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# ADAPTIVE REACTIONS OF AN ORGANISM UNDER OCCUPATIONAL CONDITIONS

A. A. Letavet

Adaptive reactions of an organism under occupational conditions are developed both in connection with the working process itself and in relation to the environment. The development of adaptive reactions is a normal and inevitable physiological process accompanying all working activities and variable environments.

The program of the Communist Party of the Soviet Union calls for the creation of maximally favorable working conditions both in respect to the length of the working day and rest time and also with respect to environment. Under these conditions man's working activity contains the greatest protective force against the action of all exogenous and endogenous harmful factors and is the foremost factor of health and longevity. A most important quality of man in the communist society will be his high working ability both in physical and in mental labor.

## Adaption Reactions and the Working Process

The high working capacity of man in the physiological aspect is a complex resultant of a purposeful development of adaptive reactions of an organism in overcoming fatigue.

The mechanism of the development of high working capacity as a result of overcoming fatigue can be observed in trace adaptive phenomena arising during man's work. The period of subsequent rest is characterized by phase changes in working capacities: a phase of low capacity, restoration of the initial level, phase of high working capacity. These phases were traced and proved by many authors (M. I. Vinogradov, Yu. V. Fol'bort, V. S. Farfel' and others).

The trace effect from strenuous muscular work that has been performed can be developed and retained for a certain time in all systems and organs whose activity when performing work was elevated to a new, higher functional level: the nervous system as a system of regulation and coordination, the endocrine apparatus, the cardiovascular system, the respiratory system, the effector apparatus-muscle system. This trace effect to some degree can be likened to the electronic memory of a calculating cybernetic machine.

As the experience of sport training shows, the trace effect after work reaches a sufficient degree of evidence and stability only if the work was performed before the advent of distinct phenomena of fatigue. The adaption of an organism to a higher level of working capacity and the ability to cope with difficulties arising in this case are developed only if the organism is placed under conditions to combat them. If we solve only easy tasks, a difficult task will never be solved.

Thus, fatigue which is characterized by a state of low working capacity can play, under certain conditions, the role of a factor fostering the development of a stable and high working capacity in man.

It would be erroneous to think that what has been stated on the role and development of the adaptive reactions of an organism for achieving high working capacity concerns only man's muscular work. These problems to the same and even greater extent pertain to mental or primarily to mental work not associated with considerable physical efforts. This type of man's activity will be predominate under conditions of highly mechanized industrial processes.

We can easily imagine that the volume of information arriving at the operator of a control panel concerning the course of automatic processing will be very appreciable and the analyzor system of the worker is faced with a difficult task--to cope with this flow of information, to evaluate it properly, and to give the proper directing reactions.

A study of the labor of workers on various control panels and also of the driver personnel of the Moscow subway, which was carried out at the Institute of Labor Hygiene and Occupational Diseases showed that in the various systems of the workers in these categories substantial functional shifts arise which sometimes were unexpected. The level of these shifts are usually in good agreement with the volume of information being received and processed or with the threat of emergency situations. Sometimes the character of these shifts resembles the same under strenuous physical work.

As is known, during strenuous muscular work there occurs an energy mobilization from the liver of sugar reserves which are acutely needed by the working muscles. When working on the control panel the muscles consumed a negligible amount of sugar, at the same time its vigorous supply into the blood channel takes place. As a result, as the investigation showed, the blood sugar level considerably increases: in subway dispatchers by a factor of 1.4, in dispatchers of the Vnukovo airport under conditions of the usual volume of information, by 1.5, and in workers on the producers control panel of the television broadcasting station, by a factor of 1.6 as opposed to the initial level. In cases of especial stress the shifts were even greater: the blood sugar level doubled at the peak hours in the airport dispatcher and also increase twofold in the subway driver when the fuses overheated and the train stopped for only a minute where it should not have stopped. It turns out that such an automatic adjusted mechanism of regulation such as the supply of sugar into the blood channel during physical work, also acts during mental work, and the more intense and emotional is the work, the more vigorously the process occurs.

EKG recordings were made of the subway engineers while tracking trains. Expressed changes, very similar to pathological were obtained on EKG of the experimental and completely healthy engineer during just the above-mentioned extraordinary occurrence--the emergency stop of the train for one minute. However, these changes bore a purely functional character and after ten minutes the EKG returned to normal. At the same time the author noted many other deviations in the physiological functions of the organism (an abrupt increase in the number of heart contractions, an increase of arterial pressure, etc.).

Returning to the problem of the development of adapted reactions during man's working activity, it is necessary to acknowledge that this development in persons of modern administrative professions should probably occur more complexly and require a longer duration than in professions of physical labor. If we acknowledge that high working capacities occur by overcoming fatigue, the process of the occurrence here is considerably more difficult and sometimes direct breakdowns resulting in a morbid condition can be in it.

When training cadres for modern control professions (control panels, dispatchers services, driver professions, etc.) we must have not only the necessary knowledge, but also the adequate working qualities. It is evident that we must develop such methods of teaching and training which in the shortest possible time would lead to the development and reinforcement of the adaptive reactions of an organism to given conditions of activity.

Each job or fulfilled training exercise gives rise to a certain extent to a directed increase in working capacity corresponding to that form of fatigue which must be overcome. At the same time we can speak about the development of the over-all high working capacity which is expressed in any form of work. Evidently, the over-all high working capacity is the consequence of the basic rearrangements in an organism, of the fundamental adaptive changes which have a generalized value.

