Pre-nosology diagnostics

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Abstract

The present paper deals with prenosological diagnostics as methodology of an estimation of functional states of an organism. Highlighted is its first practical application in space medicine, at long influence of stressful factors, including such factor unusual to terrestrial organisms as weightlessness. Demonstrated is the methodology’s wide recognition and use in various areas of medicine and physiology. Health is considered herein as process of the continuous adaptation of an organism to environment conditions. Thus, shown is the connection between transition from health to illness and decrease in adaptable possibilities. Transition from health to illness, exhaustion and failure of mechanisms of adaptation are described in detail. The classification dividing the prenosological states into physiological norm, prenosological, premorbid and pathological states is used herein. Prenosological studies including diagnostics, screening and control are considered.

Keywords

Prenosological, Space medicine, Stress, Adaptation, Premorbid

Imprint


ity of cosmonaut’s organism to adapt to the spaceflight environment and readiness to perform duties correctly and completely. Health definition in the WHO Charter as state of complete physical, mental, and social well being complies with the space medicine requirements and yet is not exhaustive. Evaluation of the health state of spacecrew members must proceed not from the philosophical, qualitative definition but from the specific, practical one that will open up possibilities of measurement and evaluation of the level of health [1–4].

Space medicine gave rise to a fundamentally new approach to health evaluation in light of the present-day theory of adaptation and the doctrine of homeostasis [5–7]. The essence of this approach is that health is considered to be a process of continuous adjustment of organism to its environment and the adaptive potential is the measure of health. Transition from health to disease is caused by a reduction of the adaptive potential, degradation of the ability to react adequately to social, labor, and usual everyday stresses. A large number of transitory or pre-nosological states develop in-between health and disease. Results of mass screening showed that 50 to 80 % of population have various prenosological states [8]. This means that the majority of people need not just medical or disease diagnostics but pre-nosology diagnostics, i.e. determination of degree of loss of adaptability or level of deviation from the norm. With space medicine, methods and approaches of pre-nosology diagnostics are among the most common and advancing instruments for evaluation of health level.

Evaluation of health level
In the turmoil of modern life most people are subjected, to one or another degree of emotional or physical stress-es. This is particularly true for people dwelling in extreme climate, geographic and social environments. All these produce stresses. Low stress level is always good to organism as it stimulates the ability to adapt (adjust) to the continuously changing outer world. However, an excessive stress, permanent emotional pressure, depression, failures, heavy physical loads and inadequate rest lead to severe straining of the regulatory systems of organism, overstrain and eventual exaustion.

This classification was experimental substantiated in the first monograph on pre-nosology diagnostics published by V.P. Kaznacheev, R.M. Baevsky and A.P. Berseneva in 1981 [9]. With time the classification was elaborated further by space medicine and applied physiology. A 10-grade scale was proposed to evaluate four levels of health depending on the extent of regulatory systems straining [3].

Our concept of pre-nosology diagnostics places emphasis on the informational aspect of health on the ground that controlling mechanisms, i.e. informational or regulatory, are of primary importance for the optimal functioning of such complex biological system as human organism. Function of a living system is a behavior pattern that keeps integrity of structures and consists of successive levels of metabolism, energy and information exchange, and temporal organization (R.M. Baevsky, 1979, 2003, 2006). Irrespective of whether we consider a cell, organ or whole organism, their functioning can be described by a single algorithm that includes four stages:

1) renewal of structures with energy and matter expenditures;
2) generation and expenditure of energy by control commands;
3) reception, processing and transmission of command (signal) information for initiation of metabolism and energy exchange regulation;
4) temporal matching of structure, energy and information-level functioning.

Key principles of pre-nosology diagnostics
Adjustment or adaptation to a changed environment is attained at the cost of the functional resource or a certain "biosocial pay". Every moment organism spends life resources and then renews them by, specifically, rest and sleep. Expenditure and renewal of the resources by organism and its individual systems is actually what the life process is. Adaptation, one of the fundamental properties of organized matter, is a result and means for resolution of internal and external contradictions of life. Organized matter exists and forms on the borderline between life and death, health and disease through their collisions and intertransitions. "Pay" for adaptation that went beyond the limit of "biosocial budget" and demands extra efforts from organism cuses breakage of the adaptation mechanism.

