

SYSTEM SECURING INTEGRITY OF ORGANISM AND ITS INTERNAL ENVIRONMENT STABILITY – FORGOTTEN HEALING POWER

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*The ancient Grecian wisdom is: physician heals but nature recovers.
The question is: do we know and take advantage?*

Introduce

Fundamental condition of every living organism is its integrity and **stability** of its internal environment. In order to secure this fundamental condition, the organism is endowed with systems, which **permanently control** the stability of internal environment and **regulate** every deviations and **steady-state errors**. It means that the system should permanently, every moment, collect data information about important parameters of internal environment, process them, and then secure regulating measures to reach the stability over and over. More, there is necessity to collect information from **outer environment**, to process and analyze them, and to react. **It represents to collect permanently thousands of data information, to process them immediately and to take measures to reach permanent integrity and stability.** The principle, how the system acts, is the same as other systems: sensors pick-up data, the data are transported to the processing center, and then the central unit takes regulation measures, which are transferred to the effectors. However, biological systems are much more complicated. Firstly, most of functioning parts of system are doubled. Secondly, the system is arranged hierarchically from lowest level (molecular, intracellular level) to higher and higher levels (cellular and intercellular communication, level of tissues, organs) up to the highest central levels. This organization is absolutely necessary due to the fact that the system is securing the most important functions of living organisms and every error could cause life-threatening condition. Every level comprises own regulating tools and there is the statute validity: every higher level is activated when lower level is not sufficient to regulate the error and, at once, the lower level is switched off or follows instructions (orders) from higher level. In sense of systemic point of view, the body is a complex integrated information and regulatory system comprising subsystems, which cooperate and interact on different levels permanently, every life moment. The stability is not a stable state but it is a dynamic process of many different biochemical reactions. The integrity is secured with healing, regenerating, and reparatory (of damaged structures) processes. **The system acts on pre-programmed functions and functions learned within the course of life.**

The goal is to reach permanent stable balance of inner environment – dynamic homeostasis as a principle condition of life and health.

Body regulatory system

The system is acting (under normal circumstances) independently on the will of the organism – the will is often mistaking and so life functions could be fatally endangered. Failure in regulation means serious health jeopardy. The most important regulatory role represents 3 interacting subsystems (in following text named as systems due to the fact that they are, in some sense, independent): **autonomic (vegetative) nervous system (ANS)**, **hypothalamo-pituitary-suprarenal axis (HPA)** (cooperated and interacted with other parts of endocrine system – humoral regulation), and **immune system (IS)**. The system is collecting data from inner environment through sensors – receptors (permanent – baro- and chemoreceptors etc.) or developed on demand (insulin receptors etc.), signaling molecules, and other ways; from outer environment through senses, speech, thinking etc. Then the information is transported through nerves, hormones and other molecules to the processing centers (vasomotoric, subcortical, cortical etc.)

and then the measures backward into the effectors (tissues, organs). The regulation is realized on cellular, humoral and nervous system levels.

Elementary parameters of homeostasis

- 8 Osmolality.
- 9 Acidobasic balance.
- 10 Natremia.
- 11 Potassemia.
- 12 Calcemia.
- 13 Phosphatemia.
- 14 Magnesemia.
- 15 Cholesterolemia.
- 16 Proteinemia.
- 17 Glycemia.
- 18 Energetic metabolism and oxygen consumption.
- 19 Blood pressure. Heart frequency.
- 20 Body temperature.
- 21 Renal function. Urine content.

As we can see, the deviations of some of the **parameters are (at once) symptoms of many civilization diseases** (atherosclerosis, diabetes, cardiovascular diseases etc.).

Regulated systems – brief and simplified information (examples)

-Cardiovascular system.

Heart parameters:

- Heart frequency (chronotropy)
- Strength of contraction (inotropy)
- Atrio-ventricular transfer (dromotropy)
- Myocard irritability (bathmotropy).

Regulation: nervous (**ANS**, parasympathetic and sympathetic), humoral – **HPA** (adrenaline, acetylcholine) and cellular (Starling's law).

Vascular system parameters:

-Local (concerning organs.) Parameter: Organ vascular circulation.

Regulation: chemical (end-products of metabolism are vasodilators), nervous (**ANS**), humoral (quinines, adrenaline – **HPA**, etc), cellular (endothelium relaxation factor EDRF = NO)

-General (concerning all body). Parameter: Blood pressure. Blood volume.

Regulation: **ANS** (sympathetic, parasympathetic), **HPA** (adrenaline), humoral (renin-angiotensin system, aldosterone, atrial natriuretic peptide, antidiuretic hormone, renal function).

