98 units) indicates that a prolonged stay at low barometric pressure does not significantly influence these indicators, although in the animals of the second group there is a more noticeable tendency toward a decrease.

Data from an investigation of blood sugar also indicate /206
the absence of signicant disturbances in liver function. In experimental animals subjected to the experiment for 40 and 98

*Aspartic transaminase
**Alanine transaminase

days, the blood sugar content fluctuates between 94 and 150 mg percent and is almost the same as in the control rats (94-148 mg percent).

Thus, animals that spent an extended period of time (100 days) in conditions of low barometric pressure, corresponding to an altitude of 10,000 m (198 mm hg) in a pure oxygen atmosphere, displayed no changes which were pronounced and dangerous for their life and overall condition.

Firmly developed chain conditioned motor reflexes are not disturbed in the conditions of the experiment; they completely retain their structure and the time characteristics of the individual units.

Changes in the water-salt exchange during the first 30 days were expressed by a decrease in the hydrophilic nature of the skin, a decrease in the amount of chlorides in the blood and an increase in their elimination with the urine, and also by the weight loss of the experimental animals. There are indications of a certain suppression of the biosynthesis of deoxy-ribonucleic acid in the parenchymatous liver cells, indicating the suppression of growth processes in this tissue. These changes become less pronounced in proportion to the inclusion of adaptation mechanisms.

As compared with the control experiment in the high-altitude experiment the body weight of the animals significantly increased (as in the case of human beings in a 62-day experiment at an altitude of 7,000 m), which, evidently, must be referred to the direct influence of the rarefied atmosphere on the metabolic processes of the organism.

CHAPTER V

AN EXTENDED STAY IN CONDITIONS OF A CHANGED GAS MEDIUM AND THE REACTIVITY OF THE ORGANISM /207

An extended stay by a man in a closed cabin of limited volume in conditions of an artificial atmosphere, relative limitation on motor activity and isolation, and significant nervous-psychological strain is accompanied by definite changes in the functional condition of different systems of the organism.

A study of the adaptive reactions of the organism in these unusual conditions of existence, must come down in the final analysis to a study of the reactivity of the organism, particularly if we consider that the biological essence of reactivity is uninterrupted equilibrium, that is, adaptability of the organism to changing environmental conditions.

The concept of the reactivity of the organism is very closely connected with resistance. The mechanisms of reactive changes in life activity, determining the resistance to different experimental effects, may be manifested both in a decrease and an increase in resistance.

In response to the effect of unfavorable factors, specific and nonspecific reactions, aimed at preserving the relative constancy of the external environment, may arise in the organism. The specific reactions producing an increase in the stability of the organism arise under the repeated effect of one stimulus or another, such as overheating, oxygen deficiency, and so forth.

An increase in the resistance of the organism caused by the action of some one factor (for example, oxygen deficiency) but being manifested in the presence of the influence of a number of other extreme factors (acceleration, sharp temperature fluctuations, great physical loads, and so forth) is an example of the nonspecific reactions of the organism. For example, in the case of the action of a microbic stimulant on the organism an immunity to the given stimulant appears and, at the same time, a nonspecific reactivity is formed.

In order to reveal the functional changes arising in different environmental conditions and characterizing the state of the overall reactivity of the organism, it is necessary to periodically apply maximum functional loads. Such influences sharply raise the requirement for a well-coordinated functioning of the systems providing for life support of the organism and the development of protective and adaptive reactions. The degree of change in physiological systems enables one to judge the state of the reactivity of the organism as a whole.

One of the basic factors acting upon a man in airtight compartments is his air environment.

From the theoretical and practical point of view it is extremely important to clarify whether the resistance of the organism to the effects of extreme factors changes with a change in the gas environment. The establishment of such a dependence could serve as an additional criterion for the physiological determination and selection of the most efficient gas medium in airtight cabins for maintaining a high reactivity of the organism not only in normal conditions but also under the influence of extreme factors.

Some gas medium parameters, permissible in normal flight, may prove to be unfavorable in emergency situations for example, during explosive decompression, acute hyposia, high accelerations, and so forth.

As applied to a pure oxygen atmosphere this problem is of particular interest, since terrestrial creatures on our planet did not run into high oxygen contents in natural conditions in the process of their evolutionary development and did not develop adaptive mechanisms corresponding to this influence. It must be assumed that it is precisely for this reason that the process of adaptation to new living conditions, in particular to an extended stay in an atmosphere with an elevated $pO_2$2, will proceed more slowly and complexly than the process of adaptation to factors met within everyday life.

We succeeded in finding only one work (Bancroft, Dunn, 1965) dedicated to the study of the influence of rapid decompression (ascent during 0.2-1 sec from an altitude of 10,670 m to 40,000 m --2mm Hg) on the organism of animals preliminarily conditioned to a pure oxygen atmosphere. /209

It was found that the longer the animals (dogs) stayed in a vacuum, the more time was required for the restoration of their vital functions. If the time spent with pressure decreased to 2 mm Hg was 120-180 sec, then up to 80% of the animals perished.

However, this study did not contain comparative data on the survival rate of the animals of the control and experimental group after the pressure drop. Actually, the authors were studying the influence of acute hypoxia on the organism and did not attribute independent significance to the decompression itself, its amount and rate, and also did not consider the effects of preliminary oxygen breathing on the ability to endure hypoxia.

The first research on the influence of explosive decompression on the organism of animals was conducted in 1935. A large amount of factual material has now been accumulated and theories have appeared which explain the mechanism of the pathological shifts in the case of explosive decompression. In the opinion of most investigators, the basic harmful factor in the case of explosive decompression is the sudden increase in pressure and expansion of gases in the air-carrying cavities of the human and animal body (in the stomach and intestines, and especially, in the lungs). The significant increase in intrathoracic pressure observed here causes a number of reflex reactions on the part of respiration and the cardiovascular system. These reactions are the result of a powerful flow of interoceptive impulses, arising due to stimulation of the mechanoreceptors, abundantly present in the lung tissue, air-carrying passages of the mediastinum, the large vessels, and the heart.

The degree of traumatic damage to the lungs depends on the initial pressure in the lungs, that is, on the air density before the drop, the phase of respiration during which the pressure drop occurs, the condition of the lung tissue and respiratory passages, the presence of compensating clothing, and other conditions.

Edelman et al. (1946) discovered ruptures in the lung tissue /210
and petechial hemhorrages in dogs in the case of a pressure drop from an altitude of 3,000 to an altitude of 15,000 m during 0.02 sec. Henry and Cook (1945) showed that with the presence of protective clothing the lung tissue of the same animal withstood a pressure three times higher than with the absence of compensating mediums.

Inflammatory processes in the tracheae or bronchi, accompanying the accumulation of mucous, may increase the danger of damage to the lungs in the case of explosive decompression.

The physiological mechanism of the structural and functional changes which appear in the organism under the influence of atmospheric pressure drops and means and methods of protecting against the effects of this factor were worked out in our country by groups of scientists under the direction of L. A. Orbeli, In animals (dogs and cats) neither life-endangering damage to the internal organs nor massive air embolism was observed even in the case of a pressure drop of 0.95 atmospheres during 0.8-0.08 sec up to an altitude of 20,000 m and more (I. M. Khazen, Ye. I. Kuznets, 1956; A. G. Kuznetsov, 1957; D. Ye. Rozenblyum, I. M. Khazen, F. I. Pozhariyskiy, 1957, and others).

It has also been shown that after explosive decompression (from 3,000 to 11,600 m) the frequency of appearance of altitude pains increases, amounting to 88%, while in the case of a slow ascent to the same altitude decompression disorders are observed only in 62% of cases (Hitchkoch, 1954). In our investigations of ascent in an altitude chamber at a rate of 2 m/sec at an altitude of 7,500 - 11,000 m with 23 participants of a mountain climbing expedition (86 ascents), altitude pains did not appear in a single case .

The influence on the organism of explosive decompression for thousandths of a second has been studied in recent years. The data obtained testify to the increasing danger of decompression, since the degree of changes observed to a significant degree is determined by the rate of drop. Thus, in the case of a pressure drop of 0.5 atmospheres and more, taking place with a speed of 0.008-0.012 sec. the white rats tested died in 60-65% of the cases as a result of rupture of the lung tissue. The same drop, but performed over 0.8-1 sec., was, as a rule, accompanied by reversible functional changes.

Comparative physiological studies showed that drops in barometric pressure lasting microintervals of time cause significant respiratory and circulatory disturbances, in which the degree of expression of these disturbances depends on the type of animal concerned. Mice and rats prove to be least resistant to a pressure drop. The conditioned reflex activity of white rats is significantly disturbed in the case of a pressure drop. Conditioned motor reflexes are restored four to five days after the effects of a pressure drop (I. M. Khazen, Ye. I. Kuznets, 1956). /211

It was of interest to investigate the influence of rapid pressure drops on conditioned motor reflexes, the performance of which is possible only with a high level of analytical synthetic activity of the cerebral cortex.

In our investigations we studied the influence on the animal organism of pressure drops taking place at a speed of 0.012 - 0.008 sec.

The experiments were conducted in a special pressure-drop chamber, which was installed in a large altitude chamber used as an auxiliary container.

In addition to the investigation of chain conditioned motor reflexes in the animals (G.P. Doronin) we also used the usual roentgenography and kinofluorography (12-24 frames/sec) of the thoracic and abdominal organs at the moment of pressure drop and immediately after the end of the experiment (A. R. Mansurov).

X-ray studies were conducted on 21 rabbits and 26 rats. Chain conditioned reflexes were investigated on 11 white rats. The survival rate was determined on 10 rabbits and 68 white rats. In all, 135 animals were subjected to 47 experiments.

The conditioned reflex activity was investigated before the effects of pressure drop and at different periods after the pressure drop until the complete restoration of developed food-acquiring reflexes.

Stable results, indicating completed synthesis of conditioned motor reactions into a single chain of food-acquiring motions, were obtained in control experiments conducted before the pressure drop.

During an   to the initial altitude the behavior of the animals did not significantly change--only a certain intensification of the orientation reaction was observed during the first minute of the ascent. After a drop for 0.8 sec /212
the correct chain of food-acquiring motion appeared in 25-35 minutes, although some inhibitions were noted here, especially in the reaction to the starting stimulus of the chain. The time of the first link of the motion chain increased on the average by 104%, the second link--by 49%, and the third link scarcely changed in its duration. Twenty-four hours after the pressure drop the speed of response reaction to the chain stimulus was the same as in the control experiment before the pressure drop.

In spite of the retention of the positive change after a pressure drop, all test rats displayed a clear disturbance of the more complex link connected with the stress of the inhibiting process --the reaction of shutting off and inhibiting stimulus. After the pressure drop an adequate reaction in comparison with the norm was noted in only 60% of the cases. The time taken for switching on an inhibiting signal doubled (to 5.5 sec).

Studies conducted 24 and 48 hours after the pressure drop showed that during the course of the first days there is normalization not only of positive chain reflexes, but also of adequate reaction to the application of a conditioned inhibition stimulus.

After complete restoration of conditioned reflex activity the test animals were subjected to a pressure drop of the same magnitude (0.5 atmospheres), but at a speed of 0.008-0.012 sec. At this rate of drop severe damage to the structure of lung tissue appeared and in most cases the experiment ended with the death of the animal during the first minute after descent from the final altitude. The direct cause of the death of the animal was the severe damage (rupture) of the lung tissue during the drop, which was indicated by the release of foaming bloody fluid from the respiratory openings and the result of pathomorphological studies. The restoration of chain conditioned motor reflexes was investigated on the rats which remained alive after the pressure drop. During the first two to three hours the condition of the animals was severe: the rats maintained an immobile position with half-closed eyes; the fur was disheveled. There were no motor reactions to conditioned stimuli. Often a genative reaction was observed /213 upon switching on the "triggering" link. Even to a stimulus similar to an unconditioned reinforcement (knocking on the feed tray), only an orientation reaction was observed, which points to the suppression not only of conditioned but also of unconditioned reflexes.

Response reactions to the chain stimulus began to appear three to four hours after the pressure drop. The mobility of the animals was significantly decreased, there were no intersignal reactions, and chain motor reflexes proved to be substantially disturbed. The duration of the first link sharply increased (by 187%) while the second link increased by 80% and the third by 41%. Response motor reaction to several stimuli of the chain completely ceased. It is characteristic that in this case instead of moving to area no. 1 a rat moved to area no. 4, that is, a reaction, corresponding to an inhibiting stimulus, was observed. At the same time adequate reaction to conditioned inhibition most often was absent and a negative reaction was observed. This indicates that restoration of conditioned motor activity took place in phases.

On the second day after the pressure drop the time taken for fulfilling individual links of the chain reflex approximated the original values to a considerable degree however, some disturbances in the structure of the food-acquiring chain continued to exist. Sometimes an imperfect chain was observed in which there was no motion to the second stimulus. Adequate reaction to the application of conditioned inhibition usually appeared, although the time required for turning off the inhibiting signal remained increased by 17%.

The system of complex food-acquiring reflexes which had been developed was restored two days after the pressure drop.