Fig. 1 shows the conceptual diagram of health measurement. From the diagram it is evident that homeostasis maintenance requires involvement of mechanisms responsible for mobilization of functional reserves, i.e. activation of relevant systems of regulation. Level of health or adaptive potential of organism are also dependent on individual characteristics of organism and environmental factors affecting its life.
The ability of adaptive mechanism to ensure stable adaptation to environment hinges on the functional reserve (FR) of organism. High functional reserve provides an adequate level of functioning (LF) of the main systems without increasing the degree of tension (DT). The dependence between FR, LF and DT can be expressed as a simple equation:

$$LF = FR \cdot DT.$$  

The equation shows that to retain adequate LF of organism or separate systems on the background of various stresses, DT must grow in sync with FR reduction. The equation should be regarded as a model describing the ratio of adaptive and homeostatic reactions of organism. The ratios of LF, DT and FR at different functional states can be quite diverse. The state of physiological norm can be observed against both the normal and increased level of functioning. At pre-nosological states, LF can be normal or high or reduced depending on FR. Premorbid states develop due to low FR and as a function of DT; they are characterized by either high or low LF.

Equation $LF = DT \times FR$ is a base of the pre-nosological approach to health evaluation. The technology of pre-nosology investigations should involve calculation of all three components of the equation. However, the key position is occupied by the DT measurement. The main reason is that this index is the most dynamic indicator of adaptation level. Another argument for the choice is that DT is a key parameter in pre-nosology diagnostics, as it can be measured using a comparatively simple and proven method of heart rate variability analysis (HRV). It should be noted that the method was designed by space cardiologists and first applied in early orbital flights of animals and humans. HRV was tested in different disciplines of medicine and physiology and now is broadly applied in researches of autonomic regulation and stress level [10–13]. Finally, the third argument for choosing DT and giving priority to HRV is that they offer the opportunity to perform intimate evaluation of the functional state of organism leaning upon knowledge about the sequence in which levels and mechanisms of regulation are mobilized.

As a rule, in case of a pre-nosological state, level of functioning (LF) of the main systems (cardiovascular, respiratory, digestive, excretory) does not alter much. That is the reason why the traditional clinical measurements of pulse rate, blood pressure, expiratory volume etc. do not help recognize states in-between the norm and pathology. However, if homeostasis is provoked by challenging environment and DT remains high for a long period of time, there is a risk that organism will pass into a pre-nosological or even premorbid state.

Besides, in addition to the traditional premorbid states we think it reasonable, along with early or initial pathological developments in organs and systems (pre-ulcerous, pre-hypertonic, etc.), to refer to premorbidity also such predecessors as overstrain and regulation depletion, manifested by non-specific signs of the general adaptation syndrome.

### Classification of the pre-nosological states

State of the whole organism as a result of functional system activities is determined by the optimality of command signals, ability of control mechanisms to sustain equilibrium between organism and environment, or its adaptation. The adaptive function of organism requires energy and information and in this connection we may speculate on the "cost of adaptation" as a function of the degree of regulation straining and expenditure of the functional reserve. Adaptation-induced change in the level of functioning of a system or its components does not necessarily break homeostasis provided the regulatory mechanisms are not overstrained and the functional reserve is not depleted.
Overstrain and depletion are the causes for adaptation failure and disease. Pathological states as an aftermath of regulation disarrangement make grade four in the classification of pre-nosological states. A detail description of each of the four functional states is presented in table 1.

This classification was fairly widely accepted owing to the proposed analogy with the traffic lights. The green light gives the right to feel free and go the chosen way. In terms of health the green means that at the moment there are no serious deviations to care about. The yellow light signals to take a pause and look closely about before proceeding further. It means that some changes have occurred and that care must be taken to reestablish the normal health level. The red light alarms that it is time to visit the doctor for diagnostics and treatment. Already in 1980s, a roughly similar to the "traffic lights" classification was applied advantageously in mass pre-nosology examinations [8, 9, and 14]. The pre-nosology health evaluation campaigns were accepted by the broad public. For instance, factory workers took them much more seriously than the traditional prophylactic medical examinations aimed at detecting diseases. Quantification of the level of regulation strain is crucial for estimation of the reserve potential or adaptability of organism. Any stress causes the reaction of regulation straining and mobilization of the functional reserve which happens constantly. However, one and the same factor may strain regulation moderately in some people (working level of functional straining) and increase sharply the regulation strain in others. All depends on the functional reserve of organism, stamina, initial individual health level.

Transition from health to disease is instigated by overstrain, exhaustion and break of adaptation. The sooner we predict this turn of event, the higher will be chances to retain health. Thus, the problem comes down to finding ways how to measure the level of regulation strain in own organism to be able to control health. Pre-nosology monitoring is a practical step toward dynamic tracking of the regulation system functions, and detection of incipient signs of overstrain of organism, organs and systems. Instead of waiting for disease symptoms, the pre-nosology approach to evaluation of health, functional state of organism is aimed at detecting regulation changes and take timely appropriate actions for health improvement and prophylaxis.