The most important means to develop and reinforce such generalized adaptive changes in an organism is undoubtedly physical education and sports. The assertion can seem paradoxical that physical labor even in the form of strenuous muscular work does not make such extensive and complex demands on physical development as those made on a man working in the control system of modern mechanized and semi-automated production. But this is true. A man at the control panel must have an all-round physical development. A person, who during physical education or sport training repeatedly came face to face with overcoming of difficulty, demanding a rise in the various systems of the organism to new functional levels, copes with greater ease with the described complex system of stresses in an organism than a physically untrained person who did not experience these functional increases. Probably disruptions in the higher nervous activity resulting in neurosis or various somatic disorders can occur sooner in such an untrained person.

The practical task issuing from what has been stated is to achieve directed development of adaptive processes characterizing high working capacity by means of different methods of education and training. The possibility of directing the development of these processes must be borne in mind especially during training for professional activity which makes high demands on the physical and intellectual sphere of man.

It goes without saying that a high degree of fitness in persons working in modern control professions must be achieved not only by training and development of adaptive reactions of an organism, but also as a result of the creation of maximally favorable environments for these professions, the establishment of an adequate regime of work and rest, a rational (in the psychophysiological sense) device of the control panel itself (the information signals, their arrangement, color, control instruments, etc.).

When speaking about possible mechanisms of adaptive reactions arising during man's activity it is necessary to acknowledge that we can hardly isolate any one mechanism and make it responsible for the entire development of these complex phenomena in the whole organism.

A particular role in the development of adaptive reactions in an organism is played by the higher division of the central nervous system, the cerebral cortex. Adaptive changes in an organism can occur not only by a direct stimulus but also by signals around it. Adaptive changes that are specific for working processes can also be developed under the effect of conditioned stimuli (K. M. Bykov and associates).

An essential role in the adaptive processes associated with the development of a high level of fitness and with the overcoming of fitigue must belong to the adaptive-trophic function of the sympathetic nervous system (L. A. Orbeli et al.). Hormonal mechanisms (the hypophysis, adrenal cortex) undoubtedly have a definite value.

## Adaptive Reactions and the Environment

Man during occupational activity is subjected to the action of extremely diverse physical and chemical factors of the environment of a variable intensity (meteorological conditions, noise, vibrations, electromagnetic waves, ionizing radiation, aerosol and gas contamination of the air, etc.). The task of hygienic measures is to keep the intensity, concentration, or dose of these factors within limits which during systematic or prolonged action on the organism will not cause substantial deviations from the normal conditions in it. The numerical values of these intensities, concentrations, or doses have been established by our system of hygienic normalization. However, a broad spectrum of adaptive processes having a certain degree of specificity depending on the acting factor occurs in an organism under environmental conditions which are not beyond the limits of the established normal indexes. However, extraordinary circumstances can arise where the acting force of the environmental factors rapidly and abruptly increase and where the existing adaptive level is no longer adequate.

As an example of the adaption of the human organism to changing environmental conditions we can cite the development of adaptive processes when working under high temperature environmental conditions (air temperature, infrared irradiation).

Man has universal, amazingly well-coordinated and purposeful adaptive mechanisms to varying environmental temperature conditions. These vast adaptive potentialities are remarkable and, perhaps, a particular human property separating him from other animal organisms and playing the major role in providing him with the power over nature. As a result even when man stays under an air temperature exceeding the body temperature, the phenomena of disorders of thermal balance and, as a result of this, hyperthermia of the organism may not ensue.

A gradual improvement in the functions ensuring adaptation of the thermoregulation apparatus to unfavorable environments (perspiration, vasomotor reactions, respiratory system, metabolism, etc.) occurs in workers in the so-called hotshops during the process of productive work without special adaptive measures.

In the interesting dynamic observations carried out by A. B. Lekakh on a group of workers at Dnepropetrovsk plants over a number of years it was shown how development of the perspiration system of an organism occurs, how its quantitative potentialities are developed especially in those cases when it is virtually the only resource for maintaining heat balance. The adaptive development of the activity of other systems and processes were also shown along with perspiration: nervous regulation, function of the cardiovascular system, metabolic processes, etc. At the same time the very gradual character of the perfection of adaptive functions was established, which must be rigorously taken into account during industrial training and education.

However, in certain jobs there can occur extreme thermal conditions when the usual adaptive levels prove to be inadequate and the development of special measures directed toward an increase of the heat resistance of an organism is required.

An increase in the heat resistance of an organism can be achieved: 1) by a specific (heat) effect on the organism and 2) by a nonspecific (general) effect. The adaptive processes developing here can occur both by improvement in the thermoregulation system (and this is the main way) and by an increase in the resistance of the organism and retention of working capacity on disturbances in thermoregulation, increase in body temperature, and of other shifts in the internal environment of an organism, as was shown by K. M. Smirmov.