In the next stage of our investigation it was extremely important to establish the influence of a multiday stay in a pure oxygen atmosphere at a total pressure of 198 mm Hg on the ability to withstand explosive decompression. The drop was performed (over 0.008 sec.) from an altitude of 10,000 m to a practically complete vacuum (2 mm Hg, an altitude of 40,000 m). Here we determined the survival rate of the animals and recorded electrocardiograms, and electromyograms of the abdominal muscles and the nature of the change in respiration. X-ray and morphological studies were /214
conducted before and after the action of explosive decompression.

Table 50 presents data characterizing the survival rate after the action of explosive decompression of control animals and animals subjected to a prolonged exposure to an altitude of 10,000 m in a pure oxygen atmosphere.

TABLE 50

SURVIVAL RATE OF ANIMALS AFTER THE ACTION OF EXPLOSIVE DECOMPRESSION IN MICROINTERVALS OF TIME (FOR 0.008 SECONDS)

Type of animal	Control		Test animals--multiday stay in pure oxygen atmosphere	
	Number of animals in experiment	No. lost	No. of animals in experiment	No. lost
Rabbits	5	1	5	3
White rats	33	5	35	16

From Table 50 it is seen that a preliminary multiday breathing of pure oxygen aven at a total pressure of 198 mm Hg, has an unfavorable effect on the resistance of the organism to explosive decompression, which correspondingly is reflected in the survival rate of the animals.

The literature contains information on the positive influence of high oxygen concentrations on certain physiological functions of the organism and increased resistance to different extreme influences: acceleration, sharp temperature changes, high carbon dioxide concentration, accumulation of carbon monoxide, vestibular disorders, and so forth (S. T. Agarkov, A. N. Namyatnyy, 1962; A. G. Zhironkin et al.,1965, and others).

As far as the ability to withstand acute hypoxia after different periods of stay in a hyperoxic medium is concerned, the available information is very limited and contradictory. Thus, A. G. Zhironkin et al. (1965) established that a long-term (up to 10-day) stay by animals in an atmosphere containing 63% oxygen at ground level pressure increases their resistance to acute hypoxia. Ye. M. Sazonova (1959) indicated an intensification of the contracting function of the myocardium in the case of inhaling a gas mixture containing 60% oxygen. However, most of these studies were short-term in nature and did not reveal the dynamics of the changes which occur in the organism during an extended stay in hyperoxic conditions. Therefore, experiments conducted to explain the resistance of the organism to acute hypoxia after different periods of stay in an air medium enriched with oxygen (imitation of cabin depressurization) has important theoretical and, particularly, practical significance. /215

We studied the ability to endure acute hypoxia at different periods of stay in an atmosphere with a high partial oxygen pressure. In studies on human beings the altitude resistance was determined both before and after an extended (10-day) stay by the subjects in an airtight chamber containing 54% oxygen at normal atmospheric pressure, an air temperature of 22°, and a relative humidity of 78%.

In order to determine the time to unconsciousness the subjects were "raised" in an altitude chamber at a rate of 15m/sec to an "altitude" of 7500 m wearing an oxygen mask. At this altitude the subjects in turns removed their masks and conducted an investigation to determine the time to unconsciousness. The experiment was stopped upon the appearance of severe functional disorders (pronounced tachycardia, the appearance of cramps or indications of fainting), and also upon the first request of a subject.

As a result of these studies it was established that the time to unconsciousness at an altitude of 7500 m after hyperoxia (54% oxygen) decreased in subject N-ov by 10.6%, and in subject M-ov by 33.8%, being respectively 6 minutes 10 seconds and 6 minutes 20 seconds.

Staying in a rarefied atmosphere after the prolonged action of hyperoxia on the organism required much greater exertion on the part of the cardiovascular and other systems of the organism.

An investigation of the cardiovascular system upon performing work on a veloergometer (with a power of 1200 kgm/min for 5 minutes) showed that, after a 10-day hyperoxia, adaptation to a load significantly worsened: the amplitude of pulse reactions sharply increased; restoration of physiological indicators after performing work was retarded in nature.

All this indicates that as a result of a man spending a prolonged period of time in hyperoxic conditions there is a weakening of the mechanism responsible for combatting a subsequent oxygen insufficiency. Presenting the organism with high demands, for example, decreasing the partial oxygen pressure in the inhaled air with an ascent to an altitude of 7500 m, or hypoxia developing in the organism upon the performance of high intensity work leads to an insufficiency of the above mentioned physiological compensatory and adaptive mechanisms. /216

We also obtained similar data indicating a lowering of a man's resistance to the effect of acute hypoxia, great physical loads (running on a treadmill) and accelerations after an extended (62-day) stay in the artificial atmosphere of an airtight chamber at an altitude of 7,000 m (pressure 308 mm Hg, oxygen 53% "high-altitude").

For aviation and space medicine it is very important to show how the resistance of the organism to acute hypoxia changes not only before and after a stay in a hyperoxic medium, but also directly during the action of high oxygen concentrations.

A series of experiments on animals was set up with this purpose in mind.

White male rats weighing 170-200 g each were used for the experiments. Two series of experiments were conducted. In the first series of experiments the animals were kept for 10 days in a two K-NZh chamber, 0.8 m^3 in volume and specially equipped for a long-term stay, containing on the average 89% oxygen (fluctuating from 83 to 97%) at ground level pressure. In the second series of experiments the oxygen content in the chamber was, on the average, 53% (47-58%), and the animals spent 20 days in the chamber. The 2K-NZh chamber was equipped with an external oxygen regeneration system, for maintaining the given parameters of the gas medium. The oxygen content of the chamber was controlled with the aid of a gas analyzer. The temperature of the chamber fluctuated between 17 and 22°, the carbon dioxide content--from 0.3 to 1%. The resistance of the animals to acute hypoxia (survival time at an altitude of 12,000 m) was determined in a 30-liter capacity chamber, located within the large 2K-NZh chamber, in order to maximally approximate the conditions of the experiment to conditions which could arise in flight in the case of cabin depressurization. In determining the altitude resistance the animals

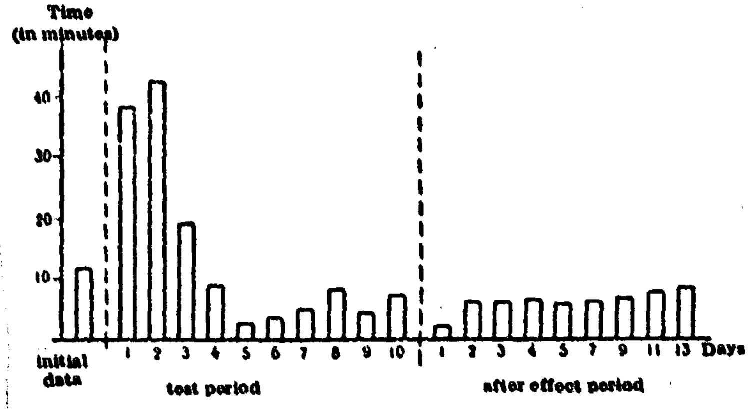


Fig. 29. Survival time of animals at an altitude of 12,000 m after different periods of stay in an atmosphere containing 89% oxygen.

were placed in the pressure chamber without disturbing the hermeticity of the medium by means of special adaptation of the large 2K-NZh chamber and then raised to an "altitude" of 12,000 m at a rate of 25 m/sec. A "landing site" was established at this altitude and the survival time determined. The experiment was stopped upon the appearance of cramps and agonal breathing in the animals. During the period of influence of hypoxia and after "descending" to ground level pressure the behavior of the animals was continuously observed, the rectal temperature was measured, and the rate of cardiac contractions and respiration recorded.

Resistance to acute oxygen starvation in the first series of experiments (89% oxygen) was determined up to the long-term experiment (as a control), daily during the stay in an atmosphere with a high oxygen content and for 2 weeks after replacing the hyperoxic medium with an ordinary atmospheric medium. In the second series of experiments (53% oxygen) the altitude resistance was determined in the initial condition (control), every five days spent in the medium containing 53% oxygen, and for 10 days during the after effect period. In all, 219 experiments were conducted, of which 150 were in the first series and 69 in the second series.

The results of the first series of experiments are shown in Fig. 29. The data obtained indicate that the resistance of the animals to acute hypoxia significantly changed in proportion to the time spent in a gas medium containing a high oxygen concentration. Thus, if in the control experiment (before placing the animals in a hyperoxic medium), the survival time at an altitude of 12,000 m was on the average 11 minutes 38 seconds, by the end of the first day it had increased by more than 3 times and reached 38 minutes 18 seconds, and on the second day it increased by almost 4 times. The sharp increase in resistance to oxygen deficiency observed /218 during the first day evidently results from a significant increase in the partial pressure of oxygen in the blood and tissues of the organism due to its excess content in the hyperoxic medium. It is as if an oxygen reservoir were created in the organism. In addition the oxygen consumption increased significantly and a high efficiency of oxidizing processes in the brain tissues was observed. From the third day the resistance of the animals to hypoxia began to decrease progressively. During this period regulatory mechanisms were switched on which limited the entrance of excess amounts of oxygen to the organism, as a consequence of which there was a decrease in the oxygen consumption of the animals, and also a decrease in the capacity of the brain tissue for oxidation, and especially for the phosphorylation connected with it (N. A. Agadzhanyan et al., 1968).

The greatest decrease in altitude resistance was observed on the fifth day spent in an atmosphere with a high oxygen content. During this period the most significant disturbances in the activity of the different physiological systems and the highest animal mortality were observed. Autopsies of the dead animals revealed massive edema of the lungs with damage to the alveoli and interalveolar septa. All the alveoli were filled with serous fluid.

Whereas for the first days a significant increase in the respiration rate, restlessness, and increased water and food consumption were observed, during the following days the picture was reversed: inhibition, refusal of food and water, and then the death of the animal. Labored breathing involving the supplementary respiratory musculature in the act of breathing was noted. A vicious circle seemed to be created where, on the one hand, there was a respiratory insufficiency due to the exclusion of a significant part of the lungs from the act of breathing (congested form of hypoxia) and on the other an inability to compensate for it by means of intensifying the external respiration function because of the toxic effect of oxygen itself. Later (on the sixth day) it was noted that functional shifts tended to level out.

The results of an analysis lead one to assume that the /219 organisms adapt to hyperoxia by changing the level of metabolic processes. This is confirmed by the fact that the rectal temperature of the rats progressively decreased in proportion to the time spent in a hyperoxic medium and toward the end of the experiment decreased on the average by 4-5° in comparison with the initial level. Our data agree with the results obtained by A. G. Zhironkin et al,(1965), which showed that in hyperoxic conditions there is a slowing of the metabolic processes in mice, caused by hypofunction of the thyroid gland, a lowering of the excitability of nerve center and a decrease in the gas exchange volume. Decreased resistance to hypoxia is particularly pronounced during the after effect period, that is after replacement of the high-oxygen medium by a normal atmosphere. The survival time at an altitude of 12,000 m decreased in this case to 1 minute 31 seconds, while in the original condition (before the experiment) it was, as we have already indicated, an average of 11 minutes 38 seconds.

The data obtained in our experiment indicate that the organism is unfavorably influenced by sharp changes in the gas composition of the environment: from a hyperoxic one to a normal or hypoxic one.

All this is confirmed by the severe changes in all vitally important functions of the organism caused by the toxic influence of oxygen. Later (for approximately, the second to third days) the resistance of the animals to acute hyposia increased, somewhat the gas exchange indices improved and the function of external respiration gradually normalized. The animals began to feed normally and increased considerably in weight. During the eleventh to thirteenth days after the influence of a hyperoxic medium the survival time at an altitude of 12,000 m was already around 8 minutes, however even on these days it did not reach the initial level. This again confirms that a prolonged (up to 10-day) stay in an atmosphere with a high oxygen content (89%) leads to severe functional disturbances in the organism.

In this regard our results do not agree with the data of A. G. Zhironkin et al,(1965), who showed that mice spending 10 days in hyperoxic conditions (63% oxygen) not only did not suffer a decreased resistance to hypoxia, but even experienced somewhat of an increase in resistance. It is difficult to give an exhaustive /220
explanation of such a difference; however, in our opinion, it is connected with the lower oxygen concentration (63%) in the experiments by A. G. Zhironkin et al. Moreover, the hypoxia was created by means of replacing the oxygen with nitrogen. This excludes the influence on the organism of the very factor of rarefaction, under which, due to the expansion of gases in the abdominal cavity and stimulation of the baroreceptors of the venae cavae, impulses enter the central nervous system which intensify

the effect of hypoxia and lower altitude resistance. The different rate of increase of hypoxia also has an effect. In the experiments of A. G. Zhironkin et al. it was approximately 6 m/sec. In this case more favorable conditions are created for the development of compensatory and adaptive reactions by the organism than in the case of an altitude chamber ascent at a rate of 25 m/sec. In our experiments it was established that the rate of increase of hypoxia has independent biological significance with respect to the nature of the response reactions of the organism to oxygen deficiency (N. A. Agadzhanyan, A. V. Sergiyenko, 1966).

We obtained somewhat different results in experiments on animals spending 20 days in an atmosphere containing 53% oxygen (Fig. 30).

