

ADSORPTION – TRANSPORT FUNCTION OF ERYTHROCYTES: IMPORTANT FACTS ABOUT NEW DIAGNOSTIC CAPABILITY

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In etiology and pathogenesis of diabetes, atherosclerosis, metabolic syndrome and many other diseases the main role pertains to metabolic disorder. But apparent changes in plasmas concentration of protein, lipids, glucose and other substances are not detected in the first stage of these diseases. This fact may be explained by earlier unknown phenomenon, called adsorption- transport function of erythrocytes (ATFE).. This function take part in quick and selective transfer of substances from blood into tissues. ATFE participate in removal of metabolites, denaturated proteins, atherogenic lipids and some other substances with heightened chemical activity from blood plasma. ATFE take part in return of protein from intersticium, increasing antiedematous potential of blood. Transport of many substances on erythrocytes surface is a changeable and adjustable process. But it allows to determination of initial changes in a metabolism of some substances.

Keywords: erythrocytes, function, transcapillary exchange, metabolism, disease diagnosis

Substantiation of existence of adsorption-transport function of erythrocytes

Fact of substances adsorption on erythrocytes surface was known in the beginning of thirties of last century [1]. 30-40 years later this phenomenon again became an object for research. In was concluded that protein adsorption on erythrocytes surface affects on deformability of red blood cells and rheology of whole blood [2]. Substances adsorbed on erythrocytes surface were considered as a reserve for their emergency supply to plasma [3].

In the studies of transcapillary exchange of protein during many decades a very important point was the «main law of lymphology». The law stated, that plasmas proteins came from blood to interstitial area are coming back to blood flow only trough lymphatic vessel. Indeed lymphostasis edemas exist, induced by block of lymph flow.. The law was also based on fact that arterio-venous difference in content of plasmas protein always means its

outlet from blood to tissues. During more precise study of this exit we found out that arterio-venous difference that determines protein content in plasma do not give possibility to calculate transcapillary balance of protein exactly, because of significant or fluctuating difference in adsorption of protein on arterial and venous erythrocyte surface. It was found that considering all (adsorbed, endoglobular, plasmas) protein, its transcapillary balance approaches to index of protein lymphatic transport to lymph [4].

Next stage in studies of substances adsorption and transport on erythrocytes surface (from 1991 year) caused by the discovery, that quantity of adsorbed glucose on erythrocytes surface increases many times in cosmonauts' body at the landing day [5].

Our experiments on animals showed that substances transfer on erythrocytes is a changeable and adjustable process. It was found that quantity and value of glucose and lipids substantially exceed the protein (between substances adsorbed

on erythrocytes protein dominates by weight). It was found that more often the quantity of some substances (bilirubin, gamma-glutamyl transpeptidase) is higher on erythrocytes surface than in plasma. Adsorption of substances on erythrocytes depends from acid-base balance of blood. Adsorption strengthens because of activity of physicochemical connections of hemoglobin (qualitative and quantitative potentialities of hemoglobin) inside the red blood cells. It is considered that on erythrocytes surface there are areas with predominant adrenalin and immunoglobulin adsorption. That's why it should be taken in consideration existence of adsorption ability of these erythrocytes. Existing and received by us data were generalized in corresponding concept [6, 7].

**SOME Important facts
about adsorption-transport
function of erythrocytes**

Results of many-sided studies during 1989-2009 years allow to make a conclusion, that regulated adsorption-desorption of substances on erythrocytes surface is a major part in the below described processes (A, B, C, D, E).

A) Guaranteeing of quick and selective transfer of substances into tissues. Erythrocytes easily flow through tighter, than erythrocytes diameter, arterial part of capillaries. Erythrocytes deformation and rotation promote this process. A new hypothesis has been arisen that during passage of each erythrocyte via blood capillaries to exist exchange and mix substances of paraendotelial exchange layer on molecules adsorbed on erythrocytes.

After that these substances firstly participate in transcapillary exchange. Some of these substances enter into interstitial space and in lymph [4].

Proportion of adsorbed substances differs from corresponded indexes of plasma. This is many differences of interstitial fluid and lymph from plasma are formulated. Selectiveness of many endogen and exogenous substances (including pharmaceuticals) inflow into tissues also stipulated (depend on different abilities of these substances to be adsorbed on erythrocytes surface) by different abilities of these substances to be adsorbed on erythrocytes surface. Percentage of strongly-adsorbed substances as increases as coming closer to erythrocytes membrane. Hormones and other active substances are also relatively quickly enter into corresponded tissues and organs.

