THE LEVEL OF ORGANISM FUNCTIONING AS AN INDICATOR OF PREMORBID CONDITIONS (REVIEW)

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Abstract

The state of the organism is the consequences of interaction with the environment, that is, the result of adaptation or maladaptation of the organism to the environment. The transition from health to illness can be seen as a process of gradually reducing the ability of a person to adapt to changes in social, educational, and production environments and surrounding conditions. Achievement of any level of functioning of an organism or its separate systems is provided through the activity of regulatory mechanisms. The mobilization of reserves occurs as a result of changes in the level of activity of regulatory systems. This is primarily due to an increase in the tone of the sympathetic department of the autonomic nervous system. In those cases where the body constantly has a deficit of functional reserves to support homeostasis, there is a state of functional stress, which is characterized by the displacement of the autonomic balance in favor of the adrenergic mechanisms and the corresponding changes in the hormonal state. In the state of functional stress, all of the basic functions of the body are within physiological norm, but the organism spends functional reserves to maintain the normal level of functioning. The process of adaptation precedes the development of a disease that results from the lack of adaptation mechanisms, their reduction and disruption. The development of maladaptation is preceded by the state of adaptability, and after the maladaptation the state of the disease develops, i.e. all the conditions that precede the disease, that is, the failure of adaptation, are united in the premorbid state. The process of identifying the states that border between the norm and the pathology, when it does not yet have signs of the disease, that is, the premorbid states, is called premorbid diagnostics. The diagnosis of premorbid states takes into account the use of methods and equipment that are designed for processing information in the range of relative functional stability of the organism with the definition of the vector of adaptation processes and that is an integral part of preventive medicine.

Key words: *Premorbid condition, functional state of an organism, functional reserves of an organism, premorbid diagnostics, preventive medicine.*

The state of the organism (its health or disease) is the consequences of interaction with the environment, that is, the result of adaptation or maladaptation of the organism to the environment. The transition from health to illness can be seen as a process of gradually reducing the ability of a person to adapt to changes in social, educational, and production environments and surrounding conditions. According to the theory of general adaptation syndrome, developed by H. Selye in 1961 [1], the reaction of the organism to any influence contains two main components - specific and nonspecific. At the same time, the nonspecific component predominates. The leading process is the mechanism of mobilization of functional reserves, which provides the release of additional energy and compensation of energy consumption of an organism in achieving the final useful adaptive result. As noted by F. Meerson in his works, the energy links of adaptive reaction are basic and implemented at the cellular level in the form of activation of the genetic apparatus of

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the cell, increase in the number and activation of mitochondria, and increase of intensity of the functioning of cell structures [2]. Achievement of any level of functioning of an organism or its separate systems is provided through the activity of regulatory mechanisms. The mobilization of reserves occurs as a result of changes in the level of activity of regulatory systems. First of all, this is due to an increase in the tone of the sympathetic department of the autonomic nervous system. In those cases where the body constantly has a deficit of functional reserves to support homeostasis, there is a state of functional stress, which is characterized by the displacement of the autonomic balance in favor of the adrenergic mechanisms and the corresponding changes in the hormonal state. In the state of functional stress, all of the basic functions of the body are within physiological norm, but the organism spends functional reserves to maintain the normal level of functioning. The process of adaptation precedes the development of a disease that results from the lack of adaptation mechanisms, their reduction and disruption [3, 4].

The development of maladaptation is preceded by the state of adaptability, and after the maladaptation the state of the disease develops, i.e. all the conditions that precede the disease, that is, the failure of adaptation, are united in the premorbid state. The premorbid state leads to an increase in the energy consumption of the human body [3, 5].

The term premorbid condition was first proposed by R. M. Baievskiy in 1974 [3]. The doctrine of the premorbid status has evolved due to researches in the field of prophylactic medicine, age-related physiology, epidemiology, which control the health of the organism, focus on its ability to adapt to new unusual environmental conditions, rather than the development of diseases in the body. The premorbid state of the organism is characterized by its normal functioning, which traces the dynamics of reducing the level of adaptive capacity of the organism. Theoretical analysis of scientific data points to a small number of researches of the premorbid states of the individual and a practical absence of models for the evaluation and correction of the premorbid states of the human body by prophylactic means and physical education and recreation classes [6, 7]. Some scientific researches about the problem of diagnostics of the level of somatic health are found in the articles [6, 7]. The premorbid state develops due to a certain set of factors having a different contribution to its structure. According to number of authors, various factors of the premorbid state development, namely, anthropometric, physiological and others [3, 7, 8, 9], are noted. However, the results of most studies do not allow complete interpretation and usage of them in preventive measures and physical education and wellness activities, which allows to conclude that this problem needs further research [5, 8].

