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BIOLOGICAL SERIES. (SELECTED ARTICLES)

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# UNEDITED ROUGH DRAFT TRANSLATION

NEWS OF THE ACADEMY OF SCIENCES OF THE USSR.
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# THE DYNAMICS OF BLOOD CIRCULATION PARAMETERS OF THE CEREBRAL VASCULAR SYSTEM DURING LONGITUDINAL GRAVITATIONAL LOADS

Yu. Ye. Moskalenko, O. G. Gazenko, A. A. Shurubura,
I. I. Kas'yan, O. V. Graunov

The study of reactions of an organism to gravitational loads is one of the basic problems of space biology. Therefore, many articles and reports have been published in recent years devoted to results of investigations of the effects of changing gravitational poles on the various systems of man and animals. On the basis of available indirect data it is possible to conclude that one of the most sensitive systems in this aspect of space flight is the cerebral blood circulation system because of the peculiarities of its structure and the high intensity of cerebral blood flow. There are no reports in available literature which relate to the study of this part of the cardiovascular system under conditions of a changing gravitational field. This is undoubtedly caused by methodical difficulties in studying cerebral blood circulation even under normal conditions not to mention the complications caused by the characteristics of an experiment in changing gravitational fields.

In recent years we have developed methods for studying cerebral blood circulation during the effect of overloading (Moskalenko, et al., 1962; Moskalenko, 1962), as a result of which corresponding methods were developed. The first stages in investigating changes in the filling of cerebral cavity with blood during maximum loads of ± 1 g (Moskalenko, et al., 1963) convinced us that the cerebral vascular system possesses a very high sensitivity the redistribution of blood in the organism which is caused by longitudinal gravitational loads.

In connection with this we extended the investigations in the direction of studying the peculiarities of the dynamics of blood circulation parameters in the cerebral cavity under longitudinal gravitational loads, paying particular attention to elucidating compensatory possibilities in this part of the cardiovascular system, to differentiating phenomena of a passive mechanical nature from active reactions of cerebral vessels and to elucidating several factors which basically underly the reactions of cerebral vessels to gravitational effects.

## Methods

Sufficient information on the condition of the cerebral vascular system during certain effects, particularly during gravitational loads, can be obtained by means of simultaneous recording of several circulation parameters. Taking into account current methodical possibilities and the peculiarities of the experiment during the study of gravitational effects, we chose for recording two circulation parameters : the change of volume of blood within the cerebral cavity; the change in pressure at various points within the cerebral cavity.

As we have shown earlier (Moskalenko, 1963), these two parameters during experimental conditions, which exclude terminal conditions, give sufficient information to make it possible to judge the condition of the cerebral vessels.

To record changes in the filling of the cerebral cavity with blood, we used the electroplethysmograph method. In distinction from the electroplethysmograph which we had used earlier (Moskalenko, et al., 1962, 1963) the present investigations were conducted with an arrangement in the outlet block of which was applied a circular phase-sensitive detector circuit (Fig. 1,a)(the electrical circuits of the generator and amplifier, not shown in Fig. 1, differed little from the circuits which we described earlier). Application of the phase-sensitive detector made it possible to eliminate the basic shortcoming of highly sensitive electroplethysmographs with a bridge circuit of the input attachment – the non-linear dependence between changes in electrical conductivity of the investigated object and the current at the output of the instrument near the balance point of the bridge (Fig. 1,b). This led to considerable simplification in tuning the instrument and eliminated errors arising in the direction of shift of the electroplethysmograph during a change in the phase voltage sign on the bridge diagonals (segments A—A in Fig. 1,b).

We recorded cerebral pressure by means of tensoelectric manometers. Tensometer wires with a base of 15 or 10 mm were glued to a celluloid membrane of 20 mm diameter which was the reason for the cone-shaped manometer housing which, at the apex, transformed into an insert of 5 mm diameter which was screwed into the skull of the animal. Such a form of the inner cavity of the manometer made it possible to extinguish the pressure wave reflected from the membrane; this reduced distortion while recording pulse fluctuations.

The inner cavity of the manometer, filled with a physiological solution, was connected through a slit in the dura mater with the subarachnoid space of the brain. Manometers were switched in to a standard tensoelectric device, type UTS-1-VT-12.

To get some idea of the reasons causing reactions of the cerebral vessels in response to gravitational loads, together with simultaneous recording of the two circulation parameters mentioned above, in several experiments we looked for changes in the general arterial pressure, in the force of respiratory movements of the animal and oxygen tension in the brain tissue and also changes in the pressure dynamics within the spinal cord cavity. Recording of arterial pressure, pressure in the spinal cord cavities and respiratory movements was accomplished by means of tensometers. Oxygen stress was recorded by the polarographic method on a device suggested by Ye. A. Kovalenko (1962).

The processes which we studied were recorded on a K 12 21 oscillograph (recorded on photographic paper 10 cm wide). All of the separate blocks were mounted into a single device, the scheme of which is shown in Fig. 2. Pressure sensing devices and electrodes in an organic glass mounting were screwed into apertures of 5 mm diameter which were trepanned in the skull and spine. The sensing device for respiratory movements (RM) was mounted on a stand to which the animal was fastened, and the sensing device for arterial pressure (AP) was connected with a cannula which was inserted in the femoral artery. The scheme of the distribution of sensing devices and electrodes is shown in Fig. 3.

Experiments conducted on dogs, cats, rabbits, and rats under a general urethane (1 g per 1 kg of weight) intraperitoneal narcosis. In all, 64 experiments were conducted, in each of which the animal was subjected to 15-20 separate tests on a rotating stand which made it possible to create longitudinal gravitational loads up to ± 1 g, and several experiments were conducted on a centrifuge which created acceleration up to 10 g.

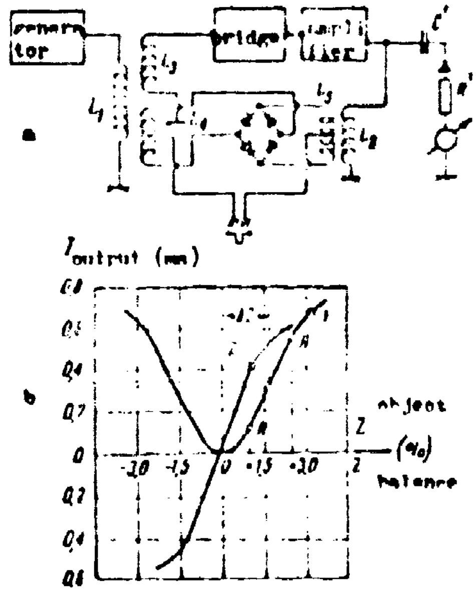
a
generator
bridge
amplifier
$L_1$
$L_2$
$L_3$
$L_4$
$C'$
$R'$
b
$I_{output}$ (ma)
0.8
0.6
0.4
0.2
0
0.2
0.4
0.6
-2.0
-1.5
0
+1.5
+2.0
1
2
object
Z
(%)
Z
balance

Fig. 1. a- the block scheme of the electroplethysmograph with phase-sensitive circular detector; b- function between current at electroplethysmograph output (1-with conventional detector, 2-with phase-sensitive detector) and the resistance of the investigated object near the balance point of the bridge.

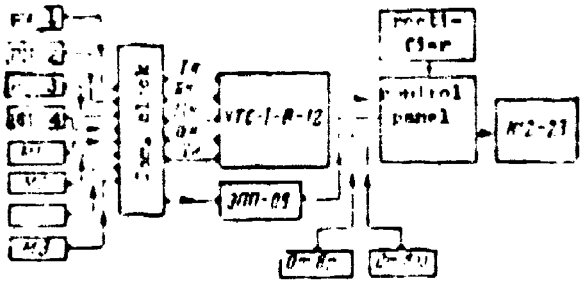
amplifier
control panel
VTC-1-R-12
K2-21
EMP-09

Fig. 2. General block-scheme of the arrangement

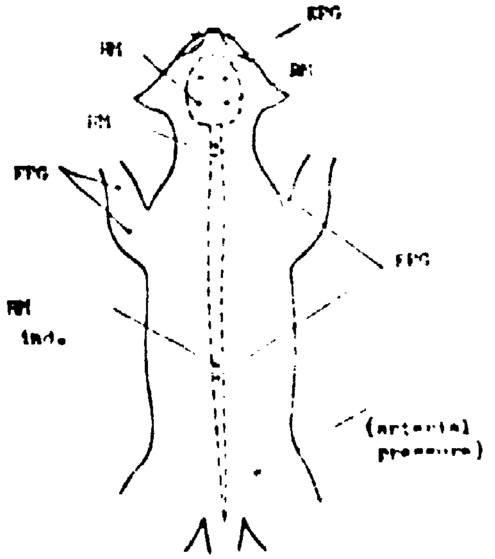
EEG
HM
EEG
EEG
EEG
HM
ind.
(arterial pressure)

Fig. 3. Scheme of the distribution of pressure indicators and electrodes under conditions of acute experience

## Results Obtained

Before us, first of all, stood the task of elucidating the general pattern of changes in the intracranial circulation system under gravitational loads and to establish acceleration magnitudes, during which it followed to study in detail the dynamics of the circulation parameters of the cerebral vascular system.

With this aim, we conducted a series of experiments on dogs, in which we recorded the intracranial electroplethysmograph (EPG) during circulation in a centrifuge during a gradual (in the course of 2 minutes) increase in the number of revolutions from zero to quantities which created an overload of nearly 10 g. At the beginning of circulation, the level of the intracranial EPG differed little from the original but later deviated significantly and then remained fixed during further increase in the overload. In other words, at the beginning of circulation we observed reactions from the side of the intracranial vessels which prevent excess filling or destruction of the cerebral cavity, but during an increase in the number of revolutions the volumetric reserves of the cerebral cavity are exhausted which is evidenced by the stabilization of the EPG level during further increase in the gravitational load. The load quantities under which these phenomena are observed are shown in Table 1.

From Table 1 we can conclude that detailed study of the dynamics of circulation parameters of the cerebral vascular system is most expedient to conduct during longitudinal gravitational loads from 0.2 to 2.0 g. Actually, at the beginning of these limits there lies a threshold of cerebral vascular sensitivity to longitudinal gravitational loads; at the average loads, active reactions are observed from the brain vessels and during accelerations lying close to the upper limit, phenomena arise which show that the volumetric reserves of the intracranial cavity system are already exhausted.

Proceeding from these data, in further series of experiments we applied gravitational loads lying within the indicated limits. To assure accuracy in apportioning the reaction and to simplify analysis of the results obtained, in all of the above cited experiments jump-like changing gravitational loads were applied. The time of their accumulation consisted of approximately 0.2-0.5 sec and then the load remained fixed for 10-30 sec.