From the data presented in Fig. 30 it is obvious that resistance to acute hypoxia in the process of a prolonged stay in a medium containing 53% oxygen also varies significantly. On the fifth day of the effect of 53% oxygen the altitude resistance increased by 30% in comparison with the initial data, which, as we have already indicated, is probably the result of better blood oxygenation. On the tenth day of the experiment, as a result of significant disturbance of the regulatory and compensatory mechanisms, there was as a rule, a pronounced decrease in altitude resistance. On the whole it amounted to 69% of the initial level. A still more significant decrease of the ability to withstand hypoxia was observed on the fifteenth and twentieth days of the experiment. The altitude resistance on the fifteenth day decreased by more than five times and on the twentieth day by ten times in comparison with the initial level.

It is obvious that a cumulative effect is observed in the case of a prolonged (more than 10-day) stay in an oxygen-enriched medium. /221

Immediately after replacing a medium containing 53% oxygen with ordinary atmospheric air the resistance to acute hypoxia, as in the first series of experiments, sharply decreased. The survival time at 12,000 m was, in all, 40 sec (8% of the initial level). However, already by the fifth day after the replacement of the gas medium the altitude not only reached its initial values, but even somewhat exceeded them. By the tenth day it was the same as in the control experiment, while in the first series of experiments (89% oxygen) complete restoration of altitude resistance was not reached even after two weeks.

It is interesting to note that while in the first series of experiments (89% oxygen) 52% of the animals died while in the

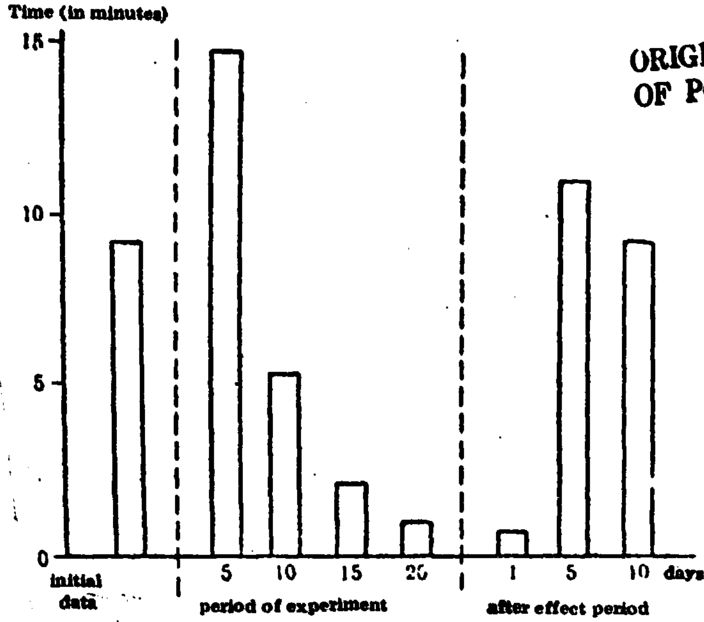


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Fig. 30. Survival time of animals at an altitude of 12,000 m after different periods of stay in an atmosphere containing 53% oxygen.

2K-NZh chamber, in the second series of experiments with a 53% oxygen content the animals did not die, although they clearly showed the symptoms of acute hypoxia.

The results of the experimental investigations provide the basis for assuming that the problem of the periods of time spent in a hyperoxic medium has independent biological significance, referring, in particular, to the ability to withstand acute hypoxia. /222

It is well known that one of the manifestations of acute hypoxia, of the toxic effect of high oxygen concentration, is the appearance of cramps. As a rule, the cramps were generalized with the predominance of the tonic phase. Earlier we had shown that hypoxic cramps usually were absent in the case of an altitude chamber ascent at a rate of 25 m/sec, and if they appeared, they were extremely insignificant and were primarily of a clonic character (N. A. Agadzhanyan, A. V. Sergiyenko, 1966).

We established that there is a definite relationship between hypoxic cramps and the duration of a stay in a hyperoxic medium. The appearance of cramps in most animals when determining the altitude resistance in a 10-day and, especially, in a 15-day experiment is not without interest, although in the initial period and in a 5-day stay in hyperoxic conditions (53% oxygen) with ascent to an altitude of 12,000 m cramps were observed in almost no experiment.

Thus, the results of the investigations conducted agree with the data given in the literature; that a prolonged stay in an atmosphere containing high oxygen concentrations at ground level pressure has a pronounced toxic effect on the organism. At the same time, brief hyperoxia improves oxygenation of the organism and thus significantly decreases the danger of the development of acute oxygen starvation in the case of depressurization of the medium of habitation with significant rarefaction of the atmospheric air.

Investigations conducted in an atmosphere containing 53% oxygen showed that this concentration also effects men and animals. In the case of a prolonged stay in such a gas medium the oxygen has a cumulative effect, the result of which is a significant decrease in the resistance of the organism to acute hypoxia. Therefore the use of such a medium for a prolonged period is not expedient in aviation and astronautic technology.

The study of the combined influence of extreme flight factors /223 on man is one of the important problems of space physiology. This is connected, first of all, with the fact that in real flight it is possible for the air regeneration and purification system to break down, for the cabin to become depressurized, and so forth.

There is information that the combined influence of explosive decompression, oxygen deficiency, vibrations, high temperature, and hypoxia has a more significant effect on the organism than each of these factors separately (Yu. M. Uspenskiy, 1943; Ye. V. Gubler, 1962; Megel et al, 1963; Furry, 1961; A. N. Namyatyy, 1966; N. A. Agadzhanyan, 1968, and others).

In research on animals it has been established that the ability to withstand acute hypoxia depends not only on environmental conditions, mainly the gas composition and temperature conditions in an airtight chamber, but also on the duration of the stay in the conditions of an artificial atmosphere (N. A. Agadzhanyan, A. V. Sergiyenko, 1969, 1970).

The literature contains information to the effect that the addition of carbon dioxide to the gas mixture to be inhaled increases the resistance of the organism to hypoxia (V. V. Strel'tsov, 1933; I. R. Petrov, 1949; M. Ye. Marshak, 1969, and others). A number of studies by native and foreign authors also are dedicated to the investigation of the ability to withstand acceleration after a stay in an atmosphere with a high carbon dioxide content; however, the opinions of the investigators are contradictory.

We studied the ability to withstand acute hypoxia and lateral acceleration (8 g) after a prolonged stay by man and animals in an atmosphere with an increase up to (pCO_2 = 45 mm Hg) carbon dioxide content.

With the participation of eight subjects, six long-term experiments were conducted in an atmosphere with a high carbon dioxide content (pCO_2 = 22.8, 30.4, 38 and 45 mm Hg) under normal and low (405 mm Hg) barometric pressure. The experiments were performed in an altitude chamber 8 m^3 in volume, specially equipped for extended human occupation. A hypercapnic medium was created due to the carbon dioxide exhaled by the subjects and automatically maintained at a strictly predetermined concentration with the aid of gas analyzers. The partial pressure of oxygen was 150-165 mm Hg, the temperature 22±1°, the relative humidity 60±10%. A high carbon dioxide content in the

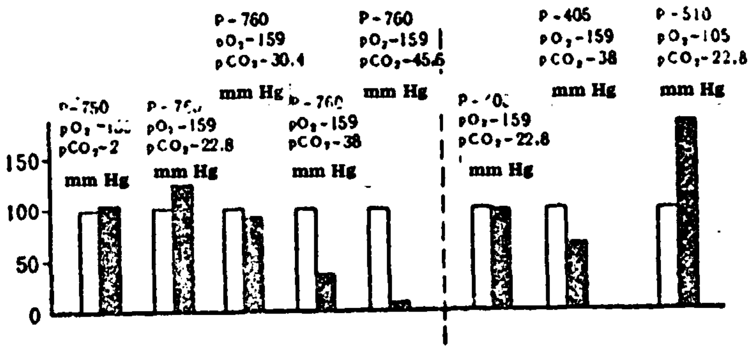

Fig. 31. Time to unconsciousness at an altitude of 7500 m after a prolonged stay in a hypercapnic medium. /224

White columns--before influence of carbon dioxide; black columns--after influence of carbon dioxide.

chamber was maintained for 5 days, and for the remaining time (before and after the creation of a hypercapnic medium in the chamber) the gas composition corresponded to the earth's atmosphere.

The total duration of each experiment was 10 days.

Investigations of the ability to withstand acute hypoxia and accelerations were conducted before and after the long-term experiment in a hypercapnic medium.

From the data presented in Fig. 31 it is obvious that after a 10-day stay in an altitude chamber with a normal gas composition the time to unconsciousness of the subjects practically did not vary. With an increase in the carbon dioxide concentration in the chamber to pCO_2 = 22.8-30.4 mm Hg, the time to unconsciousness for subject O-v increased from 5 minutes 57 seconds to 7 minutes 35 seconds (a 27% increase), and the time to unconsciousness for subject Og-v from 10 minutes 42 seconds to 12 minutes (a 12% increase). Subject D-v in all cases withstood acute hypoxia well. Probably, this is connected with the fact that earlier he had been acclimatized to high mountain conditions several times over the course of a long period of time. according to the results of an investigation of physiological /225
reactions, and according to subjective indicators, the altitude resistance of all subjects was better after the influence of hypercapnia than before the experiment. A further increase in the carbon dioxide concentration chamber (pCO_2 = 32 mm Hg and more) produced a sharp decrease in the altitude resistance of subjects and more significant changes in the physiological reactions of the organism (see Fig. 35).

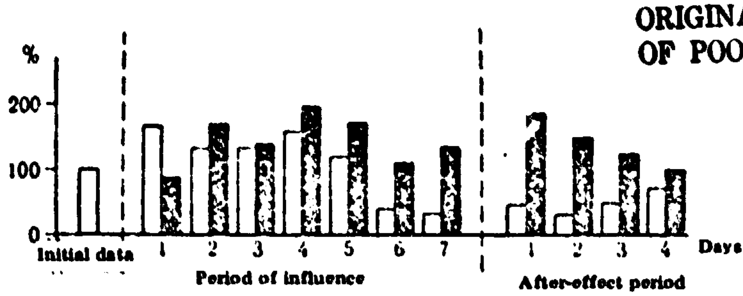

Fig. 32. Survival rate of animals at an altitude of 12,000 m (in percent) as compared with the initial level after different periods of stay in a hypercapnic medium with a pCO_2 of 45.6 mm Hg. White columns--at normal pressure; black columns--with low pressure in the chamber.

The most significant decrease in altitude resistance, from 50 minutes to 3 minutes 35 seconds, was observed with an increase in the pCO_2 in the chamber to 43-45 mm Hg. This is connected with the fact that an increase in the pCO_2 in the inhaled and alveolar air of more than 40 mm Hg causes severe disturbances in the functional systems of the organism. In addition, as a result of the pronounced hyperventilation resulting from the specific effect of carbon dioxide on the respiratory center, on the one hand, the energy consumption for intensive work of the respiratory musculature increases, and, on the other hand, hypoxic reactions are more clearly manifested against the background of such hypercapnia (I. R. Petrov, 1949; N. A. Agadzhanyan, A. V. Sergiyenko, 1970, and others). Similar data were obtained in experiments on animals (Fig. 32).

The investigations showed that up to a certain level hypercapnia in combination with hypoxia has a stimulating influence on the organism. The intensification of the reaction on the part of the respiratory organs and the cardiovascular system in these conditions improves blood oxygenation and prevents the harmful consequences of hypoxia. An increase in the partial pressure of carbon dioxide facilitates the transfer of oxygen from the blood into the tissues and decreases the oxygen consumption (M. Ye. Marshak, 1969, and others). Moreover, due to the local vascular-expanding effect of carbon /226 dioxide there is an improvement in the blood delivery, and consequently, the oxygen delivery to such vitally important organs as the brain and heart (N. V. Sanotskaya, 1966), which also leads to an increase in the resistance of the organism to oxygen deficiency. However, this adaptive effect is not long-lasting.

Extreme hypoxia (less than 8% oxygen) cannot intensify, but, on the contrary, suppresses ventilation reaction to carbon dioxide, and high carbon dioxide concentrations (more than 6%) produces a weakening or even a disappearance of respiratory reactions to hypoxia.

Data on the ability to withstand acute hypoxia after a prolonged stay in a hypercapnic medium agree with the results of experiments conducted on a centrifuge (M. A. Agadzhanyan, Ye. B. Shul'zhenko et al., 1971). It has been shown that a man's resistance to a lateral acceleration of $+8G_x$ after a stay in an atmosphere with an elevated carbon dioxide content was, as a rule, decreased (Table 51).

As is seen in Table 51, in the case of only one subject (D-ov) was the duration of the effect of acceleration somewhat greater after a stay in an atmosphere with a high carbon dioxide content (pCO_2 = 22.8 mm Hg) than in the control experiments.

TABLE 51

INFLUENCE OF AN ALTERED GAS MEDIUM WITH AN ELEVATED CARBON DIOXIDE CONCENTRATION ON THE ABILITY TO WITHSTAND ACCELERATIONS OF $+8G_x$

Subjects	Duration of Effect of Accelerations of $+8G_x$		
	Background Data	With pCO_2 = 22-38 mm Hg; P = 760 mm Hg	With pCO_2 = 38 mm Hg; P = 405 mm Hg
D-ov	3 min 26 sec	4 min 14 sec	--
A-n	7 min 05 sec	1 min 02 sec	5 min 24 sec
N-v	16 min 21 sec	8 min 21 sec	9 min 30 sec

With an increase of more than 22 mm Hg in the pCO_2 in the chamber, the ability to withstand accelerations worsened for all subjects.