The process of identifying the states that border between the norm and the pathology, when it does not yet have signs of the disease, that is, the premorbid states, is called premorbid diagnostics. Diagnostics of the premorbid states takes into account the use of methods and equipment that are designed for processing information in the range of relative functional stability of the organism with the definition of the vector of adaptation processes [3, 4, 10].

Premorbid diagnostics is an integral part of preventive medicine. The current analysis of the premorbid diagnostics, the deterioration of the health of children, adolescents and people of working age in Ukraine shows the relevance of this problem and emphasizes its main task that is to define the ways to manage human health [2, 6]. However, despite a large number of studies, most of the existing methods are based on the definition of the functional capabilities of the body, which is insufficient to measure the amount of health, and even more so for the determination of the premorbid state of the organism [3, 7–10]. For a comprehensive assessment of the health of an organism, it is important to know not only the functional capabilities of the organism (the level of capacity of the organism), but also qualitative indicators of health (level of well-being, period of recovery of the organism). According to the results of various researchers, about 80% of children of junior school, high school and people of working age are in the premorbid states [3, 4, 7]. There is a large number of studies devoted to the early detection of children's premorbid conditions, which confirms the relevance of this problem [3, 4, 6–8].

So in many studies for the purpose of correction of the premorbid state it is suggested to use means of physical fitness, which influence the optimization of functional reserves of the cardiovascular and respiratory systems of the organism. Research results of R.M. Baievskiy, T.G. Omelchenko, M.V. Malikova, N.V. Bogdanovskaya and others show the priority factors in the structure of the premorbid states

and require the development of typical correctional health programs [3–6, 8].

This diagnosis is based on the fact that the transition from health to disease passes through a series of successive stages, during which the body adapts to new conditions of existence, changing the level of functioning and tension of regulatory mechanisms. They can be characterized as:

1) normal adaptation reactions;

2) the tension of the adaptation mechanisms (short-term, or unstable adaptation);

3) overloading and failure of adaptation processes.

In the case of long-term adaptation, the number of mitochondria increases, that is the main way of adaptation is the change of energy metabolism. It is the lack of energy that determines regulatory, metabolic and structural changes. Compensation mechanisms are starting to work, which are, in fact, markers before illness. Then comes the phase of reversible changes, and only after it morphological damage to structures occurs.

There are three parameters describing the stage of adaptation of an organism, according to the opinion of many authors:

1) the level of functioning of the system;

2) the tension level of regulatory mechanisms;

3) the amount of the functional reserves.

In the premorbid diagnosis, the classification of functional states of the organism is used [6, 10].

The norm is a class of functional states with sufficient functional (adaptive) capabilities of the organism. An assessment of the functional state of the body is impossible without the use of concept of norm. The methodological aspect of the norm allows to approach its definition in the applied, scientific sense as an expression of a functional optimum, as pointed out by R. M. Baievsky in 1979. In this regard, it is often believed that the optimum is consistent with the average data. But biological systems are always characterized by instability, which manifests itself in the variability of their functional characteristics. Therefore, the individual norm is always concrete and specific, which is established depending on the conditions in which a person exists. There are four main types of norm, such as statistical, clinical, ideal and physiological. The statistical norm is described by the corresponding deviations from the mean value. Clinical norm characterizes the importance of indicators in individuals without manifestations of the disease. The ideal norm reflects the state of a person, which is in the best of pleasant conditions. The physiological norm indicates the maintenance of a sufficient level of functional capabilities of the organism [5].

