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Composition of the Blood and Reflection of the Health State of Human Body

Alexander Poletaev

Federal Research & Clinical Center for Reanimatology and Rehabilitation;
MRC Immunculus - Biomarker Group, Moscow, Russia.
*Corresponding author E-mail: a-b-poletaev@yandex.ru

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Blood (blood plasma) is a special all-pervading substance, functionally co-tuning all organs, tissues and cells of the body. To some extent blood is similar to the Ether of the ancients. In addition to performing house-keeping functions, blood is a medium for the transfer of huge amounts of information, which is continuously exchanged between all the compartments and structures of the macro-organism and its microbiome. This information is transmitted mostly in the form of chemical signals (peptides, micro-RNA, extracellular DNA, the products of the microbiome, antibodies, etc.), the totality of which controls lots of biological processes. Blood is not only a controlling, but also a reflecting environment: dynamic changes in the composition of this environment carry information about the smallest changes in the state of individual populations of cells, tissues, organs and the body as a whole. The prospects of practical using of information about the state of the organism, transmitted by blood and reflected in individual's serum immunoreactivity profiles are analyzed.

Keywords: Blood plasma, peptides, Micro-RNA, Autoantibodies, Disease markers, Preventive medicine.

Blood

Blood has long been perceived as a kind of sacred substance that can, in particular, rejuvenate the body and stimulate tissue regeneration. Ovid in "Metamorphosis" talked about return to youth Jason's father after replacing an old blood by a new one. Hippocrates believed that the consumption of new blood can change the mental and physical properties of a person. Pliny and Celsius reported that the sick and elderly Romans drank the blood of dying gladiators, because it was believed that it has a healing and rejuvenating effect. Many such examples are given in the article Butkevich[1]. These views have recently been confirmed in experiments, indicating a real anti-aging effect of the blood of young rats on the brain of old animals[2].

Blood (blood plasma) can be considered as a special substance that binds together, i.e. functionally matches all the organs, tissues and cells of the body. Blood is an all-pervading, peculiar environment, to some extent similar to the Ether of the ancients (all-filling entity, providing the transmission and distribution of interactions between all objects of the Universe). On the one hand, the blood performs house-keeping functions – brings oxygen and nutrients to the tissues and takes out the products of catabolism, and on the other hand is a medium for the transfer of huge amounts of information, which are continuously exchanged between the numerous structures of the macro-organism and its microbiome. This information is transmitted, for the most part, in the form of chemical signals.

Multiple chemical signals of blood plasma – hormones, growth factors, cytokines, chemokines, extracellular nucleic acids, antibodies, etc., creates

a highly ordered information environment that controls lot of simultaneously occurring biological processes of the human body. It is important that the blood is not only the controlling, but also the reflecting medium – dynamic changes in its composition reflect the smallest changes in the state of individual cells, tissues, organs and the body as a whole. The "mirror of chemical signals" reflects any beginning pathological events that accompany existing diseases or can lead to future diseases. Besides this "mirror" allows to objectively and impartially assess the dynamics of an individual's aging. It is only important to learn how to use this magic mirror.

Of course, it would be very tempting to have at your disposal and all the necessary technical equipment and have a powerful mathematical apparatus that allows you to identify and analyze the correlation between changes in the content of thousands of molecular components of blood in different functional states of the body. This would allow to engage in a systematic "bridging" between the whole set of dynamic changes occurring at the molecular, cellular, tissue and other levels and the functioning of integral living systems in norm and pathology. However, even if we had everything necessary for the analysis of everything at once, it is not necessary to amuse yourself with deterministic illusions a la Laplace («*The Brain that this moment would know all forces acting in nature, and relative location of its component parts ... for him, there would be nothing unclear in the future and in the past...*»[3]). Let's not forget that living systems, like any super complex systems, are characterized by a high degree of uncertainty (indeterminacy, stochasticity).

Blood peptides

The peptides (oligopeptides, i.e. containing less than 50 amino acid residues) are hormone-like molecules involved in the regulation of many physiological functions. Peptides are functioning as intercellular and intersystem communicators in many cases. In particular, changes within the ratios between several dozens of pro-inflammatory and anti-inflammatory cytokines in blood set resultant vectors of development of systemic and local immuno-inflammatory and regenerative processes. Oligopeptides participate in the modulation of neurophysiological mechanisms of the most motivations, regulate circadian sleep-awake rhythms, as well as the mechanisms of learning and memory[4, 5].

Micro-RNA and extracellular DNA in the blood

A separate "Kingdom" is presented by circulating in the blood many thousands of short (usually 18-25 nucleotides) interfering micro-RNA molecules, potentially able to quickly control gene expression and, accordingly, participate in the regulation of a wide range of physiological processes[6]. It is assumed, although even less studied, the regulatory properties of extracellular blood DNA[7].

Exogenous regulatory molecules in the blood

Since the beginning of the XXI century, biologically active molecules of non-organism origin involved in the regulation of body functions have attracted considerable attention. For example, recently it was found that molecules synthesized by the symbiotic microflora directly participate in the regulation of the physiological functions of the host-organism. For instance, short-chain fatty acids of microbial origin, act as specific ligands that bind some forms of olfactory chemoreceptors of vascular walls and participate in the regulation of vascular tone[8]. Products of partial hydrolysis of food, entering the general blood flow from the intestinal villi, can affect the emotional status of children and adults: for example, peptide ligands of opiate receptors derived from our food or exorphines[9].