Considerable experience shows the unconditional effectiveness of increasing the heat resistance of an organism as a result of adequate (heat) adaptation with the proper selection of the thermal parameters, optimal intervals between adaptations, with their sufficient duration, etc. This system of adequate training has found wide practical application in training of mining rescue crews in the coal industry. At the same time this system has a number of faults: it is complex and cumbersome since it requires the creation of special heat chambers, a considerable systematization in its behavior and considerable periods of time, and its result is nevertheless inadequately stable. Therefore, a search for methods of increasing the stability of an organism to a broad spectrum of actions, including resistance to intense thermal effect is completely justified.

As the results of the investigations accumulated up to the present show, as nonspecific methods of increasing thermostability we can use: a) various methods of hypoxia adaptation; b) physical exercises; c) drugs.

Among the latter group of drugs for increasing the thermostability of an organism in experimental conditions, dibazol has been used independently and in conjunction with hypoxia with positive results (F. T. Agarkov at the Donets Institute of Labor Physiology) as well as certain low-molecular aminothiols which lower the total oxygen requirement and increase the efficiency of its utilization (Ye. I. Kuznets at the Institute of Labor Hygiene and Occupational Diseases, USSR Academy of Medical Sciences).

It is necessary to note that a certain portion of the specificity associated with phenomena of tissue hypoxia which an organism suffers upon overheating is concealed in the apparent nonspecificity of these methods of increasing thermostability.

Numerous investigations, frequently with rather contradictory results on which we do not have the opportunity to dwell, were carried out with respect to adaptive reactions of man and animals to low temperature environment (A. D. Slon, I. R. Petrov, B. B. Koyranskiy, K. M. Smirnov, I. S. Kandror, etc.). These investigators showed the considerable possibilities of the development and improvement of man's adaptive reactions to cold (or as they sometimes say, "hardening"). At the same time substantial differences were noted in the course of these adaptive reactions in man and animals under natural environments: whereas in animals the basic role is played by chemical thermoregulation, in man its role is negligible and apparently, like for high temperatures, the first place is occupied by the regulation of heat exchange and an increase in resistance to changes in the internal environment. K. M. Bykov and A. D. Slon write concerning the role of the nervous system in these processes: "We have grounds to assume that underlying the physiological mechanism of hardening in the broad sense of this word is the adaption of the force and mobility of nervous processes and the steadfast change of the cortical mechanisms of regulation."

The dynamics of adaptive reactions to low environmental temperatures under conditions of man's labor activity were distinctly shown for the example of construction workers and refrigeration workers the microclimate laboratory of the Institute of Labor Hygiene and at Occupational Diseases (A. Ye. Malysheva et al.).

We cannot deny the certain possibility of a specific or nonspecific increase of resistance to other physical and chemical factors acting on an organism during occupational work. However, the possibilities here are evidently more limited since in respect to them there do not exist such well-developed natural adaptive mechanisms as in respect to the effect of heat and cold.

For example, the development of any noticeable useful adaptive phenomena doesn't occur at all with respect to vibration, as was shown by A. M. Volkov with respect to workers in the railroad industry. Therefore, the human organism is, so to speak, helpless against this physical factor. This apparently explains the recently observed increase in the number of cases of vibration sickness.

The important role of adaptive processes under the effect of toxic substances need hardly be considered. That which is termed "habituation" is more likely an increase in the thresholds of the receptor system than a true increase in resistance as a result of the active development of adaptive processes. The use of various biologically active chemical substances (for example thiolic substances) for protection or replacement of important biochemical structures damaged by a toxic substance (for example the enzyme systems), although it is frequently quite effective, it cannot be relegated to the category of adaptive processes and reactions in our meaning of this phenomenon.

As useful adaptive processes upon entrance of toxic substances into an organism, we can examine the processes of the conversion of these substances in the organism to those less aggressive, and also in certain cases the storage processes. At the same time cases can occur where upon repeated effect of a toxic substance a hypersensitivity to it develops (the phenomenon of allergy).

There are no important possibilities for the development of adaptive reactions with respect to inhaled nontoxic dust (for example, silicide). The fibrous process developing in lungs cannot be considered as a beneficial adaptive reaction. Conversely, this process leads to a deterioration of the functional potentialities of the respiratory system and blood circulation. Stimulation of phagocytosis is possible to a certain degree but quantitatively its effect cannot be adequate to protect the organism.

Therefore, with respect to those factors of the industrial environment under which the role of adaptive processes is very small, a system of sanitary engineering preventive measures is especially needed.

When studying the essence of adaptive processes as applied to occupational conditions we run into great difficulties. Large scale investigations are necessary with the participation of various medical and biological specialities in order to transfer the problem from the stage of phenomenology to the stage of the practical application of the results in the shortest time.

# EXPERIMENTAL BIOLOGY AND NEW CONCEPTS OF IMMUNOGENISIS

N. N. Zhukov-Verezhnikov, I. N. Mayskiy, G. P. Tribulev

Recently the mutation-clone theory of the formation of Burnet antibodies has acquired a certain popularity. As is known this theory is based on the hypothesis that cells, capable of producing each given antibody, pre-exist, having been formed by the elements of millions of random antibodies.

Thus it is necessary to ask yourself the question: is it only with some mutations that we can analogize the origin of cells which produce antibodies, and whether or not there are in modern genetics other types of mechanisms changing the heredity of cells which would be used as the basis for developing a genetic hypothesis of the formation of antibodies?