Albumin-globulin index of proteins adsorbed on erythrocytes surface is higher than in plasma.. It is known that albumin attaches to itself many other substances. Correspondingly attached to adsorbed albumin substances are included to a number of substances transported on erythrocytes surface.

B) Participation in removal of metabolites, denatured proteins, atherogenic lipids and other substances with heightened chemical activity from blood plasma. Erythrocytes are natural sorbents of substances with high chemical activity. They participates in metabolites deletion from blood plasma as well as denatured proteins, atherogenic lipids and other substances with high chemical activity. At the same time during denaturation process proteins' adsorbing ability increases. Absorbability of atherogenic lipids is higher in comparison with non-atherogenic lipids. Proteins and lipids with increased absorbability partially displace (replace) glucose from erythrocytes' surface. Owing to those peculiarities many «dedicated to deletion» substances firstly enter to liver and other structures of reticulo-endothelial

system. At interstice of other tissues such substances often compose aggregates that due to size come back to blood flow with lymph only [4].

Aggregated and glycated substances appreciably lose their activity and toxicity. During lymph motion many toxic substances transform, at the same time aggregates come to a standstill in lymph nodes.

Glucose has a relatively high absorbability on erythrocytes surface. In special conditions glucose partially displaces native proteins and most lipids from erythrocytes surface. That is why number of glucose transported on erythrocytes under hormones effect can increase or decrease in some times.

C) Mechanism of protein return from interstium – additional anti-edematous factor. Red corpuscle participates in creation of new anti-edematous (contradictory) factor. Part of adsorbed glucose always goes to tissues. On the place of departed glucose mostly proteins are adsorbed on erythrocytes surface. Correspondingly protein concentration in parietal layer of venous part of capillaries decreases. The gradient of protein concentration is change. Correspondingly increase protein return from interstitium (tissue) to blood.

This mechanism was strengthened by known erythrocytes volume increase (as well as adsorption area) during their saturation by carbon dioxide [8]. This process is a part of morpho-functional anti-edematous potential of blood. Concept of protein return from interstice to blood through blood capillary walls doesn't contradict to known data about frequent formation of edemas during diabetes, hypoproteinemia, anemia, and other pathologies, when level of protein adsorption on erythrocytes surface decreases. At

the same time adsorption area decreases in lungs during erythrocytes saturation by oxygen. Abilities of lymphatic system in water and protein transportation from lungs are limited. That is why when energy metabolism and correspondingly glucose utilization in lungs decreased a possibility of acute edema of lungs increases.

D) Maintenance of substances content in plasma within «normal» range. Plasmas and adsorbed on erythrocytes pool of substances are closely connected to each other. Not only in control groups, but in people with diseases. In human and animal during experiments with different influences a positive correlation between substances in plasma and substances on erythrocytes surface usually reveals. At blood dilution and concretion proportion of substances content in these two pools changes slowly. For example, at blood dilution by physiological solution in vivo protein concentration in plasma change as well due to "ejection" of a part of a protein from erythrocytes surface to plasma. In vitro «ejection» is less expressed. Buffer-stabilizing effect of adsorption-desorption substances on erythrocytes surface is a primary and simple «part» of complicated system of keeping constant concentration of some substances in blood plasma.

E) Establishment of conditions for biochemical processes on erythrocyte surface. Concentration of some substances in adsorbed layer on erythrocytes surface may be ten times higher than in plasma. Among adsorbed substances enzymes are found, including proteases and lipases. In patients with chronic diseases of liver a multiple increase of number of enzymes and proteolytic activity of substances adsorbed on erythrocytes surface is often found. It allows supposing that in

some cases a condition for biochemical processes are created.

Determination of initial Changes in a metabolism of some substances

Characteristics of adsorption-transport function of erythrocytes allow to reveal initial infringements of a metabolism. There many more aspects, including peculiarities of «lavage» getting from erythrocytes surface. Known methodology of erythrocytes «washing» removes into washing away (eluate) only 35-55 % of substances adsorbed on erythrocytes surface. Our methodology allows removing into eluate 85-95 % substances adsorbed on erythrocytes surface. Correspondingly data received by us differ not only quantitatively but also they are often completely different from conclusions given by other authors [2]. Full «washing» often conducts to erythrolysis.