TABLE 1

Change in level of intracranial EPG under gradually increasing gravitational loads

| Direction of acceleration | Beginning of fluctuations in level of intracranial EPG, g units | Stabilization of level in intracranial EPG, g units |
|---|---|---|
| Feet - head | 0.4-0.6 | 1.2-2.5 |
| Head - feet | 0.3-0.4 | 1.0-1.5 |

## A. Changes in Level of the Recording Quantities

The experiments which we conducted showed that the levels of intracranial pressure, of pressures in the ischemic and cervical regions of the spinal column and the intercavial the EPG changed substantially during positive and negative gravitational loads (Fig. 4). Changes in intracranial pressure and pressure in the cervical and lumbar regions of the spinal column, proportional to the amount of load (Table 2), occur immediately after the beginning of the reaction and further, during the rest of the time they remain constant in the majority of experiments. In some cases, especially during loads causing outflow of blood from the brain, during the reaction some normalization of the intracranial pressure level and a pressure increase in the lumbar region of the spinal column are observed. Upon restoration of the original position of the body, pressures in the cerebral cavity and spinal column rapidly return to normal. Under loads causing an influx of blood to the head, the restoration of the intracranial pressure level frequently occurs through a phase of a short-lived pressure increase lasting 5-15 sec.

Changes in the intracranial EPG level were similar in the majority of cases to the changes which we obtained earlier in experiments with rats (Moskalenko, et al., 1963).

However, in cats and dogs the intracranial EPG contains a number of peculiarities which are more noticeable in these animals.

TABLE 2

Change in pressures of various regions of the cerebral spinal cavity during longitudinal gravitational loads

| Magnitude of load, g units | Magnitude of pressure change (cm water column) | | |
|---|---|---|---|
| | Inside the cranium | In the cervical region of the spinal cord | In the lumbar region of the spinal cord |
| 0.2 | 0.5-1.5 | — | 0.8-2.0 |
| 0.6 | 2.0-3.0 | 0.1-0.5 | 2.0-4.0 |
| 1.0 | 3.0-5.0 | 0.3-1.0 | 4.0-7.0 |

1. Under loads on the order of 1 g causing outflow of blood from the head, in many cases we observed a reaction opposite to that which occurred in experiments with rats, and in particularly, the amount of blood filling the brain increased. Such a reaction is observed only when definite load magnitudes are reached. In these same animals at loads on the order of 0.2-0.3 g the direction of change in the intracranial EPG level coincides with the curves which we observed earlier, and indicates a decrease in blood filling of the intracranial cavity. Beginning with a load of 0.4 g, there appears a clearly expressed physiological component of the reaction which normalizes the intracranial EPG level within 5-8 seconds after the beginning of the reaction. Upon further increase of the load this active reaction increases, and already at loads on the order of 1 g a reverse reaction is observed which is caused not by the mechanical displacement of the blood column but by the physiological component (Fig. 5).

2. At times we observed changes in the intracranial EPG level which were the opposite of those typical during similar reactions in that the EPG level in these cases changed jump-like, in the beginning and at the end of the reaction (Fig. 6). It is difficult to relate such rapid changes in EPG level to indices of active physiological reactions, although several authors (Mchedlishvili, 1963) believed that the speed of reactions in the vascular system of the brain can be very large. This would more likely be caused by small displacements of brain mass resulting from gravitational forces which show up in jump-type changes in electrical conductivity between electrodes.

Such an assumption is not unrealistic in as much as the possibility of displacements in brain mass resulting from gravitational forces is shown in the work of Adey, et al. (1961); A. I. Naumenko, et al., (1962) propose that small displacements of brain mass are observed constantly, facilitating the transfer of the pulse wave within the cranium.

3. In many experiments, the beginning moment during actions causing the influx of blood to the head, and upon cessation of actions in the case of outflow of blood from the head, the filling of blood in the cerebral cavity decreases sharply for several seconds (Fig. 7). A similar decrease in blood filling reminds one, by appearance, of a momentary spasm of the brain vessels caused during a change in longitudinal gravitational load. It is possible that the phenomenon is basically caused by the emergence of ischemic anoxia in the brain during longitudinal overloads, the symptoms of which were observed during such reactions by the subjects of Rossanigo and Meineri (1961), and Duvoisin, et al., (1962) and others.

4. In studying the dynamics of blood filling the cerebral cavity during longitudinal gravitational loads, it was noticed that after the first reaction in a given experiment the sign of the intracranial EPG level does not return to the original upon cessation of the reaction but occupies some sort of intermediate value between its position during the reaction and the original (Fig. 8). However, after all of the subsequent reactions of the same sign, the intracranial EPG level rapidly returns to normal. This fact can be explained if it is assumed that under normal conditions, the volume of blood in the cerebral cavity of animals is not some sort of constant quantity but can fluctuate within certain limits; but during the change in the level of blood filling in the cerebral cavity either above or below these limits, active or passive compensitory mechanisms tend to bring

the volume of blood in the cerebral cavity back to the original limits.

In favor of such an assumption are the results of Geigel's hydrodynamic calculations (1905) which show that during small changes in blood volume in the cerebral cavity, the total resistance to blood flow in the brain vessels remains unchanged.

5. In comparing changes in the intracranial EPG level during longitudinal gravitational loads from 0.2 to 1.5 g on various types of experimental animals (rats, rabbits, cats, and dogs) it is possible to notice that cats, and especially dogs, have active regulatory processes which are observed under lighter loads than for rats. However, the phenomena indicating destruction of normal activity in the central nervous system observed in these animals under somewhat greater loads in comparison with rats (Table 3). Rabbits react in a special way to longitudinal gravitational loads. These animals have both a sensitivity threshold and a threshold of destruction of activity in the central nervous system which are very small.

Because mobility in the vertical plane for rats, cats, and dogs, and consequently their conditioning to longitudival gravitational loads the vertical plane which arise when the body position is changed in are approximately the same, then it can be assumed that differences in thresholds of sensitivity to overloads for these types of animals are caused by unequal development of their central nervous systems. Peculiarities of rabbits' reactions to longitudinal gravitational loads and also several experiments which we conducted on rates, which for a month are found under conditions of limited mobility, make it possible to conjecture that the magnitude of the sensitivity threshold in the intracranial circulatory system to longitudinal velocities are determined also by ecological pecularities. This supposition is confirmed by a series of experiments in which we recorded the dynamics of intracranial EPG level under loads placed simultaneously upon two rats, one of which was acclimatized to hypoxia and the other was the control subject (Fig. 9). It is evident from this figure that under identical loads (0.8 g) a change in intracranial EPG in the control animal indicates an active physiological reaction, but in the acclimatized animal the stimulus still does not attain threshold value.

However, we are still not assuming that there is sufficient factual material to warrant convincing confirmation of our assumptions; still necessary are detailed comparative physiological investigations of the peculiarities of intracranial EPG and other indices in various types of animals which differ by level of development of their central nervous systems and their ecologies.

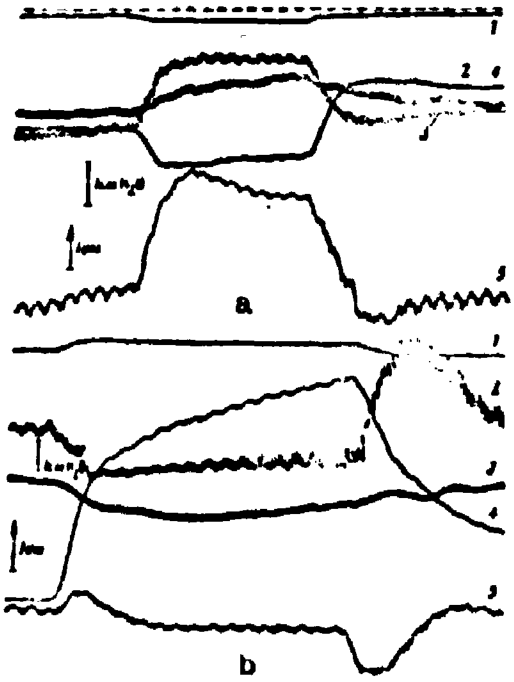

Fig. 4. Changes in intracranial pressure (2), pressures in the cervical (3) and lumbar (4) regions of the spinal cord and intracranial EPG (5) of cats under positive (A) and negative (B) longitudinal gravitational loads of 0.8 to 1 unit of action. Indexof time is 1 sec.

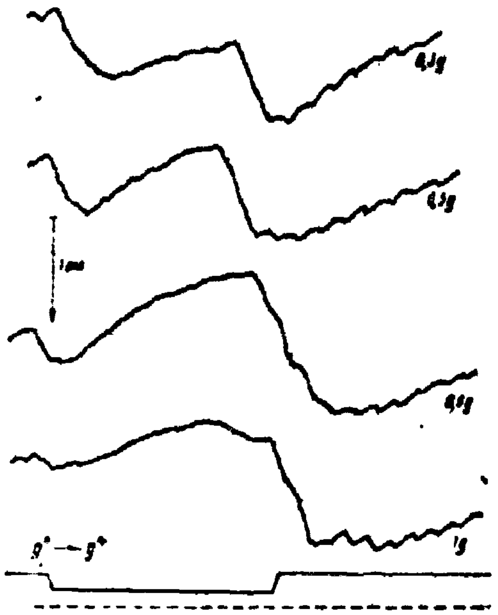

Fig. 5. Changes in level of intracranial EPG of a cat under several increasing gravitational loads.
Time index is 1 sec.

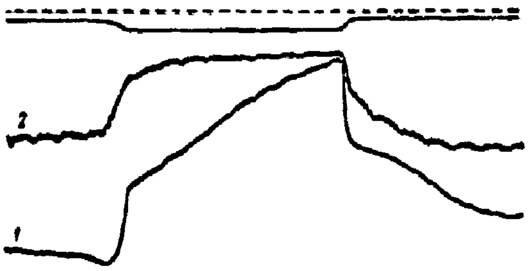

Fig. 6. Jump-like change in level of intracranial level of EPG (1) and intracranial pressure (2).
Time index is 1 sec.

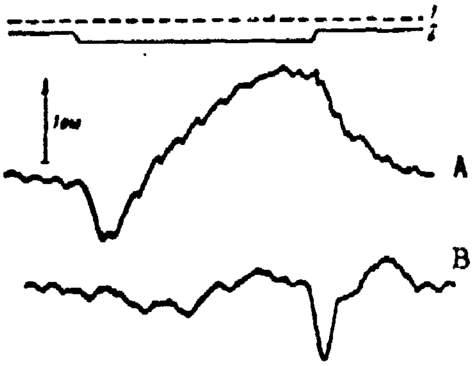

Fig. 7. Short duration decrease in blood filling of the cerebral cavity during influx of blood to the head (EPG is the curves). 1- index of time is 1 sec; 2- index of action. A- negative acceleration; B- positive acceleration.

