RM-75-21

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May 1975

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A peculiarity of the present developments in biology and medicine is the wide use of various analytic methods that accumulate great amounts of experimental data. This trend has made us acutely aware of the necessity to systematize the facts received, to reveal the clear regularities, and to conceive the processes taking place in the organism as a whole. Such motivation provides a new approach to biological and medical processes: a systems approach. It is the investigation of all functions of an organism in both normal and pathological states from the point of view of its systemic organization.

At present different system approaches have been proposed in biology for studying the general processes of an organism, as well as to the functions of specific organs, e.g. the brain, lungs. Such systems investigations have been made by Bertalanffy, Rappoport, Mesarovic, Sadovsky, Ashby, McCulloch, and others.

However, maximal interest and attention must focus on those conceptions, hypotheses, and theories which have already shown a visible, constructive effect in concrete scientific explorations. For this reason, I should like to call your attention to the theory of the functional system, proposed by Academician P. Anokhin, an eminent Soviet neurophysiologist. The elaboration of this theory in the USSR began in 1935, and its principal propositions were made before Wiener's cardinal ideas in cybernetics.

According to Anokhin, the functional system is an elementary unit of any integrative activity of an organism. It represents a dynamic, central-peripheral formation, the activity of which is directed to the achievement of a final useful effect--the result of the action of the entire system.

The principal difference between the functional system theory and other system theories lies in the system-organizing factor as an important aspect in system formation. The most popular system theories proceed from the assumption of "interacting elements which consist of multiplicities," more or less ignoring the factor of action result. The functional system theory holds that any multiplicity becomes a system only when its separate components find the general final effect, which unites these components in a system. Thus, only a useful result is a real system-organizing factor, dynamically uniting the organism's sub-systems in an hierarchical interaction of integrative activity within the organism as a whole.

The second principal feature of a functional system is its logical, operational structure which consists of concrete main points. If we analyze the whole organism from a system point of view, one may inquire which result is final and adaptive. The answer to this question--concerning those factors necessary to provide a life--was given in the nineteenth century by K. Bernard: "The constancy of the internal state or, as it was named by Cannon, 'homeostasis,' is the necessary condition of free, independent life." This means that in the case of changes of environmental factors--e.g. temperature, feeding substances, dangerous factors for the organism--life is possible only when the homeostasis of an organism is maintained. But the organism, seen as a system maintaining homeostasis, consists of separate systems whose action results are the maintenance of internal status constants.

The peculiarity of the functional system theory is that it helps to analyze maintenance mechanisms of separate homeostasis constants, as well as the mechanisms for maintaining the existence of the organism as a whole. This special aspect of the theory permits study from an entirely new angle of such medical problems as the formation of steady arterial hypertension.

The advantage of a systems approach to solving the arterial hypertension problem becomes clear when we consider that most authors emphasize only one leading factor in the genesis of this disease. Hering, for example, supposed that the leading factor in the development of arterial hypertension is a functional disturbance of pressoreceptors in vessel walls. Goldblat and his colleagues thought the leading factor to be renal tissue hypoxia, followed by activation of the rhenineangiotensine complex. In 1973, Gayton et al. saw the imbalance of liquids in the organism as the leading role in arterial hypertension formation.

According to the functional system theory, the level of arterial pressure, which is necessary for maintenance of important vital functions of the organism, is realized by the specific functional system. This system selectively unites central as well as peripheral apparatuses to maintain the level of arterial pressure which is needed for normal organism life. Any deviations in arterial pressure in response to physical, emotional, or internal (e.g. hormonal factors) stimuli, are normalized by the activity of the whole system, the principle of self-regulation.

The pressor and depressor mechanisms within the system are balanced. In case of an increase in arterial pressure, the depressor mechanisms are activated. This is realized in excitation of special pressoreceptors situated in the vessels' wall; in increase of vagal impulsation to the medulla to inhibit the vasomotor centre; in deceleration of heart rate; in decrease of blood flow; in increase of diuresis; in activation of some humoral depressor mechanisms, etc. All of these system processes in a normal state are enough to decrease the high arterial pressure.

Analogously, in the case of a decrease in arterial blood pressure, the pressor mechanisms are activated to normalize the level of blood pressure.