In the course of time influence of acceleration, the frequency of cardiac contractions rose and the arterial pressure increased from 110-120 to 170-180 mm Hg. The electrical systole of the heart (the Q-T interval) and the systolic index, determined according to the Fogel'son-Chernogorov method, decreased relatively, the amplitude of the T spike lowered and a shift in the S-T interval was noted. These changes were maintained for 10-15 minutes during the aftereffect period. Disturbances in the rhythm of cardiac activity (in the form of extra systoles) were noted in two subjects (A-n and D-ov).

An analysis of the results of these investigations showed that evidently, hypercapnia and respiratory acidosis, which, as is known, even develope in the case of a shorter stay in an atmosphere with a 3-5% carbon dioxide concentration, are the basic mechanism of the above-mentioned shifts. /227

The decrease in the rate of cardiac contractions and respiration observed during the operation of acceleration was very likely the result both of the influence of carbon dioxide on the tonus of the vagus nerve and of the inhibition of the sub-cortico structures. The decrease in the systolic index in these conditions evidently indicates a lowering of the contractive ability of the myocardium under the influence of hypoxia and elevated carbon dioxide concentrations.

The changes shown on the EKG confirm the opinion of L. I. Fogel'son (1957) that the changes in the T spike in the case of a prolonged stay in an atmosphere with an elevated carbon dioxide concentration are of a two-phase nature. Thus, T. N. Zheludkova et al. (1964), in the case of the short-term (for 6-12 hours) action of a gas mixture with a 3-5% carbon dioxide concentration, noted an increase in the T spike, while in our investigations, on the contrary, after a more prolonged (4-5 days) stay in such an atmosphere, there was noted a decrease in its amplitude.

Thus, the results of these investigations indicate that after a multiday stay in an atmosphere with an elevated (pCO_2 more than 30 mm Hg) carbon dioxide content the ability of a man to withstand acute hypoxia and lateral acceleration is significantly lowered.

As investigations on human beings and animals showed, in evaluating and normalizing the parameters of the gas medium in inhabited airtight cabins it is necessary to determine the influence of the maximal permissible concentration of oxygen and other gases not only according to data on changes in the physiological reactions of the organism in the course of a long stay in artificial atmospheric conditions, but also according to the subsequent results, characterizing the ability to withstand extreme influences after different periods of stay in different gas media.

CONCLUSION /228

We have examined experimental data on the physiological basis of different parameters of an altered gas medium and the principals of the formation of an artificial atmosphere for airtight compartments.

The materials presented indicate that the creation of an artificial atmosphere for airtight compartments entails a series of biomedical and engineering problems requiring extensive study for their solution.

The general requirement for an atmosphere for airtight cabins may be formulated as follows: the atmosphere with respect to pressure, content of oxygen and other gases, temperature, humidity, concentration of ions and harmful impurities must provide for stable human working efficiency in flight, satisfy the necessary comfort requirements, be safe for the organism and be capable not only of being controlled, but also of being regenerated by simple and reliable means.

In spite of the fact that modern aircraft are equipped with airtight cabins, hypoxia, which may occur in an emergency situation, represents the greatest danger for man. In investigations with human participation and in experiments of animals we have shown that in conditions of oxygen deficiency there appear functional disturbances in different physiological systems of the organism and, primarily, in the function of the higher sections of the brain.

The explanation of the deeper mechanisms of the disturbance of brain activity under the effects of hypoxia, correlation of the bioelectrical activity with conditioned reflex activity and metabolic processes, and study of the "chemical" congradients of the reaction of the brain to the effects of hypoxia are problems for further investigation.

The establishment of optimal barometric pressure in spacecraft cabins also has important significance for the gas medium parameters. The literature and our own experimental data indicate /229 that, from the physiological point of view, the total pressure of the gas medium in spacecraft cabins, especially in the case of extended flights, should be maintained below atmospheric pressure. This is to decrease the danger of the influence of explosive decompression in the case of cabin depressurization, to decrease gas leakage from the cabin, to decrease cabin weight and energy consumption for ventilation, to improve heat regulation and to create the most favorable conditions for entry and exit from the cabin in outer space conditions. The relative percentages of the gases in the spacecraft atmosphere changes in correspondence with the pressure change: the oxygen concentration increases and nitrogen decreases. The remaining parameters remain without significant changes.

We established that it is possible for a man to spend a long (62-day) time in an airtight chamber with a reduced atmospheric pressure, corresponding to an altitude of 7,000 m (308 mm Hg) and a normal partial pressure of oxygen (160-180 mm Hg).

A further decrease in the barometric pressure in airtight cabins (below 300 mm Hg), probably, is inexpedient due to the danger of the appearance of decompression disorders in crew members.

Although up to the present time in the space flights of Soviet and American astronauts there have been no cases of the appearance of altitude pains, the possibility of their appearance is not excluded, particularly in the case of an extended space walk, when the pressure in the space suit is decreased. As we have already indicated, the presence of an inert gas, for example nitrogen, is necessary in order to prevent the development of atelectasis of the lungs. At the same time, in the case of decompression it is precisely because of the presence of nitrogen in the atmosphere that altitude pains occur, the occurrence of which may be avoided only by inhaling pure oxygen.

The question naturally arises of whether nitrogen is necessary for supporting life in the above-mentioned condition.

Our experimental data showed that animals survive for several months in a single gas atmosphere of pure nitrogen at a pressure of 198 mm Hg. Berry and Smythe (1962) also did not discover any significant metabolic disturbances in mice that spent 3 weeks in a pure oxygen atmosphere at a pressure of 226 and 187 mm Hg (9,000 and 10,200 m).

However, judging by Allen's experiment (1962), a categorical denial of the biological role of nitrogen for the activity of the animal's organism is premature. The author showed that in the conditions of pure oxygen at a pressure of 190 mm Hg there is observed a retardation of the development of the vascular system of chick embryos, and assumed that the cause of this was the absence of nitrogen in the gas medium. /230

Our investigations have shown that in the case of a prolonged (100-day) stay by animals at an altitude of 10,000 m (198 mm Hg) in a pure oxygen atmosphere there is observed a lengthening of the pregnancy period (by 5-7 days), the appearance of stillborn offspring and a retardation in weight increase as compared with control animals born in normal conditions. The necessity for further investigations in this direction is obvious. It is also efficient to use an inert gas in the atmosphere of a spacecraft cabin because of the danger of fire and meteorite collision.

It has been shown that if the atmosphere of an airtight cabin contains pure oxygen at low pressure (196 mm Hg) then the rate of combustion is doubled due to the absence of nitrogen. The fire danger connected with the use of pure oxygen at a pressure of 258 mm Hg was also confirmed in long-term (9-14 day) experiments, conducted with human beings (Welch et al., 1961, and others). As far as heat conductivity is concerned, oxygen is inferior to nitrogen and other inert gases. Consequently, in a pure oxygen atmosphere it is necessary to have more cooling (Schaefer, 1964).

It is necessary to conduct further investigations with respect to discovering the most efficient atmosphere for manned airtight cabins, in particular, with respect to studying the biological role of inert gases and the possibility of their practical application. The best variant would be the creation of systems providing for automatic cabin control of an optimum artifical atmosphere depending on the particular concrete flight conditions.

At the same time it is necessary to seek means of increasing the resistance of the organism to different unfavorable influences.

We studied hypoxic hypoxia and developed means of increasing /231 the resistance of the organism to oxygen deficiency both by means of pressure chamber training and mountain acclimitization, and also by means of chemical and hormonal stimulation of the processes of adaptation to hypoxia.

These results showed that active mountain acclimatization is a promising method not only for the purposes of increasing the resistance of the organism to hypoxia, but also to various other extreme factors (acceleration, high temperature, great physical loads), to long isolation, monotony of surroundings, sharp fluctuations of temperature, humidity, and increased ultraviolet, infrared and cosmic radiation. Mountain acclimatization is, moreover, a means of curing and preventing many pathological processes which may arise in astronauts in flight.

The result of the high mountain expeditions we conducted show that after mountain acclimatization, the resistance of the organism to the appearance and development of altitude pains is increased.

Around 100 chamber ascents to an altitude of more than 7,000 m (7500 - 12000 m) were conducted with the participation fo 26 subjects. Here, after mountain acclimatization, no case of the appearance of altitude pains was found, although most of the subjects spent more than 30 minutes at altitudes exceeding 7400 m without oxygen, and in addition, some of them performed quite heavy physical work according to a special program.

There are also indications of this in the work of foreign authors. Thus, Hurtado and Clark (1950) note that mountaineers (inhabitants of the Andes) manifest great resistance to altitude pain. Combining mountain acclimatization with physical training of subjects, Balke and Wills (1958) also observed an increase not only of altitude resistance but also of resistance to decompression sickness.

The rate of decompression also influences the appearance and development of altitude pains. While altitude pains are manifested in 5-25% of cases with a chamber ascent to an altitude of 7500-12000 m at a rate of 15-25 m/sec, with a decrease in pressure at a rate of 2 m/sec decompression sickness did not appear in any of 19 subjects (N. A. Agadzhanyan, 1968).

Increasing the resistance of the organism to the effect of environmental factors is a very complex biological problem. The investigations of physiological processes on the cellular and molecular level, conducted in recent years, show that the principles of tissue restructuring both in the simplest organisms and in the more highly organized animals are approximately the same. /232

It has been established that for the most effective development of increased resistance to any stimulus it is necessary to be trained to this stimulus, and also for the organism to be acclimated to different meteorological factors.

The repeated action of a complex of stimuli leads to the development of complex functional interrelationships, in which the entire stimulus complex is combined into a single hole. The above mentioned regularities of the resistance of the organism to environmental factors emphasize the important significance of the "specificity" principle in the development of this process. However, these data in no way contradict the fact that increasing the resistance to one stimulus may change the reaction of the organism to the effect of another stimulus, as a result of which the resistance to the new stimulus is either increased or decreased ("nonspecific" change in resistance).

Research has shown that changes in cellular chemism during the long-term action of different extreme factors are basically of a

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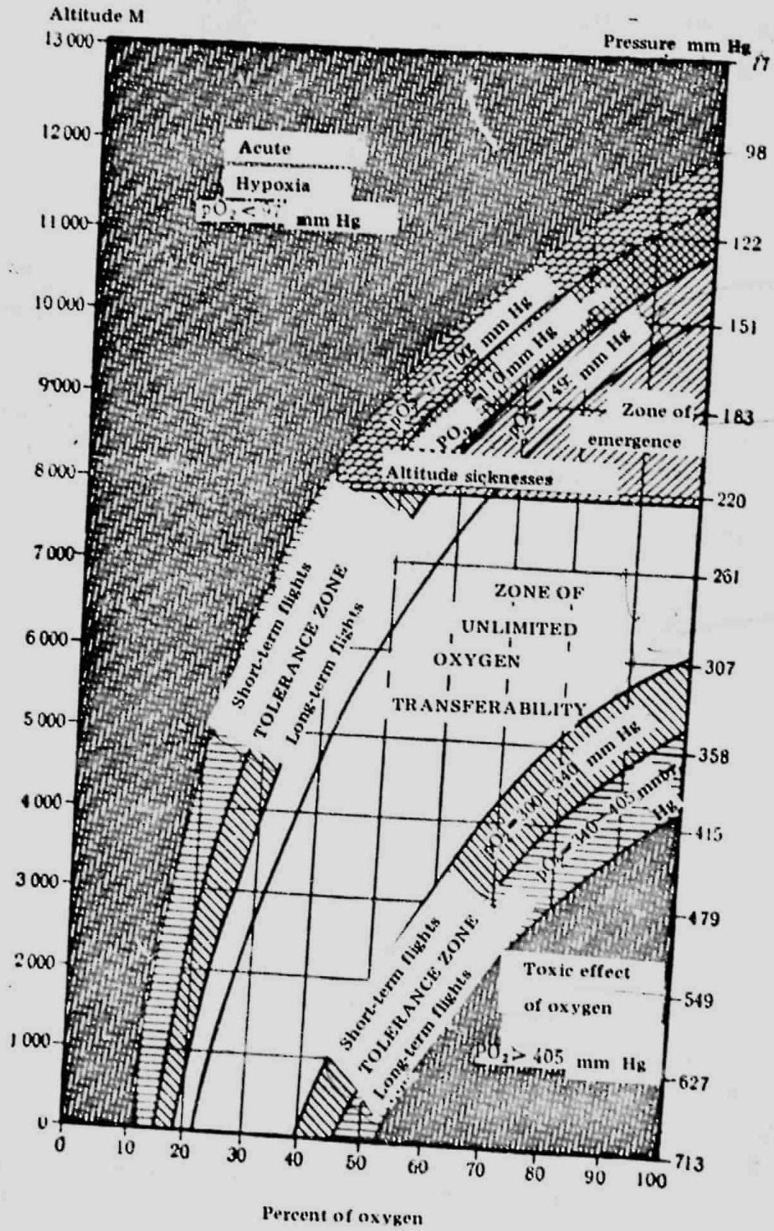

Fig. 33. Limits of the tolerable parameters for the gas medium of manned cabins (in mm Hg)

similar nature. Similar features in cellular adaptive reactions are also noted if we compare animals on different levels of cylogenetic development. All this gives ground for assuming that cellular adaptation is based on reactions formed in the process of the evolutionary development of the animal world.