In addition to mutational alterations, we consider the existence of numerous forms of cell alterations as proved. This is the hereditary adaptation, transduction and lysogenicity in bacteria, as well as other forms of transmission of heredity characteristics through chemical substances, which as a whole can be called the phenomenon of transformation, including the phenomenon of bacteriophagia.

Our team, being occupied over the course of many years with an investigation of such alterations in bacteria, as well as attempting to reproduce them for somatic cells, arrived at the conclusion that the solution to the riddle of the mechanisms of the formation of antibodies should be sought within the frameworks of typical genetic phenomena, which can be combined under the single term "transformations." It is necessary to state that Burnet within the past ten years closely approached to this conclusion twice and twice rejected it.

We had to solve whether further investigations of the mechanisms of antibody formation should be carried out within the frameworks of the analogy with mutational processes or whether the analogies with the phenomenon with genetic transformation should be considered when developing a theory of immunity. But for this purpose we must become more familiar with the basis for the latter analogy.

The laboratories of the Institute of Experimental Biology of the USSR Academy of Medical Science in recent years have obtained data on microbiological and cytological models, which enable us to judge certain fundamental characteristics of genetic transformations in general and also to propose a certain classification of such kind of phenomena and to consider whether or not a place for the mechanism of antibody formation is found in this system. Underlying this classification must be characteristics yielding the input information, i.e., the substance which penetrates into the cell and causes directed changes of some particular hereditary properties. We will start from the assumption that such a substance can be not only DNA, which Avery established in experiments on the transformations of pneumococci, but also RNA and, finally, proteins.

Let us examine a diagram characterizing these three types of genetic transformations.

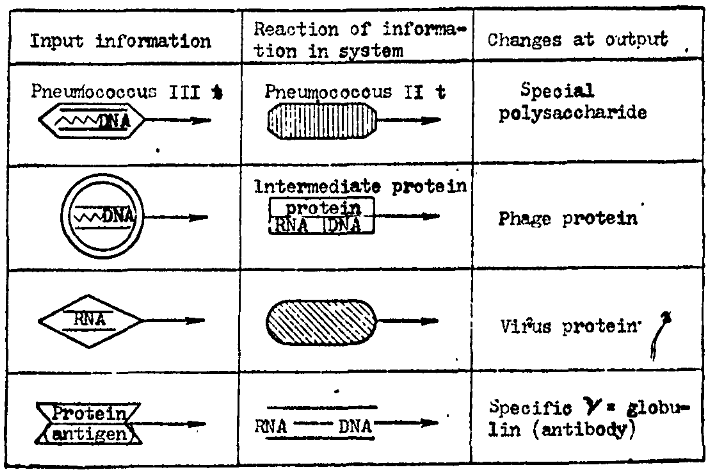


Fig. 1.

Figure 1 shows the features of the transformation process in relation to the type of carrier of the input information. It is not difficult to see that whatever the nature of the carrier of input information, proteins or polysaccharides will always be at the output of the system. However these types of transformations are distinguished by the extent to which the number of characteristics are involved in the alteration process. We will examine an extreme case where transformation encompasses, like an avalanche, the bulk of characteristics upon formation of bacteriophages. This case is especially important for our study because the end product of transformation, phage protein, has many properties of an antibody. The latter investigation, performed at our institute by A. P. Pekhov, N. I. Rybakov, and B. A. Mishchenko, made it possible to refine what enormous changes occur inside a bacteria cell when it receives transforming information from a virulent bacteriophage. In order to analyze properly the process of the formation of bacteriophages, we, together with A. P. Pekhov and Buyko, also made ultra-thin sections of free phages.

Bacteriophages are divided morphologically into a nucleus containing DNA and protoplasm containing phage protein, which is the end, and especially interesting, stage of transformation.

Thus we can consider as proved that bacteriophages T-2 and 1327 use the nuclear material of bacteria by means of transformation for building their own nucleus; this is fully confirmed biochemically. In this case the introduction of new information into the bacteria cell leads to a radical change in the direction of biosynthesis, on the strength of which complete transformation of molecular and biological structure is accomplished with the appearance at the input of that protein, information about which was carried to the cell by the phage DNA and which we saw on the ultra-thin section of phages in the form of phage complimentary plasma.

For our study it was especially important that the so-called intermediate protein, which does not enter either into the structure of the bacteriophage or into the bacterial structures, participates in the transformation of bacterial structures to phage structures. Inhibition of its formation by means of antibiotics stops the formation of phage DNA. This shows that protein bodies can have an inducing effect with respect to DNA. No less important are the cases where the introduction of phage DNA does not lead to a radical transformation of the cell substrates, but is limited only to a change in individual characteristics.

This is one of the most interesting phenomena in contemporary biology, the so-called lysogenization, where the DNA in phages is incorporated into the nuclear apparatus of bacteria. It is noteworthy that under certain effects, for example nuclear radiation, bacterial cells instantaneously again start to produce bacteriophages. In this case the transformation ability of phage DNA is, so to speak, fully restored. This process is in a rigorous quantitative dependence on the intensity of ionizing radiation. It is necessary to point out that this transformation and most radiosensitive model was irradiated by our institute on satellites and spaceships in order to investigate the genetic conditions in the orbits which the first cosmonauts Yu. A. Gagarin and G. S. Titov flew.

Certain data characterizing the type of transformation which is associated with phage DNA are as such. We see that the extent of transformations varies within wide limits and in essence such transformations can secure the most diverse changes of protein. The second type of transformation associated with RNA is no less instructive. Here a transition to protein as a carrier of information is seen.