Therefore, the norm for any indicator includes not only the average value, but also a series of deviations from it. These deviations are connected with the nature of biological indicators, and with individual variability, specificity. The individual optimum of the organism does not always (or rather, very rarely) coincides with the average indicators. Individual norm is always concrete and specific. However, the set of individual indicators gives only a static image of the current state of the organism, which by comparison can be attributed to a certain class of states. The notion of norm includes the ability of an organism to adapt to certain effects of factors of the environment. Human organism constantly adapts to changes in the environment associated with the time of day, working environment, and so on. The adequacy of the response of the organism to the action of one or another factor is the one of the important components of the norm [4, 5, 9].

The premorbid states are the states in which optimal adaptive capabilities of the organism are provided with higher than normal tension of regulatory systems. This leads to increased expenditure of the functional reserves of the body, the increase of energy-information provision of the interaction of physiological systems of the body to support homeostasis. A characteristic feature of the premorbid states is the presence of increased functional tension of adaptation mechanisms. It is possible to distinguish three stages of functional tension: moderate, expressed and sharply expressed [7, 8, 9].

Examination and forecasting of the premorbid states of health of people of working age are based on the analysis of physiological mechanisms ensuring the activity of a person. The spectrum of modern researches is based on a number of scientific fields, including the study of parameters of psychophysiological potential of a person. In these studies, premorbid diagnostics takes a first place as a marker for possible physical and psycho-emotional stresses [7].

The deterioration of health of population occurs due to an increase in the number of premorbid states. This requires the development of techniques that allow to predict them. Currently there are three main criteria of the premorbid state commonly accepted such as the level of functioning of organs and systems, the state of functional reserves and the measure of tension of regulatory mechanisms [10, 11].

Thus, the formation of premorbid state most often occurs in a non-specific way depending on the individual characteristics and adaptive capabilities of the organism, which significantly reduces the possibilities of the methods of parametric statistics [4–6]. In this case, it is recommended to study the correlation between the investigated features, the calculation of nonparametric statistical criteria processing [4–6].

Conceptual definition of the concept of "cause-effect relationship" implies the existence of functional (or correlation) relationships, which consider the role of causative factors and risk factors in the manifestations of morbidity [6, 12, 14]. Changing the frequency and quality of one of the factors entails a change to another. The change in the first part of the interacting phenomena is considered a cause, and the change in the second is a consequence. The causal link between the health determinants and health is a statistical connection [13, 14].

The causal nature of the epidemiological link is expressed by the difference in the rates of morbidity, depending on the revealed correspondences with one factor or another. The presence of this is evidenced by the quantitative relationship between the strength of the hypothetical risk factor (level and duration of exposure) and the severity of the effects (level of morbidity) by the type of dose-effect [4, 5].

Thus, the study of the intensity of regulatory mechanisms is the study of the dynamics and interconnection of indicators of homeostasis, the influence of factors on the development of the premorbid state. For forecasting, the following statistical methods can be used: correlation, regression and dispersion analysis [4, 5].

Another perspective way of the premorbid diagnosis is the application of the principles of information theory and the calculation of indicators of information analysis of entropy (IEA). The possibility of using the IEA to measure the tension of regulating mechanisms is confirmed in the study of the peculiarities of the lifestyle of modern youth [6]. Separation of subjects under regular physical activity allowed to identify the risk factors that are most pronounced in the group of people not engaged in physical culture. The calculation of the relative entropy indicators allowed establishing a hierarchy of risk factors that increase the regulation level and form an unhealthy lifestyle. Thus, the use of statistical methods allowed assessing the process of formation of the premorbid status [4, 6, 15–17].

In turn, a significant increase in tension, which leads to a decrease in functional resources, makes the biological system unstable, sensitive to various actions and requires additional mobilization of reserves [6, 7, 19, 20]. This condition, associated with the tension of regulatory mechanisms, was called the state of poor adaptation. In this state, specific changes of individual organs and systems become more significant [21–23]. Therefore, it is entirely permissible to speak about development of initial manifestations of premorbid conditions, when changes already indicate a manifestation of a possible pathology. Premorbid conditions are conditions characterized by a decrease in the functional capacity of the body and manifest in the form of two stages, namely: 1) with the predominance of non-specific changes while maintaining homeostasis of the main vital systems of the body, including the cardiovascular system; 2) with the predominance of specific changes on the part of certain organs and systems, homeostasis of which is violated, but due to the mechanisms of compensation the manifestation of the disease can be expressed or it is in the initial phase and is compensatory in nature. An essential feature of this class of functional states is that they develop and flow with overloading of regulatory mechanisms [24–26].