On the basis of the results of an analysis of our experimental investigation and the data in the literature we already consider it possible to recommend tolerable and optimal oxygen concentrations with respect to short-term (3-5 days) and long-term (up to 2 months) stays in the artificial atmosphere of airtight cabins. These recommended gas medium parameters are shown in Fig. 33 and Table 52.

TABLE 52 /234

GAS MEDIUM FOR INHABITED PRESSURIZED SPACECRAFT CABINS (mm Hg)

Parameter	Short Flights (to 3-5 days)		Long Flights (to 2 months)	
	Permissible Values	Optimal Values	Permissible Values	Optimal Values
Total pressure	307-760	380-405	307-760	380-405
Partial pressure of oxygen	97-405	150-170	115-250	150-170

The indicated values will be made more precise in correspondence with the accumulation of new experimental data in proportion to the increased duration of flight.

For a final solution of the problem of the selection and formation of the most efficient gas medium for manned airtight chambers it is necessary to use the broadest complex of physiological investigations using different pressures and gas compositions, and to investigate resistance to other extreme factors of flight after different periods of stay in an artificial atmosphere: acceleration, vibrations, significant temperature and humidity fluctuation, and so forth.

There is no doubt that persistant and systematic investigative work on this most important medical and biological problem will lead to the successful development of scientifically well-founded principles for the formation of an optimum gas medium for airtight cabins.

Scientific ideas born out of practical work and good theoretical and technical outfitting of medical and biologival research create all the possibilities for the successful solution of the practical scientific problems of our time.

REFERENCES

Agadzhanyan, N. A., Extinction of Conditioned Motor Electrical-Defensive Reflexes in Rarefied Atmospheric Conditions. Zh. vyssh. nervn. veyat., 1956, Vol. VI, No. 2, p. 260.

Agadzhanyan, N. A., The Physiological Basis of the Total Pressure and Oxygen Conditions in Flying Vehicles, doctoral dissertation, Moscow 1968.

Agadzhanyan, N. A., The Problem and the Physiological and Hygienic Basis for an Efficient Gas Environment in Spacecraft Cabins, Zh. kosm. biol. i med., 1969, No. 5, p. 3.

Agadzhanyan, N. A.,Vakar, M. I., Chernyakov, I. N., Variation in Blood Oxygenation at High Altitudes in Relation to the Effectiveness of the Viscosity-Gravity Constant, Voyenn.-med. zh.,1959, No. 5, p. 29.

Agadzhanyan, N. A., Vakar, M. I., Tsivilashvili, A. S., et al., Reaction of the Human Cardio-Vascular System to Hypoxia, Voyenn.-med. zh., 1969, No. 2, p. 65.

Agadzhanyan, N. A., Kuznetsov, A. G., Functions of the Organism in Conditions of Adyanamia and Isolation. Reports of the Scientific Session of the Department of Biological Sciences of the Academy of Sciences, USSR, in honor of the fifth anniversary of the launching of the first artificial earth satellite, Moscow, 1962, p. 25.

Agadzhanyan, N. A., Bizin, Yu. P., Doronin, G. P., Kuznetsov, A. G., Changes in Higher Nervous Activity and Certain Vegetative Reactions in the Case of a Long Stay in Conditions of Adynamia and Isolation, Zh. vyssh. nervn. deyat., 1963, No. 6, p. 953.

Agadzhanyan, N. A., Kalinichenko, I. P., Characteristics of an Investigation of Gas Exchange in Rarefield Atmospheric Conditions, Fiziol. zh. SSSR, 1965, Vol. 51, No. 7, p. 793.

Agadzhanyan, N. A., Zharov, S. G., Kalinichenko, I. R., Kaplan, Ye. Ya. et al, Influence on the Human Organism at Different Decompression Rates, Voyenn.-med. zh., 1965, Vol. 10, p. 49.

Agadzhanyan, N. A., Sergiyenko, A. V., Nature of Variation in Altitude Resistance in Relation to the Decompression Rate, Voyenn.-med. zh., 1966, Vol. 4, p. 59.

Agadzhanyan, N. A., Davydov, G. A., Nature of Variation in Gas Exchange With Extreme Degrees of Atmospheric Rarefaction, Fiziol. zh. SSSR, 1967, Vol. 53, No. 4, p. 421.

Agadzhanyan, N. A., Sergiyenko, A. V., The Ability to Withstand Acute Hypoxia After a Long Stay by Animals in a Medium With a High Oxygen Content, Fiziol. zh. SSSR, 1959, Vol. 55, No. 12, p. 1487.

Agadzhanyan, N. A., Zakharova, I. N., Kalyuzhnyy, L. V., Changes in EEG and Conditioned Feeding Activity After Brief Hypoxia. Zh. vyssh. nervn. deyat.,1969, Vol. XIX,No. 2, p. 369.

Agadzhanyan, N. A., Mirrakhimov, M. M., Gory i rezistentnost' organizma (Mountains and Resistance of the Organism), Moscow, 1970.

Agadzhanyan, N. A., Sergiyenko, A. Z., The Ability to Withstand Acute Hypoxia After Different Periods of Stay in a Medium With an Elevated Carbon Dioxide Content, DAN SSSR,1970, Vol. 191, No. 2, p. 487. /236

Agadzhanyan, N. A., Dvorzhak, I., Kalyuzhnyy, L. V., Moravek, M., Variation in EEG and Behavioral Reaction With Different Levels of Hypoxia, zh. vyssh. nervn. deyat., 1971, Vol. 21, No. 1, p. 176

Agadzhanyan, N. A., Rybakov, B. K., Influence of Hyperoxia on the Coagulating and Anti-coagulating Systems of the Blood, Exper. Khir. I anesteviol., 1971, No. 6, p. 77.

Agadzhanyan, N. A., Usakova, N. A., Influence of Acute Hypoxia on the Organism of Animals with "Deneverated" Sinocarodid Zones, DAN SSSR, 1971, Vol. 198, No. 1, p. 236.

Agadzhanyan, N. A., Shevchenko, Yu. V., Correlation of Changes of Different Functional Systems of the Organism Under the Influence of Increasing Hypoxia on Intact and Narcotisized Animals., DAN SSSR, 1971, Vol. 198, No. 2, p. 471.

Agarkov F. T., Namyatyy, A. N. Organizm cheloveka i zhivotnogo v usloviyakh vysokoy temperatury vneshney sredy. Materialy konferentsii (The Human and Animal Organism in Conditions of High Environmental Temperature. Conference materials) Donetsk, 1962, p. 149.

Alifanov V. N., Spetsial'nyye funktsional'no-diagnosticheskiye issledovaniya serdechno-sosudistoy sistemy i dykhaniya vo vrachebnyy ekspertize letnogo sostava grazhdanskoy aviatsii. Avtoref. dis dokt (Special functional-diagnostic Investigations of the Cardiovascular System and Respiration in a Medical Examination of Civil Aviation Flight Crew. Author's Abstract of Doctoral Dissertation) Moscow, 1968.

Altukhov, G. V., The Influence of a Rarified Atmosphere On the Higher Nervous Activity of Man and Animals, VIII. Vsesoyuzn. "cezd fiziol., biokhim. i farmakol. Doke. (Eighth All Union Congress of Physiologists, Biochemists, and Pharmocologists. Reports.) Moscow, 1965, p. 24.

Altukhov, G. V., Balakhovskiy , I. S., Malkin, V. B., Bioelectrical Activity of the Brain and Blood Saturation With Oxygen in the Case of Acute Hypoxemia., Voyen.-med. zh., 1954, n. 11, p. 30.

Altukhov, G. V., Agadzhanyan, N. A. Characteristics of the Development of and Changes in Conditioned Reflexes in the Case of Breathing Oxygen under High Pressure, Zh. vyssh. nervn. deyat., 1959, 9, 6, p. 865.

Altukhov, G. V., Agadzhanyan, N. A. A Study of the Higher Nervous Activity of Man and Conditions of a Prolonged Stay in a Rarefied Atmosphere., Zh. vyssh. nerv. deyat., 1961, 9, 4, p. 586.

Al'bitskiy, P. M. O vliyanii kislorodnogo golodaniya na azotistiy obmen veshchestv v zhivotnom organizme. Diss. (The Influence of Oxygen Starvation on the Nitrogen Metabolism in the Animal Organism. Dissertation) St. Petersburg, 1884.

Anichkov, N. N. Experimental Research on Anemia of the Brain. Vestn. khir. i pogran. obl., 1929, Vol. 16-17, 48-49, p. 105.

Anichkov, S. V., Belen'kiy, M. L. Farmakologiya khimioretseptorov karotidnogo klubochka. (Pharmocology of the Chemoreceptors of the carotid body.) Leningrad, 1962.

Anokhin, P. K. New Data on the Functional Heterogeneity of the Recticular Formation of the Brain Stem, Zh. vyssh. nervn. deyat., 1959, Vol. 9, 4, p.489.

Apollonov, A. P. Oxygen Supply for High Altitude Flights in the book: Aviatsionnaya meditsina (Aviation Medicine) Moscow, 1953.

Apollonov, A. P., Mirolyubov, B. G. Pains in the Joints, in the book: Vopr. fiziologii i gigiyeny vysotnykh poletove (Problems of the Physiology and Hygiene of High Altitude Flights.) Moscow, 1938.

Ardashnikova, L. I. The Mechanisms of Adaptation of Short-term Oxygen Deficiency in the book: Kislorodnaya terapiya. (Oxygen Therapy), Kiev, 1952, p. 77.

Ardashnikova, L. I. The Significance of Different Chemoreceptor Regions in the Regulation of Respiration in the Case of Oxygen Deficiency. Trudy In-ta norm. i pat. fiziol. AMN SSSR, Vol. 3, Moscow, 1959, P. 64. /237

Ardashnikova, L. I., Shik, L. L. The Mechanism of the Effect of Acute Hypoxemia Respiration, in the book: K regulyatsii dykhaniya, krovoobrashcheniya i gazoobmena. (Regulation of Respiration, Circulation, and Gas Exchange.) Moscow, 1958, P. 25.

Asratyan, E. A. Fiziologiya tsentral'noy nervnoi sistemy. (Physiology of the Central Nervous System), Moscow, 1953.

Akhmedov, K. Yu. Vneshnyeye dykhaniye i ego regulyatsiya v usloviyakh vysokogornoi gipoksii. Avtoref. dis. dokt. (External Respiration and its Regulation in Conditions of High Mountain Hypoxia.) Author's abstract of doctoral dissertation. Dushanbe, 1967.

Balakhovskiy, I. S., Mansurov, A. R., Yazdovskiy, V. I., The Influence of Breathing Pure Oxygen on the Lungs of White Rats, Byull. eksper. biol. i med., 1962, Vol. 53, No. 2, p. 43.

Barbashova, Z. I. Akklimatizatsiia k gipoksii i eë fiziologicheskiye mekhanizmy. (Acclimitization to Hypoxia and its Physical Mechanism.) Moscow-Leningrad, 1960.

Barbashova, Z. I. The Dynamics of Increasing the Resistance of the Organism and Adaptive Reactions on the Cellular Level in the Process of the Adaptation to Hypoxia, Usp. fiziol. nauk, 1970, Vol. 1, No. 3, p. 70.

Belay, V. E., Vasil'ev, P. V., Glod, G. D. The Mechanism of the Adaptation of White Mice to a Hypercapnic Gas Medium, in the book: Problemy kosmicheskoy biologii, (Problems of Space Biology), 1968, No. 8, p. 204.

Belitser, V. A., Tsybakova, Ye. T., Biokhimiya (Biochemistry), 1939, No. 4, p. 516.

Beregovkin, A. V., Buyanov, P. V., Malkin, V. B. Respiration and Gas Exchange in an Acute Hypoxic Test, in the book: Aviatsionnaya i kosmicheskaya meditsina (Aviation and Space Medicine), Moscow, 1963, p. 72.

Berkovich Ye. M., Okhnyanskaya, L. G. Trudy AMN SSSR, 1952, No. 16, p. 63.

Breslav, I. S. vospriyatiye dykhatel'noi sredy i gazoperferendum u zhivotnykh i cheloveka, (Acceptance of the Respiratory Medium and Gas Perferendum in Animals and Man), Leningrad, 1970.

Bernshteyn, S. A., Changes in the Fundamental Parameters of Hemodynamics in the Case of Oxygen Deficiency in the Inhaled Air, Fiziol. zh. AN USSR, 1966, Vol. 12, No. 5, p. 649.

Brestkin, M. P., The Influence of Increased Barometric Pressure on Higher Nervous Activity, Zhurn. vyssh. nervn. deyat., 1952, Vol. 2, No. 3, p. 450.

Brestkin, A. P., Zhironkin, A. G. (Cited by A. G. Zhironkin et. al.)

Vanyushina, Yu. V., Functional Shifts in the Cardiovascular System after the Influence of Hypodynamia, in the book: Aviatsionnaya i kosmicheskaya meditsina, (Aviation and Space Medicine), Moscow, 1963, p. 92.

Vasilenko, M.Ye., Gazenko, O. G., Gramenitskii, P. M., and others, Changes in Altitude Resistance with Altitude Chamber Training,in the book: Funktsii organizma v usloviyakh izmenennoy gazowoy sredy (Functions of the Organism in the Conditions of an Altered Gas Medium) Moscow-Leningrad, 1958, p. 37.