These assertions permit us to examine in greater detail the process of the formation of antibodies from the point of view of the transformation theory. As was already stated we can assume that the protein antigen introduces appropriate information into cells of the lymphoid system which leads to the transformation of the structure of cell RNA, which directly, or through some kind of specific chains, modifies gamma-globulin being constantly produced by this cell. As a result, at the output of the system we find a specific antibody capable of selectively reacting with the protein used as the carrier of the input information. There is no doubt that in this case the process of transformation differs considerably from other types, which N. F. Gamaleya emphasized in his time.

The first characteristic is that not DNA or RNA, but protein starts this chain reaction. But it was shown above that in principle protein cannot be such a carrier of information.

The second characteristic of the process of antibody formation, if it is considered as a transformation reaction, is that only a partial or very unique change of a substrate is noted at the output. Here transformation concerns not the entire protein molecule as is observed, for example, on the formation of protein of bacteriophages having many antibody properties. We are concerned about the changes in the amino acid chain of gamma-globulin within a narrow segment which includes only several amino acids. In addition we must acknowledge that this change is not fully adequate for the quota of information which is brought to the cell by the protein antigen as an input to the system, since these local changes in the gamma-globulin molecule are probably not direct, but a mere image in the active portion in the antigen molecule.

Finally, as a third distinction we need emphasize that in this case the same cell substrate, namely gamma-globulin or its analogs, is always subjected to specific transformation. This last characteristic is the key to the main series of argument in behalf of the transformation theory as opposed to the mutation theory. Actually, it is not improbable that such a rigorously specialized function as the production of labeled gamma-globulin would be in the final stage regardless of the random mutational phenomenon. If it will be proved that this function has mainly some kind of starting forms in preceding evolution, the fate of the mutation theory will be solved once and for all.

We consider the ability of organisms to react to certain antigens without previous immunization as such starting forms of reaction. Serological tests with the participation of normal antibodies are a particular case of such a reaction.

About ten years ago we formulated the concept of the so-called primary immunological reactivity. The hypothesis was expressed that a reaction of the antigen-antibody type is accomplished without previous immunization, is widespread in nature, and has a general biological significance. Numerous data confirming this hypothesis have been obtained in recent years.

Figure 2 summarizes the data obtained by O. Ye. Vyazov and team (Konyukhov, Murashova, Lishtvan, Titova, and Volkova) during the three White Sea expeditions. In Fig. 2 it is shown that the proteins of marine animals which stand high in an evolutionary sense are able to react serologically without previous immunization with the proteins of animals standing at a lower step of development. The same pertains to the immunological interrelationships of the sexual cells of these animals. Figure 2 shows that such interrelationships extend to embryonic development, where the protein of tissues which are at higher stages of differentiation reacts by a antigen-antibody type with the proteins of the tissues of early anlagen. The principle of primary immunological reactivity was finally proved; it reflects fully the regular evolutionary phenomena of a transformation character which have nothing in common with accidental mutations.

Therefore, it is quite proper to think that the production of antibodies by lymphoid cells is a regular evolutionary echo of a formerly widespread primary immunological reactivity.

Just as in the process of specialization, the ability for intracellular digestion was secured only for a definite catagory of cells, mainly Metchnikoff's phagocytes; precisely the same is the ability to develop special globulins and to transform them under the effect of antigens secured only for a specific catagory of cells whose function is protection by means of transforming special proteins. The protective function is inherent to these cells, but they can serve as a source of pathogenic auto-antibodies, whose value was recently shown again by I. N. Mayskiy, this time for pathogenesis of cancer.