-Respiratory system.

Parameters: Respiration rhythm. Ventilation capacity.

Regulation: central nervous (inspiration and expiration nerves), **ANS** (Hering-Breuer reflex, carotide sinus chemoreceptors), chemical (arterial blood pCO₂, pO₂, pH, atmospheric pO₂), **HPA** (hypothalamus).

-Digestive system.

Parameters: Gastrointestinal movement. Digestion juices production. Absorption. Nutrition intake.

Regulation: **ANS**, **HPA**, humoral (gastrointestinal tract hormones, glucose and amino acids plasma concentrations etc.), cellular (local organs own regulation).

-System of thermoregulation.

Parameter: Body temperature.

Regulation: **HPA, ANS.**

-Acido-basic balance. Fluids and mineral balance.

Parameter: Blood and extra-cellular liquid pH, volume and mineral content.

Regulation: Respiration, gastrointestinal (metabolism) and renal function – **ANS, HPA**, humoral and reflex mechanisms.

-Immune system.

Basal parameters: WBC, differential count, phagocytic activity, respiratory burst, cytotoxic activity, complement activity, immunoglobulines.

Regulation: **HPA, ANS**, humoral and cellular regulation (cytokines etc.)

Certainly, the examples above described serve as a brief information of some systems regulation; another information is possible to find in corresponding literature. Undeniable fact is that **ANS and HPA participate (fully or partly) in all regulatory mechanisms to secure homeostasis.**

Problems to contemplate

-The systems securing homeostasis represents very powerful system enabling to keep stability and integrity of organism much better than any artificial human (medical) influence. The efficiency of the system is approved: the system is able to keep homeostasis (and its parameters) within normal limits for many years of life. **Aging process is one of the causes that the system loses its efficiency.**

-Aging process (and also the chronic diseases, which are with aging process connected) is going together with **oxidative stress** (surplus of free radicals over antioxidants).

-Aging process is connected with reducing of own **energy production**. It means, on cellular level, the reducing of **mitochondrial activity**. Cellular energy production depends on sum of mitochondria and energy production of every mitochondrion. Mitochondria are very receptive to **free radicals** damaging influence.

-**Stress** is one of the most important free radicals producers. That is why stress accelerates aging processes and deteriorates chronic diseases and vice versa.

-The efficiency of **regulatory systems (ANS, HPA) depends on energy supply.**

The medicine comes with its healing methods when regulatory systems fail to keep homeostasis. Then there are the medicaments on the right place: antidiabetics, betablockers, statines, diuretics, hormones, diet arrangements etc. These measures are able to correct pathologic parameters within normal limits but with some disadvantage:

-Process leading to disease (i.e. aging) continues

-Medicaments have different side effects what need to calculate their benefits with their hurtfulness

Possible chances

There is an opening of an old-new dimension: to slow down the aging processes and to increase the energy supply. That means the support of efficiency of regulatory systems. All that means the **better health state, the better living conditions**. Using power and possibilities of own regulatory systems could bring lower medicaments requirement, reduce of their side effects, and lower costs. The question is, if official structures have interest in this way.

The chance is to utilize the powerful efficiency of organism's own regulatory systems, mainly ANS. This is possible by use of some ways.

Stress management

The stress includes the complex of reactions of the organism to the signals and changes of outer and inner environment as a complex of reactions of the organism's ANS and HPA to stabilize the

homeostasis: balance between organism and environment. Many of stress definitions are known but for practical purposes are less useful (Selye, Lazarus, Ganong). For practical use is very apt, however compromise, definition by Schreiber: stress is any influence of environment (inner, outer: physical, chemical, biological, political, labor, social, psychological) endangering health of some sensitive individuals. That means: the most important factor determining health stress disorders (and also stress diseases) is individual perceptiveness of the organism to the stress. Some sensible organisms or organisms under some specified conditions, esp. organisms unable to defend against stress or less resistant to stress (what could be caused by many different inner and outer factors), can this normal adaptation syndrome change to diseases from adaptation (or stress diseases) with different damaging influence to health state: inhibition of immunity, coronary heart disease, myocardial infarction, high blood pressure, peptic ulcer, stress disorders of menstruation, aging, asthma (and some other allergy diseases); stress negatively influence also ulcerous colitis and bowel irritant syndrome; the migraine depends some on stress, the attacks are more intensive and frequent under emotional and physical stress; manager's syndrome

For practical purposes there is a need of some method allowing **measure the stress, particularly the individual perceptiveness**. Many different methods have been developed to measure stress and individual perceptiveness to stress, mostly psychological and laboratory tests, and questionnaires. These tests reflect the possibility of organism to cope with stress, its ability to control stress etc. The psychological methods, much as they brought progress to the problems of stress measurement, are less or more depending on subjective reactions, valuation, and answers of test person. Not-till the **heart rhythm variability analysis came with possibility of objective evaluation of stress, activity of regulatory and adaptation systems, esp. the activity of ANS (sympathetic and parasympathetic)**.