The role of biologically active microbiota products, as well as derivatives of our daily food entering the blood, is getting down to be disclosed. The structure and functions of numerous small RNAs and extracellular DNAs and regulatory peptides (oligopeptides) of blood plasma also have been investigated insufficiently. The high lability of most of them, as well as the complexity or high cost of dynamic measurements of their content greatly hinders their study. In this respect, the obvious advantage belongs to the other, probably the most numerous and most diverse macromolecules of blood, namely antibodies. In addition, it should be noted that antibodies are characterized by an extremely wide range of antigenic (epitopic) specificity, i.e. molecular-functional variants. It is very important that antibodies are characterized by high stability in vivo and in vitro, that permits operating with antibodies not only to trained researchers, but to laboratory doctors with using

simple and cheap equipment of typical clinical laboratories.

Immune reflection

New opportunities for research of an organism in norm and pathology, were opened as a result of transformation of views on a role of a biological role of the immune system. The beginning of this transformation was laid by Elia Mechnikoff, who believed that the fight against harmful microbes is no more than one of the particular manifestations of much more wider homeostatic functions of the immune system[10]. In the last 20 years, it has come to realize that the immune system is a reflective system, which accurately reflecting any changes occurring in the body. As a result, today the biological role of the immune system is considered not so much from the "classical" microbiological positions, but based on the following provisions[11- 14]:

- The immune system provides a constant screening of the molecular structure of the body.
- The immune system is involved in molecular-cellular homeostasis, primarily through participation in auto-clearance and auto-repair processes.
- The immune system is involved in the functional adjustment (co-tuning) of many different cells, tissues and organs for the orderly and harmonious functioning of a whole organism.
- Many "alien" entities are present in a healthy body permanently or for a long time (normal microflora, fetus), not causing a pathological immune response[15], but bringing obvious benefits to the host organism[16].
- The immune system fights against harmful microorganisms, but ignores the non-threatening "foreign", and actively preserves and promotes the integration of useful "foreign" in the structure of the host organism[12, 15].
- Natural autoantibodies and auto-reactive lymphocytes are the main tools of immune reflection and immune clearance of the body.

Serological studies on antibodies to pathogenic microbes, for example to HIV-1 antigens or *Chlamidia trachomatis*, etc., have long been routine – elevated titers of specific antibodies against microbial antigens indicate the presence of appropriate viruses or bacteria in the body. Parenteral administration of self-antigens, such as human chorionic gonadotropin (HCG) in pharmacological dosages, also lead to an increase of antibodies to HCG[17]. Similarly, the increase in the production of self-antigens causes an increase in the synthesis of antibodies to them. For example, an increase in the expression of insulin receptors, for many months and years precedes the development of type-2 diabetes, is accompanied by an increase in anti-receptor antibodies[18]; increased synthesis of apoptosis regulatory protein p53 leads to the rise of antibodies to p53[19]. These and similar examples illustrate the phenomenon of immune reflection, i.e. the ability of the immune system to respond to changes in the content of any antigens in the body by quantitative changes in the production of appropriate antibodies. The corresponding antibodies are involved in the implementation of the basic (archetypal) function of the immune system – its participation in the body's clearance from the excess of any molecules that potentially can disturb homeostasis[13]. Antibodies mark particles or molecules intended for disposal by macrophages and stimulate phagocytic activity in dozens and hundreds of times. The content of autoantibodies of different specificity can vary significantly, but serum levels of autoantibodies of the same antigen specificity are similar in all healthy adults[20]. In the pathology, accompanied by the death of certain specialized cells, the synthesis of autoantibodies to their antigens prominently grows.

Autoantibodies as markers of disease

Today it has become common place to talk about the rise of serum levels of certain autoantibodies, as markers of conditions and diseases, not attributable to a cohort of autoimmune, for example, in stroke, cancer, myocardial infarction, complicated pregnancy, etc.[12, 15, 21, 22]. The development of any chronic disease is associated either with the activation of certain cell types of cell death, or with abnormalities in the expression, secretion or utilization of their antigens. The persistent increase in the extracellular content of any autoantigen is accompanied by an increase in the production of autoantibodies to this antigen[23]. Thus, the transient increase in autoimmune reactions caused by tissue damage or disorders represent a universal physiological response of the immune system, aimed at increasing clearance of damaged tissue and activation of regeneration.

The possibility to use the phenomenon

of immune reflection of pathological changes in practical medicine was realized with the help of ELI-Test technology based on the analysis of serum immunoreactivity profiles, i.e. on selective changes in serum content of autoantibodies of certain specificity[13]. It is important that the increased production of certain antibodies can be detected after a few days from the beginning of the pathological process, long before the clinical manifestation of the disease. Therefore, the analysis of changes in the markers of future disease ("mirror of antibodies") provides an opportunity to "work" with the disease ahead of the curve, i.e. months and years before its clinical manifestation. Such approaches allow us to move from words to action, in relation to the needs of preventive medicine.

Notification

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