Interpretation of data about transport of substances on erythrocytes surface is not simple. At interpretation of data received during experimental and clinic studies, not only direct indexes were important but also secondary indexes of this function [9]. The parameter total (in plasma and on erythrocytes surface) transport of substance in blood is important. The parameter of a parity of transport of substances on erythrocytes surface and in plasma is important. It is important to reveal a degree of insufficiency of adsorption- transport function of erythrocytes. We have unexpectedly received low parameters of transport on erythrocytes surface aspartate aminotransferase and alanine aminotransferase at patients with coronary heart disease. Probably it has been connected with insufficiency of adsorption- transport function of erythrocytes.

Let's consider some diagnostic aspects of adsorption- transport function of erythrocytes in connection to diabetes and atherosclerosis.

Detection of first stage diabetes of type 2

In our experiments on narcotized animals under insulin effect a quantity of glucose decreased firstly among substances, adsorbed on erythrocytes, then in plasma, lastly its content decreased in lymph. Adrenalin simultaneously increases content of adsorbed and plasmas glucose [5]. Owing to this entrance of glucose to tissue sharply increases.

According to our data, normally, after food intake, glucose content increases owing to substances adsorbed on erythrocytes. Part of erythrocyte adsorbed glucose always enters to tissues, including regulatory structures. It starts insulin mechanism of carbohydrate metabolism regulation. Chronic stresses, frequent caloric food intake, disbolism are accompanied with continuous transport of glucose on erythrocytes surface. It leads to heightened glucose entrance inside erythrocytes. But increase (higher than norm) of glucose content inside of erythrocytes leads to its joining with hemoglobin. As far as percentage of glycated hemoglobin increases, ability of erythrocytes to adsorb on its surface proteins, lipids, carbohydrate and other substances decreases. Relative decrease of glucose transport on erythrocytes, in my opinion, disturbs adequate regulation of carbohydrate metabolism. This, probably, is an additional reason for development of «tolerance» to insulin. Gradually the bigger part of glucose enters plasma – symptoms of diabetes of type 2 show up.

The above written can prove presence of early (latent) stage of diabetes,

which is characterized by continuous transfer of increased volume of glucose on erythrocytes surface [11].

To a question of diagnostics of an atherosclerosis

In norm on erythrocytes surface mostly atherogenic lipids transported. Lipids often take first place by number of molecules between organic substances adsorbed on erythrocytes. After food intake at moderate change in metabolism, change of lipids transport in blood happens because of molecules adsorbed on erythrocytes. These lipids enter into wall layer of blood capillaries, which are not subject to atherosclerotic changes. In interstitial space in liver when lymph is moving atherogenic lipids are collapsed, deleted or transformed to less pathogenic formations. At deficiency of the above written links including deficiency of adsorption-transport function of erythrocytes, a content of atherogenic lipids in plasma increases, which increases risk of atherosclerosis appearance. It is known that number of atherogenic lipids in plasma (and accordingly risk of atherosclerosis development) increases at diabetes, liver diseases, kidney diseases, podagra, obesity, arterial hypertension, chronic poisoning, and chronic exposure processes. These facts can be explained by adsorption-transport function of erythrocytes. During increase of adsorption of glucose and protein on erythrocytes with heightened chemical activity leads to partial «discharge» atherogenic lipids to plasma.

Adsorption-transport function of erythrocytes also decreases when hemoglobin joins with other substances, particularly at increased accumulation in erythrocytes of lipid peroxidation production.

Studies of adsorption-transport function of erythrocytes at clinic just be-

gan [11, 12 and other]. Predominance of adsorption of one substance can damage adsorption and metabolism of other substances, making preconditions for pathologies, that can't be defined by blood plasma analysis at their initial stage. These are so called latent (initial, beginner) pathology [11]. It is important to know, what metabolic imbalance occur at this initial stage.

An initial stage inflammatory diseases (with temperature), increase of transport of glucose on erythrocytes surface is marked. The increase in activity sympathetic-adrenal systems also is accompanied increase in transport of glucose on erythrocytes. But at many other things diseases and conditions transport of substances on erythrocytes surface was not studied. Wide and repeated researches are necessary. Unification of a method is necessary.

As far as new data will be accumulated, theoretical and practical understanding of adsorption-transport function of erythrocytes will be increased and specified. Clinical and diagnostic relevance also will be increased.

Studies of pharmaceutical substances' influence on this function are just beginning. It is possible to accelerate our researches at cooperation. Financing is necessary. With offers on scientific and other cooperation to address by e-mail (tatrauf@mail.ru <mailto: tatrauf@mail.ru >a theme of the letter – a science).

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