One of the best of situation of influence of outer environment to the organism is stress in conditions of long lasting space flights. That is why the studies of stress during long lasting space flights are basic for the estimation of adaptation mechanisms and regulatory systems activity - esp. the tension of both parts of autonomic nervous system of the organism. The very useful method of estimation of activity of the regulatory systems is analysis of heart rate variability. The method is exact (when measurement is provided under standardized conditions), easy, economic, and possible to repeat on demand; it is one of acceptable indicator of general health; so the space medicine has brought a new dimension of estimation of general health to conventional (mostly preventive) medicine.

The method of HRV analysis in preventive medicine is based on large scale studies provided in Russia within the last 20 years on different groups of industrial and rural regions as well as of different age and sex-together about 20.000 of studied persons.

Basal principles and importance of heart rate variability analysis

Heart rhythm is almost never fully regular, also healthy heart has physiological, normal **arrhythmia** = rhythm irregularity known as respiratory (sinus) arrhythmia. The variability of heart rhythm refers to degree of fluctuation of the length of the heart beat intervals. Two people could have exactly the same average heart rate and yet when the variation is precisely measured in milliseconds it can be demonstrated that there is variance between individual beats and that degree of variance is different for different individuals under different conditions. This degree of variance between different beats is called **heart rate variability HRV**. Variability is the opposite of stability: as higher variability so lower stability and vice versa. **Low variability (high stability) is typical for sympathetic activity responsible to manage regulatory functions of organism by load - stress. High variability (low stability) is typical for parasympathetic activity**, as we can see during sleeping and/or anesthesia.

Basal functions the organism depends on those not (or very moderately) depending on the will-they are independent, automatically managed and controlled, as respiration, metabolism, cardiovascular system, hormonal and immune system, digestive tract etc. These systems are subject of control and regulation of **autonomic (vegetative) nervous system (ANS)** constituted from two parts: sympathetic and parasympathetic. The system comprises own hierarchy, periphery and higher vegetative centers as vasomotoric center (regulating tonus of vessels) and highest subcortical sympathetic centers (managing hypothalamic-hypophyseal-suprarenal system). Certainly, the main role to control and manage plays brain

cortex. The system is receiving information from outer environment (main source are senses) and inner environment-status of organs (main source are special receptors in vessels, lungs, heart and other organs, as baro-, chemoreceptors etc.). The most important function of ANS is to secure and provide **balance between environment and organism (adaptation), homeostasis**. After the information are processed first the lowest parts of ANS are activated, only when this activation is not sufficient to keep balance (adaptation), and/or the load is too high, then the higher parts of regulation are activated. Activity of each ANS part is well reflected in **heart rhythm variability**.

For analysis of HRV there was developed by Russian and German scientists a unique device **!TESLAGRAPH** or **!KARDIVAR** with software **ISCIM 6-Dynacons (Dynamic Control, of Stress)**. The complex is taking standard ECG record recognizing R-peaks within 5 minutes measurement under standardized conditions. The record is then processed in PC. On the processed information there is possible to evaluate the load of organism, state of stress, degree of variability, activities of different parts of ANS.

Cardiovascular system (and its heart rate variability) is so used as an indicator of activities of ANS (sympathetic and parasympathetic parts and their different levels) and adaptation reactions of organism.

Stress management and mitochondrial medicine

The aim of mitochondrial medicine is to keep, restore (or at least partially restore) cell functions and their viability (and functions of cells structures and cells organells), in sense of prevention and of an additional method to conventional medicine; here, the mitochondrial medicine, in any mean, does not replace (and cannot replace) therapeutic methods of modern conventional medicine, but significantly can increase efficiency of conventional medicine. Non-irrelevant fact is the direct therapeutic effect of means of mitochondrial medicine, esp. the effect of **Coenzyme Q-10**. In the field of securing the cell energetic levels and protection against cell (and its structures) damage caused by increased development of ROS (i.e. environmental pollution, enormous mental and physical load, ageing, influence of some medicaments and medical methods etc.), and **lack of ROS (free radicals) scavengers**.