With such powerful self-regulatory mechanisms for maintaining arterial pressure, it becomes clear that under normal conditions it would be impossible for an organism to maintain either steady arterial hypertension or constant hypotension. But WHO statistics show that millions of people throughout the world suffer from hypertension. What factors, then, can disrupt these self-regulating mechanisms?

Experiments carried out by Anokhin and others showed that one of the leading causes in the disturbance of self-regulating mechanisms is uninterrupted, negative emotional influences, e.g. emotions of rage, fear, melancholy. In these emotional states the excitation, starting at the level of limbic-reticular brain structures, spreads to the brain cortex in ascending and descending directions, via the autonomic nervous system and the hormonal-hypo-physical apparatus. These mechanisms increase the level of arterial pressure. Under these circumstances, the depressive mechanisms for self-regulated arterial pressure are no longer sufficient to resist the powerful pressor influences on blood vessels. The arterial pressure decreases only when the negative emotional excitations cease. If they continue in prolonged conflict situations, constant arterial hypertension can result.

Experiments done in our laboratory show the role of uninterrupted negative emotional excitations which induce steady arterial hypertension in rabbits. The electrical stimulation of the ventro-medial hypothalamic area in rabbits with chronically implanted electrodes was in all cases followed by an emotional reaction of fear. These animals were then placed in special stands and given uninterrupted stimulation of negative emotional sites for many hours.

These experiments helped us to model an acute emotional stress in a conflict situation. We also recorded blood pressure in the arteria femoralis and respiration rates, and made electrocardiograms and electromyograms.

The following results were obtained. The electrical stimulation of a negative emotional centre of the hypothalamus led to an increase of arterial pressure of 30-40 mm Hg. Within the first hour of a negative stimulation, the arterial pressure progressively decreased, meaning that in this stage of emotional stress, the domination of depressive mechanisms in the self-regulation of arterial pressure is noticeable. Later, however, arterial pressure rose considerably, which indicated the weakening of the depressive reaction, and steady domination of pressive influences was observed. At this stage of emotional stress, changes in heart functions (e.g. extra systoles, architmia, ECG-disorders) occurred and some animals showed symptoms of acute cardiac insufficiency. Electrono-microscopic observations have revealed some phenomena typical of myocardial infarction in this stage of constant emotional stress.

Therefore, after long, uninterrupted conditions of stimulation of hypothalamic negative emotional sites, it was possible to model a whole natural history of hypertension disease development--from its transitory stage to a steady, constant stage with features of myocardial infarction.

However, it is necessary to emphasize that there are some peculiarities in constants which form homeostasis. But in these cases, the operational structure of the functional system practically remains the same.

Let us analyze other constants of the internal state of the organism, for example, the level of nutritious substances in the blood. The functional system maintaining this constant or final adaptive result has the same structure. There are special receptors which are sensitive to the changes of nutritious substances in the blood (peripheral and central), special apparatuses of the central nervous system which perform regulating functions, and concrete effectoral mechanisms. At this stage of system maintenance of the constants of nutritious substances in the blood, it is possible to notice some difference in comparison with efferent components of the functional system's maintenance of arterial pressure. In the latter case, the level of arterial pressure in the blood is provided by the interrelation of pressive and depressive factors, exceptionally by the intrinsic factors of the organism. For regulation of the level of nutritious substances in the blood, external mechanisms are also of importance--i.e. the behavior of a man or an animal in its environment, resulting in the maintenance of this important constant of homeostasis. The functional system theory also contributes greatly to the revelation of concrete human and animal behavioral mechanisms which, as we know, lead to the achievement of the final adaptive result of an organism in a concrete situation.

The operational structure of the functional system for the general behavior of man and animals must explain the ensuing questions: a) what result must be received? b) when must it be received? c) what mechanisms must provide this result? and d) how is the system informed about the sufficiency of the result received?

The answers to most of these questions can be given in the first stage of the functional system, the stage of afferent synthesis. The following processes can be chosen at this stage:

1) All kinds of information are united in the central nervous system forming the basis for decision making. It includes dominating motivation (social and biological for man), memory, situational and trigger afferentations.