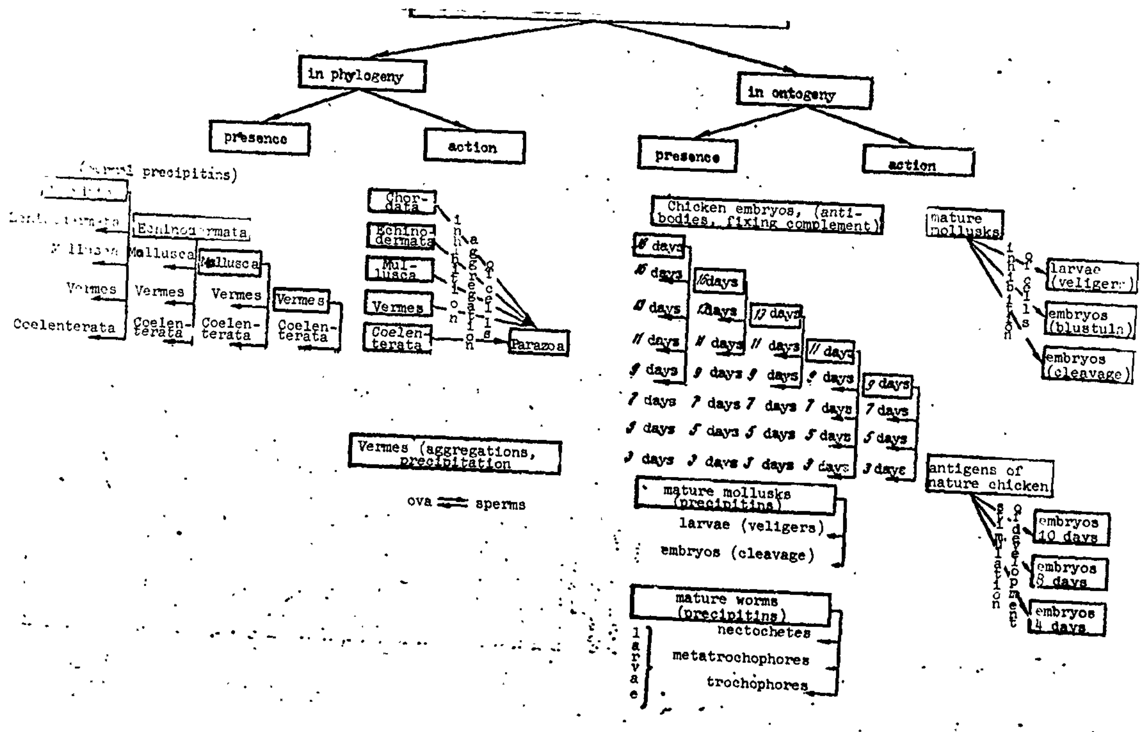
in phylogeny
in ontogeny
presence
action
presence
action
Echinodermata
Mollusca
Vermes
Coelenterata
Chordata
Parazoa
Vermes (aggregations, precipitation
ova sperms
Chicken embryos, (antibodies, fixing complement)
mature mollusks (precipitins)
larvae (veligers)
embryos (cleavage)
mature worms (precipitins)
nectochetes
metatrochophores
trochophores
larvae
mature mollusks
embryos (blastula)
antigens of mature chicken
embryos 10 days
embryos 8 days
embryos 4 days

Fig. 2.

As regards the chemical mechanism of primary immunological reactivity, it will be investigated. It is possible that in a chemical sense a certain general law exists, where on a change of proteins during development of RNA or DNA a mirror-imprinted trace of previous forms of protein body is preserved, which creates the possibility of reactions between evolutionary "old" and "new" formations. From our point of view it is this law in a modified and specialized form which underlies the production of antibodies by cells of lymphoid tissue. Therefore, serological immunogenesis seems to us to be a completely regular phenomenon which is remote from random mutation by its nature.

The above-cited example of the formation of phage protein shows what in principle can be the fine mechanism of transformation which results in the appearance of a protein antibody.

Such are the basic features of a traditional immunology of the transformation theory of immunogenesis. This hypothesis, it seems to us, opens the road for new experiments and can promote a further conversion of clinical aspects and theoretical immunobiology.

# POSSIBILITIES OF PROTECTIVE ADAPTATIONS OF AN ORGANISM AND THEIR LIMITS UNDER CONDITIONS OF MAXIMUM G-FORCES AND WEIGHTLESSNESS

V. V. Parnin, O. G. Gazenko, and V. I. Yazdovskiy

The entire world is aware of the vast achievements of Soviet science in man's conquest of space which took place in 1961: the flight of Gagarin, the world's first spaceman, and the flight of Titov in the "Vostok-2" in which he spent more than a day. These enormous scientific achievements are not only important per se, they present us with a number of new problems.

Numerous investigations have shown that the most powerfully acting factors of spaceflight are acceleration, weightlessness, cosmic radiation, and emotional tension which affect a living organism at various stages of spaceflight. Acceleration accompanied by considerable emotional tension has its greatest effect during rocket acceleration and entrance into the dense atmospheric layer on return of the spaceship to earth.

For the biologist and doctor, all investigations pertaining to the problem of flight safety are a particular, dominating factor—the protection of man and his possible companions, live earth organisms, from the injurious effects of spaceflight factors.

Naturally, the development of this problem is first of all associated with a manifold consideration of the conditions and factors which can noticeably effect the vitality of an organism, with those that are a potential or real danger to him.

It is quite possible that further investigations of the physics of outer space and biological experiments will reveal some kind of additional, still unknown conditions or such conditions whose effect we heretofore have not paid due attention. Here it is pertinent to note that success in solving biological problems depends on the overall progress of scientific investigations of space.

The possible physiological (biological) effects and tolerable limits, with respect to force and duration, of various factor or set of factors have been estimated on the basis of accumulated experience or in special experiments on animals and then on man. If the probability of an injurious action is detected, methods of increasing the organism's resistance are sought by developing his natural compensatory mechanisms or by using appropriate protective adaptations.

The physiologist's natural endeavor to exclude any discomforting influence of flight factors is limited by obstacles of a technical nature. The result of this is usually a rational compromise combining certain requirements of the living organism and the possibilities of the spaceship.

The effect of g-forces acting on an organism must be considered in relation to their direction. When g-forces act along a body in a foot-head direction, the person experiences small g-forces (6-8 fold) for a very short time, 0.3 sec. When the g-forces act along the body in a head-foot direction, a person can withstand for the same time twice the g-forces as when acted on in a foot-head direction. The endurance time considerably drops with greater g-forces.

The greatest resistance of an organism and effect of acceleration are observed when the latter is acted on in a direction perpendicular to the longitudinal axis of the body (transverse acceleration). However, in this case disorders of respiration, hemodynamics, and nervous regulation occur. At certain values of the exposure and magnitude of acceleration, all these shifts can reach critical values.