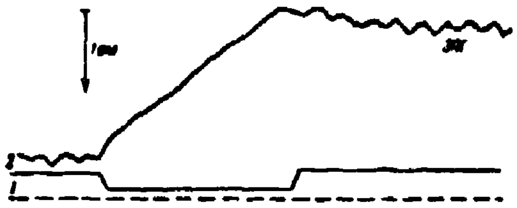

Fig. 8. Dynamics of the level of intracranial EPG during the first action in the given experiment. Index of time is 1 sec. 1- index of time; 2- index of action.

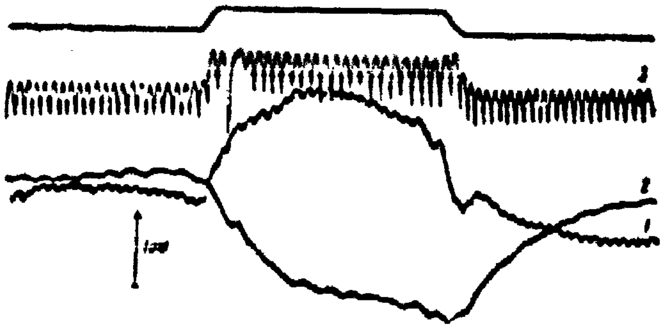

Fig. 9. Dynamics of the level of intracranial EPG in a controlled rat (3) and rats conditioned to hypoxia (2) in response to identical (0.8 g) action. 1- respiratory movements of the controlled animal Index of time – 1 sec

TABLE 3

Change in thresholds of sensitivity and disturbances of regulation in intracranial blood circulation in different types of animals as a function of the development of the central nervous system (CNS) and ecology

| Type of animal | Threshold of sensitivity of the brain vessels, in g units | Threshold of disturbances in the regulation of intracranial blood circulation, in g units |
|---|---|---|
| Rabbits | 0.3-0.5 | 0.5-0.8 |
| Rats | | |
| Control | 0.5-0.8 | 0.8-0.12 |
| Held under conditions of hypoxia | 0.8-1.0 | > 1.0 |
| Held under conditions of limited mobility | 0.3-0.4 | 0.6-0.8 |
| Cats | 0.4-0.6 | 0.8 - > 1.0 |
| Dogs | 0.3-0.5 | 1.0-1.5 |

## B. Periodic Fluctuations

The dynamics of the level of intracranial pressure and blood filling of the cerebral cavity under longitudinal gravitational loads are accompanied by changes in the parameters of periodic components of these parameters — pulse and respiratory waves whereby, just as in relation to the dynamics of the pressure level, in the intracranial EPG are observed more significant changes than on the curve of intracranial pressure. Thus for example, in Fig. 10a, it is obvious that within 5-10 sec after the beginning of the action on the intracranial EPG respiratory waves increase significantly — by 6-10 times — during the same time that respiratory waves of intracranial pressure increase by only 2-3 times.

It should be noted that the dynamics of the amplitude of respiratory waves, both of the intracranial EPG and of intracranial pressure do not always correlate with the range of respiratory movements of the experimental animal. This follows, in particular, from the experiments shown in Fig. 10a where the amplitude of respiratory movements remained unchanged all of the time. In other experiments we observed that sometimes increased frequency of respiratory movements during the reaction was accompanied by a decrease in the amplitude of respiratory waves in the intracranial EPG (Fig. 10b). Possibly this incongruity in amplitude of the respiratory waves with the respiratory movements was caused by the fact that except for changes in conditions of venous blood from the skull during respiration, there also occur active changes in the tone of the intracranial vessels, as was shown in the work of K. Sh Nadareyshvili (1962). In other respects, the general picture of change in the amplitude of respiratory waves in all types of experimental animals does not differ from the phenomena which were described by us earlier in studying the peculiarities of intracranial EPG in rats (Moskalenko, et al., 1963).

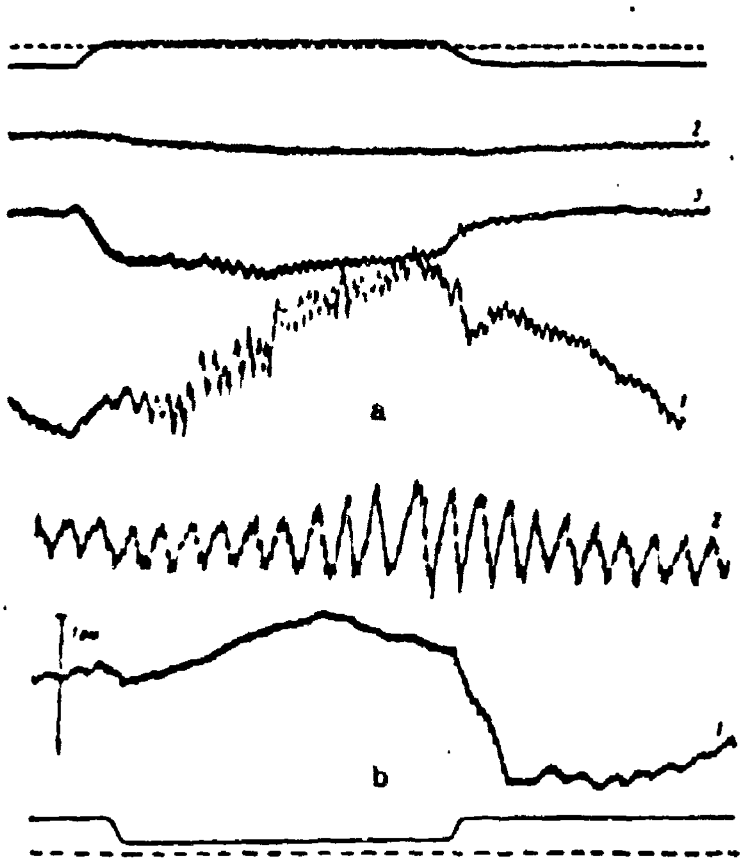

Fig. 10. a, b — Dynamics of the level and respiratory waves of intracranial EPG (1) respiratory movements of an animal (2) and intracranial pressure (3) under longitudinal gravitational loads. Index of time — 1 sec

Substantial changes under gravitational loads are observed in the amplitude of pulse waves. Thus, in Fig. 9a it is apparent that within 10-15 sec after the beginning of the reaction, the amplitude of pulse waves of tho intracranial EPG increases by 5-8 times. Pulse fluctuations in intracranial pressure also increase.

However, a complete interrelationship between changes in amplitude of pulse waves of the intracranial EPG and in intracranial pressure is not observed.

It should be noted that we were not able to register any kind of dynamics in pulse pressure waves in the lumbar and cervical regions of the spinal cord in either cats or dogs, in as much as the pulse waves on the curves we obtained were very poorly shown.

Changes in amplitude of pulse waves of the intracranial EPG and of intracranial pressure during longitudinal gravitational loads are accompanied by substantial changes in their form (Fig. 11). This showed up especially clearly during reactions accompanying the outflow of blood from the head.

Passing from the most general concepts about the effects of changing gravitational fields on living organisms, one can conclude that changes in circulatory parameters of the cerebral cavity can be caused by several reasons. Passive changes in blood filling of the cerebral cavity and in intracranial pressure are possibly the result of disproportionation of blood in the organism. Besides, under the influence of longitudinal gravitational loads it is possible to observe the disproportionation between the liquid phases which fill the cerebral and spinal cord cavities with blood and spinal fluid.

Active changes can occur in the tone of the cerebral vascular system which are reactions of the intracranial vessels to changes in blood filling which are caused by the effect of a longitudinal gravitational load.

For the characteristics of passive changes in the circulation parameters of the cerebral cavity, we, as in earlier experiments, elucidated by calculations the qualitative functions in the change of their level. In as much as our earlier calculations furnished an analysis of the passive change in blood filling of the cerebral cavity, in the present work we tried to elucidate the nature of passive change in the level of intracranial pressure and the dynamics of its periodic components under longitudinal gravitational loads.

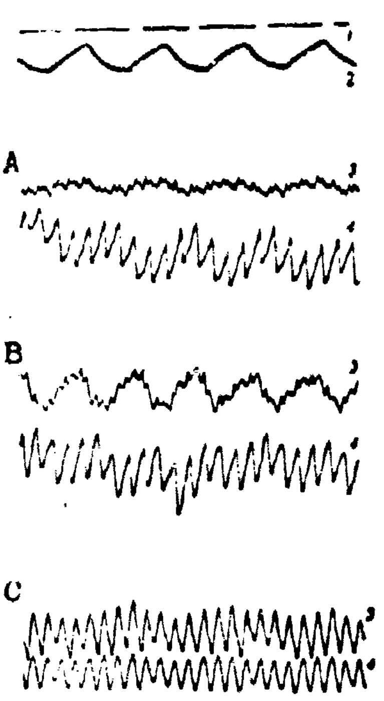

Fig. 11. Pulse and respiratory waves of intracranial EPG (4) and intracranial pressure (3) in norm (A), under negative (B) and positive (C) longitudinal gravitational load of 1 d. 1- index of time, 1 sec; 2- respiratory movements

In calculating, we proceeded from the model which reflects the following peculiarities of the intracranial circulatory system a. Changes in blood volume in the cerebral cavity result from displacement of cerebral spinal liquid in the spinal cord cavity. b. Displacements of cerebral spinal liquid in the spinal cord cavity occur through an opening of limited size as characterized by parameter A. c. The arterial and venous systems of the brain posses definite coefficients of elasticity $\alpha_a$ and $\alpha_b$ where upon $\alpha_b >> \alpha_a$. d. The spinal cavity in which occurs a displacement of cerebral spinal liquid during an increase in the volume of blood in the cerebral cavity posses some elasticity $\alpha_{c\,p}$. e. We think that there is no direct connection between the volumes filled by arterial and venous blood.

The first four conditions accepted by us correspond to a real picture of the structure of the vascular system of the brain, because the elasticity of the cerebral cavity, the counter forward motions of the cerebral spinal liquid between the brain and spinal column cavities, and the elastic properties of the spinal sac were shown in the classical investigations on intracranial blood circulation (Becher, 1962; Ewig, Lulies, 1924; Hurthle, 1927; Sepp, 1928; Bowsher, 1958 and others).

The last condition (e) leads to the result that we are not viewing capillaries as the agent of interaction between arterial and venous volumes. Such a simplification of the model is justified by the fact that the rapidly flowing processes which we are examining in the cerebral cavity result from the direct interaction of the arterial and venous systems of the brain, bypassing the capillary canal (Naumenko, et al., 1962, and others). It should be noted that the model which we accepted is a simplified scheme of the extremely complex architecture of the vascular system of the brain which makes it possible to analyze qualitatively only the separate sides of the rapid, passive mechanical changes in circulation parameters of the intracranial cavity.