Maladaptation is a state with a sharp decline in the functional capabilities of the body in connection with the violation of compensation mechanisms. In this state, as a rule, there are various diseases in the stage of subcompensation or decompensation [5, 6, 10]. This majority of violations is manifested by the cardiovascular, respiratory, digestive, excretory systems [6].

I.M. Sechenov noted that the existence of organism without an external environment is impossible; according to I.P. Pavlov, the animal organism as a system exists among the surrounding nature only due to the continuous equilibrium of this system with the external environment, provided by certain reactions of the living system to external stimulation. In general, the doctrine of health can be defined as a science of the laws of the harmonious unity of biological, physical-chemical and informational exchange processes both within the body and with the environment surrounding it [26, 32, 33].

The human organism facing modern scientific and technological progress with continuous stress (social, psycho-emotional, etc.) must be considered as a dynamic system that continuously adapts to environmental conditions by changing the level of functioning of individual systems and the

corresponding tension of regulatory mechanisms [29–32]. Adaptation to new conditions is achieved by the expenditure of functional resources of the organism. An organism constantly spends its vital resources and constantly refills them during rest and sleep [33–35]. The state of an organism is determined by the optimality of actions that control the ability of mechanisms to balance the organism with the environment, its adaptation to the environment. Support of the normal level of functioning of the basic systems of the body is the main task of mechanisms of homeostasis. In order for the fluctuations of the homeostatic parameters to be kept within normal limits, constant work of functional regulatory systems is required. The activity of adaptation mechanisms requires a certain tension of regulatory system which is a level of stress depending on the functional reserves of the body [29, 36–38]. The more are the functional reserves, the lower tension of regulatory systems is required to maintain homeostasis [29, 39, 40].

Adaptation reactions to a large extent depend on the individual characteristics of the organism (sex, age, type of regulation), and also on environmental conditions. The state of an organism, as a result of the activity of various functional systems and organs, is determined by the optimality of the managing actions, their ability to balance the organism with the environment, its adaptation to the conditions of existence, and the adequate level of functioning of the basic systems and organs to the requirements of the environment [4–7, 41, 42].

Functional reserves of regulatory systems can be explained by the equation (R. M. Baievsky, 2017): level of functioning = tension level x functional reserves. This equation shows that in various actions to maintain an adequate level of functioning of the organism as a whole or its separate systems, an increase in the amount of stress is required, which is pronounced the more, the lower are the functional reserves [5]. Maintenance of homeostasis within the body and between the organism and the environment is the main condition for the existence of a living system. The homeostatic properties of an organism are the result of the simultaneous action of numerous and complex organizational mechanisms, among which one of the important central places is autonomic regulation of the body, its organs and tissues. After researches made by K. Bernard, I. M. Sechenov and W. Cannon, a new step in the development of the idea of homeostasis was made by N. Wiener, who proposed to apply the theory of control in the modeling of homeostatic systems. The ability to balance with the environment, or the adaptive capacity of the body, is one of the most important features of the living system. It should be noted that the reduction of the adaptive capacity of the organism, associated with changes in physiological functions, in particular, with the change myocardial-hemodynamic homeostasis, is characterized by an increase in blood pressure, a decrease in the external work of the heart [46]. However, in the premorbid conditions observed changes in physiological parameters, as a rule, do not go beyond the so-called clinical norm and therefore usually remain out of the attention of doctors during the preventive medical examination of the population. As a result, as it is known that only the failure of adaptation with the development of specific disease becomes the basis for medical treatment. In the best case, with the earlier detection of the initial signs of the disease, specific measures of secondary prevention may be applied. To assess the level of functioning of the cardiovascular system which is the leading homeostatic system of the organism, a special indicator is developed that is the index of functional changes (IFC). It is calculated in points according to the following formula: IFC = 0.011 * HR + 0.014 * SAP + 0.008 * DAP + 0.014 * A + 0.009 * BM – 0.009 * H-0.27, where HR is the heart rate (bpm), SÀP and DAP – systolic and diastolic blood pressure (mm Hg), A – age (years), BM – body weight (kg), H – height (cm). Interpretation of IFC is carried out according to the following scheme: satisfactory adaptation – up to 2.59; tension of adaptation mechanisms – 2.60–3.09; unsatisfactory adaptation – 3.10–3.49; maladaptation – 3.50 and above [14, 18].