Table 1. Classification of the functional states in pre-nosology diagnostics

<table>
<thead>
<tr>
<th>No.</th>
<th>Functional state</th>
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<tbody>
<tr>
<td>1</td>
<td>Physiological norm</td>
</tr>
<tr>
<td></td>
<td>Satisfactory adaptation to environment. Sufficient functional potential of organism. Homeostasis is maintained with minimal regulation straining</td>
</tr>
<tr>
<td>2</td>
<td>Pre-nosological states</td>
</tr>
<tr>
<td></td>
<td>Organism-environment equilibrium is maintained through mobilization of the functional reserve and, consequently, regulation straining. Adaptive potential of resting organism is lowered and adaptability to stresses is reduced. Homeostasis is achieved only by regulation straining</td>
</tr>
<tr>
<td>3</td>
<td>Pre-morbid states</td>
</tr>
<tr>
<td></td>
<td>Unsatisfactory adaptation. Low functional potential. Homeostasis only due to extreme regulation straining and mobilization of additional compensatory mechanisms</td>
</tr>
<tr>
<td>4</td>
<td>Failure (break) of adaptation mechanisms</td>
</tr>
<tr>
<td></td>
<td>Sharply reduced functional potential. Impaired homeostasis. Specific pathologic changes on organ and system levels</td>
</tr>
</tbody>
</table>

Pre-nosology diagnostics: Methodology

The theoretical developments above are objectified through methods and technologies of investigations. First of all, we should point it out that methodology and all the more technology of pre-nosology diagnostics may vary significantly with application areas in medicine and physiology. Much depends on purpose of investigations. Therefore, methodology and technology of pre-nosology diagnostics in preventive medicine may have little similarity with those in rehabilitative, sport, not to mention space medicine.

In context of purpose, the pre-nosological investigations can be divided into three groups:
1) pre-nosology diagnostics;
2) pre-nosology screening
3) pre-nosology monitoring

In a broad sense, pre-nosology diagnostics is interpreted as making a so-called pre-nosology diagnosis or, more exactly, evaluation of the functional state of organism within the norm-pathology interval, between health and disease. Classification of the states given above can and must be modified to fit the needs of various areas of medicine and physiology. Modifications do not imply revision of fundamental but rather practical aspects of adapting principles and terminology to the objectives of one or another field of application. For instance, medicine and physiology of labor are concerned with evaluation...
of human ability to work; preventive medicine, with determination of the necessity and content of health improving and prophylactic measures, and urgency of visiting a doctor; rehabilitation medicine, with the progress of recovery from a disease. In all cases pre-nosology diagnostics serves to evaluate current functional state of organism, level of deviation from the norm and how close the deviation approaches to disease.

Pre-nosology screening is selection of people with functional states of organism that need to be improved, may not permit to work, require secondary care in medical institution etc. Public healthcare is short of these methods and technologies; instead, it has to handle perplexing medical and social issues using crude inaccurate. For example, working capacity examination relies on the nosological approach unsuitable for separation of groups of normal people with pronounced regulation strain; they are in the premorbid state though disease symptoms are still unapparent. Time must pass till break of adaptation when the need to limit workload will be obvious. Pre-nosology screening on this stage has received widespread acceptance in preventive medicine, mass health examination, and medical flight certification. The first practical steps of pre-nosology diagnostics were made in pre-nosology screening. Effectiveness of the method was demonstrated in nationwide health examination campaigns conducted in the USSR in 1970–80s [8, 9]. Pre-nosology screening can be useful in different industries where it is important to identify employees with undesirably high levels of regulation straining, lowered functional reserve or risk of pathology.

Pre-nosology monitoring is a dynamic functional state check of essentially healthy people. In fact, this is a process of tracking the state of healthy human doing his job. The most illustrative example of pre-nosology monitoring is provided by space medicine that can be called the cradle of the prenosological approach. In the course of long-term space mission cosmonauts, rigorously selected healthy people, are regularly subjected to medical and physiological examinations. The reason is to see the trend and extent of shifts in the functional state of cosmonauts. If the functional state shifts toward pathology is paralleled by DT growth, intervention is urgent including release of workloads, change in diet or training program, prescription of prophylactic medication, etc. Pre-nosology monitoring can be beneficial to health check of shift personnel operating complex systems, evaluation of recovery from severe disease, functional state of sportsmen preparing for tournaments, etc.