On the basis of the conditions listed above, a system of differential equations was composed, the solution of which, with respect to the amount of change in intracranial pressure $\Delta p_{inc}$, takes the form;

$$\Delta p_{inc} = \frac{1}{\alpha_a + \alpha_b}\left[f(t) - \beta e^{-\beta_1 t}\int_{-\infty}^{t} f(\tau)\, e^{\beta_1 \tau}\, d\tau\right] \tag{1}$$

$$\left(\beta = \frac{A}{\alpha_a + \alpha_b};\ \beta_1 = \beta + \frac{A}{\alpha_g C}\right).$$

where f(t) is a function depending upon changes during pressures in the arterial $\Delta p_a(t)$ and venous $\Delta p_b(t)$ systems.

$$f(t) = \alpha_a \Delta p_a(t) + \alpha_b \Delta p_b(t).$$

Considering that a change in blood pressure during longitudinal gravitational loads occurs jump-like or

$$\Delta p_a = \begin{cases} 0 & t < 0 \\ a & t \geq 0 \end{cases} \ \text{и}\ \Delta p_b = \begin{cases} 0 & t < 0 \\ b & t \geq 0 \end{cases}, \tag{2}$$

we obtain

$$\Delta p_{inc} = \frac{\alpha_a a + \alpha_b b}{\alpha_a + \alpha_b}\left[1 - \frac{\beta}{\beta_1}\left(1 - e^{-\beta_1 t}\right)\right]. \tag{3}$$

Equation (3) shows that during sharp changes in a longitudinal gravitational load, intracranial pressure must change quickly, but after this the level of intracranial pressure is gradually partially re-established. A similar picture of the change in intracranial pressure was observed in an experiment; in all of the trials, the ıtracranial pressure, in distinction from intracranial EPG, changed ɪry sharply but then somewhat returned to normal. Consequently, ıe can conclude that during longitudinal gravitational loads, the 'namics of the level of cerebral spinal liquid pressure reflects passively mechanical side of intracranial hemo-dynamics. Com- ıring equations (3) with the results of computations which we did ırlier shows that there is no parallel between changes in blood .lling of the cerebral cavity and changes in intracranial pressure ıring rapidly evolving processes. These two processes are con- ɪcted with the complicated dependence which, during jump-like ıanges in blood pressure changes into a ratio of the two exponents. ; is interesting to note that the assumption of the presence of a ımilar connection based on experimental data was advanced by ɪbrazzini,(1940) and Ryder, et al., (1950).

Having assumed in equation (1) that a change in $\Delta p_a$ occurs by periodic law, it is possible to trace the relationship between ıe form of arterial pressure pulse wave and the form of intra- 'anial pressure wave which it causes.

Assuming that

$$\Delta p_a = \sum_n C_n \cos(\omega_n t + \varphi_n).$$

ıere $C_n$, $\omega_n$ and $\varphi_n$ are respectively the amplitude, frequency and ıase of the M-th harmonic of the pulse wave.

Equation (1) in this instance assumes the form:

$$\Delta p_{ino} = \sum_n A_n \cos(\omega_n t + \varphi_n + \psi_n). \quad (4)$$

From this it is apparent that the transformation of pulse luctuations in arterial pressure to pulse fluctuations in cerebral spinal liquid pressure is accompanied by the appearance of an additional phase shift $\psi_n$ for each primary harmonic. This leads to distortion of the initial form of pulse fluctuations.

The fact that the form of the pulse wave of intracranial pressure is significantly more complex than the arterial pulse has long been known. The complexity of the intracranial pulsation form can also been seen in the curves of Fig. 11. So this consequence of Eq. (4) has factual foundation. However, it should be noted that some authors (Becher, 1922; Hurthle, 1924; Bering, 1955 and others) have explained such a complication in the form of pulse fluctuations of intracranial pressure by interference of the cranial pulse wave with a wave reflected from the caudal part of the spinal cord. We shall not bring into the discussion the relative acceptability of such a point of view; we shall only note that these assumptions were expressed, in our view, without sufficient factual basis or any kind of computations which would confirm them. The data which we have obtained showing an insignificant quantity of pulse waves in the lumbar region of the spinal cord also fail to support this assumption.

In as much as Eq. (1) is linear with respect to $\Delta p_a$ and $\Delta p_b$, then it is possible to view the reaction of intracranial pressure to a complex reaction (occurring simultaneously are periodic changes in blood pressure — pulse waves — and a jump-like change in pressure — a reaction to a longitudinal gravitational load) $\Delta p_{inc}$ as the sum of the separate components of the reaction. It follows from this that under various conditions of blood pressure, changes in the amplitude and form of the pulse wave of intracranial pressure will not be observed. And actually, as is apparent in Fig. 11, the form of pulse ave of intracranial pressure under loads causing an influx of blood o the head does not change.

However, from this same figure it is apparent that under a load ausing outflow of blood from the head, the form of pulse waves of ntracranial pressure changes substantially. On the basis of data n the dynamics of intracranial EPG level which show that the tone f brain vessels decreases in this case, one can conclude that a hange in the elastic properties of the brain vessels leads to hanges in the form of pulse waves of intracranial pressure.

This finds confirmation in formula (4). Additional phase shift $_n$ depends upon the characteristics of vessel elasticity so that uring an increase in arterial elasticity ($\alpha_a$ increasing), the phase hift decreases. Thus, a distortion of the pulse wave according to he form in pulse fluctuations of intracranial pressure decreases. onsequently, the form of pulse waves of intracranial pressure hanges but pulsation amplitude increases. In Fig. 11 it is apparent hat pulse waves of intracranial pressure undergo just such changes uring gravitational loads causing the outflow of blood from the ead.

By similar considerations, assuming that under gravitational oads conditions of the outflow of cerebral spinal liquid into the pinal cavity are changing, it is possible to show that during a ositive load the respiratory waves of intracranial pressure must ncrease, and during a negative load they must decrease. This assumption also corresponds with experimental data.

Based upon computations which show passive changes in intracrani-l pressure during longitudinal gravitational loads, it is possible o make the following conclusions:

1. The general form of changes in level of intracranial pressure and amplitude of respiratory waves (arising at once after the beginning of the reaction and remaining thus until its end) reflects the pecularities of the cerebral cavity structure and is not connected with any kind of phenomena of active physiological reactions of the brain vessels.

2. Changes in form and amplitude of pulse fluctuations of intracranial pressure testify to the change in tone of the intracranial vessels. A change in the amplitude of respiratory waves during the course of the action several seconds after its inception also indicates active physiological reactions.

3. Compiling the results of the above computations with computations which we did earlier (Moskalenko, et al., 1963) and with experimental results, it is possible to conclude that the passive mechanical factor plays a substantial role in the dynamics of circulation parameters of the vascular system of the brain, but a number of peculiarities in these dynamics testifies to the active reactions of the vascular system of the brain.

The dynamics of the level of intracranial pressure and especially intracranial EPG during longitudinal gravitational loads observed in the experiment indicate the existence of active physiological reactions of the brain vessels which, as was shown by us earlier (Moskalenko, et al., 1963), are specific for the system of intracranial blood circulation. Proceeding from current concepts of the mechanisms of brain blood circulation regulation (Blinova, Marshak, 1963; Klosovskiy, 1963; Mchedlishvili, 1963; Lassen, 1953; Sokoloff and Kety, 1960; Shenkin, 1961, and others), one can conclude that during disproportionation of blood in the organism under the influence of gravitational forces, active reactions in the system of intracranial circulation can be caused by several reasons. From them it is possible to extract the direct influence of changes in arterial pressure upon the tone of intracranial vessels (so-called mechanical regulation, or autoregulation), the influence of change in the gas medium of the brain — oxygen deficit and accumulation of carbon dioxide (chemical regulation) and nervous reflex reactions of the brain vessels resulting from stimulation of the different receptor zones during action on the organism of longitudinal gravitational loads (nervous regulation). Unfortunately, we still do not have at our disposal sufficient facts for analyzing the role of each of these regulatory mechanisms of intracranial blood circulation and to trace the relationship between them. Therefore, we shall present below separate concepts with respect to the possible role of the first two of these mechanisms.

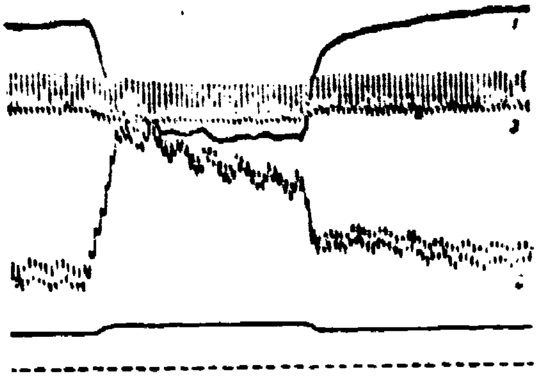

Fig. 12. Changes in intracranial EPG (1), intracranial (2) and arterial (3) pressures under a longitudinal gravitational load of 0.8 g.

The dependence of brain vessel tone upon changes in arterial pressure is determined by the fact that the smooth muscles of the vessel walls react to an increase in intracranial pressure by constricting (Folkow, 1953; Levy, 1958; Zurav, Kaŕmer, 1959, and others). This phenomena also assures autoregulation of intracranial blood circulation during changes in general arterial pressure. To elucidate the possible role of autoregulation of intracranial circulation during longitudinal gravitational loads, we regulated in several experiments changes in general arterial pressure (Fig. 12) simultaneously with intracranial EPG. In the majority of cases we found that the general arterial pressure changes not more than by 5-8%. The quantities which we obtained agree with the data of Lindberg, et al, (1960) with respect to changes in aortic pressure longitudinal loads.

However, it is possible to consider that the amounts of change in arterial pressure can be more significant in some cases as a result of changes in heart activity which occur during longitudinal loads. Thus, for example, in separate trials at loads of nearly 1 g causing the outflow of blood from the head, we observed the emergence of an alternating rhythm of heart contractions. Changes in heart activity during longitudinal loads of nearly 1 g as a result of a change in the tone of the sympathetic region were noticed in the investigations of Lamb and Roman (1961).

One can assume from this that some normalization in the level of intracranial EPG observed in many experiments for several seconds after the beginning of the action, occurs due to autoregulation of the tone of brain vessels resulting from changes in general arterial pressure.

However, the fluctuations in arterial pressure observed in the majority of experiments were all small. Therefore, to confirm this assumption it is necessary to obtain additional information on the threshold of brain vessel sensitivity to changes in arterial pressure.