Even small changes in the traditionally measured parameters of pulse rate, blood pressure, body mass change the value of this integral index, indicating the direction of change in the functional state of the organism. The action on the organism of the environmental factors is constant, systematic and, being a stressor, leads to the development of the tension of regulatory systems of the body [10, 43].

Normally, this tension has a working character and ensures that the body achieves an individual functional optimum. It does not cause negative consequences, and after rest the complete recovery of initial normal functional state is marked. By reducing the adaptive capacity of the body in response to normal activity loads, there is an increased functional tension of the adaptation

mechanisms [44, 45]. Gradually, in the absence of adequate preventive measures, moderate functional tension converts into expressed, and then sharply expressed. In the case where ordinary activity loads are inadequate or with a significant reduction in the adaptive capacity of the organism (for example due to a disease) and insufficient recovery, a sharp increase in functional tension leads to overloading of regulatory mechanisms and then to their exhaustion. In this case, the premorbid conditions develop, as the initial stage of occupational diseases. But traditional occupational pathology practically begins with the second stage of premorbid conditions, when specific changes of certain organs and systems whose homeostasis are violated are already appearing. In this case, due to the mechanisms of compensation, the manifestation of the disease may be slightly expressed or it is in the initial phase and is compensatory in nature [6, 8, 9]. It is clear that it is fundamentally important to discover the signs of the disease at the first stage of premorbid conditions, when non-specific changes are predominant in preserving the homeostasis of the vital systems of the organism, including the cardiovascular system [46].

The central place in the diagnostics is the study and evaluation of the organism's response to the stressful environmental effects and the determination of the tension of regulatory systems and functional reserve. The leading method for determining the tension of regulatory systems is the analysis of cardiac rhythm variability (HRV), which is now widely used worldwide [5, 13, 14]. It is possible to analyze the degree of tension of regulatory systems by many methods: by studying the blood levels of the hormones of adrenaline and norepinephrine, by changing the diameter of the pupil, by the amount of sweating, and so on. But the most simple and accessible method, and most importantly, that allows continuous dynamic control, is a mathematical analysis of the heart rhythm [46]. It is known that changes of heart rhythm are a universal operational response of an organism to any action of the factors of the environment. However, the traditionally measured mean pulse rate only reflects the final effect of numerous regulatory influences on the blood circulation apparatus, characterizing the features of the already existing homeostatic mechanism. One of the important tasks of this mechanism is to balance the sympathetic and parasympathetic parts of the autonomic nervous system [47, 48]. One and the same heart rate may correspond to various combinations of activity of the system's links that controls the equilibrium of the autonomic system. This provides the basis for considering the SA node as a sensitive indicator of adaptive reactions of the organism in the process of its adaptation to environmental conditions. If the body is represented as a cybernetic system, the blood circulation system can be considered as the one of the main executive mechanisms acting as an intermediary between the leader (central nervous system, autonomic nervous system, system of humoral and hormonal regulation) and controlled (locomotor apparatus, muscular system, internal organs) contours [46, 49, 50]. This allows considering the activity of the cardiovascular system as a process of interaction between autonomic and cardiovascular homeostasis [51, 52]. Cardiovascular homeostasis is aimed at providing adequate blood supply to organs and tissues. Informational processes in cardiovascular homeostasis are determined by chrono- and inotropic effects on the myocardium, carried out inside and outside the heart reflex mechanisms, vascular reactions, cardiopulmonary actions. Comparison of the results of a large number of clinical and clinical-physiological observations and studies shows that some violations of normal functioning of the body can be regarded as a special type of pathology – "disease of homeostasis", according to the definition of Kassil. These include states caused by insufficiency, excess or inadequacy of the adaptive systems of the body. With a certain condition they can be attributed to disorders of the functions associated with the process of aging, some functional disorders, depletion of the nervous system, endocrine apparatus, diseases such as autonomic dysfunction, and so on [53–57].