According to the opinion of most investigators, disorders of gas exchange in the lungs play an appreciable role here. Disorder of compensatory mechanisms leads to a critical state, a sharp disruption of performance, with subsequent disturbance of vital functions.

It is important to elucidate not only the maximum permissible values of g-factors, but also to have a clear concept of the essence of the physiological shifts taking place here and the possible methods of overcoming them.

In experiments on animals we investigated the state of external respiration, hemodynamics of pulmonary circulation, and the degree of blood oxygenation during transverse g-forces of magnitude 3, 6, and 9.

It was shown (A. Kiselev, etc.) that at 3-g the pulse pressure in the right ventricle remains unchanged. At 6-g, as a rule, it increases an average of 16% during rotation of the centrifuge, and at 9-g increased by 62% in comparison with the initial level.

The results of measuring the circulation time and the oxygen level in the arterial blood are interesting. A direct dependence of the degree of blood oxygenation on the circulation time was noted, which testifies to the active participation of the hemodynamics of pulmonary circulation in oxygenation of blood during transverse accelerations.

Thus, in spite of the decrease in aeration of the lungs owing to their decrease in ventilation, an active rearrangement of circulation in the pulmonary system can, within certain limits, ensure maintenance of the necessary level of blood oxygenation.

It is quite probable that the limit of compensatory possibilities in this case is determined by the character of the circulation response. There are reasons to suppose that there is an inequality of the volumes of blood ejected by the right and left ventricles, with predominance of the stroke volume of the right ventricle.

If the latter supposition is valid, it is difficult to imagine, taking into consideration the progressive deposition of blood in the lungs, that man can stay for a reasonably long time under conditions of increased gravity.

In order to forecast the onset of the critical phase and to determine the time of onset of decompensation with any combinations of magnitude and duration of g-forces, it is important to set up certain tests, mainly electroencephalographic.

A definite phase relationship in the change of bioelectrical activity of the cerebral cortex has been found. Experiments were carried out on rabbits subjected to transverse accelerations from 2- to 14-g on a centrifuge.

The first phase originated with the start of centrifuge rotation and was expressed by a drop in the voltage of the biopotentials, by a decrease in the number of slow waves, and by an increase of rapid oscillations. At the same time an increase in respiration rate and number of cardiac contractions was noted.

The second phase was characterized by an increase in the synchronization of the cortical biopotentials, by the appearance of slow rhythms and spindles. The frequency of cardiac contractions and respiration remained high.

The third phase was distinguished by an evident synchronization of the biopotentials. As a rule it occurred at higher than 6-g and was accompanied by a decrease in rate of respiration and heart contractions (extrasystoles and arrhythmia were observed in 30% of the cases).

Depending on the initial character of the bioelectrical activity of the cerebral cortex induced by g-forces, we detected three types of changes in the biopotentials, from the picture of which it was not difficult to determine the time of onset of the second phase, the "phase of primary decompensation."

An analysis of the data showed that the relation between the onset time of the phase of primary decompensation and the magnitude of the g-force has the form of a rectangular hyperbola.

The picture was very similar to that observed on the EKG during hypoxia or in the presence of ionizing radiation.

A further development of the work was the attempt to reveal the mode of action of g-forces on the central nervous system. In particular, we tested the effect of aminazine (chlorpromazine) as an agent blocking impulsation at the level of the reticular formation of the mesencephalon. The administration of aminazine (up to 10 mg/kg) removed the response of bioelectrical activity, respiration, and the cardiovascular system to the effect of g-forces; critical disorders did not develop under such experimental conditions.

Attempts in the indicated directions seem quite promising. It is necessary and, it seems to us, possible to select tests, forerunners of functional disorders, which could serve as a diagnostic criterion for evaluating the condition of a cosmonaut and, quite possibly, would be one of the common signals for switching on protective adaptations.

Objections can always arise in the sense that the results obtained in laboratory experiments on a centrifuge cannot be fully applied to solve problems associated with actual flight.

The difference of conditions is evident. In an actual flight the g-forces are combined with a complex of other factors, the main one, of course, being the emotional tension of the cosmonaut. A comparison of the data obtained from centrifuge tests and on takeoff on an actual flight, yields instructive material. Gagarin and Titov, according to their subjective impressions, unanimously evaluated these tests as very similar.

On the other hand, the fact is noteworthy that the pulse and respiration rate and other objective indexes of the state of certain physiological functions during flight noticeably differed from those recorded on the centrifuge. It is difficult to doubt that this is the result of definite emotional tension. As far as can be judged from recent publications, analogous data were obtained during the flights of Shepard and Grissom.

At the same time we cannot but see numerous new problems and tasks, some of which are dictated by the logic of investigations and others by the practical needs of the astronauts. Other fields of space biology and medicine are less developed. As an example we could site the effect of weightlessness on the human and animal organism.

A comparison between data obtained in ground experiments under the acceleration effect of a centrifuge and the acceleration effect during takeoff of the "Vostok" spaceships with Gagarin and Titov on board, showed an almost complete analogy. However, the physiological reactions in flight were somewhat higher, mainly due to emotional stress.

As a result of ground experiments and manned spaceflights, the limits of the maximum tolerable magnitudes of prolonged accelerations have been marked, and preliminary results of the possibility of increasing the physiological resistance of man to the acceleration effect by the conditioning method have been obtained.