Many medical studies and three international congresses on themes of **Coenzyme Q-10** (and other mitochondrial medicine means, as antioxidants etc.) approved effective use of these means by different chronic diseases of metabolism (diabetes of both types and diabetic complications, obesity, arteriosclerosis), muscular and neurological (Parkinson's disease, Alzheimer's disease, multiple sclerosis, muscle dystrophies etc.), cardiovascular diseases (esp. coronary heart disease, hypertension, cardiomyopathies etc.), chronic degenerative and inflammatory joints and spinal diseases (osteoarthritis, osteochondropathies, spondylosis), malignant diseases (important reduction of side effects of radiotherapy and chemotherapy, acceleration of regeneration of the white and red blood cells etc.), immune system diseases (allergies, asthma etc.), dental diseases as parodontosis and many others. The very positive effect was approved in sport medicine esp. in acceleration and improve the quality of regeneration processes after heavy training load and during sport competitions; in addition to that, the means of mitochondrial medicine are not listed as restricted doping means.

Significant effect is in the field of stress management and management of stress situations, where means of mitochondrial medicine secure realization of all processes of stress management and support development of stress reserves in systems responsible to manage the stress situations (mental and physical) - the autonomic (vegetative) nervous system, hypothalamo-pituitary-suprarenal system (HPA axis), subcortical sympathetic centers and central nervous system, what is important for workers with very high personal responsibility, operators of complicated systems, and workers with high mental demand (aircraft pilots, speed-train pilots, flying navigators , bank and enterprises managers etc.) as well as patients suffering from chronic diseases.

The deficiency of energetic resources in healthy organism (on the cell level) is characteristic for long-term adaptation mechanism (3). Thank to this mechanism the synthesis of proteins and nucleic acids is activated what increase power of mitochondrial apparatus in the cell resulting in increase of adaptation capabilities of the organism. To keep these adaptation mechanisms functionally capable then the informational, energetic, and metabolic reserves are essential - when the reserves are inadequate, the functional insufficiency of the organism develops leading to restricted ability of the adaptation to different environmental influences, esp. under conditions of moderate or mild load, to worsening of chronic diseases and acceleration of aging processes.

The method of heart rate variability analysis is actually very important method for estimation of functions and activities of autonomic (vegetative) nervous system and of adaptation reactions of the organism for evaluation of practical mitochondrial therapy effect.

Conclusion: perspectives, possibilities

-Using the heart rate variability (HRV) analysis is possible to estimate the **status, activity, tension and efficiency of autonomic nervous system** in total as well as its parts and levels. The efficacy of therapy (or other methods as acupuncture, meditation, **mitochondrial medicine means**, alternative medicine, etc.) is detectable by control HRV measurements. The system VariOtact enables to measure not only standard HRV parameters (SDNN, HR, RMSDD, Power HF, LF, VLF, etc.), but, in addition, some very important parameters as **stress index SI** and so forth.

-Using the means of mitochondrial medicine (Carnosine, Coenzyme Q10, Vitamin C with bioflavonoids, special compound of antioxidants, colostrums and, eventually, other diet supplements individually designed due to patients' disorders, there is the chance positively influence many different health disorders and diseases, which are related to chronic diseases and aging processes:

- Increase of energy production** of all cells of the organism, esp. of autonomic nervous system

- Reduction of tension of sympathetic part of ANS, reduction of stress (stress index etc.), increase of variability, regeneration of sympathetic activity when exhausted: to achieve the most important purpose – **balanced activity of ANS and its functional ability to control and regulate appropriate systems, i.e. dynamic homeostasis**. Then the ANS could take over (fully or partly) its lost controlling and regulating capability. This could be very advantageous **support of conventional medicine** in sense of reducing the dosages of medicaments (and/or reducing their combinations), reducing the side effects of medicaments, and **increase quality of patients' life conditions** (diabetes, coronary heart disease, hypertension, Parkinson's and Alzheimer's diseases, atherosclerosis, immune system disorders, osteoporosis etc.)

- Reduction of oxidative stress** is very important factor **slowing down the aging processes (inhibition of oxidative mitochondrial damage), and reducing the symptoms of chronic diseases**, where the oxidative stress is involved

- Reduction of stress** is another **important** factor reducing the **oxidative stress**.

Use of mitochondrial medicine method may be very advantageous method for those interesting in treating the patients seriously, with aim to help them really. The efficiency of therapy of any kind should be successfully monitored concurrently with estimation of ANS status with use of heart rate variability analysis.