In all probability, one of the phenomena of autoregulation of brain vessels is also the short duration spasms of brain vessels during the inflow of blood to the head. However, the fact is significant that in this case the curve for the change in intracranial EPG level by appearance reminds one of the function which is derived from the curve for change in intracranial pressure. In spite of the fact that this indicates the passive mechanical nature of such spasms, it is nevertheless possible to assume that they have some physiological activity, since on the one hand, it is difficult to imagine a mechanical model of such a phenomenom, and on the other hand there is data (Blinova, Marshak, 1963) showning that there exists a dependence between changes in tone of the vascular wall and the sharpness in growth of intravascular pressure. Besides, we noticed in a number of experiments that these spasms are accompanied by a significant increase in pulse fluctuations of intracranial pressure which also indicates the active nature of this phenomenon.

Thus, changes in arterial pressure as a mechanism of autoregulation of the tone of the intracranial vessels is one of the reasons for active physiological reactions in the vascular system of the brain during longitudinal gravitational loads.

Along with changes in general arterial pressure under longitudinal gravitational loads, significant changes are observed in the perfusion pressure of blood in the brain, since the disproportionation of the blood in the organism causes substantial changes in venous pressure (Henry, et al, 1951, and others). Changes in blood filling of the venous part of the vascular system of the brain could be the reason for the destruction of its blood supply and could cause a defficiency in oxygen tension and an accumulation of $CO_2$ which would cause active changes in the tone of the intracranial vessels, because the vasodilative action of $CO_2$ is well known.

To elucidate the role of this factor in the active changes which we observed in blood filling of the cerebral cavity during longitudinal gravitational loads, we simultaneously with the intracranial EPG and intracranial pressure, recorded in several experiments the dynamics of oxygen tension in the fibers of the brain. As a rule, in the beginning and sometimes at the end of the action, oxygen tension in the brain fibers decreases somewhat, but after 4-8 sec it returns to the original level (Fig. 13). In some experiments, oxygen tension in the brain tissues remains somewhat decreased during the whole experiment.

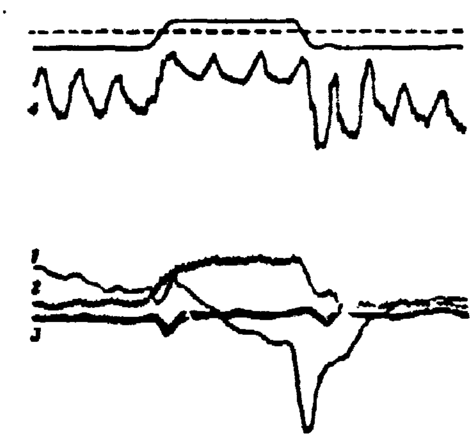

Fig. 13. Dynamics of intracranial EPG (1), intracranial pressure (2) and oxygen tension (3) under a longitudinal gravitational load; 4- respiratory movements

Obviously, during short-term longitudinal gravitational loads we scarcely observed the active reactions of the brain vessels which are caused by changes in tension of gases in the brain tissues, because these reactions arise, as a rule, after the level of oxygen tension in the brain tissue returns to normal. However, during more prolonged actions at a magnitude of nearly 1 g, for 15-20 sec after their beginning in some experiments, there suddenly begins a significant (sometimes in the form of several waves) increase in blood filling of the cerebral cavity. As a rule, this increase in blood filling of the cerebral cavity is accompanied by a sharp intensification of pulse and respiratory waves in the intracranial EPG.

These facts are difficult to explain by appearances of autoregulation of the brain vessels, all the more so because the polarogram registered in several of such experiments shows changes in the level of oxygen tension within the brain tissues which are in the opposite phase to blood filling fluctuations. Most likely, with an increase in the duration of the action there occurs an accumulation of $CO_2$ in the brain tissue which causes the switching in of a new regulating mechanism.

Thus, the data which we obtained leads us to believe that active physiological reactions in the intracranial vessels during longitudinal gravitational loads are caused, first of all, by the reaction of the vascular system of the brain to changes in intravascular pressure which arise immediately after the beginning of the action, and after a certain time, if the blood supply to the brain is lower than the necessary level phenomena are observed which indicate the switching in of a chemical mechanism which regulates intracranial blood circulation.

## Conclusions

1. During longitudinal gravitational loads there are observed substantial changes in the circulation parameters of the intracranial cavity which are caused by phenomena of a passive mechanical nature and by active changes in the tone of the intracranial vessels.

2. The threshold of sensitivity of the vascular system of the brain to longitudinal gravitational loads lies within the limits of 0.2 to 0.5 g, the magnitude of which depends upon the peculiarities of the ecology and conditioning of the animals under experiment,

and also, in all probability, upon the development of the central nervous system.

3. The data obtained show that under longitudinal gravitational loads, organs of the central nervous system function under conditions of insufficient blood supply which cause definite compensitory reactions on the part of the vascular system of the brain, reactions of an automechanical and chemical nature.

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# EMOTIONAL STRESS OF COSMONAUTS DURING SPACE FLIGHTS

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As a result of the flights of Gagarin, Titov, Nikolaev and Popovich Soviet scientists received voluminous valuable scientific data on the effect of a complex of space factors on the human organism. A careful analysis of the material obtained will enable further development of the methods of selecting and preparing cosmonauts for new flights.

This work analyzes the neuropsychological stress which arises in cosmonauts before launch, in different flight periods, and also under the effect of acceleration on earth.

As a test to determine the functional state of the organism we measured the pulse rate. As is known, the frequency of heart contractions is an integral index which characterizes the reaction of the organism to the effect of various factors including those encountered in space flight.

Thus, for example, when an organism is subjected to acceleration of a different direction, substantial changes of pulse rate are observed. The degree of these changes depends directly on the magnitude and length of acceleration (Babushkin et al., 1952; Kotovskaya et al., 1962).

An increase in pulse rate caused by emotional stress can be observed in parashuting and also before catapulting (Reznikov and Grayfer, 1937; Povalyaev, 1939; Lukin, 1952; Gozulov, 1955; and others).

Consequently, in our opinion, a comparison of the pulse rate change in cosmonauts recorded during different periods of flight and under earth conditions reflects the character of the organism's reaction to the effect of space flight factors.

As is known, just before the spaceships were launched an increased heart contraction rate was observed in the cosmonauts. Table 1 introduces data on the changes in pulse rate 8 days (P-0), 4 hr(P-1) and 5 min (P-2) before launch. It is evident that the pulse rate increase was expressed most by Popovich and least by Titov. In the period immediately before launch the former's pulse rate had increased 101.7% compared with what it was 8 days before launch, and the latter's, 55%.

Such differences in prelaunch pulse rate increase may be connected to the dissimilar character of flying assignments, a difference in training of the cosmonauts and the pecularities of their characters and other factors.

The significant increase in Gagarin's pulse rate in the prelaunch period (by 68.7% compared with the P-0 data) should be explained by emotional stress connected to the singularity and responsibility of his task, the first attempt by a man to penetrate cosmic space.

TABLE 1

Changes in pulse rate (PR) 4 hr (P-1) and immediately before launch (P-2) compared with the results observed 8 days before the flight experiments (P-0) (average data)

| Cosmonauts | PR at P-0 | PR at P-1 | PR at P-2 | PR, % with respect to P-0 in the period | |
|---|---|---|---|---|---|
| | | | | P-1 | P-2 |
| Gagarin | 64 | 65 | 108 | 101,5 | 168,7 |
| Titov | 60 | 60 | 107 | 100,0 | 155,0 |
| Nikolaev | 64 | 72 | 112 | 112,5 | 175,0 |
| Popovich | 58 | 56 | 117 | 96,5 | 201,7 |

In the prelaunch period Titov's pulse rate increase was less than Gagarin's, which was evidently caused by a decrease in emotional stress. The fact is that the first flight proved the possibility of a man staying in space, the safety of the ship construction, that space flight factors could be endured etc.

It would seem that in the group flight of Nikolaev and Popovich there should have been a further decrease of emotional stress; however the data on pulse rate changes testify to the contrary. This evidently can be explained by the greater complexity of the group flight compared with the experiments conducted by Gagarin and Titov (lengthening and complicating the flight program etc.). Also, in the prelaunch period Popovich's greater increase of pulse rate (compared with the other cosmonauts) had individual characteristics: easy excitability, an expressed lability from the side of the autonomic functions, etc.

We should consider the relatively low level of Popovich's pulse rate in the initial state. As is known, during the prelaunch period and acceleration the pulse rate increase is more significantly expressed in persons with a tendency towards bradycardia than in those with tachycardia (Perlina, 1957; Rozenblat, 1962; and others). Evidently, this also partially explains the more significant increase in Popovich's pulse rate.

A comparison of the level of emotional stress observed before the real space flight and before the corresponding tests on earth, rotation on the centrifuge, shows than in the latter case the stress was considerably lower. The differences in the pulse rate measurements affirms this. Thus, just before the effect of acceleration on the centrifuge the pulse rate of most of the cosmonauts did not exceed 90 beats a minute. The increase in the heart contraction rate occurred in the final seconds before rotation. Differences in the level of emotional stress are explained by significant differences in the character and responsibility of the experiments on earth and in flight.

The greatest increase in the heart contraction rate compared with that of the prelaunch period was observed in the period when the ship was put into orbit (Table 2).

TABLE 2

Pulse rate (PR) of the cosmonauts during launching into orbit (period A) compared with the P-0 and P-2 periods (average data)

| Cosmonauts | PR in the P-0 period | PR in the P-2 period | PR in period A | PR increase in period A with respect to P-0 | | PR increase in period A with respect to P-2 (acceleration) | | PR increase in period A due to emotional factor | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | in absolute magnitudes | % | in absolute magnitudes | % | in absolute magnitudes | % |
| Gagarin | 64 | 110 | 120 | 56 | 88 | 10 | 9 | 46 | 79 |
| Titov | 69 | 107 | 112 | 43 | 62 | 5 | 5 | 38 | 57 |
| Nikolaev | 64 | 112 | 119 | 55 | 86 | 7 | 6,0 | 48 | 80 |
| Popovich | 58 | 117 | 120 | 62 | 107 | 3 | 3 | 59 | 104 |

Note: P-0 is the data obtained 8 days before the flight, P-2 was obtained directly before the launch at the 5 min readiness.

Comparing the pulse rate during the active portion and in the prelaunch period (P-2) allows us to explain its increase mainly due to the effect of acceleration, since the level of neuro-emotional stress in these periods was sufficiently high. Under the effect of acceleration the pulse rate increase in all the cosmonauts averaged 3-10 beats a minute (3.0-9.0%) compared with the initial state (P-2), the largest increase being expressed in Gagarin (9%) and the least in Popovich (only 3%).

The heart contraction rate increase during the active portion of the flight was mainly determined by emotional stress as is evident from comparing the pulse rate in this period and eight days before launch. Thus, for instance, Gagarin's pulse rate during the active portion on the average increased 88.0% compared with the P-0 period and only 9% compared with the P-2 period. Evidently, the pulse rate increase when the ship was being put into orbit was basically caused by emotional stress. About the same data appear when other flight experiments are analyzed. Just as in the prelaunch period, emotional stress was most strongly expressed in Popovich and least strongly in Titov. The causes were evidently the same as when the prelaunch results were analyzed.