Under orbital flight conditions on a spaceship, the main influencing factor is weightlessness (the absence of the earth's gravity field) acting also against a background of appreciable emotional tension and with a certain radiation background.

Weightlessness is one of the basic factors of spaceflight. There is no doubt that it can be eliminated by creating artificial gravity in the ship. However, whether this is completely necessary and what magnitudes of artificial gravity should be recommended are problems requiring further experimental solution.

It is necessary to point out that our information relative to the physiology of weightlessness is limited because all attempts to imitate this unique state on earth are quite difficult and for all practical purposes not successful.

Investigations on special stands submerged in water and on airplanes and, in part, on ballistic missels have an important, but nevertheless auxiliary value in the solution of this complex problem. The main way, of course, is a direct experiment in an orbital flight where the weightless state can be maintained indefinitely.

Not once has the danger arisen that sensory, somatic, and vegetative disorders will limit man's stay under weightless conditions.

Biological experiments in orbital flights made a definite contribution to this problem. In the experiments with Laika, Belka, Strelka, Mushka, Pchelka, Chernushka, and Zvezdochka it was shown that a definite tendency for return of the basic physiological indexes to the initial level after expressed shifts during takeoff was noted as soon as the animals were in a state of weightlessness.

During the first two hours the dogs revealed certain changes in the functional state of the heart, which were expressed by a change in the intensity of the heart tones, prolongation of the duration of the first tone, and an increase in the time of ejecting the blood from the heart into the large vessels.

These changes disappeared rather rapidly, but after 8-10 hr certain functional changes of the heart appeared again.

For example, according to the EKG data, a drop in the systolic index to 23-26% and certain changes of the T-wave were noted. During the flight of Belka and Strelka, an appreciable quickening of the pulse and respiration rate and an increase of arterial pressure were observed in both animals at this period. These changes were not detected by the end of the 24-hr orbital flight.

The described picture fits into the frame of functional shifts which per se do not lead to noticeable circulation disorders. However, certain phenomena related to neurohumoral regulation of the cardiovascular system are noteworthy and deserve special mentioning.

It was shown as early as in the experiment with Laika that the return time to normal of the number of heart contractions in the weightless state after the end of acceleration was about 3 times greater than with the same accelerations on earth. Moreover, subsequent analysis of the EKG showed that during the first 4-6 hr of orbital flight the oscillations of the frequency of heart contractions (the difference between the maximum and minimum value of the cardiac rhythm for 10 sec) underwent considerable and ever growing fluctuations over the normal values in the animals.

The relative instability of the rhythm of heart contractions, although less expressed, remained until the end of weightless flight. The respiration depth and rate were also distinguished by noticeable irregularity.

It is necessary to point out that an analogous, although less expressed picture of the fluctuations of the rhythm was observed on the EKG of Yu. A. Gagarin.

All this indicates a certain instability, lability, of the central apparatus regulating vegetative functions. We get the impression of some kind of a periodic, wavelike change of first the sympathetic and then parasympathetic influences.

We can assume that the sensory sphere and changes in afferentation under weightless conditions, the probability of which has been postulated by many authors, are quilty in this.

Disorders of spatial analysis and the development of vestibular symptoms could serve as an especially distinct and demonstrative confirmation of this point of view.

Something similar was observed in certain investigations during experiments on aircraft with multiple alternating effects of brief g-forces and weightlessness. However, the conditions of these experiments differ from a prolonged stay in complete weightlessness.

The results of manned flights were awaited with understandable impatience. Yu. A. Gagarin was in a state of weightlessness for more than an hour, Shepard 5 min. The duration of the flight was comparatively short, the program of work, strenuous. No disorders in the sensory and motor spheres were noted in either one.

The scientific data obtained furing Titov's flight were of great value. He noted the phenomenon of discomfort under weightless conditions, especially after a five-hour stay in a weightless state.

A change in afferentation is observed under weightless conditions. This is clearly confirmed by certain disorders of spatial analysis and the development of vestibular symptoms, which were aggravated upon abrupt turns of the head or during observation of rapidly moving objects.

Under spaceflight conditions, especially with weightlessness, there arises a complex and quite dynamic picture of the interaction of many nervous instruments (afferent systems), on the basis of which are formed the functional state of the central nervous system, its tonus, and the current activity of the organism. The weightless state places a number of nerve-receptor instruments under unusual conditions of functioning since a gravity stimulus adequate for them disappears.

In spaceflight where there is no effect of a gravitational field and the usual afferentation from the otolithic receptor is reduced and perhaps modified, the afferentation from the skin receptors and probably from other receptors is partially reduced and changed. Consequently, the normal volume of afferent impulses from these analyzors is reduced and against this background, possibly, there could easily occur a relative predominance of afferentation from the labyrinth apparatus of the inner ear and, with time, irritation which can lead to extreme reaction, to blurring of coordination, and to the development of the motion-sickness syndrome.

This scheme of the physiological effect of weightlessness on an organism is in need of experimental verification and refinement.

In a practical sense it is important to emphasize that the nervous system has an expressed flexibility and considerable compensatory potentialities, which permit restoration of lost normal contact with the outside world by substituting some functions by others.

However, we still do not know how far this principle can act under weightless conditions.

The final word belongs to further scientific experiments.

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