Vvedenskiy, N.Ye., Ob izmenenii dykhatel'nogo ritma pri razdrazhenii bluzhdayushchego nerva elektricheskim tokom pazlichnoy chastoty (The Change in Respiratory Rhythm upon Stimulation of the Vagus Nerve by Electrical Current of Different Frequencies) St. Petersburg, 1889.

Veselkin, G. N., Zykina-Gramenitskaya,Ye. S., The Role of the Basic Vascular Reflexogenic Zones in the Development of the Fever Reaction, in the book: Fiziologicheskiye mekhanizmy likhoradochinykh reaktsiy (Physiological Mechanisms of Fever Reactions). Leningrad, 1957, p. 125.

Vishnevskiy, A. A., Shik, L. L., Berezin, I. P., Use of Oxygen under High Pressure, Eksper. khir. i anesteziol., 1967, Vol. 1, p. 3.

Vladimirov, G.Ye., The Nucleic Acid Content in Small Lymphocytes of the Spleen and Liver Cells of Irradiated White Rats with Protection by Cystamine and Without It, Tsistologiya (Cystology), 1961, Vol. 3, No. 5, p. 560. /238

Voitkevich, V. I., The Hemopoetic Properties of the Blood Serum of Men during a Stay in the Mountains, Materials of the Symposium "Vysokogor'ye i krasnaya krov'" ("High Mountains and Red Blood"), Frunze, 1968, p. 28.

Voytkevich, V. I.,Izuchenie nekotorykh fiziologicheskikh zashchitnykh reaktsiy i ikh mekhanizmov pri dlitel'nom nakhozhdenii cheloveka i zhivotnykh v usloviyakh gipokcii. Diss. dokt. (A Study of some Physiological Protective Reactions and their Mechanisms in Man and Animals during a Long Stay in Conditions of Hypoxia. Doctoral dissertation, Leningrad, 1969.

Voronin, L. G., Dorokin, G. P., A Study of the Influence of a Rarefied Atmosphere on the Function of the Central Nervous System by means of Chain Conditioned Motor Reflexes, Zhurn. vyssh. nervn. deyat., 1965, Vol. 15, No. 5, p. 831.

Vyadro, M. D., The Problem of the Pathogenesis and Expert Evaluation of Hypoxic Collapses in a Flight Crew. Voenn.-med. zh., 1958, No. 3, p. 60.

Gayevskaya, M. S. Biokhimiya mozga pri umiranii i ozhivlenii organizma (Biochemistry of the Brain upon the Death and Revivification of the Organism), Moscow, 1963.

Gazenko, G. G. Shepelev, E. Ya., Metodika issledovaniya gazov krovi (A Method of Investigating Gases in the Blood), Moscow, 1953.

Genin, A. M. Some Principles of the Formation of an Artificial Environment in Spacecraft Cabins, in the book: Problemy kosmicheskoy biologii, (Problems of Space Biology), Moscow, 1964, No. 3, p. 59.

Genin, A. M., Zharov, S. G., Kaplan, E. Ya., et. al. Investigation of the Long-Term Action of an Oxygen Atmosphere at Low Pressure on Animals and Man, 18th Congress of the International Astronautical Federation, Belgrade, 1967. (Reprint)

Gershuni, G. V., Problemy fiziologicheskoy akustiki (Problems of Physiological Acoustics), Moscow, 1949, No. 1, p. 13.

Gramenitskiy, P. M., Ob usloviyakh i mekhanizme razvitiya dekompressionnykh narusheniy. Diss. Dokt., (The Conditions and Mechanism of the Development of Decompression Disorders. Doctoral Dissertation, Leningrad, 1967.

Gubler, Ye. V., The Role of "Natural" Hypothermia in Oxygen Starvation and the Influence on its Course of a Low Environmental Temperature, Usp. sovr. biol., 1962, Vol. 53, No. 3, p. 306.

Dedyulin, I. M., Kislotno-shchelochnoye ravnovesiye i dykhamel'naya funktsiya krovi cheloveka v usloviyakh razrezhennoy atmosfery (The Acid-base Balance and Respiratory Function of the Human Blood in Conditions of a Rarefied Atmosphere), Leningrad, 1941.

Dembo, A. G., Kreps,Ye. M., Methods of Investigating the Function of External Respiration, in the book: Fiziologicheskiye metody v klinicheskoy praktike (Physiological Methods in Clinical Practice), Leningrad, 1959, p. 59.

Dianov, A. G., Kuznetsov, A. G., The Possibility of Replacing the Nitrogen of the Air with Helium in Spacecraft Cabins, in the book: Aviatsionnaya i kosmicheskaya meditsina (Aviation and Space Medicine), Moscow, 1963, p. 162.

Davydov, G. A.,Nikolayev, V. P., Dynamics of the Changes in Alveolar Air Composition during a Human Stay at High Altitudes, Patol. fiziologiya i eksper. terpaniya, 1972, No. 1, pp. 39-44.

Yegorov,P. I.,Vliyaniye ponizhennogo partsial'nogo davleniya kisloroda na organizm cheloveka. Diss. (The Influence of a Reduced Partial Pressure of Oxygen on the Human Organism. Dissertation), Leningrad, 1936.

Zhironkin, A. G., Panin, A. F., Sorokin, P. A., Vliyaniye povyshennogo partsial'nogo davleniya kisloroda na organizm cheloveka i zhevotnykh (The Influence of a Reduced Partial Pressure of Oxygen on Man and Animals), Leningrad, 1965.

Zal'tsman, G.L.,Fiziologicheskiye osnovy prebyvaniya cheloveka v usloviyakh povyshennogo davleniya gazovoy sredy. (The Physiological Fundamentals of the Stay in Conditions of Increased Pressures of the Gas Medium), Leningrad, 1961.

Zvorykin, V. N.,Vliyaniye razrezhennogo vozdukha na vysshuyu nervnuyu deyatel'nost', Avtoref. diss. kand. (The /239
Influence of Rarefied Air on Higher Nervous Activity. Author's Abstract of Candidate Dissertation.) Leningrad, 1951.

Zilov, G. N., Funktsional'noye sostoyaniye vysshikh tsentral'noy nervnoy sistemy i gazovyy obmen v usloviyakh giperoksii. Avtoref. diss. dokt. (The Functional Condition of the Higher Sections of the Central Nervous System and Gas Exchange in Conditions of Hyperoxia. Author's Abstract of Doctoral Dissertation.), Moscow, 1956.

Ivanov, D. I., Malkin, V. B., Chernyakov, I. N. et. al., Changes in the Basic Physiological System during an Extended Stay of a Man in Conditions of Reduced Barometric Pressure and Restricted Space, in the book: Aviatsionnaya i kosmicheskaya meditsina (Aviation and Space Medicine), Moscow, 1963, p. 202.

Ivanov, K. P., Kislorodnoye golodaniye i temperatura (Oxygen Starvation and Body Temperature), Leningrad, 1968.

Isabayeva, V.A., Vliyaniye ponizhennogo atmosfernogo davleniya na vysshuyu nervnuyu deyatel'nost'. Avtoref. diss. kand. (The Influence of Reduced Atmospheric Pressure on Higher Nervous Activity. Author's Abstract of Candidate's Dissertation), Moscow, 1954.

Isakov, P. K., The Structure of the Respiratory Cycle and Gas Exchange in the case of Breathing in Special Conditions., Byull. eksper, biol. i med., 1947, Vol. 23, No. 3, p. 22.

Kakurin, L. I., Katkovskiy, B. S., Kozlov, A. N., Mukharlyamov, N. M., The Influence of Hypokinesia on Several Indicators of the Efficiency and Functioning of Human Respiration in the book: Aviatsionnaya i kosmicheskaya meditsina, (Aviation and Space Medicine), Moscow, 1963, p. 226.

Kalinina, M. K., Alyukhin, Yu. S., Fiziol. zh. SSSR, 1969, Vol. 55, No. 12, p. 1481.

Kalinichenko, I. R., Izmeneniye funktsii vneshnego dykhaniya pri dlitel'nom prebyvanii cheloveka v razrezhennoy atmosfere s povyshennym soderzhaniyem CO_2 i normal'nym pO_2. Diss. kand. (Change in the Function of External Respiration during an Extended Stay in a Rarefied Atmosphere with an Elevated CO_2 content and Normal pO_2. Candidate's dissertation), Moscow, 1966.

Kalyuzhnyy, L. V., Agadzhanyan, N. A., Zakharova, I. N., Correlation of Changes in the EEG and Conditioned Reflex Feeding Activity in Rabbits under the Affects of Increasing Hypoxia. Zhurn. kosm. biol. i med., 1967, No. 5, p. 38.

Katkovskiy, B. S. Nekotorye osobennosti potrebleniya kisloroda pri fizicheskoy rabote posle dlitel'nogo ogranicheniya dvigatel'noy aktivnosti cheloveka. Diss. Kand. (Some Characteristics of the Oxygen Consumption during Physical Work after a Prolonged Limitation on the Motor Activity of a Man. Candidate's Dissertation), Moscow, 1966.

Kovalenko, Ye.A., Izmeneniya napryazheniya kisloroda v tkanyakh pri gipoksii. Avtoref. diss. dokt. (Changes in the Oxygen Pressure in the Tissues in the case of Hypoxia. Author's Abstract of Doctoral Dissertation), Moscow, 1966.

Kovalenko, Ye. A., Chernyakov, I. N., Tissue Oxygen under Extreme Flight Conditions, Pr. kosm. biologii, Vol. 21, Moscow, 1972.

Kolchinskaya, A. Z., Nedostatok kisloroda i vozrast (Oxygen Insufficiency and Age), Kiev, 1964.

Konza, E. A., Fiziol. zhurn. SSSR., 1970, Vol. 56, No. 7, p. 1064.

Korzhuyev , P. A., The Problem of Oxygen Reserves in Animal and Human Organisms. Materials of the Symposium "Kislorodnyy rezhim organizma i ego regulirovaniye" (The Oxygen Regime of the Organism and its Regulation), Kiev, 1966, p. 127.

Korobkov, A. V., dostizheniye vysokoy rabotosposobnosti v usloviyakh ogranichennoy podvizhnosti. Materialy nauchnoy konferentsii. (Achieving High Efficiency in Conditions of Limited Mobility. Materials of the Scientific Conference.), Leningrad, 1961, p. 3.

Kreps, Ye. M., Ugol'naya angidraza v evolyutsii funktsii dykhaniya. Carbon Anhydrase in the Evolution of the Respiratory Function. Trudy Fiziol. in-ta imeni Pavlova, Leningrad, 1945, No. 1, p. 77.

Koshtoyants, Kh. S., Belkovye tela, obmen veshchestv i nervnaya regulyatsiya (Albumin Bodies, Metabolism, and Nervous Regulation) Moscow, 1951.

Kreps, Ye. M., Verzhbinskaya, N. A., Chenykayeva, Yu. Ye., et al., The Influence of Chronic Hypoxia on the Hemoglobin, Myohemoglobin, and Cytochrome Content and on the Activity of the Cytochromoxidase and Carboanhydrase of the Blood and Tissues., Fiziol. zh. SSSR, 1956, Vol. 42, No.2, p. 149.

Kuznetsova, A. G., Breathing Oxygen under Excess Pressure at High Altitudes, in the book: Aviatsionnaya meditsina, (Aviation Medicine), Moscow, 1959.

Kuznetsov, A. G., Agadzhanyan, N. A., Bizin, Yu. P., Kalinichenko, I. R., et. al., The Nature of the Change in the Respiratory Function and Cardio-vascular System during Extended Stay under Conditions of Reduced Barometric Pressure, in the book: Aviatsionnaya i kosmicheskaya meditsina (Aviation and Space Medicine), Moscow, 1963, p. 318. /240

Kuznetsov, A. G. Agadzhanyan, N. A., Dianov, A. G. Zharov, S. G., Influence on the Organism of an Extended Stay in the Conditions of an Artificial Atmosphere. Materials of the 15th International Congress on Astronautics, Warsaw, 1964.

Kulik, A. M., Analysis of the Causes Producing Hypoxic Phenomena in Patients with Respiratory and Circulatory Disorders, in the book: Voprosy regulyatsii dykhaniya v norme i patologii (Problems of the Regulation of Respiration in Normal Conditions and Pathology), Moscow, 1959, p. 34.

Kulik, A. M., Regulyatsiya dykhaniya pri raznykh vozdeystviyakh na organizm. Avtoref. diss. dokt. (Regulation of Respiration in the case of Different Influences on the Organism. Author's Abstract of Doctoral Dissertation), Moscow, 1967.

Kurshakov, N. A., Troitskiy, N. A., A Method of Investigating Gas Exchanges in the Lungs, Klin. med., 1951, Vol. 29, No. 5, p. 12.

Lauer, N. V., Kolchinskaya, A. Z., The Oxygen Regime of the Organism. Materials of the Symposium "Kislorodnyy rezhim organizma i ego regulirovaniye" (The Oxygen Regime of the Organism and its Regulation), Kiev, 1966, p. 3.