In spite of the significant pulse rate increase in the cosmonauts during the active portion of the flight, it must be mentioned that none of them had a pulse rate higher than 160 beats per minute. In the literature there is evidence that the upper critical limit of the pulse is 180 ± 10-20 beats a minute. If we note the good physical preparation of the cosmonauts (and for athletes the pulse rate limit must be raised), then the pulse rate shifts during the active portion of the flight are very far from the critical value. This agrees with the data evaluating their activity. The cosmonauts took observations, maintained radio communications with earth stations and their state of health was good. They noticed a certain difficulty in breathing, a squeezing of the chest cage during acceleration and a difficulty in performing motor acts.

During orbital flight, the length of which was different for each flight experiment, the pulse rate gradually approached the initial level, the pulse rate recorded eight days before launch. The rate of normalization was different; for Popovich the initial pulse rate was attained in the 14th orbit, for Nikolaev in the 13th orbit. Throughout the flight Titov's pulse did not normalize, evidently due to the appearance of cosmic motion sickness (Komendantov, Kopanev, 1962), and also because the level of emotional stress began to increase significantly during the second half of the day because the more responsible portion of the flight, the period of returning to earth, was approaching. For a fully understandable reason, the shortness of the flight, Gagarin's pulse was higher than the initial data for the whole flight.

The data about pulse rate normalization in the cosmonauts agrees with the results observed in animals when they were launched into space. Under weightless conditions the pulse rate in animals, having been increased by the effect of acceleration, returned to the initial level about three times slower than it did on earth (Chernov and Yakovlev, 1958; and others). This is evidently caused by a change in the regulation of the cardiovascular system under weightlessness.

During the ship's descent a number of unfavorable factors acted on the cosmonauts: noise, vibration, acceleration etc., the determining effect on the organism was evidently that of acceleration, the magnitude of which was about identical during all the flight experiments.

Material concerning pulse rate change during descent is given in Table 3. These data differ somewhat from the results obtained when the ships were put into orbit. Thus, the emotional stress was considerably less during descent; the difference in the pulse rate change affirm this. During launching into orbit, due to emotional stress the pulse rate increased by 57-104%, during descent it increased by only 21-62%.

TABLE 3

Pulse rate (PR) in cosmonauts during descent (period B) to earth (from the moment of firing the breaking rockets to catapulting) compared with the pulse rate in the penultimate orbit (period C) and in the last minutes of weightlessness (period N-K) (average data)

| Cosmonauts | PR in period C | PR in period N-K | PR in period B | PR increase in period B, with respect to period C | | PR increase in period B with respect to period N-K * | | PR increase in period B due to emotional factors | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | in absolute magnitudes | % | in absolute magnitudes | % | in absolute magnitudes | % |
| Titov | 87 | 105 | 107 | 20 | 23 | 2 | 2 | 18 | 21 |
| Nikolaev | 66 | 75 | 92 | 26 | 39 | 17 | 23 | 9 | 16 |
| Popovich | 61 | 83 | 143 | 82 | 134 | 60 | 72 | 22 | 62 |

* (acceleration)

During descent acceleration exerted a more significant effect directly on the cardiovascular system than during launching into orbit. During descent the pulse rate increased on the average by 2-72% with respect to the N-K period, while during launching the increase was only by 2-9%. In our opinion the similar directivity of pulse rate changes during descent is explained by the large magnitudes of acceleration and chiefly because before the effect of this factor, the cosmonauts were weightless for an extended period, which substantially decreased their resistance to weightlessness.

During an analysis of the results obtained from the flights of Titov, Popovich and Nikolaev, we noted a certain dependence of pulse rate change under the effect of acceleration on the length of the stay under weightlessness (Table 3). The shorter the time of orbital flight, the less the heart contraction rate increased and converesely. Titov's pulse rate increase during descent averaged 2% compared with the N-K period. Nikolaev and Popovich, who were under weightlessness 4 and 3 times longer, had increases of 23 and 72% respectively.

The more expressed heart contraction rate of Popovich compared with Nikolaev's evidently can again be explained by individual properties of regulation of the autonomic functions, a tendency towards bradycardia, and consequently a more significant pulse rate increase during the effect of flight factors as indicated below.

During descent the cosmonauts took observations and maintained radio communications. According to the words of the cosmonauts, they withstood the acceleration satisfactorily, although the difficulty in breathing was expressed to a greater degree than during launching.

In the training on earth, together with a moderate pulse rate increase the cosmonauts's state of health, as a rule, was good and their emotional stress was expressed to a lesser degree than in the flight experiments. During space flight the level of emotional stress depends very much on the tasks of the flight experiments, on personality characteristics and to a significant degree it determines the direction of the physiological reaction. Therefore, when the cosmonauts are in orbit we must devote particular attention to determining emotional stability and the typological properties of higher nervous activity, since, all things considered, the force of the excitation and inhibition processes and their interrelationship are the basis of the different physiological changes in the prelaunch period.

An analysis of the physiological shifts during launching and descent allows us to conclude that in the first case, the pulse rate increase was caused mainly by emotional stress, while during descent, by the effect of acceleration. An extended stay under weightlessness by the cosmonauts before descent is important here; due to this their resistance to acceleration is somewhat decreased. While we did not record a noticeable decrease in work capacity, the pulse rate did increase. Possibly, a longer stay under weightlessness might cause more serious changes, Therefore, we must devote particular attention to investigations of the effect of extended weightlessness on the adaptation properties of the human organism.

## CONCLUSIONS

1. The level of emotional stress observed in cosmonauts during space flight depends on the complexity of the flight experiments and the training and personality characteristics of the cosmonauts.

2. When the cosmonauts were under weightlessness for an extended period (3-4 days), we observed a certain decrease in their resistance to acceleration which was expressed in more significant shifts of the pulse rate. A certain dependence of these shifts on the time under weightlessness was noted.

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# A SYMPOSIUM ON APPLIED MICROBIOLOGY (IN STOCKHOLM, SWEDEN)

Ye. N. Mishustin and N. D. Ierusalimskiy

This symposium on applied microbiology was established by a decision of the VIII International Congress of Microbiologists at Montreal from July 29 to August 3, 1962. Taking part in the symposium were the International Association of Microbiologists, UNESCO, the Swedish Academy of Sciences and other organizations.

The aim of the symposium was to discuss the most effective directions of investigation in applied microbiology connected with satisfying the material needs of mankind and, in particular, those of the population of economically underdeveloped countries. Both official documents and the papers submitted to the first plenary assemblies concerned this. Nevertheless, there was a definite break between setting up the organizations of the symposium and maintaining the work of a number of its members. At times the scientific reports were random in character and did not agree with the basic task of the symposium. While there were enough general reports, there were few concrete ones on the problems of help to economically lagging countries.

There were representatives from 33 countries among the participants: 74 from Sweden, 43 from the USA, 22 from England, 20 from the FGR, 19 from Norway, 16 from Holland, 14 from Italy, 11 from France, and from 1-7 delegates from the other countries. In all there were 306 delegates.

The symposium opened at 3 o'clock on 29 July in the chamber of the Swedish parliament. In his opening speech the president of the symposium, the famous Swedish scientist Tiselius, concentrated on the aims of the meeting. He emphasized that this meeting, in which not only scientists but also directors of government institutions and industrial enterprises were participating, would allow planning a program of effective research directed towards increasing agricultural and industrial resources and also towards improving sanitary measures. This is particularly important for raising the prosperity of underdeveloped countries. Both the international character of the symposium and the close connection of applied microbiology to many sides of human activity must help to fulfill the plotted task.

He also emphasized that the brilliant accomplishments of contemporary physics can overshadow the meaning of biological research for most people. However, the role of the latter in increasing the prosperity of nations cannot be valued too highly.

Brouhult (Sweden) delved into statistical data describing population increase and on the tasks before biologists in supplying the material wants of nations. He devoted particular attention to training scientific cadres devoted to solving this problem.

The minister of culture of Israel, M. A. Eban, stated that the aims of science must be humane and directed towards improving the lives of people. The brilliant achievements of science in the

20th century include deep contradictions. These achievements have led to conquests over diseases and to a population increase but they have also placed humanity on the verge of annihilation by atomic energy. The wide practical consequences of scientific discoveries have made the internal connection between science and politics inherent. Therefore, science deprived of social ideas is just as inconceivable as politics disregarding the achievements of science. There must be an organic connection between them to ensure that science develops in the interest of people.

He concentrated on the problems connected to the discovery of political independence by many underdeveloped countries. He stated that their being free and politically equal does not mean that they are economically equal. Achieving the latter is tied to the development of science and, primarily, to training scientific cadres. Science cannot be isolated in the laboratory. It must be connected to life and its needs.

The exchange of opinions on the basic tasks of the symposium continued on July 30. The representative of the Rockefeller Foundation, Harrar (USA), touched on the possibility of microbiological assistance to the development of young countries in medicine, agriculture and industry. He noted the role of science in the struggle against disease, in supplying and processing foodstuffs for man and animals, in obtaining biologically valuable compounds and also in regulating soil processes. He emphasized the ever increasing role of microbiology for mankind.

Borgstrom, the director of the nutrition laboratory at Michigan University (USA), reported on the problem of satisfying the needs of the earth's growing population. He emphasized that today's needs must not be the only basis of using nature. It is erroneous to examine the satisfying of current requirements withoug calculating the possible consequences of exploiting natural resources. In particular he emphasized the possibility of the wide uses of the ocean's riches to solve nutrition problems.

A professor from the University of Ohio (USA), Birkeland, spoke about the development of science and the progress of humanity. He noted that our natural resources can be rationally used only on a scientific basis.

After hearing the general reports and the exchange of opinions on them there were several plenary and a considerable number of sectional meetings. At most of them the discussion concerned the results of concrete scientific investigations having more or less practical value. At times very specific questions were discussed, the sterilization of milk or the hypogeal culturing of morel fungi. Nevertheless the basic group of reports was of undoubted interest.

The themes of the plenary sessions were: 1) microbiology and the mobilization of food resources; 2) investigations in the area of applied immunology; 3) perspectives and horizons of applied microbiology; 4) achievements in technical and engineering microbiology; and 5) mechanisms of biochemical reactions.

The work at the sectional meetings concerned these questions: 1) documentation and information in the area of applied microbiology; 2) production and use of amino acids; 3) protecting plants from microorganisms and insects; 4) soil microbiology; 5) fermentation and preservation of organic matter; 6) water microbiology; 7) transformation of hydrocarbons; and 8) engineering work in microbiology.