Methodology and especially technology of pre-nosology diagnostics vary significantly with type of investigation. Methodology is generally understood as a basic scheme of investigation, stages and methods. Technology is specific procedures, details of investigation and description of instruments, methods of data processing and analysis. Technologies are often patented and licensed, as they provide a complete tangible or information result. We shall now consider methodology of pre-nosological investigations and outline some of the technologies from this standpoint.

Object of pre-nosology investigations is healthy people or sometimes patients recovering from diseases. The key criterion of choosing a contingent is a request to evaluate health but not to make diagnosis. This is a matter of principle, as we work in the field of prenosology. When we apply the pre-nosological approach to patients on the stage of recovery, we proceed from the assumption that even a sick organism possesses some store of adaptation potential and functional reserve to regain normal health state. In essence, treatment has the goal to mobilize the functional reserve of organism, to stimulate its adaptation potential. However, the point is that being unable to assess results of its effort the level to which health has regained (less straining of regulation systems, growth of the functional reserve), traditional medicine still uses the criteria of disease. Therefore, pre-nosology diagnostics helps traditional medicine to control health recovery using the arsenal of own methods to evaluate the progress from disease to health or from pathology to the norm. In all cases pre-nosological investigation is a process of recognition guided by a simple logical rule and sophisticated mathematical techniques. It is always noninvasive, comfortable and quick. These characteristics of the pre-nosological methodology are of fundamental importance because object of investigation is healthy human. As long as one is healthy and does not feel symptoms of disease, one is not mentally ready to any, even a very simple medical procedure.

Innumerable recreation centers and fitness clubs attract clients with the promise to improve quality of life and to raise mood by reducing diet, taking supplements to aid sleep or per-
forming exercises that will increase strength and elasticity of muscles. As a rule, all these do not imply sufficient monitoring or evaluation of the initial functional status of organism.

Healthy person must be motivated for a specific type of examination. Unfortunately, healthy lifestyle gets implanted very slowly. Some companies, private in particular, launch wellness programs for high-priced and qualified staff. Health of senior officers and generals has been standardized first in the US army and now in Russian army. In sport, health maintenance is a pivot for success. There are some though still few cohorts of people who regard pre-nosology investigations as important and indispensable. For others, comfort, noninvasiveness and short time of investigation are motivators for brooding on whether give preference to costly and time-consuming clinical examination which is effective only when there are symptoms of a disease or pre-nosological investigation that can delay disease.

We must not hold back an important principle of pre-nosology diagnostics which is use of data-intensive methods of investigation. This means that a very short and methodically simple investigation must generate massive and valuable information sufficient for stating conclusions about regulation activities, functional reserve and functioning of the vital body systems. The principle lays the ground for development of concrete technologies. An obvious example of how the principle works is a broad application of heart rate variability analysis in pre-nosological investigations. Another example is designing the method to evaluate level of the cardiovascular functioning by complex parameter FCI (functional change index) deduced from simple traditional measurements of pulse rate and blood pressure.

Pre-nosology diagnostics technologies are diverse and to a large degree dependent on type of pre-nosological investigation. In addition to the main indices of pre-nosology diagnostics (FL, DT, FR), consideration must be also given to the cause-and-effect factors such as environment, lifestyle and anamnesis. This explains the presence of questionnaires and socio-ecological survey among the pre-nosology diagnostics technologies. Flow chart of any technology can be divided into three parts, i.e. information collection (1); processing and analysis (2); data evaluation and conclusions (3). Algorithm of pre-nosology diagnostics implements the abstract theorems above in the form of conclusion concerning the functional state and adaptation potential of organism.

To begin with, we should note that information collection during pre-nosological investigations is arranged in a comfortable, quick and highly productive manner. In contrast to patients in hospitals and outpatient clinics, objects of pre-nosology diagnostics are, as a rule, healthy people. Their interest in this examination is driven, on the one hand, by the form and content of conclusions they receive and, on the other, simplicity and comfort of technologies. Mass examination, specifically, is often performed at production site during work time and, therefore, requires comfortable and time-efficient technologies.

Measurements of height, body weight, muscle strength and blood pressure usually take 2 to 3 minutes each; ECG recording for HRV analysis takes 5 minutes. Filling out the questionnaire also is not a problem. The questionnaire must contain no more than 15–20 questions with multiple choice answers. Information collection must utilize dedicated software tools as much as possible including databases storing individual files with results of measurements.