2) Next is the stage of "decision making"--one of the complex and responsible moments in the behavioral system which is realized when all of the above signals are processed. At this stage, the system is released from excessive degrees of freedom, taking only one form of action to achieve the optimal result in a concrete situation.

3) After stage 2 is the formation stage of the acceptor of the action result. This apparatus consists of all the features of the future result, before the action directed towards obtaining a real result is performed.

We must point out that the stage of activity of the system directed towards obtaining a result includes a peculiar "efferent integral" of the motor somatic functions and their autonomic provision. As mentioned above, a result of the system activity is the starting point of the successive stages in the activity of a system. If the parameters of the result correspond through feedback to the properties of the acceptor of action results previously formed, the given stage in the system activity is finished and this information can be used by the organism for other purposes. If the parameters of the achieved result do not correspond to the properties of the acceptor of the action result formed by afferent synthesis, an orienting-investigative reaction is immediately induced. This evokes reorganization in afferent synthesis; a new decision is made to achieve the result needed for the system, a new action directed towards obtaining the result is formed.

The operational structure of the functional system permits analysis of the internal structure of any kind of system, including, for example, social-economic systems. The concept of the functional system as a locked, self-regulated organization formed the basis of physiological cybernetics. When Norbert Wiener visited Anokhin's laboratory in the USSR in 1960, he admitted that the physiological cybernetics research there surpassed the trends in cybernetics as the whole.

At the present time in the USSR, intensive research is in progress upon principal links of various partial functional systems of the organism. The complex of analytical and systems investigations are being melded to help establish a conceptual bridge between the molecular-cellular level of physiological processes and the integrative function of the whole organism. In particular, the analysis of the functional system in the ontogenetic development of functions has led to the creation of a new principle of development, the so-called "systemogenesis." According to this principle, the ontogenetic development is selectively realized through systems. The functional system and their separate components, which provide man and animals with the most essential adaptive functions, mature first. The basic principles of systemogenesis are the heterogenic developments of structures, and the consolidation of separate components of the system and its minimal provision.

A detailed analysis of key mechanisms of the functional system presented a new opportunity to appreciate the participation of cortical neurones in the integrative action of the brain. This led to the new scientific field, "functional neuro-chemistry," the study of the changes in the chemical reactions of the central nervous system in the realization of specific functions.

The functional system theory brought about a new conception of emotions which help the organism to evaluate its requirements and their satisfaction. As a rule, complete coincidence of the properties of the acceptor of action with the incoming signal about the result of action through feed-back is always accompanied by positive emotions which sanction the success of the action performed. And conversely, any disagreement provokes unpleasant, biologically negative emotions contributing to a rapid meeting of the arisen requirements.

Functional systems theory, used as a method for analyzing self-regulating adaptations of an organism under pathological conditions, helped to formulate the principal features of compensation of disrupted functions. It revealed the mechanisms of compensatory adaptations in surgical operations, such as total ablation of a lung, where the process of compensation embraces such executive apparatuses of the respiratory functional system as the heart, hemocytes, saturation of erythrocyte with haemoglobins, buffer properties of blood, and others. At the same time, key mechanisms of the functional system adaptation and resistence under extreme conditions were revealed.

Many years of research on the physiological properties of baroceptors of the aortic arch and mechanisms forming emotional stresses now permit successful use of the functional system theory in the pathogenesis of the neurotic form of hypertension disease. Here I would like once more to draw your attention to the problem of hypertension disease. According to the WHO bulletin, deaths from cardiovascular diseases in developed countries take the first place. Thus, the problem of treatment and prevention of hypertension disease is international, and may be a suitable topic for investigation in IIASA.

I would also like to add that the Institute of Normal Physiology of the USSR, the Academy of Medical Sciences in Moscow (whose chief, Prof. K.V. Sudakov, is a pupil and former colleague of Academician P. Anokhin) and the Institute of Cardiology in Moscow, are investigating the genesis of arterial hypertension using the systems approach from the point of view of the functional system theory. The unity of efforts between physiological laboratories of the IIASA member countries with the Institute of Normal Physiology and Cardiological Institute in Moscow under IIASA will promote the investigation from a system point of view of the pathogenesis of hypertension disease.