It is clearly evident that in this short article we cannot give a full report on the work of the symposium in its entirety. The difficulties are tied not only to the great volume of work but also to the fact that the material of the symposium was not printed and this discussion can only be based on aural reports. Many conferences ran simultaneously and the small number of Soviet representatives precluded our having people in every section. Therefore we will survey only those reports which were most interesting to us.

Among the plenary reports Braun's (USA) "Microbe Genetics and Applied Microbiology" is worth noting. He noted that explaining the laws of microbe variability has value for practical aims. Establishing the role of nucleic acids in forming the properties of genotypes and phenotypes uncovers the possibility of cultures having new properties. There have been achievements in producing cultures for a number of purposes (antibiotics, vitamins, amino acids, etc.). The transition to a biological concept concerning hereditary substances and the explanation of the role of DNA are opening great possibilities of producing microbe cultures with these valuable properties. Lately substantial results have been obtained in controlling the synthesis of enzymes in a microbe cell by means of the complex effect of inhibitive and inductive substances of the cell. Wide genetical possibilities are being opened by the phenomena of transformation, transduction and conjugation in microbes. The speaker spent some time on the works of the French school (Monod, Jacob and Wollman), which has created a concept about the structure of bacterial chromosomes. Genetic achievements have great value for classification work. They have undoubted value for medical purposes also since existing methods can change the antigen properties of microbes.

A number of reports were devoted to the production of proteins from hydrocarbons. Champagnat (France) reported on this question. The basic task of the works conducted under his direction in the British Petroleum Co. laboratory is the deparaffination of diesel fuel (gas oil) with the help of aerobic yeast. The cultured biomass can be used as a nutrient protein. The table gives data on the composition of 10 important amino acids in the two specimens of protein preparations obtained in the firm's tests.

The sulfur-containing amino acids are insufficient in the microbe preparations but they have a surplus of lysine, leucine and threonine. Therefore when they are added to food these preparations can be sources of the named amino acids.

TABLE

The composition of amino acids in protein preparations produced from diesel fuel and their optimum ratios as calculated by the nutrition and agriculture organization of UNESCO (FAO)

| Amino acids | Data | | |
|---|---|---|---|
| | British Petroleum Co. | | The nutrition and agriculture organization of UNESCO |
| | 1 | 2 | |
| Lysine | 12 | 7 | 4.3 |
| Phenyl-alanine<br>Tyrosine | 7 | 5.4 | 2.8 |
| Tyrosine | | | |
| Leucine | 8.8 | 7.7 | 4.8 |
| Isoleucine | 3.3 | 5.0 | 4.2 |
| Methyonine + cystine | 2.4 | 2.4 | 4.2 |
| Tryptophan | 1.3 | 1.3 | 1.4 |
| Valine | 7.4 | 5.2 | 4.2 |
| Threonine | 7.4 | 4.9 | 2.7 |

Senez (France) gave an historical survey from which it is particularly evident that research into hydrocarbon microbiology in France was first begun in the laboratories of the British Petroleum Co. but then this connection was interrupted. This report introduced data on the distribution in soil and sea of microbes which oxidize these or other liquid hydrocarbons. Microbes which oxidize pentanes and cyclohexanes are rarely encountered while the oxidation of n-hexane and the higher molecular hydrocarbons of a limited number are observed more often. Dehydrogenases (DPN) participate in the oxidation of cyclic groups of aliphatic and aromatic hydrocarbons. From the latter aromatic acids which can have practical value are formed. In particular Miles Laboratories (Indiana, USA) are studying microbiological oxidation of naphthalene. Poster Laboratories (Texas, USA) are studying the oxidation of gaseous hydrocarbons. The task of producing protein preparations from gaseous hydrocarbons evidently has not yet been accomplished anywhere.

Casas-Campillo (National Polytechnical Institute, Mexico) reported on experiments in culturing asporogenic yeast of the genera Candida, Torulopsis, Rhodotorula, Cryptococcus, Pityrosporus and others on hydrocarbons. About 30 strains which grow well on kerosene were selected. Very many of the active strains were of the genus Rhodotorula. Unfortunately, while the composition of kerosene can vary tremendously, no data were given on the chemical composition of the test kerosene. It was shown that this requires a greater number of petroleum products consisting of hydrocarbons of a lower molecular weight. The optimum source of hydrogen is ammonium phosphate. In the deep culturing of one strain of Rhodotorula maximum growth is attained in the 5-6th day. The optimum quantity of kerosene is 3%. In 4 days the biomass reaches 5-6 g/liter which is 14-23% of the given kerosene. The biomass consisted of 47-52% of protein and many lipids, 15-26%.

The question of culturing hydrocarbons brought on a lively discussion at the meetings of two sections. Besides the delegates, the prominent microbiologist Foster (USA), a representative of ESSO, Jevanoff, the director of yeast factories in England, Dowson and others took part in the discussion. The speakers noted the huge practical value of these investigations and also the great technical and economical difficulties standing in the way of their realization. They indicated the excessive optimism of Champagnat and that he had somewhat underevaluated all these difficulties. The petroleum firms, British Petroleum Co. and ESSO, are first of all busy deparaffinating diesel fuel to increase its quality. The work has been carried farthest in that direction. But the problem can also be solved in a different aspect; for example, the production of nutrient protein from different fractions of petroleum, from the waste water of petroleum refineries or from gaseous hydrocarbons, thus using the oxidizing activity of microbes to obtain these or other chemical substances. All these questions are still far from practical solution.

The problem of producing physiologically active substances was considered at the plenary and one of the sectional conferences. The representative of the Anglo-Swiss firm CIBA, Wettstein, devoted his report to the biosynthesis of pharmacologically active substances by microorganisms, with particular attention to the production of vitamins $B_2$ and $B_{12}$, lysergic and 6-aminopenicilloic acids, the transformation of every kind of steroid, and also the synthesis of tetracycline, rifamycine, cephalosporin, various viral antibiotics etc. The speaker also reported on the biosynthesis of ferrioxamines, cyclic polypeptides containing iron among which are both biostimulators and antibiotics.

The report of Chain (Italy) touched on questions connected with using antibiotics. Having briefly described the history of the work in antibiotics, he noted that they have revolutionized medicine. At present up to 700 antibiotic substances have been reported but only a comparatively small number of them are being used in clinical practice. Nevertheless, a large number of different diseases are cured by antibiotics. The successes in using antibiotics in medicine prompt the question of their wide use in economically lagging countries. Chain listed the antibiotics which should be recommended for wide use in medical practice. He also emphasized the huge role of applied antibiotics in feeding farm animals. Industry must supply antibiotics not only to medicine but also to animal husbandry.

The Japanese submitted many reports on biologically active substances. Most of all we noted the report of Arima from the Institute of Applied Microbiology (Tokyo). He treated the production of enzymes by microorganisms. Together with the common enzymes, amylase, invertase, pectinase, and protease, the author counted another 20 microbic enzymes which can be used in practice: varidase, streptokinase, penicillinase, glucosidase, hyalonidase, lipase, catalase, keratinase, ribonuclease, deaminase, adenylic acid, naringinase, hesperinase, glucoisomerase, lactase and others. Several of these are produced only on an experimental scale but others are already in production or are being put into production.

In Japan, 460 strains (14 different genera) of bacteria, 98 strains of Actinomyces and 224 strains (19 genera) of fungi are used to produce enzymes. It is interesting that they are using mucleotides (as a scent producer) to improve the taste of food products. In [illegible] will this different types of nucleases are important not only for research but also for industry.

Chibata (Japan) devoted his report to the production of isoleucine from threonine with the help of Serratia marcescens. By various methods the author showed that the threonine added to the culture in a number of steps was converted into isoleucine. The given bacteria can dehydrogenize (with the formation of α-ketobutyric acid) not only natural threonine but also its optic isomer. The obtained results are new and interesting in a scientific sense. It is, however, difficult to say to what degree such a means of producing one amino acid from another is economically justified.

In his report Tsuanoda (Japan) examined the effect of aeration on the formation of glutamic, α-ketoglutaric, succinic and lactic acids by a culture of bacteria (of the genus Brevibacterium). The oxygen absorption rate was determined both by the sulfite method and by a direct gas analysis of the input and output air. It was observed that the data of these two methods can noticeably diverge. It was established that during intensive aeration chiefly glutamic and ketoglutaric acids are formed, during insufficient aeration succinic acid and during the lack of aeration, lactic acid. Under optimum conditions more than 40 g/liter of glutamic acid accumulates in the culture fluid. Thus, the work is not only theoretically but also practically interesting.

Karlstrom (Sweden) reported on a method of producing bacterial mutants which can produce amino acids. The method is based on changing the capacity to synthesize one or another amino acid and simultaneously changing the relationship of the mutants to certain analogs of that amino acid which have a depressing or stimulating effect. By using these circumstances one can easily select the desired mutants.

The reports of Manc (Czechoslovakia) and Peterson (USA) on steroid transformation resembled survey reports; they contained abundant factual but not new material.

Problems of soil microbiology were touched at both plenary and sectional meetings. In his report, "The Role of Microbiology in Agricultural Practice," having described soil as a living system, Katznelson (Canada) mainly discussed the Rhizosphere. This is the theme of his investigations and in the report he offered material characterizing the microorganisms of the rhizosphere, the effect of soil type on the microflora in the root and near-root zones, the yearly conditions etc.

Increasing the light intensity increases the microbe population, particularly that of the Pseudomonas, but it does not affect the number of fungi. In the root zone of plants which were more strongly illuminated the nematodes were more richly established.

For wheat the maximum number of bacteria was observed at 15°, and for soybean at 30°. Asporogenic dark-colored fungi dominated on the roots of wheat at the high temperature and at the low temperature, asporogenic fungi with hyaline mycelium.

For soybean Phycomycetes, Rhizoctonia and Gliocladium were richly established at the high temperature; and Fusarium and Cylindrocarpon at the low. Nematodes also decreased in number when the temperature was lowered but not to the same degree as for the wheat.

For wheat the maximum number of bacteria were observed at low humidity. The fungous population decreased only during the highest humidity, higher than in the test. Under these conditions Fusarium, [illegible], Mucor, Trichoderma and Helminthosporium dominated; they were not observed on the roots.

In his report, "Microorganisms and Fertile Soils," Ye. N. Mishustin noted that the present period of agricultural development is connected to wide chemicalization. However, this does not take away from the large role of the biological factor in farming. The high cost of mineral fertilizers, and in some cases their insufficiency makes it adviseable to maximally use the forces of nature and first of all the microbiological soil processes which mobilize substances nutritional to plants.

The value of the biological factor is particularly demonstrated by the example of nitrogen. Even in countries which widely use mineral nitrogen, less than 25% of agricultural requirements for this element are supplied by mineral fertilizers. The activity of nitrogen-fixing bacteria cover the rest. Symbiotic nitrogen fixers are especially important for farming but this does not exclude the wide use of nitrogen-absorbing bacteria living freely.