Lebedinskiy, A. V., Levinskiy, S. V., Nefedov, Yu, G., A Unique Experiment by Soviet Scientists, in the book: Aviatsiya i kosmonavtika (Aviation and Cosmonautics), 1964, No. 11, p. 24.

Livanov, M. N., Nekotorye voprosy sovremennoy elektroentsefalografii. (Some Problems of Modern Electroencephalography), Moscow-Leningrad, 1960.

Lifshits, A. V., The Influence of Hypoxemia on Higher Nervous Activity., Fiziol. zh. SSSR, 1949, Vol. 35, No. 1, p. 3.

Malkin, V. B., Razumeyev, A. N., Izosimov, G. V., Investigation of the Bio-electrical Activity of the Cerebral Cortex and some Sub-cortical Formations in the case of Acute Hypoxemia, in the book: Kislorodnaya nedostatochnost' (Oxygen Insufficiency), Kiev, 1963, p. 104.

Mansurov, A. R., Agadzhanyan, N. A., Doronin, G. P., The Ability to Withstand Explosive Decompression after Prolonged Breathing of Pure Oxygen at an "Altitude" of 10,000 Meters, Tezisy dokl. X Vsesoyuzn. s"ezda fiziologov (Summaries of Reports of the Tenth All-Union Congress of Physiologists), Yerevan, 1964, Vol. 2, No. 2, p. 57.

Marshak, M.Ye., Regulyatsiya dykhaniya u cheloveka (Regulation of Human Respiration), Moscow, 1961.

Marshak, M.Ye., Fizidogicheskoye znacheniye uglekisloty (Physiological Significance of Carbon Dioxide), Moscow, 1969, p. 143.

Mirrakhimov, M. M., Ocherki o vliyanii gornogo klimata Sredney Azii na organizm (Outline of the Influence of the Mountain Climate of Central Asia on the Organism), Frunze, 1964.

Moiseyev, Ye.A., Zur Kenntnis des Corotissinsraflex, (Information on the Corotissin Reflex) Z. exp. Med., 1927, No. 53, p. 696.

Namyatyy, A. N. O temperature vydykhayemogo al'veolyarnogo vozdukha i fiziologicheskom znachenii eё izmeneniy pri rabote v usloviyakh obshchego intensivnogo teplovogo vozdeystviya. Diss. kand. (The Temperature of Exhaled Alveolar Air and the Physiological Significance of its variations during work under conditions of a General Intensive Heat Influence. Candidate's Dissertation), Donetsk, 1966.

Nefedov, Ye. G., Zaloguyev, S. N., The Problem of the Habitability of Spacecraft, Zhurn. kosm. biol. i med., 1967, Vol. 1, No. 1, p. 30.

Ol'nyanskaya, R. P., Isaakyan, L. A., Metody issledovaniya gazovogo obmena u cheloveka i zhivotnykh (Methods of Investigating Gas Exchange in Man and Animals), Leningrad, 1959.

Oparin, A. I., The State and Problems of the Investigation of the Origin of Life, in the book: Abiogenez i nachal'nye stadii evolyutsii zhizni, (Abiogenesis and the Initial Stages of the Evolution of Life), Moscow, 1968.

Orbeli, L. A., The Nervous System Under Reduced Pressure, /241 Sov. nauka, 1940, No. 10, p. 66.

Pavlov, I. P., Polnoye sobraniye sochineniy (Complete Collected Works), Moscow-Leningrad, 1951.

Palladin, A. V., Results and Problems of an Investigation in the Biochemistry of the Brain, in the book: Biokhimiya nervnoy sistemy (Biochemistry of the Nervous System), Kiev, 1954, p. 7.

Parin, V. V., Meyerson, F. Z., Ocherki klinicheskoy fiziologii krovoobrashcheniya (Outline of the Clinical Physiology of Circulation), Moscow, 1965.

Parfenova, O. I., Livanov, M. N., Biocurrents of the Brain in Conditions of Reduced Barometric Pressure, Byull. eksper. biol. i med., 1945, No. 20, p. 36.

Palosh, L. A., Fibrinolysis as a Physiological and Pathophysiological Process, in the book: Fibrinoliz (Fibrinolysis), Budapest, 1970, p. 7.

Pashutin, V. V., Lektsii po obshchey patologii (Lectures in General Pathology), St. Petersburg, 1881.

Petrov, I. R., Kislorodnoye golodaniye golornogo mozga (Oxygen Starvation of the Brain), Leningrad, 1949.

Petrov, I. R., Rol' tsentral'noy nervnoy sistemy, adenogipofiza i kory nadpochechnikov pri kislorodnoy nedostatochnosti (The Role of the Central Nervous System, Adenohypophysis, Adrenal Cortex in the Case of Oxygen Defficiencies), Leningrad, 1967.

Petrun', N. M., Gazoobmen cherez kozhy i ego znacheniye dlya organizma cheloveka (Gas Exchange Through the Skin and its Significance for the Human Organism), Moscow, 1960.

Redf''d, A., Evolution of the Respiratory Function of the Blood, Usp. sovr. biol., 1934, Vol. 3, No. 3, p. 322.

Rozenblyum, D.Ye., Adaptation to Oxygen Starvation in the Case of the Short-term and Repeated Effects of Decreased Barometric Pressure, Byull. eksp. biol. i med., 1943, Vol. 16, No. 1-2, p. 6.

Rozenblyum, D.Ye., Pozharskiy, F. I., Khazen, I. M., An Analysis of the Changes of the Respiratory and Circulatory Functions in the Case of Large and Rapid Pressure Drops, in the book: Voprosy aviatsionnoy meditsiny, (Problems of Aviation Medicine), Moscow, 1957, p. 9.

. Rossolovskiy, N. A., Acclimatization to a High Mountain Location as a Method of Increasing Resistance to Anoxia, Trudy III Uzbeksk. konfer. fiziol. biokhim. i farmakol. (Reports of the Third Uzbekistan Conference of Physiologists, Biochemists, and Pharmacologists), Tashkent, 1951, p. 11.

. Savitskiy, N. N., Kislorodnaya terapiya (Oxygen Therapy), Leningrad, 1940.

. Sanotskaya, N. V., Changes in the Tissue Oxygen Pressure in the case of Hypoxia and Hyperoxia, Byull. eksper. biol. i med., 1961, Vol. 51, No. 6, p. 33.

. Sanotskaya, N. V., The Influence of Carbon Dioxide on the Oxygen Pressure on the Brain and Skeletal Muscles in the case of Acute Hypoxia, Byull. eksper. biol. i med., 1962, Vol. 54, No. 9, p. 46.

Sanotskaya, N. V., The Influence of Carbon Dioxide on the Oxygen Pressure on the myocardium, Fiziol. zh. SSSR, 1966, Vol. 11, No. 5, p. 556.

Sakhiulina, G. T., Anemization as a Means of Studying the Functions of the Central Nervous System, Byull. eksp. biol. i med., 1949, Vol. 28, No. 3, Sec. 9, p. 212.

. Severin, S.Ye., The Energy Supply of Physiological Functions. Ref. dokl. na X s"ezde Vses. fiziol. obshchestva (Abstracts of Reports at the Tenth Congress of the All-Union Society of Physiologists), Yerevan, 1964.

. Sergeyev, A.A., Vliyaniye uskoreniy na organizm letchika, (The Influence of Acceleration on a Pilot's Organism), Moscow, 1957.

. Sergiyevskiy, M. V., New Information on the Regulation of Breathing, in the book: Novoye v fiziologii i patologii dykhaniya (New Developments in the Physiology and Pathology of Breathing), Moscow, 1961, p. 188.

. Sechenov, I. M., The Problem of Breathing Rarefied Air, Vrach, 1880, pp. 21-22.

. Simonov, Ye. Ye., On Determining the Absolute DNA Content in Cell Nuclei, Laborator. delo, 1966, No.5, p. 263.

. Sirotinin, N. N., History of the Development of the Sickness of Mountain Sickness in the collection of works of the Kazan Medical Institute, Kazan, 1931, No. 1, p. 3.

Sirotinin, N. N., Anoxic anoxemia., Klin. med., 1941, Vol. 19, No. 3, p. 5. /242

Skulachev, V. P., New Developments in the Study of Oxidizing Phosphorylization in Mitochondria, Usp. sovr. biol., 1958, Vol. vi-xi, No. 3, p. 241.

Sokolov, V. A., Gazy Zemli (The Gases of the Earth), Moscow, 1966.

Strel'tsov, V. V., Physiological Notes on High-Altitude Flights; Pressure Chamber Experiments, Vestn. vozd. flota, 1933, No. 3, p. 22.

Strel'tsov, V. V., Vysotnyye polety i vliyaniye ikh na organizm cheloveka (High Altitude Flights and Their Influence on the Human Organism), Moscow, 1939.

Strel'tsov, V. V., Khazen, I. M., The Activity of Carboanhydrase in the Blood and Several Tissues of the Organism in the Case of Reduced Barometric Pressure, Byull. eksp. biol. i med., 1946, Vol. 21, No. 4, p. 65.

Uzhanskiy, Ya. G., Fiziologicheskiye mekhanizmy regeneratsii krovi, (The Physiological Mechanism of Blood Regeneration), Moscow, 1968.

Uspenskiy, Yu. N., Deyatel'nost' pishchevarimel'nykh organov v usloviyakh vysokogor'ya i pri poletakh na samolete. Diss. dokt. (The Activity of the Digestive Organs in High Mountain Conditions and Airplane Flights. Doctoral Dissertation), Moscow, 1943.

Khazen, I. M., Kuznets, Ye. I., The Influence of Large Drops in Barometric Pressure in Micro-intervals of Time on the Higher Nervous Activity of White Rats, DAN SSSR, 1956, No. 108, p. 5.

Charnyy, A. M., Patofiziologiya gipoksicheskikh sostoyaniy (The Pathophysiology of Hypoxic Conditions), Moscow, 1961.

Chernigovskiy, V. N., Developmental Tendencies of Certain Physiological Problems, Izv. AN SSSR, 1971, No. 5, p. 661.

Shik, L. L., Gazoobmen pri kislorodnom golodanii, Diss. dokt. (Gas Exchange in the case of Oxygen Starvation. Doctoral Dissertation,) Moscow, 1947.

Engel'gardt, V. A., Nekotorye problemy sovremennoy biokhimii (Some Problems of Contemporary Biochemistry), Moscow, 1959.

Engel'gardt, V. A., Molecular Respiration, in the book: Uchenyye zapiski Kabardino-Balkarskogo gos. un-ta., (Scientific Writings of Karbardin-Balkarskiy State University, 1967, Vol. 33, p. 7.

Yakobson, M. I., Kessonnaya bolezn' (Cassion Disease), Moscow, 1950.

Adams, J. D., Conkle, J. P. et al. Study of man during a 56-day exposure to an oxygen-helium atmosphere at 258 mm. Hg total pressure. II. Major and minor atmospheric components. Aerosp. Med., 1966, 37, 6, 555.

Allen, S. E. Further studies on the role of nitrogen in the problem of O_2 toxicity The Physiologist, 1962, 5, 98.

Alvarex-Buylla, R. A study of the chemoreceptor activity in the carotid sinus. XIX-the Intern. Congr. of Physiol., 1953.

Armstrong, H. G. Aviatsionnaya meditsina (Aviation Medicine). Translated from English, Moscow, 1954.

Balke B., Wells, J. G. Ceiling altitude tolerance following physical training and acclimatization. J. av. Med., 1958, 29, 40.

Bancroft, R. W., Dunn, J. E. Experimental animal decompressions to a near vacuum environment. Aerosp. Med., 1965, 36, 8, 720.

Banus, M. G., Corman, H. H., Perlo V. P., Popkin G. L. The sensitivity of the respiratory center to hydrogen ion concentration. Am. J. Physiol., 1944, 142, 1, 121.

Barcroft, J. Osnovnyye cherti arkhitektury fiziologicheskikh funktsiy (Basic Features of the Architecture of the Physiological Functions). Translated from English, Moscow-Leningrad, 1937.

Bargeton, D. Analysis of capnigram and oxygram in man. Bull. physio-pathol. respirat., 1967, 3, No. 3, 503.

Bartek, M. I., Ulvedal F. et al. Study of man during a 56-day exposure to an oxygen-helium atmosphere at 258 mm. Hg total pressure, IV. Selected blood enzyme response. Aerosp. Med., 1966, 37, 6, 563.

Bean, J. W. Effects of Oxygen at Increased Pressure. Physiol. Rev., 1945, 25, 1. /243

Becker-Freyseng, H., Clamann H. G. Die Wirkung langdauernder Sauerstoffatmung in verschiedenen Hohen auf den Menschen (The Effect of Continuous Oxygen Inhalation at Various Altitudes on Human Beings). Berlin, "Luftfahrmedizin," 1942, 7, s. 272.

Berry, L. J., Smythe D. S. Effect of pure oxygen at reduced pressure on metabolism changes in mice. Am. J Physiol., 1962, 203(1), 155.

Berry, C. A., Minners, H. A., McCutcheon E. P., Polland R. A. Aeromedical Analysis. In: Results of the Third U. S. Manned Orbital Flight. Manned Spacecraft Center, NASA, Houston, Texas, October 3, 1962.

Bert, P. La pression barometrique; recherches de physiologie experimental (Barometric Pressure; Physiological Experimental Researches). Paris. 1878.