In the pre-nosology approach, the primary health criterion is level of adaptation potential of organism rather than presence or absence of diseases. The ability to withstand external stress factors and to maintain normal functioning of the vital body systems, as well as relative equilibrium with the environment is the main health indicator. Mechanisms compensating deviations developing in different systems underlie the enormous variety of adaptive reactions. Actively and continuously working regulation systems optimize interrelations between organism and affecting factors. In other words, deviations that traditional medicine qualifies as diseases and refers to appropriate nosological class, the for the pre-nosology approach are the reason for concern about the ability of organism to sustain balance with its environment. If the functional reserve is sufficient, organism does not need treatment but support of an adequate level of adaptation potential.

The pre-nosology diagnostics classification of the functional states by level of adaptation to environment makes it possible to distribute the total flow of people coming for mass medical examination into four categories depending on their need in medical aid. Medical investigations
are required only to those who have been referred to the category with broken adaptation and some people in premorbid state who have serious health complaints or face with sharply deteriorated environments. Mass pre-nosology investigations [9, 15-17] showed that no more than 20-30% really need medical diagnostics and treatment. Consequently, application of the pre-nosology approach in mass medical examinations would let more effective use of the healthcare strength and resources.

Pre-nosology diagnostics as a fundament for medicine in future

Practice of the pre-nosology investigations shows clearly that recognition and evaluation of functional states of organism in-between the norm and pathology require cutting-edge techniques and technologies. In this context, leadership still belongs to space medicine concentrated on enhancement of health evaluation methodology in long-duration orbital and exploration missions. It is natural that the present-day technologies are incomparably better than 30-40 years ago. In its turn, pre-nosology diagnostics has also made a leap forward. Now we discuss not so much recognition of functional states, as their probability, pathology risk estimation, and prognostication of a probable decline of the adaptation potential. The concepts of pre-nosology screening and pre-nosology monitoring have been reconsidered.

On the evidence gathered at the end of the last century, screening is focused on differentiation of pre-nosological and premorbid states as they require different health recommendations. This was supported by the results of examining bus drivers [18, 19] and pilots using hard- and software system Ecosan-2007, and data from project Mars-500 [20-28]. We succeeded in demonstrating a high correlation of the functional state of normal people with effecting factors (regional climate, working environment, psychophysiological parameters). Transition from prenosology to premorbidity and consequent growth of disease risks are accompanied by an increase in organism vulnerability to changed conditions. For example, seasonal rise in common cold incidence involves mostly people in premorbid and pre-nosology states due to low adaptation potential. In recent years, space medicine has been enriched with the concept of adaptation risk as a criterion of pathology probability [29, 30]. In light of this concept, pre-nosology monitoring is a dynamic estimation of individual adaptation risk aimed to reveal negative trends in health state and to predict possible pathologic developments.

Advancement of pre-nosology diagnostics is objective necessity, as it may build a bridge between the Western and Oriental models of medicine. The Russian healthcare system reproduces the so-called Western model, i.e. medicine is oriented at diagnostics and treatment of concrete diseases on the nosology principle. All types of pathology are related to specific organs and systems; medical specialties become more and more narrow. It is well known that Oriental medicine (Tibetan and Chinese in particular) sees human organism as a comprehensive whole. Its primary goal is to study health and ways to keep it. Different pains are considered to be health disorders that can be removed by various actions on whole organism, since a single organ pathology is linked with disorders on the level of whole organism.

In Russia and majority of the West countries doctors’ duty is, first and foremost, to diagnose correctly. This means precise location of a pathologic process and its characterization on the cell and even subcell levels. In doctors’ opinion, only precise diagnosis gives reason to prescribe treatment, typically drugs. They disregard the fact that the “aimed pharmacological blow” to the site of pathology impacts the entire organism and may cause an irreparable damage to healthy organs and systems.

Methods of pre-nosology diagnostics showed that no matter the treatment mode, it begins with mobilization of the functional reserve of organism (straining) and only afterwards, in a while, reaches local effects, provided a correct individual dosage and period of treatment. The reverse transition from disease to health is no less complicated. Sometime in future medicine will have technologies of assessing the therapy efficacy and conducting dynamic pre-nosology monitoring of rehabilitation.

Medicine of the future must be sure focused on maintaining health of healthy people. Methods and means of treating diseases will, of course be perfected; however, priority will be set on the energetic development of methods of health maintenance and improvement that could be integrated into the healthcare system. This is where the theoretical and practical knowledge of pre-nosology diagnostics will gain recognition and furtherance.
Statement on ethical issues
Research involving people and/or animals is in full compliance with current national and international ethical standards.

Conflict of interest
None declared.

Author contributions
The authors read the ICMJE criteria for authorship and approved the final manuscript.

References
4. Baevsky RM, Berseneva AP. Pre-nosological diagnostics in health state evaluation. Валеология. 1993; p. 131. [in Russian]