He noted the possible role of microbiological methods in determining soil requirements for fertilizers, the role of the microbiological processes in increasing fertilizer effectivity (mineral and organic) and rendering the soil harmless of herbicides and fungicides, etc.

The role of microorganisms in the treatment of agrotechnical problems is large since treating the soil sharply changes the character of soil processes and, in the final result, this affects the size of the harvest.

A number of reports were devoted to the inactivation of herbicides in the soil is etermined by many factors (climate, soil type, Jensen divided the herbicides used in agriculture into these groups: a) "harmonic herbicides," of which 2,4-D is an example, which are active against higher plants but affect soil microflora relatively weakly; similar herbicides can be decomposed by extremely different organisms; b) compounds similar to nitro derivitive of phenol which alter metabolism and possess considerable general toxicity; they can be decomposed by a relatively small group of microorganisms; c) simple aliphatic compounds which are distinguished by their stability in the soil; the following order is given as an example of their progressive stability: allyl alcohol → monochlorascetate → dichlorpropionate → trichlorascetate; d) compounds which are extremely active in nature but weak against soil microorganisms, simazin is an example; this phenomenon can probably be explained by their weak solubility; e) inorganic compounds, e.g., chlorates and sulfonates, which can be transformed by microbes if they have organic substances which can donate electrons; without this they are stable.

There is a definite dependence between the stability of compounds and their structure. Para position of chlorine or the $NO_2$ group favors rapid decomposition. Meta position gives the reverse effect. Increasing the Cl atoms in the presence of carbon increases the stability of compounds. Replacing oxygen by sulfur in urea and its derivitives increases the stability of these compounds.

Wieringa (Holland) devoted his report to decomposition of aromatic compounds by microorganisms. From the upper turf he isolated a great number of microorganisms capable of decomposing aromatic compounds. It is particularly easy to decompose toluene. In all he isolated about 100 cultures which decompose phenol, cresol and other aromatic compounds. Several of these organisms form brown and black bodies of a humic nature. It is assumed that free radicals are formed which can polymerize into stable humic acids.

In "Microbiological Decomposition of Pesticides," Alexander (USA) reported on a similar theme. He noted that the stability of pesticides depends on their chemical nature. He studied the destruction process of a significant series of chemical compounds (phenoxyalkyl-carboxyl acids, chlorophenols, halogenic compounds of the aromatic acids, derivitives of triazine, thiocarbamates and derivitives of benzoic acid). Manometric, spectrophotometric, tracer and chromatographic (paper and gas) techniques were used. He reported methods of transforming several of these compounds under the effect of soil microorganisms.

A number of reports given at the session concerned separate sides of the life of the soil micro-population. Thus, Furusaca (Japan) analyzed the bacterial activity in a heterogenic system. This was done to study the sulfate reduction process occurring in very wet soils during summer.

By determining the hydrogenase activity of the soil by Warberg's method, the soil's capacity to reduce sulfates can be established indirectly. The author considers that the hydrogenase activity of the soil is mainly caused by the bacteria Desulfovibrio. It was established that sulfate reduction can be depressed and that it depends on the pH and the concentration of oxygen acceptors. The activity of these factors depends on the presence of soil particles. For a more detailed analysis he conducted tests with substrata containing silico-gel and resin particles.

The author expressed the thought that in a heterogenic medium the chemical activity of microbes can change due to the cells being partially covered by solid bodies, the concentration of hydrogen ions on the surface of the solids touching the microbe cells, due to changes in the physiological function of the cells under the influence of the particles surrounding them, etc.

Thus, the activity of microbes progresses differently in soil than in a liquid medium.

Rangaswami (India) reported on tests studying the soil of rice paddies. The tests covered several years and were statistically processed.

It was established that when the rice is growing and the soil flooded, the number of microorganisms decreases. After the rice has been harvested and the water let out of the paddy, the microorganisms begin to multiply rapidly. The optimum moisture content for fungi and Actinomycetes to reproduce is close to 20% of full water capacity. Bacteria multiply more actively at 40% of saturation.

During the first phase of rice growth bacteria dominate the rhizosphere; when it ripens fungi and Actinomycetes begin to noticeably increase. After the harvest Actinomycetes multiply vigorously.

Mineral fertilizers affect the soil microbe population very little but manure increases the quantity of fungi and bacteria.

The rhizosphere effect of rice is in general well known. In the deeper layers of the soil the rhizosphere is poorer in microorganisms. Also the number of fungi and bacteria relatively increases in it.

In his report Sasson (Morocco) touched a number of practical questions connected to the possible role of microbiology in raising the productivity of soil. He considers that the work of microbiologists makes possible not only knowing the composition of the soil micropopulation but also actively regulating its processes.

In the African countries, Morocco in particular, a significant portion of the territory does not have enough moisture. The welfare of the population is organically connected to assimilating these lands, which can be done only through measures of an international nature. The microbiological properties of soils which can be assimilated are poorly defined and this situation must be clarified. These soils must be studied not only by microbiologists but also by other specialists.

This speaker spent some time on methodical questions. He feels that in soil studies we must find out not only the size of the microbe population but also the state of the remaining types and groups of microorganisms which determine the productivity of the soil. Keeping in mind the climatical conditions of the territory, we should devote particular attention to those microorganisms, especially the nitrogen-fixers, which have adapted to drought.

One sectional meeting concerned questions of the biological fixation of atomospheric nitrogen. Chairman Bond (England) reported in detail mainly on symbiotic fixation of atmospheric nitrogen. Presently there are up to 190 nonleguminous plants which are capable of fixing atmospheric nitrogen in a symbiosis with microorganisms. Up till now no one has studied these plants, but, in the opinion of the author, they can have a determining value in agriculture. While most of these plants, belonging to genera Elaegnus, Casuarina, Alnus, Ceanthus etc., are trees and bushes, they still can be used in mixed planting or their leaves gathered for feed or compost.

A considerable number of [illegible] symbiotic nitrogen fixers are not published and, therefore, we did not spend time on the physiological questions connected [illegible] assimilation of molecular nitrogen.

After Bond's report there was a lively exchange of opinions. The reports took note of the value of Bond's work. But it was stated that the leguminous grasses, many of which are very active nitrogen fixers, are no doubt more important for practical agriculture. The need of future study of the possibilities of using free nitrogen fixers in practical agriculture was also emphasized. Evidently, this can be promising for rice fields where blue-green algae, many of which can assimilate atmospheric nitrogen, grow vigorously. It was also noted that the principle of the activity of "azotobacterin," which is rather widely used in agriculture in the USSR, is not sufficiently clear.

There was an interesting session devoted to the protection of harvests from pests. These reports were heard:

1) Dekker (Holland), "Internal Therapy of Plants with a Special Calculation of the Effect of 6-azauracil"; 2) Zaitlin (USA), "Future Possibilities of Controlling Plant Virus Diseases"; 3) Baigent (New Zealand), "Pseudomonas Siringa Phage Harmful to Siringa"; 4) Rangaswami (India), "The Role of Antibiotics in Suppressing Phytopathogenic Microorganisms in the Soil"; 5) Kiraly (Hungary), Phenol Metabolism in Diseased Plants."

The film, "Biological Warfare with Insects," was shown at this session. Franz (FGR) explained the film.

The section on conservation of organic substances, directed by Nilsson (Sweden), had a number of reports devoted to the problem of [illegible] age. The last report was made [illegible] [illegible], conducted a great work on the processing of ensilage of very different feeds. They conserved by fermentation not only plant but also animal material (fish waste products, blood etc.). Most of the given feeds should be examined as difficult or impossible to ensilage. The increased silageability is attained by adding malt, meal and usually a maltase preparation. He gave the determining relationships of the components which would allow the fermenting of alfalfa, clover, fish waste products and even blood. Because maltase has attained a great value in ensuring the process of fermentation, one of the Swedish firms has begun to produce a special preparation, "Ensi-Malt," designed for ensilage.

The report of Erikson (Sweden) shone light on the nutrient value of different silages.

Certain data on changes in microflora composition during silaging were given by Langston, an employee of the Defense Department (USA). This report did not contain any new developments.

Cullough (USA), considering methods of ensuring the process of silaging, gave data on the use of sodium metabisulfate. Under the influence of this preservative, the sugar in the silage mass (alfalfa) is gradually used up. Since the acidity does not increase, this is possibly explained by the process of respiration. After 2 months the pH of alfalfa was 5.2. Thus, there is chemical preservation here. Its addition to alfalfa and wheat masses, which are rich in carbohydrates, easily ensures the ensilageability of the feed.

Malin (USA) reported on the good preservative properties of the antibiotic tylosin, an actinomycete derivitive. This antibiotic does not depress the growth of lactic bacteria but it does suppress the growth of numerous undesirable [illegible]

This synopsis allows us to conclude that the symposium had a wide profile. This and also the short time allotted to the work makes it impossible to closely detail the given problems or make appropriate conclusions on them. Nevertheless, the results of the works of the symposium were indubitably useful since it gave a concept of directed work in the field of applied microbiology in many countries and it enabled personal contacts which are always useful.

The symposium resolved to further the introduction of applied microbiological research into practice.

After the congress the members of the Soviet group visited th Institute of Microbiology of the Agricultural College at Uppsala, of which Nilsson is the head. He and his co-workers (Rydin et al are studying the process of silaging. The basic results of this work have already been given.

Considerable work is also being conducted there in the field of biological nitrogen. Fahraeus is conducting an interesting st on the mechanism of root hair tuber infection by bacteria.

The Institute is preparing for the practical application of nitrogen (alfalfa, clover and other cultures) and it is also calculating the effectivity of these preparations. Tests over many years have shown that in most cases nitrogen noticeably increases the productivity of leguminous crops. They also have tested the preparation "azotobacterin." On the soil of Sweden it proved to ineffective.

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| NAVY | 3 |
| NSA | 6 |
| OAR | 1 |
| OTS | 2 |
| PWS | 1 |
| PGE (Steensen) | 1 |
| PGE | 12 |
| RAND | 1 |
| AFCRL (CRXLR) | 1 |
| FAA (Med Lib) | 1 |

| MAJOR AIR COMMANDS | Nr. C |
|---|---|
| DDC | 20 |
| AFSC | |
| SCFDD | 1 |
| TDBDP | [illegible] |
| TDBTL | [illegible] |
| TDGS | 1 |
| AFMDC (MDF) | 1 |
| AFWL (WLF) | 1 |
| AMD (AMRF) | 1 |
| APGC (PGF) | 1 |
| ASD (ASFA) | 2 |
| ESD (ESY) | 1 |
| SSD (SSFI) | 2 |