Boothby, W. M., Luft, U. C., Benson O. O., J. av. med., 1952, 23, 2, 141.

Bowman, N. J., Dingman, E. H. An environmental conditioning system for a manned satellite. J. Brit. Interplan. Soc., 1960, 17, 10, 372.

Brooksby, G. A., Dennis, R. L., Staley R. W. Effects of Continuous Exposure of Rats to 100 per cent Oxygen at 450 mm. Hg for 64 Days. Aerosp. Med., 1966, 37, 243.

Campbell, J. A., J. Physiol.(London), 1938, 92, 29.

Campos, I., Iglesias B. Mechanisms of Natural Acclimatization. Preliminary Report on Anatomic Studies at High Altitudes. School of Av. Med., U.S.A.F., Randolph Field, Texas. Rep., 1956, 55.

Celentano, J. T., Alexander, J. B. Bioengineering for the zero G environment. Phys. and Biol. Phenomena Weightless State. Baltimore Md., Am. Astronaut. Soc., 1963, 350.

Cockett, A., Nakamura, R. M., Franks, J. J. Recent findings in pathogenesis of decompression sickness (dysvarism). Surgery, 1965, August, v. 58, 2, 384.

Colinet-Lagneaux, D., Herman-Gedang, J., Troquet, J. J. Physiol. (France), 1967, 59, 4, bis, 381.

Comroe, J., Forster, R., Dubois, A. et al. Klinicheskaya fiziologiya i funktsional'nyye probyi (Basic Physiological and Functional Probes) Translated from English, 1961.

Comroe S. H., Dripps R. D., Dumke P. R., Deming M. Oxygen Toxicity: The Effect of Inhalation of High Concentrations of Oxygen for Twenty-four Hours on Normal Men at Sea Level and at a Simulated Altitude of 18,000 feet. J.A.M.A., 1945, 128, 710.

Cook, J. F. The Inhibition of animal metabolism under decompression. J. av. Med., 1945, 16, 4, 268.

Dale W. A., Rahn H. Rate of gas absorption during atelectasis. Am. J. Physiol., 1952, 170, 606.

Daly M., Lambertsen C. J., Schweitzer A. Observations on the volume of blood flow and oxygen utilization of the carotid body in the cat. J. Physiol. (London), 1954, 125, 1, 67.

Darling R. C., Cournard A., Richards D. W. Studies on the intrapulmonary mixture of gases. J. clin. Invest., 1940, 19, 4, 609.

David-Heather M. Airmen live 17 days on pure oxygen. Missles, Rockets, 1961, 9, 4, 27, 44.

Dejours P., Labrousse Y., Raynaud J., Rirard F., Teillac A. The Oxygen Stimulation of Ventilation at Rest and During Muscular Exercise at a Low Altitude (50 m) for Human Beings). Rev. Franc. D'etudes clin. et biol., 1958, 3(2), 105.

Dickens F. The toxic effects of oxygen on brain metabolism and on tissue enzyme. Biochem. J., 1946, 40, 145. /244

Dickerson K. H. Pathophysiology of Pulmonic Toxicity in Rats Exposed to 100 Per Cent Oxygen at Reduced Pressures. MADC-ML-6403, U.S. Naval Air Development Center, Johnsville, Pennsylvania, 1964.

Dines J. H., Hiatt E. P. Prolonged Exposure of Young Rats to an Oxygen Atmosphere at Reduced Pressure. J. App. Physiol., 19, 17,1964.

Edelman N., Mittman C., Norris A., Shock N. J. appl. Physiol. 1968, 24, 1, 49.

Ernsting J. The effect of breathing high concentrations of oxygen upon the diffusing capacity of the lung in man. J. Physiol., (London), 1961, 155, 51.

Fabre J. et al. Enzyme Inhibition and Hyperoxia Rev. Med. Aeronaut., 1965, 4, 13, 45.

Farhy L., Rahn H. Anesthesiology, 1960, 21, 604.

Fay F. S. Oxygen consumption of the carotid body. Am. J. Physiol., 1970, 218, 2, 518.

Fenn W. O., Rahn H., Otis A. B. Theoretical study of the composition of the alveolar air at altitude. Am. J. Phys., 1946, 146, 637.

Fowler W., Cornish E., Kety S. J. clin. Invest., 1952, 31, 40.

Furry D. E. Protection of vibrated rats exposed to explosive decompression. Aerosp. Med., 1964, 35, 8, 773.

Gable W. D., Townsend F. M. Lung morphology of individuals exposed to prolonged intermittent supplemental oxygen. Aerosp. Med., 1962, 33, 1344.

Gauer O. Luftfahrtmed., 1944, 9.

Gesell R. The chemical regulation of respiration, Physiol. Rev., 1925, 5, 4, 551.

Grant W. Influence of carotid body on polycythemia and arterial oxygen saturation. Am. J. Physiol., 1951, 164, 226.

Graveline D. E. Maintenance of cardiovascular adopta dility during prolonged weightlessness. Aerosp. Med., 1962, 33, 3, 297.

Gray J. S. Pulmonary ventilation and its physiological regulation. Am. Lecture, Ser. 63. Springfield, 1950.

Graybiel A., Clark B. Symptoms resulting from prolonged immersion in water: the problem of zero G-asthenia. Aerosp. Med., 1961, 32, 3, 181.

Haldane J. C., Priestley J. G. Respiration. Oxford, 1935.

Haugaard N. Oxygen poisoning XI - The relation between onactivation of enzymes by oxygen and essential sulfhydril group. J. biol. Chem., 1946, 164, 265.

Helvey W. M. quoted by M. E. Roth. Space-cabin atmospheres part I - Oxygen toxicity. Washington, 1964.

Henry F. M., Cook S. F. Effectiveness of pre-flight oxygen breathing in preventing decompression sickness. J. av. Med., 1945, 16, 350.

Hemingway A. J. av. Med., 1944, 15, 298.

Hering H. Die Karotid sinusreflexe auf Herz und Gefasse (The Carotid Sinusoidal Reflexes of the Heart and Blood Vessels), Dresden, Steinkopt, 1927.

Hesser C. M. The Role of Nitrogen in Breath-holding at Increased Pressures. In: Man's Dependence on the Earthly Atmosphere. K. E. Schaefer, ed. N. Y.: The Macmillan Co., 1962, y. 327

Heymans C. On the Physiology and Pharmacology of the Coronary Vagus Centers. Erg. Physiol., 1929, 28, 244.

Heymans C., Bouckaert I. I., Dautrebande L. The Sinusoidal Carotid Respiratory Reflexes. Arch. intern. Pharmac. Ther., 1930, 39, 400.

Heymans C. Chemoreceptors and regulation of respiration. Acta physiol. scand., 1951, 22, 4.

Heymans J. F., Heymans C. On the Reflex Regulation of Respiration. Ann. physiol., 1927, 3, 471.

Hitchkock F. A. Physiological and Pathological effects of Explosive Decompression. J. Av. Med., 25, 6, 1954, 578.

Hoffman C. E., Clark R. F., Brown B. Am. J. Physiol., 1946, 145, 685.

Houston C. S., Riley R. L. Respiratory and circulatory changes during acclimatization to high altitude, Am. J. Physiol., 1947, 149, 565.

Hurtado A. Acclimatization to high altitudes. The physiological effects of high altitude. The Macmillan Company. New York, 1963, 1.

Kamakura K. Prophylaxis of hypoxia by carbamates and As mechanism. p. 319. XXIII International congress of Physiological Sciences. Tokyo, 1965, 319.

Kaplan H. P. Hematologic effects of increased oxygen tensions. Aerosp. Med., 1967, 38, 7, 676.

Kaunitz J. J. J. av. Med., 13, 1942, 267.

Kety S. S., Schmidt C. F. The determination of cerebral blood flow in man by the use of nitrous oxide in low concentrations. Am. J. Physiol., 1945, 143, 1, 53.

Kim T. S., Rahn H. Estimation of true venous and arterial pCO_2 by gas analysis of a single breath. J. appl. Physiol., 1966, 21, 4, 1338.

Konecci E. B. Human factors and Space Cabin Development, Report to the 12th Annual Conference of the American Rocket Society, New York, 1957.

Kraus H., Raab W. Hypokinetic oliscase. Diseases produced by lack of exercise. Springfield, Illinois, USA, 1961.

Kuno Jas. Perspiratsiya cheloveka (Human Perspiration). Translated from English, Moscow, 1961.

Lamb L. E., Stevens P. M., Johnson R. L. Hypokinesia secondary to chair rest from 4 to 10 days. Aerosp. Med., 1965, 36, 8, 755.

Lambersten C. Y., Kough R. H., Cooper D. Y. et al. Comparision of the Relationship of Respiratory Minute Volume to PCO_2 and pH of Arterial and Internal Yungular Blood in Normal Man during Hyperventilation Produced by Low Concentrations of CO_2 at 1 Atmosphere and by O_2 at 3.0 Atmospheres. J. appl. Physiol., 1953, 5, 12, 803.

Landgren S., Neil E. The contribution of Carotid Chemoreceptor mechanisms to the rise of blood pressure caused by carotid occlusion. Acta Physiol. scand., 1951, 23, 152.

Leituer L. M., Lianbet M. J. Carotid Body Oxygen Consumption of the Cat in vitrl. Pflug. Arch., 1971, 323, 315.

Loeschcke H. H., Koepchen H. P., Gertz K. H. The Influence of Hydrogen Ion Concentration and CO_2 Pressure in the Cerebral Spinal Fluid upon Respiration. Phlug. Arch. Physiol., 1958, 266, 6, 569.

Malmejac J., Plane P. Influence of oxygen want on functional cortical fitness. J. av. Med., 1952, 23, 2, 177,

McIlwain H. Biokhimiya i tsentral'naya nervnaya sistema (Biochemistry and the Central Nervous System). Translated from English, Moscow, 1962.

Megel H. et al. Aerosp. Med., 1963, 34, 319.

Mengel C. E., Kann H. E. Jr., Lewis A. Ma., Horton B. Mechanisms of in vivo Hemolysis Induced by Hyperoxia. Aerosp. Med., 1964, 35, 857. /246

Miller P. B., Hartman B. O., Johnson R. L., Lamb L. E. Modification on the effects of two weeks of bed rest upon circulatory functions in man. Aerosp. Med., 1964, 35, 10, 931.

Motobayaski F., Mitrai V., Ando S. 4th Internal Sympos. Space Technol. Sci. Tokyo, 1963, p. 100.

Neswald R. G. The spacecraft atmosphere. Space Aeronaut., 1967, 48, 3, 71.

Ohlsson W. T. L. A Study on Oxygen Toxicity at Atmospheric Pressure. Acta med. scand., 1947, 128, 190.

Orr C. Mezhdu zemlyey i kosmosom (Between the Earth and the Stars). Translated from English, Leningrad, 1964.

Pflesser G. Contribution Concerning the Question of the Toxicity of Oxygen. Arch. exp. Path. Pharmak., 1937, 187, 472.

Purves M. J. The effect of hypoxia, hypercapnia and hypotension upon carotid body blood flow and oxygen consumption in the cat. J. Physiol. (London), 1970, 209, 395.

Reynafarje B. Myoglobin content and enzymatic activity of muscle and altitude adaptation. J. appl. Physiol., 1962, 17, 301.

Robertson W. G., Ws Rae G. L. Study of man during a 56-day exposure to an oxygen-helium atmosphere at 258 mm Hg total pressure. VII. Respiratory function. Aerosp. Med., 1966, 37, 6, 578.

Robinson F. R., Harper D. T., Thomas A., Kaplan P. Proliferative pulmonary lesions in monkeys exposed to rich concentration of oxygen. 37th Annual Scientific Meeting. Aerosp. Med., 1966, 4, 18.

Roth E. M. Space cabin Atmospheres, Part I - Oxygen Toxicity. NASA. Houston, Texas, 1964, SP-47.

Schaefer K. E. Gaseous requirements in manned space flight. "Bioastronautics," New York, Macmillan Co., London Collier - Macmillan Ltd., 1964, 76.

Selje H. Ocherki ob adaptatsionnom sindrome (Sketches of Adaptation Syndrome), Moscow, 1960.

Stadie W., Riggs G., Haugaard N. Oxygen Poisoning. Am. J. med. Sci., 1944, 207, 84.

Strughold H. Atmospheric Space Equivalence. J. av. Med., 1954, 25, 4,420.

Taylor H. J. J. Physiol., 1949, 108, 264, 109, 272.

Violette F. Vzryvnaya dekompressiya i ee deystviye na organizm cheloveka (Explosive Decompression and its Effect on the Human Organism). Translated from French, Moscow, 1961.

Vogt F. B. Effect of extremity cufftourniquets on tilt table (sic) tolerance after water immersion. Aerosp. Med., 1965, 36, 5, 442.

. Weir F. W., Bath D. W., Gevich P., Oberst F. W. Study of Effects of Continous Inhalation of High Concentrations of Oxygen at Ambient Pressure and Temperature. Aerosp. Med., 36, 2, 1965, 117.

. Welch B. E , Morgan R. E., Ulvedal F. Observations in the S.A.M. two- man space cabin simulator. I. Logistics aspects. II. Biomedical aspects. J. Aerosp. Med., 1961, 32, 7, 583.