For operational evaluation of the functional state of the body, an analysis of the following indicators is carried out in next steps: 1) filling out a short questionnaire on health, complaints and lifestyles; 2) registration of ECG in 3 standard leads; 3) dispersion ECG mapping; 4) analysis of heart rhythm variability; 5) measurement of height and weight of the body; 6) measurement of blood pressure; 7) psychophysiological testing (measuring the speed of a simple and complex visual-motor reaction). All these surveys are carried out at rest, without any testing loads. Dispersion mapping of the electrocardiogram (ECG) is performed using three electrocardiograms and special software programs. The research is conducted in the sitting position with maximum psychological and physical comfort [6, 15].

The concept of health includes not only medical, biological and psychological aspects, but also social, economic and environmental components, therefore the degree of tension of regulating systems reflects the integral response of the human body to the whole complex of factors that affect it [58]. A healthy organism, in the conditions of a high level of functionality, responds to the effect of stimuli on the normal, working tension of regulatory systems. However, the degree of tension of regulatory systems in healthy individuals may fluctuate, where the higher intensity of stress depends on the functional reserves, which leads to an increase in the tone of the sympathetic ANS and the stability of the heart rate [59, 60]. Prevalence of sympathetic tone leads to the activation of the hypothalamic-pituitary-adrenocorticotropic system, which implements the response of the organism to the effect of stress exposure.

Therefore, an increase in the tension level of adaptation mechanisms is the initial stage of the state between health and disease. On the one hand, the functional tension is characterized by a high degree of development of elements of the stage of resistance, but on the other hand, adaptive activity proceeds on the limit of the capabilities of the organism and is accompanied by the development of relevant violations. In the state of functional tension of adaptation mechanisms there is an increase in the degree of the structural and functional organization of the biosystem [55, 61]. At the same time, the high content of corticosteroids indicates an increase in the level of functionalization, which is supported by the intensive tension of regulatory systems, where the amount of reserves is sufficient, but due to constant spending, functional reserves are not sufficiently replenished, and if there is no replenishment of reserves, the achievement of equilibrium in regulatory mechanisms becomes impossible [62]. One of the ways in which the disorder of energy and metabolic processes occurs is a shift in the autonomic balance towards sympathetic prevalence.

Human body continuously experiences the effect of factors that reject the balance of regulatory processes. At the same time, regulatory mechanisms are introduced to prevent or compensate for possible or existing shifts, i.e. adaptive mechanisms are closely related to homeostasis. That is, the state of functional stress of adaptation mechanisms reflects the maximum mobilization of the mechanisms of short-term and long-term adaptation that occurs at the limit of the possibilities of the organism.

Thus, as stated in the scientific works of V. Lisovy, V. Kapustnik and V. Korobchansky, the development of clinical forms of diseases is preceded by well-defined violations of the functional state of the organism, having a boundary character. At the same time, the timely detection of premorbid states, the establishment and elimination of risk factors for their occurrence can prevent the development of pathological process. The premorbid conditions arise from the dysfunction of those adaptive systems that are now called to ensure the stable functioning of the organism, which is why the premorbid diagnosis is based on the definition of qualitative and quantitative indicators of the adaptation process, which are measured and / or calculated as a result of the preventive examination. As a rule, border mental states are diagnosed on the basis of presence of neurotic disorders in situations and periods of risk, the precursors of somatic diseases are diagnosed on the basis of dysfunction of the relevant regulatory systems (pro- and antioxidant, thermoregulation, etc.) [8].

Conclusions. Based on the discussed above, it becomes possible to conclude that stress response is a necessary link in adaptation. It should be emphasized that during the action of extremely strong factors, the adaptive response becomes inadequate, however, in some cases, even when the normal environmental factors influence the organism, inadequate adaptive reactions may occur, which is the main example of the transition of the adaptive reaction to pathological one. Adequacy and adaptation efficiency depend on the state of adaptation mechanisms, that is, the level of functionality, the degree of regulatory mechanisms tension and functional reserves.

Conflict of interests

There is no conflict of interests.

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